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EXPERIMENTAL SURGERY IN THE USSR

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EXPERIMENTAL SURGERY IN THE USSR

[Following is the translation of seven articles in Eksperimental'naya Khirurgiya (Experimental Surgery), No. 2, Mar/Apr 1960.]

Peripheral Circulation in Venous Thrombosis

(pages 8-12)

By M. I. Oganesyan

The Department of Operative Surgery and Topographical Anatomy (Director - Prof. Kh. A. Petrosyan) of the Yerevan Medical Institute (Director - Prof. L. A. Arutyunyan). Scientific Director of the work - Prof. P. N. Mazayev.

The clinical and experimental studies of A. I. Abrikosov, D. Ye. Al'pern, F. I. Val'ker, V. V. Podvysotskiy, Ye. M. Tareyev, Baumgarten and Dietrich have shown that, in the pathogenesis of thrombosis of vessels, a leading role is palyed by (1) damage to the vessel wall, (2) retardation of the flow of blood, and (3) changes in the composition of the blood.

Many authors attribute an important role in the etiology and pathogenesis of thrombosis to infection (G. P. Zaitsev, F. S. Karganova-Myuller, Lyubarsh, and others), believing that it may be the cause of all three of the above-mentioned factors.

F. I. Val'ker, S. P. Protopopov, F. I. Sidorina, A. S. Stepanov, A. I. Fel'dman, and others have demonstrated the great importance of the nervous system in thrombosis, as a reflexly-acting system under the influence of which there may be changes in the composition of the blood, circulation, and nutrition of vessel walls.

It should, nevertheless, be emphasized that insufficient attention has been given in the literature to the

problem of the anatomical and fucntional changes in the peripheral vascular system following thrombosis of large veins.

Modern X-ray advancements permit objective documentation of the anatomical and topographical features of arteries and veins and of their functional state.

Contrast media (cardiotrast, diotrast, diodon, and others) are widely used at the present time in the diagnosis of congenital heart disease and congenital lesions of the great vessels, as well as for studies of the periperal vascular system.

It seemed extremely important to us to determine the anatomical and functional changes in the peripheral vessels upon thrombosis of the iliac and femoral veins.

In experiments on dogs, for the creation of thrombosis of veins we used 96 percent alcohol and ten percent tincture of iodine.

Using the method of intravital serial vasography, we studied the collateral circulation, the rate of arterio-venous circulation and the permeability of the vessel walls.

The experimental animals were anesthetized with morphine and barmabyl [amobarbital]. Excision of the skin, subcutaneous tissues and fascia two cm in length beneath Poupart's ligament, permitted exposure of the vascular bundle of the femur. Seventy percent solution of cardiotrast was injected, in amounts of six to seven ml, directly into the femoral artery.

For several films, we used the tunnel cassette devised by P. N. Mazayev and D. S. Mitkevich. Depending on the purpose of the experiment, we took from three to nine films at intervals of three to five seconds.

To induce thrombosis we exposed the femoral or iliac vein for a distance of five to six cm and, between ligatures temporarily applied to the vein, injected into the lumen one ml of ten percent tincture of iodine or 96 percent alcohol. Thrombosis of veins occurred ten to 15 min after injection.

By means of intravital serial vasography we studied the picture of the circulation and the state of the vessels under conditions of thrombosis of veins at different times

(30 min to eight months).

Experiments were run on 14 dogs.

In chronic experiments we performed dynamic X-ray studies. We made 846 vasograms, successively documenting the anatomic and functional changes in the peripheral vascular system.

As illustration let us describe an experiment carried out on dog Sevan, weighing 11 kg. Initially we performed vasography of the left hindlimb under normal conditions (Fig. 1). In film a is shown a representation of the arteries of the limb, including the femoral artery and its ramifications, the popliteal, the tibial, etc. Film b shows, along with the arteries, small peripheral and more proximal veins. Film c shows contrast substance only in the smaller arteries, while the veins are well shown.

In the experimental dog, thrombosis was induced in the left femoral vein by injection with tincture of iodine. Thirty minutes after this, a second vasogram was made of this limb. In three successive films (Fig. 2) performed by the same method, contrast medium was seen only in the arteries of the extremity, with the lumens of the arteries being markedly dilated, with the development of patency in a supplementary vascular network, not visible in films of the normal limb, and with marked slowing of the arterio-venous circulation and increased permeability of the walls of the blood vessels.

Contrast vasographic studies carried out eight months after experimental induction of thrombosis of the femoral vein permitted a demonstration of the changes in the peripheral vessels of the limb being studied. Thus, in the vasograms of the left limb (Fig. 3), there is, as before, marked dilatation of the arteries with the incorporation of a supplementary vascular network into the blood supply of the tissues. The venous network circulation is re-established due to the richly developed and markedly dilated collateral venous pathways. This is especially clearly seen in the film, which shows filling of the veins with contrast medium. In this it is clear that the femoral vein does not contain contrast substance, due to the presence of thrombus. At this level, a well developed and dilated collateral venous network is easily seen. Eight months after thrombosis, there was no evidence of increased vascular permeability.

Hence, it is clear from this experiment that, upon thrombosis of the femoral vein, the lumen of the arteries is enlarged by dilatation, a supplementary vascular network is included in the blood supply to the tissues, the srterio-venous circulation is greatly slowed, and the permeability of vessels is increased. Eight months afterward, vasograms show restoration of the arterio-venous cilculation due to the rich venous collateral circulation and subsistence of the increased vascular permeability.

In a series of experiments, studies were made not only of the picture of cilculation following venous thrombosis, but also of the peripheral lymph vessels at the same time.

For illustration of the blood and lymph circulation upon thrombosis of the femoral vein, let us consider the following experiment. Dog Tuzik, weighing ten kg, was first subjected to vasography and lymphography under normal conditions. Vasography was performed by injecting contrast medium (cardiotrast) into the femoral artery. In order to show the lymphatics, 25 percent thorotrast was used which was injected in amounts of 1.5 ml into the soft tissues of the paw.

In serial vasolymphograms we recorded the movements of the contrast medium through the arterio-venous channels and lymphatics.

Thrombosis of the femoral vein in this dog was induced by the injection of ten percent tincture of iodine into the lumen of the vein.

Forty days after experimental thrombosis of the femoral vein, six serial vasopymphograms (Figs 4 and 5) clearly showed the arteries of the femoral and popiteal regions and a great number of small branches, including the "reserve" vascular network. In later films there was good filling of the veins with contrast medium. This appears especially clearly in films in which the arteries no longer contain the dye. These films show the richly developed collateral venous channels, the lumen of some of these collateral veins being markedly dilated. Despite the development of a collateral venous cilculation, the arterio-venous circulation remains slow and the permeability of the vessel walls is still increased. As to the lymphatics of the limb, sequential vasolymphograms showed movement of the contrast substance along the superficial lymphatics to the popliteal nodes, and then to the in-

guinal and iliac nodes. The lymphatics were dilated and the rate of lymph circulation increased.

From this experiment it is evident that, under the influence of thrombosis of the femoral vein, the lumens of the arteries are dilated, a "reserve" vascular network is incorporated into the blood supply of the tissues, venous anastomoses develop, the arterio-venous circulation is slowed, the rate of flow of the lymph is enhanced, and the lumens of the lymphatics are dilated.

Conclusions

(1) The method of intravital vasolymphography affords the opportunity to study the anatomical, topographical, and fucntional state of the blood and lymph vessels under normal and pathologic conditions.

(2) Upon thrombosis of the major veins of the extremities, the lumens of the arteries are dilated, a "reserve" vascular network comes to be included in the blood supply of the tissues along with a collateral venous communication, the arterio-venous circulation is slowed, and the permeability of the vessel walls is increased.

(3) Under the influence of thrombosis of veins of the extremities, the lumens of the lymphatics are dilated and the rate of lymph flow is markedly increased.

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Fig. 1. Vasogram of the left hindlimb of a healthy dog. a - artery; b - artery and vein; c - vein

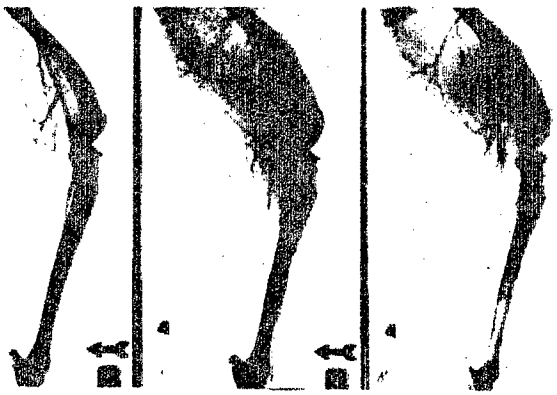

Fig. 2. Vasogram (a, b, c) of the same limb 30 minutes after thrombosis of the femoral vein. Circualtion is markedly slowed, the permeability of the vessels is increased, with diffusion of contrast medium into the soft tossues of the extremity.

Fig. 3. Vasogram (a, b, c) of the same limb eight months after thrombosis of the femoral vein. Clearly visible are the richly developed venous collaterals.

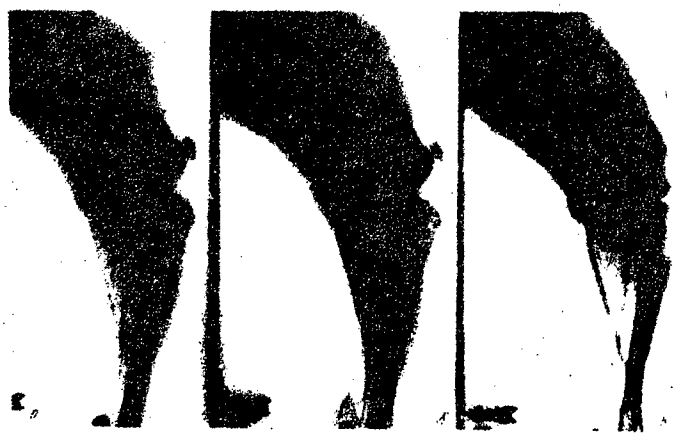

Fig. 4. Vasolymphogram (a, b, c) of the left limb of a dog 40 days after thrombosis of the femoral vein. It shows arteries, veins, and lymph vessels.

Fig. 5. (continued) vasogram (a, b, c) of the same limb. Well shown are the venous anastomoses and the lymphatics.

Submitted 22 April 1959

The Effectiveness of Extracorporal Circulation in Using Various Systems of Artificial Blood Circulation under Experimental Conditions

(pages 12-18)

By M. S. Margulis

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Despite considerable advances in the area of the surgical treatment of congenital and acquired lesions of the heart, there are many lesions for the correction of which it is necessary to cr ate conditions permitting operations on the dry heart under direct visual control. These conditions are best reproduced with the use of artificial circulation apparatus for performing the functions of the heart and lungs during the time necessary for surgery within the heart.

A complete solution of the problem of artificial circulation is exceptionally difficult from the biologic point of view. It is necessary to duplicate as nearly as possible the hemodynamic conditions which ensure sufficiently favorable possibilities for the life activity of the organism. Moreover, one must prevent disturbances in the biochemical and cytological integrity of the blood. As is known from the literature (Lillehei, et al., Kirklin, et al., Crafoord et al., L. A. Levitskaya et al.), during artificially maintained circulation there are numerous disturbances in the biochemical constitution of the blood (pH, acid-base balance, percentage content of different protein fractions), as well as changes in the formed elements of the blood.

It has been shown that these and other changes occurring in the blood during artificial circulation depend primarily on the volume rate of artificial circulation. If this is adequate, it may be possible to create hemodynamic conditions such that deviations from the normal will be very slight.

Nonetheless, there is no single view regarding the determination of the most desirable volume rate of flow. There are exponents of small volume rates (60-80 ml/kg/mn), such as Lillehei, for instance. Other authors, among whom we might mention Kirklin, Crafoord, and so forth, prefer high volume rates (80-100 ml/kg/min). S. S. Bryukhonenko

proposes that the optimal volume rate should be 120-130 ml/kg/min.

Taking into account these divergent data, we undertook some experiments in dogs on artificial circulation with the use of different volume rates.

In the present report we present the results of recent experiments on 15 dogs carried out after satisfactory mastery of the apparatus and of the methods employed.

In five of these dogs we used volume rates of artificial circulation within limits of 60-80 ml/kg/min, in four 80-100 ml/kg/min, and in six greater than 100 ml/kg/min. Anesthesia was accomplished by the subcutaneous administration of one percent morphine hydrochloride in doses of 1.5 ml per kg body weight and intravenous droplet anesthesia with 0.2 percent solution of pentothal.

Using this anesthesia and with simultaneous artificial respiration, we prepared the femoral vessels on the right and performed right-sided thoracotomy in the sixth intercostal space. We prepared both venae cavae, which were held in rubber clamps, and also the axygos vein. For artificial circulation we used the AIK apparatus, devised by the NIIEKhAI, with one arterial pump and venous outflow. The apparatus was filled with donor blood in amounts of 1000-1200 ml, stabilized with 35-40 mg heparin. Rhe deficit was made up with physiologic saline solution. The catheter of the main arterial apparatus was introduced into the femoral artery in the direction of the aorta. One of the venous catheters of the apparatus was inserted into the superior vena cava through the azygous vein and the other into the inferior vena cava through the auricle of the right atrium.

After turning on the AIK and determining the desired volume rate, by compression with the rubber clamps around the venae cavae we interrupted the access of blood to the cavity of the right atrium, after which circulation in the organism was effectuated only through the functioning of the apparatus. Artificial circulation was maintained for 30 minutes; then by releasing the clamps, the natural flow of blood was restored to the heart and its own circulatory functions were renewed. After this, the AIK was removed and the catheters withdrawn.

To create the condition of artificial hemophilia necessary during the procedure of extracorporeal circulation,

we injected intravenously, before insertion of the arterial and venous catheters, heparin in doses of 1.5-2 mg per kg of body weight. After conclusion of srtificial circulation and removal of the catheters, the heparin was neutralized with protamine sulfate injected intravenously.

Two rubber drains were placed in the thoracic cavity after 24 hours in order to remove accumulated blood and secretions. The wound itself was closed without drainage.

During the experiment, continuous measurements were made of arterial and venous pressures with the use of mercury and water manometers, the cannulas of which were inserted respectively into the brachial artery and vein. Moreover, recordings were made of the ECG and the EEG of each animal.

Hence, we observed not only the picture of hemodynamic alterations but also tests on the basis of which it was possible to judge the sufficiency of oxygen supply to the heart and brain, which, as is known, are the most sensitive to oxygen deprivation. We suggest that a comparison of these findings obtained prior to, during, and after exclusion of the heart from the circulation affords a completely adequate criterion for objective evaluation of the effectiveness of the regime of artificial circulation.

In appraising our experiments we took into account also the survival of the experimental animals. However, it should be remarked that a successful outcome of the experiments dxpends not only on the adequacy of the regime of artificial circulation but also on the effective control of artificial hemophilia, as well as on the effectiveness of the postoperative care.

Reviewing the results of the experiments (survival) and the picture of hemodynamic, EEG and ECG changes, it is possible to conclude that they depend to a significant degree on the regime of artificial circulation, and primarily on the volume rate of circulation. Of five dogs in which the volume rate during artificial circulation was from 60 to 80 ml/kg/min, three died. With a volume rate of 80 to 100 ml/kg/min, only one of the four dogs died. Of six dogs in which artificial circulation was maintained with a volume rate higher than 100 ml/kg/min, three died (Fig. 1).

Comparing the hemodynamic indices with the magnitude of the volume rate, it is possible to detect characteristic

changes. With low volume rates the arterial pressure drops to 70 mm Hg or lower, this decline sometimes representing 50 percent of the level maintained prior to artificial circulation. Soon after the experiment the arterial pressure, although it increases, nevertheless remains somewhat lower than the initial pressure. Simultaneously, as in the experiment with the dog Layma (Fig. 2), the venous pressure is sustained within limits of normal.

With volume rates of artificial circulation within limits of 80-100 ml/kg/min, the arterial pressure falls only slightly (not below 90 mm Hg) and, after conclusion of the experiment, increases again to the original level. In this, the venous pressure, although it increases, does not exceed permissible limits, as was seen in the experiment with dog Ulybka (Fig. 3).

In dogs perfused with volume rates higher than 100 ml/kg/min, the arterial pressure is maintained at a level of 90-100 mm Hg; however, it is not stable. During this time there is an increase in venous pressure with a marked jump to 150-200 mm water, as seen in dog Mavra (Fig. 4). Apparently, we are dealing here with hypervolemia observed with the use of such large volume rates.

With identical degrees of oxygenation of the blood, different states of hemodynamics due to the use of different volume rates give rise to maintenance of or changes in the corresponding possibilities of supplying oxygen to the tissues. This is seen in studies of the EEG and ECG. In animals perfused with low volume rates (60-80 ml/kg/min), after 20 minutes of artificial circulation, there is a moderate hypoxia of the myocardium, expressed as sagging in the ST segment and in smoothing out of the T waves, as in dog Layma (Fig. 5). The state of hypoxia of the myocardium is maintained to a certain extent during the period immediately after termination of the artificial circulation. The EEG also shows the development of temporary periods of hypoxia of the cerebral cortex, which disappear after termination of the perfusion (Fig. 6). This indicates that, with extracoerporeal circulation at low volume rates, there are manifestations of a certain oxygen deficit, especially if artificial circulation is continued for more than 20 minutes. With volume rates of 80-100 ml/kg/min there are no substantial changes in the ECG during artificial circulation, with the exception of a certain acceleration of the rhythm, which is a consequence of the fact that during the experiment the number of myocardial contractions begins

to coincide with the pulse of the apparatus itself (Fig. 7). The EEG also indicates the absence of any important changes during the experiment (Fig. 8). From these findings it follows that, with volume rates of 80-100 ml/kg/min (equal to the minute volume of the heart), the oxygen supply to the tissues is quite adequate.

In dogs in which artificial circulation was maintained at volume rates higher than 100 ml/kg/min, the ECG showed a slight disturbance of rhythms and conductivity, expressed as a smoothing out of the P waves during the experiment and the disappearance of this phenomenon after discontinuation of the perfusion. However, hypoxia apparently does not occur, since, upon examination of the EEG, no changes are to be seen. Consequently, with such high volume rates as were used in the last group of experiments, the supply of oxygen to the tissues is quite satisfactory, but there are changes in the ECG reflecting disturbances in the mechanism of conductivity, which, evidently, are explicable in terms of the above-mentioned hemodynamic disruption. There can be no doubt that, with volume rates in excess of 100 ml/kg/min, improvement in the conditions of venous run-off, ensuring normal or nearly normal levels of venous pressure, would increase the percentage of favorable results.

However, our data show that the most physiologic volume rate is one of 80-100 ml/kg/min in extracorporeal circulation, i. e., one which equals the minute volume of the heart at rest. With such a volume rate, a very high percentage of survivals is obtained.

Apparently, small volume rates may ensure effectiveness of artificial circulation with brief exclusion of the heart and lungs. In operations requiring exclusion of the heart for more prolonged periods, it is advisable to use a high volume rate of artificial circulation.

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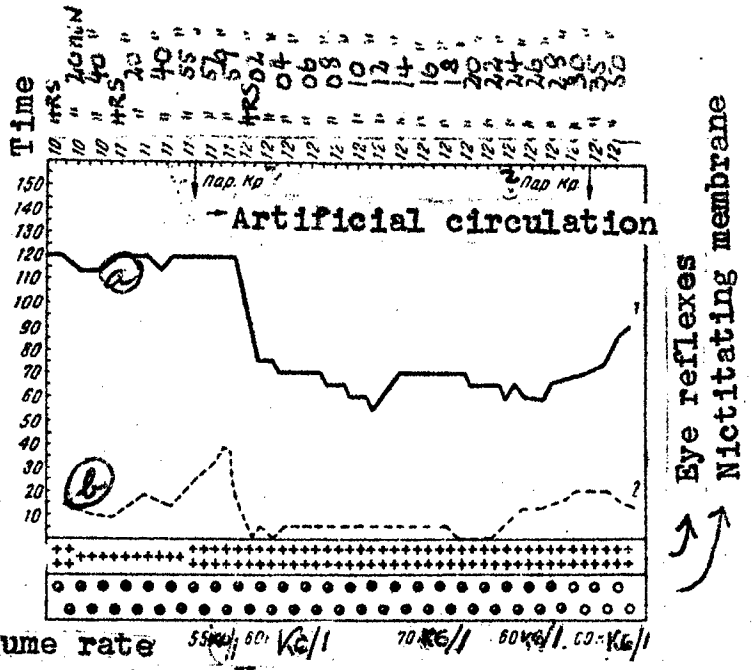
Volume rate	Number of dogs Survived	Died	Total
60-80 ml/kg body weight/min	2	3	5
80-100 ml/kg body weight/min	3	1	4
more than 100 ml/kg body weight/min	3	3	6

Fig. 1. Results of experiments as a function of the volume rate of artificial circulation.



a) Venous pressure in mm Hg
b) Arterial pressure in mm Hg

Fig. 2. Curves of arterial pressure (1) and venous pressure (2) at artificial circulation with low volume rates in dog Layma.

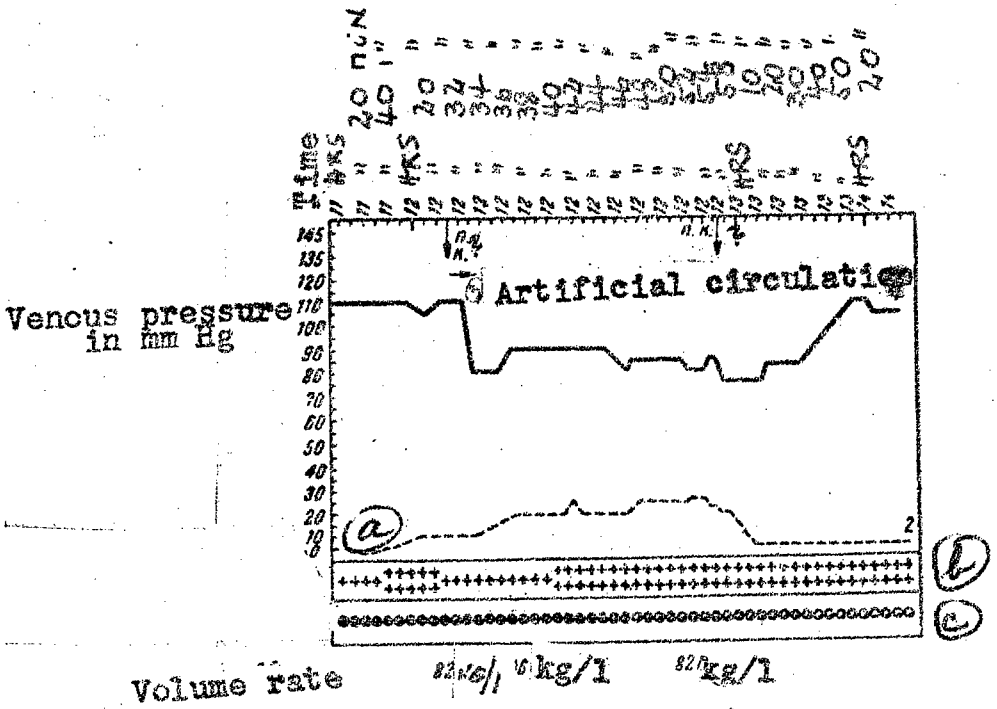


Fig. 1. Curves of arterial pressure (1) and venous pressure (2) at artificial circulation with volume rates of 80-100 ml/kg/min in dog Ulybka.

a) Arterial pressure in mm Hg.
b) Eye refl[illegible]
c) Nictitating membra[illegible]

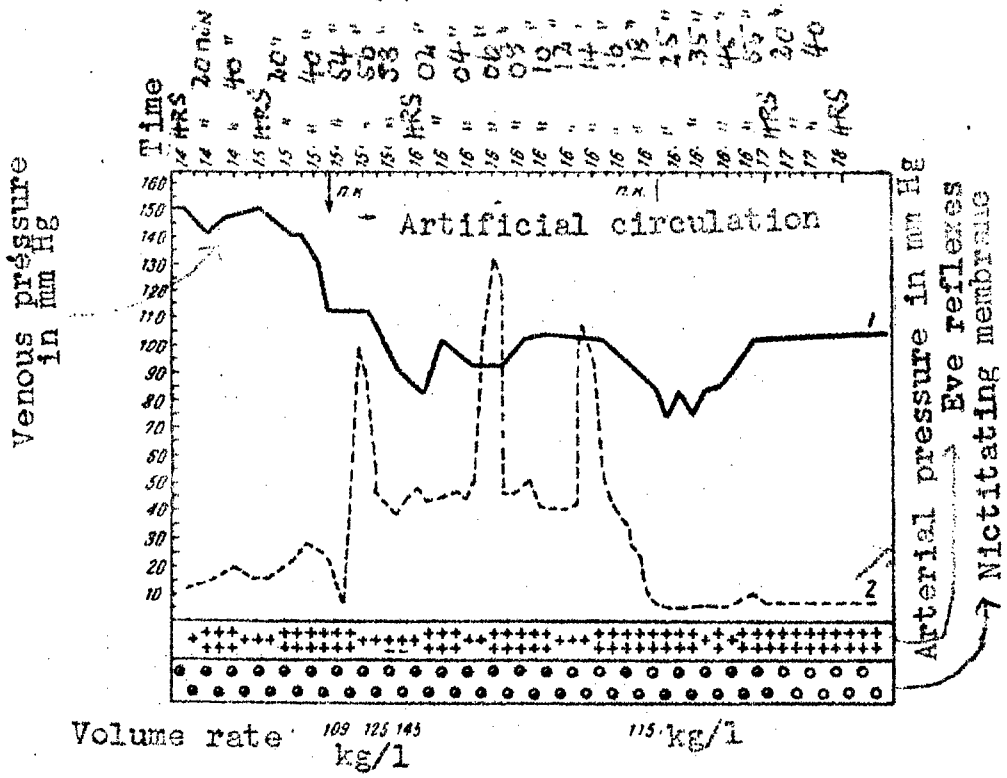


Fig. 4. Curves of arterial (1) and venous (2) pressure at artificial circulation with volume rates in excess of 100 ml/kg/min in dog Marva.

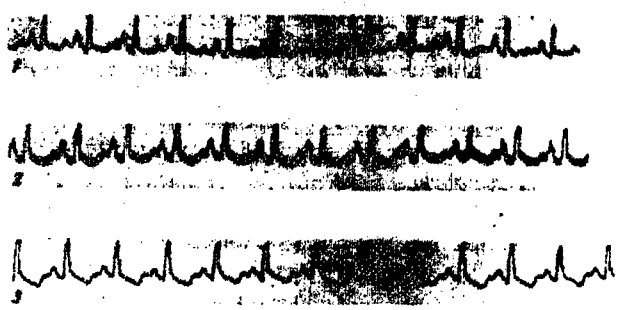


Fig. 5. ECG before (1), during (2), and after (3) artificial circulation with volume rates of 60-80 ml/kg/min in dog Layma. Reduction of the ST segment during artificial circulation.

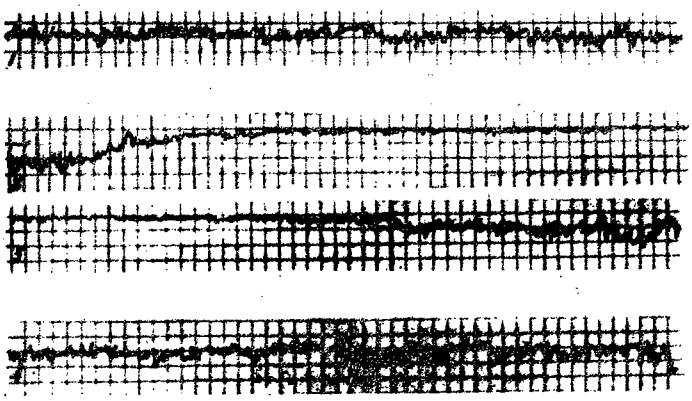


Fig. 6. EEG before (1), during (2), and after (3) artificial circulation with volume rates of 60-80 ml/kg/min in dog Layma. One of the periods of hypoxia of the cortex during artificial circulation.

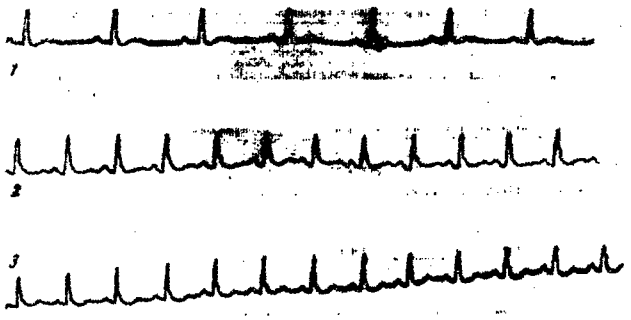


Fig. 7. An ECG before (1), during (2) and after (3) artificial circulation with volume rates of 80-100 ml/kg/min in dog Ulybka.

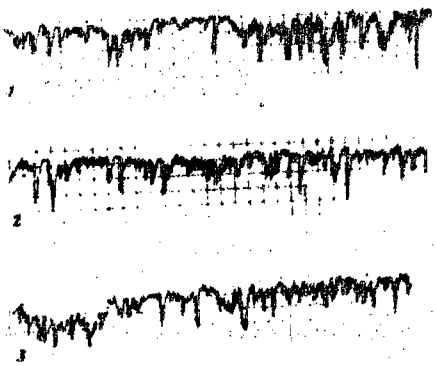


Fig. 8. EEG before (1), during (2) and after (3) artificial circulation with volume rates of 80-100 ml/kg/min in dog Ulybka.

Submitted 19 December 1959

Experience with the Closure of Patent Ductus Arteriosus with the Aid of a Mechanical Multi-Staple Suture

(pages 26-33)

By Ye. N. Meshalkin and V. I. Fufin

The Institute of Experimental Biology and Medicine (Director - Prof. Ye. N. Meshalkin) of the Siberian Division of the Academy of Sciences USSR and the Department of Thoracic Surgery and Anesthesiology (Director - Prof. Ye. N. Meshalkin) of the Central Institute of Advanced Training of Physicians (Director - M. D. Kovrigina).

More than 50 years have passed since Munro proposed surgical treatment for patent ductus arteriosus, and more than 20 years have passed since the first operation of this type was carried out by Gross. However, up to the present time there has been no unanimity concerning the best method of surgical closure of the ductus, although closure itself is considered desirable by all.

The first to carry out this operation was Gross in 1938, who ligated the ductus with two silk ligatures. In 1939 he published the first work, in which he described four cases of ligation of patent ductus with two silk ligatures; however, the author later discontinued this method.

Immediately after Gross, alosure of the patent ductus was performed by Crafoord (1941), Touroff (1940), Jones (1940), et al.

The initial successes encouraged surgeons, and the number of operations increased swiftly. According to Keys and Shapiro, by 1945, 25 surgeons had completed 139 operations. However, with increases in the number of operations, defects in the technique began to become apparent. Thus, Crafoord (1944) reported on 60 operations for closure of patent ductus with two ligatures, of which three patients had to be re-operated for insufficiency of the two ligatures.

According to Gross, recanalizations in his series reached ten precent. This stimulated Gross (1944) to wrap the patent ductus in cellophane, in accordance with experimental data obtained, in 1940, by Pierce, who showed experi-

mentally with the use of aortas and carotid arteries of dogs that free wrapping of vessels with cellophane causes first a perivascular increase in fibrous tissue, which compresses the vessel and then penetrates through it. After using this method with 28 cases and noting instances of recurrence after several years, Gross rejected this method also. In order to hasten obliteration, a number of authors (Jones, 1940; Gross, et al.; Polak, Padevceva, Bor, 1951; Crafoord, 1944) used a method involving the insertion into the lumen of sclerosing substances between ligatures. But this method also did not meet with wide acceptance because of defective features. Blalock, in 1946, proposed the application of multiple ligatures - two purse-string and two with preliminary suturing of the ductus with mattress sutures.

In addition to these methods of closing the patent ductus, a number of authors have used subaoventitial ligation of the ductus (Touroff, 1942), ligation with five ligatures (Murray, 1950), and the like.

In 1947 Shapiro and Johnson published a review article combining the statistics of 643 operations carried out by 46 surgeons. According to their findings, in 172 cases of ductus the suture method was used, and in the others the ductus was ligated. In 8.7 percent of cases there was recanalization of the ductus. These data led the authors to propose transection of the ductus, using ligation only in cases not transectable. According to Gross, recurrences after ligation of the ductus reach 20 percent (cases of recanalization and incomplete closure of the ductus). This high percentage of unfavorable results compelled him to reject the method of ligation of patent ductus arteriosus. Gross was the first, in 1939, to come out in favor of transection of the ductus.

Touroff, together with Vesell, in 1940, found it necessary to transect the ductus arteriosus when, because of injury to the pulmonary artery, it became necessary to remove the ductus arteriosus in order to effect hemostasis. In 1941 the patent ductus was transected by Crafoord. Despite this, both authors continued to be exponents of the technique of ligation of the ductus. Gross began to consider the transection of the patent ductus the operation of choice. In 1944 he published a work based on 14 operations performed by the following method: to the isolated patent ductus four clamps are applied. Between the central clamps the ductus is transected, and then the pulmonary stump is closed with two continuous sutures. With the aid of the remaining external clamp,

the pulmonary stump of the artery is drawn to one side and the aortic stump is closed with two continuous sutures. Then the clamps are removed (Gross used this method in 508 operations).

A number of authors (Wangenstein, Varco, and Baranofsky, 1949) modified this method, using three instead of four clamps. The final perfection of this method was accomlished by Potts (1953). In consists in the use of two special clamps with dentate grips applied to the pulmonary and aortic ends of the ductus, with subsequent transection of the ductus and application of mattress and uninterrupted sutures to the stumps.

In cases of short ductus arteriosus, a number of authors (Freeman, Leeds, Gardner, 1949; Conklin, Watkins, 1950; Davis, 1953) have employed an operation with the use of the Potts or Bailey clamp applied to the aorta. Another clamp is applied to the pulmonary end of the ductus, after which the ductus is cut away from the aorta. The defect in the latter is sutured with two continuous sutures, and the pulmonary stump is closed in various ways.

In the opinion of Rodriguez (1957), the author of the atlas "Cardiac Surgery", the technique of closure by transection of the patent ductus by the two above-mentioned method is the best.

In the Soviet Union the first operation for patent ductus was performed in 1948 by A. N. Bakulev (the stump of the transected ductus was sutured with silk sutures).

The majority of Soviet surgeons (P. A. Kupriyanov, 1954, 1955; B. V. Petrovskiy and A. A. Keshisheva, 1957; M. I. Perel'man, 1951; B. K. Osipov, 1950; F. Kh. Kutushev, 1959, and others) are adherents of ligation of the ductus. In reviewing the literature, it is clear that in the USSR, also, ligation of the ductus arteriosus is often followed by recanalization of the ductus (according to F. Kh. Kutushev, in 140 operations there was one recurrence), which entails a serious second operation, in which the dissection of the ductus from extensive adhesion in the adjacent regions is attended by numerous difficulties. Moreover, upon ligation of the ductus arteriosus there may be tearing or cutting through of the ligatures, especially in the presence of endarteritis or sclerotic changes.

Let us consider an example of a surgical mischance observed by us in our clinic.

Patient P., 19 years of age, was operated upon in the clinic on 24 February 1958, for patent ductus arteriosus with signs of pulmonary hypertension and sclerotic changes in the pulmonary artery and the ductus. During the operation, hemorrhage developed from the damaged pulmonary artery. In order to effect hemostasia, the ductus was transected, the pulmonary stump ligated, the aortic stump ligated with two ligatures, and atraumatic sutures appled to the defect in the pulmonary artery. Sudden death supervened nine hours after the operation due to acute exsanguination. At autopsy, both ligatures were found to have slipped from the aortic stump.

Ligation of the ductus may also predispose to the formation of aneurysms in the region of origin of the ductus from the aorta and from the pulmonary artery (Kerwin, Jaffe, 1959).

Starting with this, in 1956 one of us (Ye. N. Meshalkin) used the method of mechanical multistaple tantalum suture for closure. The arguments for the use of mechanical suture of the ductus arteriosus were the good results obtained by the author in using this method for suturing the auricle of the heart after commissurotomy, for saturing the ostium of the superior vena cava (in the operation of caval-pulmonary anastomosis), for suturing the aorta during constriction of it for tetralogy of Fallot (when the formation of anastomosis is impossible), and so forth.

Since 1956 mechanical tantalum sutures have been used for ductus arteriosus, and have been applied with different apparatuses.

At the present time, with our participation, the group of the Scientific Research Institute of Experimental Surgical Apparatus and Instrumentation has worked out a special apparatus UAP-20 (for suturing patent ductus arteriosus) (A. M. Geselevich, N. S. Gorkin, B. A. Smirnov, 1959), at the basis of which lay our experience with the mechanical suturing of the ductus arteriosus, which was the only experience recorde at that time.

Surgical closure of the patent ductus by mechanical suturing has been carried out (1) with apparatus not specifically desogned for this purpose (UUS, UKL, UKB-25) in 1956 to

1958, and (2) with apparatus specifically designed for this purpose (UAP-20) in 1958 to 1959.

Apparatus used during the first period was larger and therefore its application was associated with many difficulties. Let us present a brief description of mechanical suturing of patent ductus with subsequent transection of it.

Patient K., 18 years of age, entered the clinic on 9 October 1956 with complaints of dyspnea and easy fatiguability upon physical exertion. Following studies in the clinic, a diagnosis of patent ductus arteriosus was made. Operation was performed on 28 October by Prof. Ye. N. Meshalkin. Under intubation ether-oxygen anesthesia, the fifth rib on the left was removed and the pleural cavity entered. The pulmonary artery was considerably dilated, and a systolic thrill could be felt over the pulmonary-aortic zone. The mediastinal pleura was incised parallel to the phrenic nerve, about one to 1.5 cm behind it. The aorta was isolated and held in a clamp. Upon dissection of the pulmonary artery there was damage to its posterior wall. Slight hemorrhage was stopped by pressure with a gauze sponge. The ductus arteriosus was freed up for a distance of 1.5 cm in length and one cm in width, and its aortic and pulmonary ends were stapled with tantalum sutures, using the UKB-25 apparatus. Slight bleeding at the sites of application of the staples was observed. The ductus was then transected. Oozing began between the rows of staples from both stumps. Hemorrhage from the aortic stump stopped upon application of a nylon continuous suture, and the bleeding from the pulmonary stump stopped spontaneously. The thoracic cavity was closed in layers without drainage, through the incision, with simultaneous evacuation of air from it through a separate drain site. The postoperative course was smooth. The patient was discharged from the clinic in good condition (17 November 1956). Studies in 1959 showed the patient to be in good condition and to be active as a student (Fig. 1).

As indicated above, during the first period we used different apparatuses. These were used to close the ductus in 35 patients. Upon analyzing the material, we established that, of these apparatuses, the most suitable was the UUS, and the least suitable the UKB-25 (Table 1).

While being exponents of transection of the ductus arteriosus, during the initial period we did not, however, invariably use transection. This is explained by the following. The use of apparatuses of large size permitted, in some patient

application of mechanical sutures only to the aortic end of the ductus, and confined application to the pulmonary end to an encircling ligature, or a strengthening suture ligature. In 13 patients we succeeded in applying two rows of staple sutures. In the majority of these patients the two rows of sutures used up the entire length of the ductus. Tantalum suture is not absorbed in tissues, which excludes the possibility of recanalization. Hence, transection was carried out only in those cases in which it was possible to perform it. Of 35 operations, 19 transections were performed (Table 2).

Following transection of the ductus arteriosus, insufficiency of the medhanical sutures appeared in a number of cases. In 12 patients, upon suturing the ductus with the UKB-25 apparatus, it was necessary to apply additional atraumatic sutures, there being distinct hemorrhage in ten of these patients.

Let us consider another case history.

Patient O., 21 years of age, entered the clinic on 9 April 1957 with complaints of dyspnea and easy fatiguability. Studies showed the typical picture of patent ductus arteriosus stage I. On 19 April 1957 the patient was operated upon for closure of the ductus with mechanical sutures, using the UKB-25 apparatus, with transection. The pleural cavity was opened with a lateral incision in the fifth intercostal space. Palpation in the aorto-pulmonary area confirmed the presence of patent ductus.

The aorta and the pulmonary artery were dissected out above and below the ductus and held in temporary rubber clamps. After isolation of the ductus, it was sutured at the aortic end. The pulmonary end was ligated. The ductus was then transected. Hemorrhage developed from the aortic stump. The aorta was clamped in rubber clamps for 15 minutes. At the bleeding site, atraumatic sutures were applied. The pulmonary stump was also sutured with continuous sutures. The clamps were released. Hemorrhage did not recur. The incision was closed in layers. The postoperative course was smooth. The patient was dismissed in doog condition on the 15th postoperative day (3 May 1959).

Upon closing the ductus with the use of the UUS-apparatus, only in one instance did additional sutures have to be used.

Easy control of developing hemorrhage is ensured by compression of the aorta and pulmonary artery above and below the ductus by preliminary application of temporary rubber clamps. The use of clamps for controlling hemorrhage in the present group of patients was required in 11 cases. Of this number the aorta was clamped ten times and the pulmonary artery five times, once without clamping the aorta since the ductus was already closed on the aortic side. The aorta in our case was closed from four to 23 minutes.

In no such patient were there any signs of disturbed function of the brain or spinal cord.

The technique of compressing the main vessels is simple and cosists in crossing untied ligature and securing them with clamps (Fig. 2, above).

In two cases, with a greatly dilated trunk of the pulmonary artery and the development of hemorrhage afterward, the hemorrhage was controlled by compressing the trunk of the pulmonary artery immediately distal to the valve (Fig. 2, below).

In the second period we used a special apparatus - the UAP-20 - which is designed to suture the patent ductus arteriosus ("Grudnaya Khirurgiya" [Thoracic Surgery], 1959, No. 1, 114-118). The disposition of the staples in the suture is different from that when the UKB is used (see Fig. 3). The apparatus has a clearance of 0.5 mm.

From 19 November 1958 until 1 January 1960, we carried out 56 operations for closure of patent ductus arteriosus with the UAP-20 apparatus. In all instances the ductus was transected (see Table 1 and 2).

Let us consider the basic steps and certain technical points in the operation. Entry is lateral, with subperiosteal resection of the fifth rib. Wide incision of the mediastinal pleura permits easy and quick dissection of the aorta and pulmonary artery above and below the ductus. With the latter step, the ductus is dissected out. In the great majority of cases the ductus is dilated both on the aortic and on the pulmonary sides. This convinced us (as we have already reported) that we should suture the aorta and the pulmonary artery at the site of origin of the ductus, since dilation of vessels is completely eliminated after application of sutures. Moreover, the security of placement of sutures upon applica-

tion of them to major vessels is considerably greater.

At the time of suturing with the apparatus, the surgeon must press the lever, after preliminarily releasing the catch. The movement of the lever is transmitted to the blade of the ejector, which ejects a staple. The latter penetrates the tissues of the vessels, and, coming hard against the supporting "matrix", is bent into a B shape. The suture is thereby completed.

Pressure on the lever must be smooth, with no abrupt pressure differences, and, by the same token, without moving the instrument to one side or the other.

Repeated pressures on the lever are not recommended, since this may tear the vessel.

Upon closing the aortic end of the ductus, it is necessary to move the apparatus from within outward, since there is one extra staple in the magazine of the apparatus and the suture will in this case be more reliable (Fig. 3a).

To facilitate placing the apparatus about the ductus and the application of it to the wall of the aorta, the latter must be carefully held in a clamp. Upon application of the sutures and lifting of the stapling lever, the crook of the supporting part must be inserted slightly deeper into the operative field and cautiously moved out again, in order not to tear the atples out of the ductus.

In a similar fashion the pulmonary end of the ductus is clossed, but in this instance the apparatus must be moved from without inward (Fig. 3b) so that there will be more staples on the side of the pulmonary artery. After suturing both ends of the ductus, it is transected (Fig. 3c).

For closure of the ductus, we have used staples 0.2 mm in diameter, three mm wide, and three or two mm long. Experience has shown that those three mm long were the most reliable (Fig. 3d).

In one case the apparatus did not function, due to the fact that the ejector jammed because of a piece of tantalum from a broken staple wedging in one of the spaces of the magazine. This led us subsequently always to test the apparatus carefully before use.

Let us present our observation on patient K., who had a patent ductus arteriosus and was operated upon by the method described above.

Patient K., 19 years of age, entered the clinic on 31 August 1958 with complaints of dyspnea, easy fatiguability, and periodic episodes of syncope. A congenital heart defect was diagnosed at four years of age. On the basis of our studies in the clinic, we diagnosed patent ductus arteriosus. Operation was performed on 30 September 1958. Under ether-oxygen anesthesia and preliminary ganglionic blockade, the thoracic cavity was opened along the fifth rib on the left, with subperiosteal resection of the rib. There were no adhesions, the wound was enlarged, and the lung compressed down and backward. At the predicted site of location of the patent ductus, a systolic-diastolic thrill could be palpated. The mediastinal pleura was incised parallel to the phrenic nerve and 1.5 cm behind it. The vagus nerve together with the surrounding tissues were enclosed in a gauze tape soaked in novocaine. The aorta, above and below the ductus, and the pulmonary artery were dissected and held in rubber clamps. The ductus was isolated. The latter was about 0.5 cm in diameter and 1.3 cm in length, and entered the left branch of the pulmonary artery at a distance of 0.5 cm from the bifurcation. The pericardium was 0.3 cm from the ductus. The aortic end of the ductus, with partial implication of the aortic wall, was sutured with tantalum sutures with the UAP-20 apparatus. There was no hemorrhage. The systolic-diastolic thrill immediately ceased. At the pulmonary end, the same method was used to apply a second row of tantalum sutures. The ductus was then transected. There was no hemorrhage. The pleural cavity was dried, and 300,000 units of penicillin introduced. The incisional wound was sutured in layers. Air was removed from the pleural cavity through a temporary drain. The postoperative course was smooth. The patient was discharged in good condition on 14 October 1958.

In addition, note should be taken of the technique of isolating the vagus nerve and the recurrent nerve which arises from it. The mediastinal pleura is incised parallel to the nerve to both sides of it, which permits, for a considerable distance, dissection of the nerve and retraction of it with a gauze tape soaked in novocaine. Traction with the tape permits visualization of the recurrent nerve, which, together with the surrounding tissues through which it passes, is dissected by sharp dissection from the inferior and posterior walls of the ductus. Drawing the vagus nerve toward

the pulmonary artery permits easy application of the suturing apparatus to the ductus and suturing of the aortic end of the ductus, whereas drawing the vagus nerve toward the aorta permits the same procedure on the pulmonary end of the ductus. In 101 operations for closure of the ductus, there was not a single instance of disruption of the recurrent nerve.

We observed patient A., who died two years and seven month after operation due to the development of bronchiectasis, aneurism of the bronchial artery of the left lung, and pulmonary hemorrhage. Upon pathologic study, we discovered an excellent state of the sutures in the aorta and the pulmonary artery (Fig. 4), and there was no evidence of inflammatory reaction around them.

Of 91 patients operated upon by the method of mechanical suturing for closure of patent ductus arteriosus, 63 have been followed for differing periods of time. Of this number, 61 are virtually healthy and are working. Two others are feeling well.

Our experience with the use of the mechanical multistaple tantalum suture for patent ductus arteriosus, using different apparatusses, testifies in favor of the use of this method for closure of patent ductus.

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Fig. 1. Roentgenogram of patient K., 21 years of age, three years after closure of patent ductus arteriosus by the mechanical suturing technique.

Table 1

Use of Apparatuses for Closure of Ductus Arteriosus

ıratus	No. of operations	No. of transections	Bleeding marked	Bleeding slight	Need of additional sutures
UKB-25	31	19	10	13	12
UUS	4	3	-	1	1
UAP-20	56	56	-	6	6
Total	91	78	10	20	19

Table 2

The Use of Different Methods of Surgical Closure of Ductus Arteriosus in the Clinic

Operation	No. of operations first period	second period	Total
Closure of PAD with two rows of staple sutures, with transection of the ductus	13	56	69
Closure of PAD with two rows of staple sutures, without transection of the ductus	7	-	7
Closure of PAD with staple sutures on the aortic side and ligation of it on the pulmonary side, with transection of the ductus	6	-	6
Closure of PAD with staple sutures on the aortic side and ligation of it on the pulmonary side, without transection of the ductus	7	1	8
Closure of PAD by other means, with transection	5	1	6
Closure of PAD by other means, without transection	5	-	5
Total	43	58	101

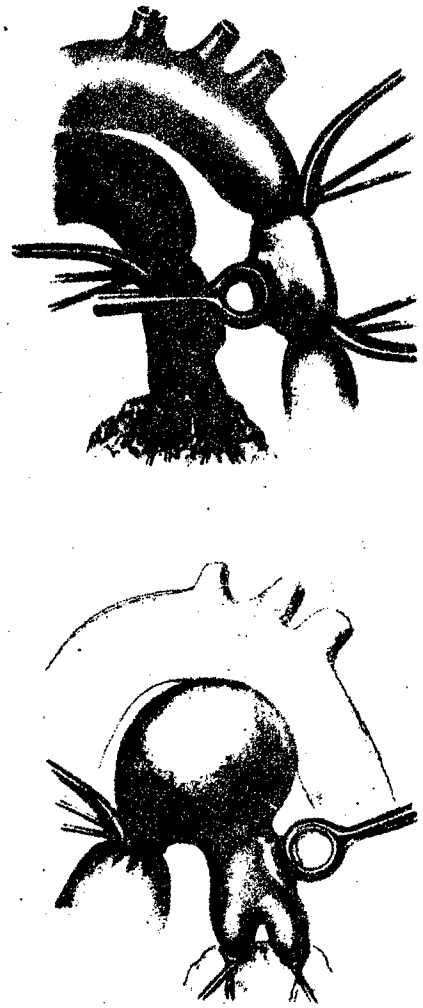

Fig. 2. Occlusion of the aorta and pulmonary arteries with temporary rubber clamps in cases of injury to the ductus. Above - compression of the left branch of the pulmonary artery and aorta; below - compression of the trunk of the pulmonary artery.

3a

3б

Fig. 3. Application of mechanical sutures to the aorta and the pulmonary artery with the UAP-20 apparatus.
(a) the moment of compression of the ductus with the UAP-20 apparatus;
(b) double row of mechanical sutures on both stumps of the ductus;

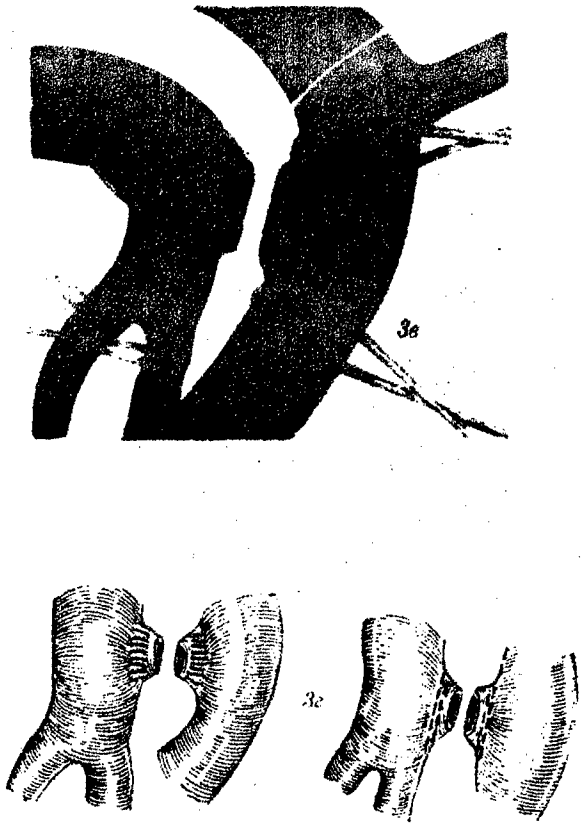

Fig. 3. (continued)
(c) transected ductus closed with mechanical sutures;
(d) scheme of positioning of mechanical sutures on ductus, as applied with the UKB-25 apparatus and the UAP-20 apparatus.

Fig. 4. The aorta of patient A., 11 years of age, two years and seven months after placement of mechanical sutures on the ductus arteriosus (photograph).

The Significance of Venous Pressure Measurements during Operations on Organs of the Thoracic Cavity

(pages 34-36)

By A. I. Bredis

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Despite the considerable advancements in the area of thoracic surgery, the mortality during operations and in the hours immediately follwoing still remain high. In some cases the patients may die at the onset of the operation - immediately after opening the thoracic cage, while in other cases, they may die several hours after an easily completed and well tolerated procidure.

We attribute great importance to variations in the venous pressure occurring during surgical intervention in organs of the thoracic cavity. Hence, throughout the entire operation, we systematically measure the venous pressure and, depending upon the readings, we regulate blood transfusion and the method of administration of blood.

The introduction of blood transfusion into daily practice has favored the growth of thoracic surgery; however, with the accumulation of experience, it has been increasigly shown that massive intravenous transfusions used during thoracic procedures in some cases not only do not help the patient but even exert an injuring effect on his condition.

It is known that operations in the chest lead to a number of hemodynamic shifts in which there is congestion in the lesser circulation, increase in the venous pressure, reduction in the arterial pressure, and weakening of cardiac activity.

In these instances massive intravenous transfusions of blood designated to pull the patient out of a serious condition, may lead to even greater increase in the venous pressure, to overstress of an already weakened heart (especially on the right), to dilatation of the right heart, and sometimes

to death.

At the present time there are potent measures in the form of intra-arterial blood injectors, which all surgeons are obligated to use during terminal states. Taking into account that in chest procedures different complications may d velop swiftly, we use intravenous transfusions, controlling the venous pressure and we are continually in readiness to use intra-arterial transfusions.

This is carried out by the following method. All major thoracic procedures are accompanied by intravenous droplet transfusions of blood. The blood is injected into the medial dorsal vein of the foot. The transfusion system is combined with a Val'dman apparatus and periodic measurements are made of the venous pressure. Prior to operations, the femoral artery is exposed in the antecubital space and, with a ligature under it, the incision is covered with a sterile bandage. A bottle of blood is arranged for intra-arterial injection and supported on a stand. If the arterial pressure begins progressively to drop during the operation and, together with this, there is marked venous hypertension, we not only do not force intravenous transfusions but even consider them contraindicated, since this may lead to overloading of the right heart and acute dilatation thereof. In these instances we discontinue the intravenous infusions and, in order to improve the coronary circulation, resort to intra-arterial transfusions. After the arterial pressure is restored and the readings approximate normal levels, and when the venous pressure has dropped nearly to normal, we renew the droplet infusion of blood and thus reinforce the effect achieved by recourse to the intra-arterial transfusion.

Such a procedure has enabled restoration of cardiac activity in a number of cases and has prevented transition from the third phase of cardiac-pulmonary insufficiency to shock state.

We regard the intra-arterial transfusion of blood as a powerful means for reversing the terminal state of the patient, and hence have introduced this method into the daily practice.

Of 41 patients with which we used intra-arterial transfusion, 14 [it should probably be 34] suffered with diseases of the lungs, one of the heart, one of the pericardium, one with tumor of the mediastinum, and four with diseases of the

esophagus.

Of 21 patients operated upon, cardio-pulmonary insufficiency developed in seven and severe shock in 14 (during operation in seven and after operation in the other seven).

Hence, the most frequent complication in operations on organs of the chest is shock, according to our figures.

In two patients with cardio-pulmonary insufficiency, we did not note the development of venous hypertension during the operation. Desiring to improve the poor state of these patients, we increased the rate of intravenous infusion and, not achieving the desired effect, had recourse to intra-arterial forced infusion of blood at a time when there was already marked cardiac insufficiency as the result of acute dilatation of the heart. Intra-arterial infusion of blood was ineffective, and the patient died.

In five patients with manifestations of cardio-pulmonary insufficiency developing at the onset of operation, proceeding on the basis of high indices of venous pressure, we discontinued intravenous blood transfusion and, wishing to raise the markedly reduced arterial pressure, immediately started intra-arterial transfusion under pressure. In all of these cases, there was reversal of the third stage of cardio-pulmonary insufficiency and successful conclusion of the operation.

In these cases, the intravenous infusion of blood for enhancement of the effect obtained was resumed only when the patient had recovered from his serious state, as shown by restoration of the arterial pressure and reduction of the venous pressure.

With a decline in the arterial pressure and also in the venous pressure during operation, the intravenous infusion of blood is changed from droplet to continuous infusion, and if there is no improvement in the arterial pressure, we continue the intravenous infusion while adding intra-arterial infusion.

With drops in the arterial and venous pressures after unseccessful intravenous transfusions, we administered intra-arterial blood to 12 patients. Of these, eight experienced reversal of their severe shock, and four died.

In fourth stage shock, when it is no longer possible to measure the arterial pressure, we do not rely on intravenous infusions but immediately resort to intra-arterial transfusion. One of two such patients was brought back from a terminal state.

According to our observations, for the reversal of the condition of shock (if the latter is not due to blood loss), 200-400 ml of blood will ordinarily suffice.

Hence, in operations of the organs of the thoracic cavity, systematic measurements of the venous pressure are of great importance. The indices of venous pressure aid in the rational utilization of one or another method of blood transfusion, help to eliminate cardio-pulmonary insufficiency and reverse the shock state, thereby reducing the mortality due to thoracic procedures.

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On Deep Hypothermia and Emergence from Itl. Report III[2]. Oxygen Balance and the Efficiency of Training for Oxygen Deficiency in Deep Hypothermia

(pages 39-45)

By Ye. V. Gubler, N. V. Alishev, N. I. Lassi, and N. B. Sokolova

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A study of the problem of the oxygen budget in deep hypothermia (rectal temperature below 20 degrees C), and also the development of measures for improving it, are important for the practical utilization of hypothermia as a method of enhancing resistance to oxygen deficiency.

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1. Presented at the meeting of the Leningrad Society of Pathologists on 11 March 1958.

2. Reports I and II published in the journal "Patologicheskaya fiziologiya i eksperimental'naya terapiya" [Pathologic Physiology and Experimental Therapy].

In many studies it has been found that the resistance to many forms of severe oxygen deprivation increases with increasing depths of hypothermia. This can be explained only by the assumption that the requirement for oxygen is reduced more than the transfer of oxygen into the body is reduced upon lowering the body temperature. At the same time, with deep hypothermia a number of serious disturbances develop also in systems providing oxygen supply to the tissues, especially the agglutination of erythrocytes in the capillaries (McBirnie et al., 1953; Gelin and Lofstrom, 1955; Lofstrom and Zederfeldt, 1956), interference with dissociation of oxyhemoglobin (A. I. Izbinskiy, 1953; Penrod, and others, 1955), and disturbances of oxidative enzymes (Ganshirt et al., 1954). Moreover, in deep hypothermia, there is not infrequently cardiac arrest which, of course, seriously interferes with the transport of oxygen (I. R. Petrov, Z. A. Rayko, and T. Ye. Kudritskaya, 1957). As shown by Z. A. Rayko et al. (1957), during the warm-up period after cessation of circulation under conditions of moderate hypothermia, there is a resumption of oxygen deficiency associated with the restoration of oxidative processes and increases in the tissue oxygen needs.

In the present work we had the opportunity to compare the groups of indices of the oxygen budget of the organism: (1) the pulmonary ventilation, oxygen saturation of the blood, and arterial blood pressure, which characterize the supply of oxygen; and (2) the oxygen requirements and the content of lactic acid in the blood, which characterize the utilization of oxygen in the tissues. In addition, we tested the effectiveness of certain anti-hypoxic measures directed at normalization of the disordered oxygen budget. As the latter we used the injection of pantothenic acid (vitamin of the B group) and preliminary training in a pressure chamber with reduction of the barometric pressure. The latter measure, as shown by N. N. Sirotinin (1955) and V. M. Pinchuk (1958), may increase the resistance not only to oxygen deficiency, but also to diseases such as pertussis, anemia, schizophrenia, pneumonia, etc.

A study of the problem of the influence of training in the pressure chamber on the tolerance of cats to deep hypothermia was carried out by the authors of the present article in conjunction with V. G. Petrukhin and V. M. Pinchuk, who supervised the preliminary training of animals in the pressure chamber and carried out the morphologic part of the study. The results of the morphologic studies are described

in a separate publication (V. G. Petrukhin and V. S. Pinchuk, 1958).

The experiments were set up on cats which were cooled, under ether-oxygen anesthesia, to temperatures averaging 11.8 degrees C in the rectum and 18 degrees C in the esophagus. Cooling was discontinued after the arterial pressure fell to zero, and, after a definite period of time, the warm-up period was begun with hot water, initially at 50 degrees C and then at 40-45 degrees. At the same time measures were carried out to restore cardiac activity. The heart was massaged through the thoracic cage, and also repeated intra-arterial injections of five ml of N. V. Petrov's salt solution and 0.05 mg noradrenalin were given (injection of noradrenalin was given to increase the arterial pressure to 30-50 mm Hg upon massage of the heart). Training in the pressure chamber was initially carried out at "heights" of five to six, and later seven to 7.5 kilometers three hours a day for six to ten days. Pantothenic acid was given in the form of the calcium salt in doses of 30 mg in two equal portions at the beginning of cooling and immediately after onset of cardiac massage (intravenously and intra-arterially. respectively).

In the experiments we studied the following pathophysiologic and biochemical indices: temperature in the rectum, esophagus and nasal passages, arterial pressure, frequency of pulse and respiration, pulmonary ventilation and oxygen consumption (with the aid of a specially-modified Mitropol'skiy apparatus), oxygen saturation of the blood hemoglobin (with the aid of a cuvet oxymeter), lactic acid content of the blood (by the method of Frideman, Cattonio, and Shaffer). In the present report we shall present the material from 66 experiments (Table 1).

The problem of the pathophysiology of deep hypothermia has been considered in detail in Report I (Ye. B. Gubler, N. V. Alishev, N. I. Lassi, 1958). Deep hypothermia is characterized by severe disturbances in circulation. In our experiments, at rectal temperatures of 10.6-20 degrees C and esophageal temperatures of 15.2-24.3 degrees C, there was cardiac arrest. True, in half of the cases, weak and quite rapid heart beats returned within several minutes, but these soon disappeared, sometimes appearing again periodically and lasting an hour or more. Nonetheless, the circulation during this period, which may be designated the period of "cardiac crisis", was insufficient to sustain tissue metabolism even under the conditions of deep hypothermia. Therefore, after a cardiac

crisis lasting more than 30 minutes, it was possible to restore complete circulatory activity with maintenance of life onlt in a small number of animals (Table 1). Not infrequently it was not possible to restore cardiac activity at all. At the same time, in 20 experiments in which cardiac crisis either did not develop during deep hypothermia or else lasted less than 30 minutes, only one cat died (three days after the experiment).

At temperatures of down to 16 degrees in the rectum (about 19 d gree in the esophagus), the oxygen need diminished slightly more rapidly than the pulmonary ventilation and the arterial pressure (Fig. 1). Simultaneoulsy, the oxygen saturation of the blood declined altogether five to six percent as compared with the original level. At the same time it became clear that the content of lactic acid in the blood increased not only after the cardiac crisis but even during anesthesia itself as well as upon cooling to 25 to 30 degrees C (Figs 1 and 2, Table 2).

Under conditions of ether anesthesia with oxygen at normal body temperatures or during mild hypothermia (25-30 degrees), it is difficult to demonstrate the presence of oxygen deficiency. Hence, it must be assumed that the accumulation of lactic acid was associated not only with oxygen deficiency but also with unequal inhibition (under the influence of low temperatures) of the activity of different enzyme systems. As the result, anaerobic glycolysis, as the more primitive phylogenetic process, presumably was inhibited less than aerobic processes. In deep hypothermia, and especially during cardiac crisis, this undoubtedly was influenced by insufficient access of oxygen caused by disruptions in circulation. However, regardless of the nature of the nature of the mechanism of accumulation of lactic acid in artificial hypothermia as well as under anesthesia, this fact in itself testifies to definite disorders in oxidative processes leading to the accumulation of unoxidized products, with all the consequences which follow from that.

After the injection of calcium pantothenate, cardiac arrest occurred at esophageal temperatures one degree lower than in controls (reliability of differences: $p = 0.997$; calculation of reliability by the Student "t" test (V. I. Romanovskiy, 1947); reliability of differences with $p = 0.95$ and above is considered quite sufficient), and the pulse during the period of cardiac crisis periodically reappeared in a greater number of experiments and was maintained for longer

periods of time than in the controls (Table 3). Restoration of cardiac activity with cardiac massage was also achieved more frequently. There was slightly quicker restoration of arterial pressure upon rewarming. However, no positive effect was apparent in the final outcome of the experiments.

Reduction in the disorders of circulation under conditions of deep hypothermia was not seen in the trained animals. Arterial pressures upon cooling and rewarming were no higher than in controls (Fig. 3). Cardiac arrest occurred at the same temperatures as in controls (Table 3). During the period of cardiac crisis, in both trained animals and controls, the pulse periodically appeared only in half the animals and remained for even shorter periods than in the controls.

Hence, improvement in the supply of oxygen to the tissues during hypothermia was evidently not seen in trained animals. Nonetheless, preliminary pressure chamber training markedly improved the tolerance of animals to deep hypothermia. Cardiac activity upon massage in trained animals was restored in all cases, and this occurred after less prolonged cardiac massage. Simultaneously there was more prolonged maintenance of respiration during the period of cardiac crisis (Table 3), which testifies to the lesser damage to the nervous system. As a result, the outcomes of experiments on animals preliminarily trained in the pressure chamber were considerably better than in controls. Of 14 control animals, only two survived after cardiac crisis lasting 55-65 minutes and in eight of the 12 which died, it was no longer possible to restore cardiac activity, whereas in experiments preceded by training in the pressure chamber, restoration of cardiac activity was observed in all cases, without exception, and six of ten cats survived after cardiac crisis lasting 60-61 minutes (Table 1).

A study of the morphologic changes in the cardiac muscle in trained animals (V. G. Petrukhin and V. M. Pinchuk, 1958) and in animals not trained (S. S. Vayl', 1958), which died or were sacrificed at various times after deep hypothermia, showed that, with equal durations of cardiac crisis, there were either vitually no pathologic changes in the myocardium of the trained animals, or else these were much less apparent than in the myocardium of the control animals, in which damage to the myocardium was quite pronounced.

Some light is thrown by the following data on the mechanism of the positive effects of oxygen deficiency training du-

ring deep hypothermia. It turned out that, at all stages in the development of deep hypothermia and of recovery afterward (except at the time of discontinuation of rewarming), increases of the lactic acid in the blood in trained animals were less than in the controls. Consequently, there was a less marked predominance of anaerobic processes under hypothermia in the trained animals. This is confirmed by the fact that, in hypothermia, the uptake of oxygen by trained animals is higher than by controls (Fig. 4).

Hence, training in the pressure chamber ensures a higher uptake of oxygen and a more complete utilization of it for oxidative processes in deep, as well as in moderate, hypothermia, which is not due to the greater supplying of oxygen to the animal by the respiratory apparatus or to external respiration. At the same time, the possibility of intensifying anaerobic glycolysis in trained animals is also maintained or even increased. This is apparent from the high rates of increase of lactic acid in the blood of trained animals during the period of cardiac crisis and also after it.

Hence, preliminary training in the tolerance of oxygen deficiency permits improvement in the utilization of oxygen during hypothermia and reduction in the accumulation of lactic acid, and ensures, in the event of need, a more effective control of oxygen deficiency by the trained organism under conditions of anesthesia and moderate or deep hypothermia, as well as after recovery from it.

What has been said permits the conclusion, which is of considerable practical importance, that training for oxygen deficiency is desirable as a preparatory measure prior to major operations under general anesthesia, and especially under hypothermia, not to speak of deep hypothermia.

Conclusions

(1) Upon cooling, under conditions of ether anesthesia with oxygen, to 16 degrees C rectal temperature (19 degrees C esophageal), the ratio of indices characterizing the access and utilization of oxygen remained favorable. At the same time, the content of lactic acid in the blood progressively increased.

(2) The injection of pantothenic acid during cooling

slightly reduced the disturbances in circulation under deep hypothermia, but did not improve the final outcome of the experiments.

(3) Preliminary training of cats to the effects of low barometric pressure considerably enhanced their resistance to deep hypothermia with marked disturbances of circulation (so-called "cardiac Crisis"), decreased the accumulation of lactic acid, and increased the oxygen consumption during hypothermia and at the onset of the period of rewarming.

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Table 1

Results of Experiments with Deep Hypothermia

Series	Length of cardiac arrest in min.	No. of animals	Results of experiments: Died: Unrestored cardiac activity	Died: During first 8 hrs	Died: On 2-7 day	Died: On 8-30 day	Survived: Total	Survived: percent
Control	28—30	9	0	0	1	0	8	89
	31—49	8	4	1	0	1	2	25
	55—65	14	8	0	2	2	2	14
	70—92	8	1	0	4	1	2	25
	121	2	2	0	0	0	0	0
With calcium pantothenate	55—72	8	3	2	1	2	0	0
	30—32	7	0	0	1	0	6	86
Training in pressure chamber	60—61	10	0	1	3	0	6	60

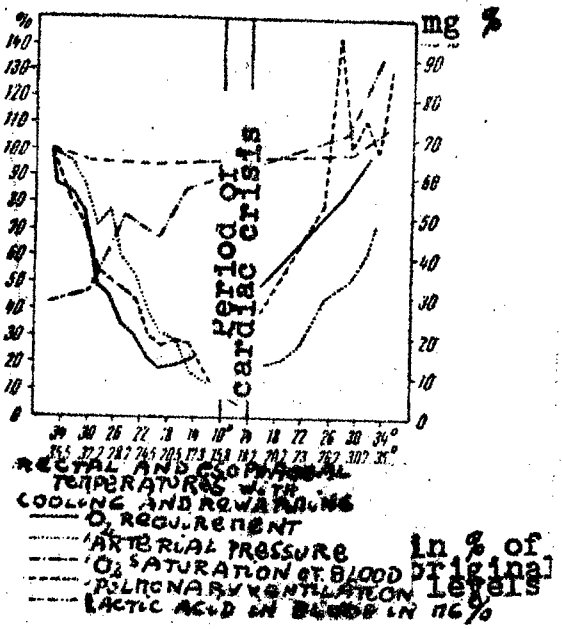

Fig. 1. Changes in the oxygen consumption, arterial pressure, pulmonary ventilation, oxygen saturation of the blood, and lactic acid content of the blood in deep hypothermia and upon rewarming afterward (average data).

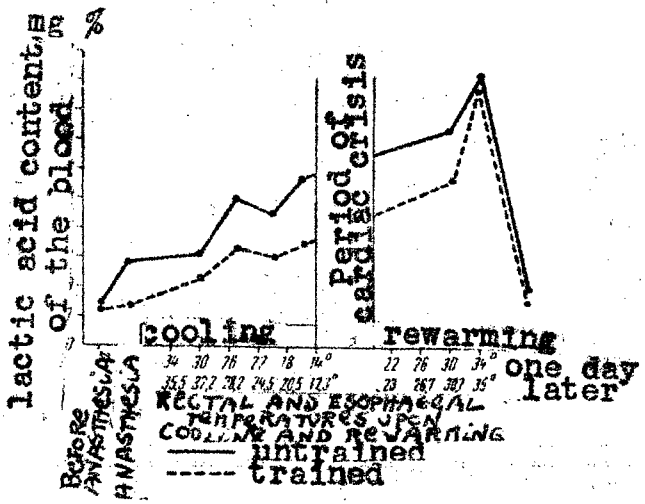

Fig. 2. Content of lactic acid in the blood in trained (in pressure chamber) and untrained cats under deep hypothermia before the onset of the cardiac crisis and during the period of rewarming after it (average data).

Table 2

The Effect of Training for Oxygen Deficiency on Changes in the Content of Lactic Acid in the Arterial Blood in Cats under Deep Hypothermia with Cardiac Crisis

No. of experiment	Content of lactic acid in arterial blood in mg percent: before anesthesia	under anesthesia	cooling — temperature of the body (rectal) 30°	25°	20°	16°	rewarming 28.1–32°	32.1–36°	18 hrs after experiment
Without preliminary training									
81		24,3			31,5		82,8		
85		21,6			39,6		56,7	117	
88		23,4			36,0		78,3		
89		23,4			53,1		—		
90		26,1			36,0		—	67,5	
91		19,8			38,7		—	96,3	
92		56,7			82,8		103,5	134,1	
93		—			39,7		80,1	98,3	
94		25,2			36,1		41,4	77,4	
97		31,5			41,5		75,6	88,2	
98	12,6	28,8					55,8		
99	22,5	35,1					73,8	122,4	27,0
100		29,7	49,5	54,0				80,1	14,4
101	17,1		32,4	55,8					
104	11,7		33,3	54,0					
110	15,3		23,4		37,0		54,0	65,7	
111	18,0				48,6		67,5	79,2	21,6
120	14,4	27,9	32,4	40,5	54,9				
121	9,9	25,2	37,8	45,9	54,0			94,8	
136	12,6		31,5		54,0	58,8	83,7		16,2
137	13,5		25,2		48,6	53,1	86,4		17,1
Average	14,76	28,4	30,68	50,04	45,7	55,9	72,27	93,4	19,26
In %	100	193,2	208,1	340,1	310,9	380,9	549,2	635,3	131,2
After preliminary training									
108			37,5	51,3			83,7	90,0	
109			31,5	44,1			60,3	72,0	17,1
114	15,3		30,6		48,8		61,2	73,8	
116	18,0		26,2	31,5			38,7	83,7	
117	17,0		25,2		29,7		40,5	64,0	15,3
118	11,8	12,6	14,4	18,9	25,2			124,2	16,2
119	9,9	14,4	16,2	19,8	19,8			91,8	
126	11,7		20,7		27,0	32,4		82,8	
128	10,8		18,9		27,0	30,6		90,0	
129	12,8		20,7		28,8	35,1		98,1	12,6
134	11,7		26,1		33,3	43,2		90,1	14,4
135	12,6		18,9		23,4	25,2		77,4	15,3
143	11,7		24,3	27,0		44,1		87,3	
144	10,8		35,1		30,6			72,0	
145	12,6		16,2		19,8	21,6		85,5	
146	16,2		22,5	26,1	20,7			83,7	
Average	13,07	13,5	24,1	31,2	27,8	33,2	56,9	85,4	16,1
In %	100	103	184	239	213	253	435	607	116

Table 3

The Effect of Training in the Pressure Chamber and the Injection of Calcium Pantothenate on Changes in the Cardiac Activity and Respiration during Cardiac Activity under Deep Hypothermia (Average Data)

Indicators \ Series of experiments		Control	With preliminary training	With injection of calcium pantothenate
Total number of experiments		41	17	8
Temperature of first cardiac arrest (onset of cardiac crisis)	rectal:	16.1°	15.8°	15.7°
	esophageal:	19.2°	18.8°	18.1°
Pulse periodically appeared in % of total number of animals (in this series)		32	53	88
Duration of maintenance of pulse (in min) during crisis lasting	28-30 min:	17.0	9.9	-
	55-65 min:	23.4	16.0	39.1
Cardiac activity restored after crisis lasting 55-65 min (in % of total number of animals in this series)		43	100	63
Duration (in min) of cardiac massage leading to restoration of cardiac activity		18.6	12.1	20
Duration of maintenance of spontaneous respiration during crisis lasting	28-30 min:	14.0	22.1	-
	55-65 min:	23.4	30.2	20.7

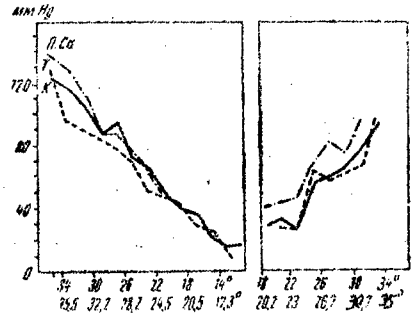

Fig. 3. Arterial pressure in mm Hg in pressure-chamber-trained animals (T), those receiving calcium pantothenate (P. Ca), and controls (K) under deep hypothermia, prior to the onset of cardiac crisis and during rewarming after it (average data). Along the abscissa - temperature in the rectum (upper scale) and in the esophagus.

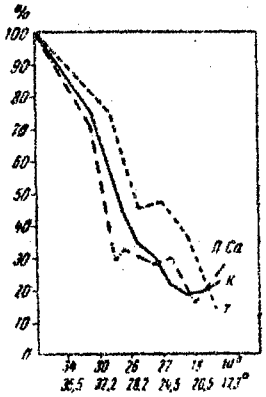

Fig. 4. Uptake of oxygen in percent of original levels (under anesthesia) in animals trained in the pressure chamber (T), those receiving calcium pantothenate (P. Ca.) and controls (K) under deep hypothermia, prior to the onset of cardiac crisis (average data). Along the abscissa designations are the same as in Fig. 3.

The Effect of Biopreparations on the Synthesis of Proteins in the Normal and in the Damaged Myocardium of the Rat

(pages 52-53)

By L. V. Polezhayev and V. L. Mant'yeva

We have shown previously that biopreparations (hydrolysates and extracts) prepared from a cardiac muscle of rats markedly stimulate regeneration of the myocardium of rats after damage inflicted upon it by means of electrodiathermocoagulation, through enhancing the processes of dedifferentiation and disintegration of tissues.

In the light of these findings, it was essential to investigate whether the above-mentioned biopreparations influence directly the process of protein synthesis in the cardiac muscle and in other tissues.

For a clarification of this problem, we set up the following experiments. Rats with undamaged and damaged hearts were given hydrolysate, for courses of two or of 13 days, every other day in doses of 0.0003 mg each. Then, two days in the two first series of experiments and 13 days following the beginning of the experiment in the third, the rats were given methionine S35 in doses yielding 2500 impulses per gm of body weight; 19 hours later the animals were sacrificed. The average results are shown in the table.

The data of the table show that two treatments with small doses of hydrolysate do not alter the intensity of protein synthesis of the brain and skeletal muscles in rats with undamaged and damaged myocardium, but change it markedly in the serum, liver, and kidneys. The treatments, and especially seven treatments, of unoperated rats with small doses of hydrolysate enhance the intensity of serum proteins by one and a half to two and a half times as compared with controls. Two treatments with small doses of hydrolysate increase the synthesis of proteins of the serum by one and a half times in rats with damaged myocardium three days after the operation. After seven treatments of rats with hydrolysate, there is a certain intensification of the synthesis of the proteins of the myocardium, liver, and serum in operated and non-operated rats. Thirteen days after damage to the myocardium, and with completion of seven treatments with hydrolysate, there is an especially great increase in the synthesis of proteins of the kidneys.

Hence, there is reason to assume that biopreparations of myocardium may influence regeneration of the myocardium by means of activating the processes of protein synthesis.

The Creation of Chronic Cardiac Aneurysms in Rabbits

(pages 53-54)

By D. S. Sarkisov, T. M. Darbinyan, B. M. Tsukerman, and L. D. Krymskiy

Chronic aneurysm of the heart is not readily produced in animals. For this purpose ligation of the coronary arteries is used, in which the myocardial infarct which regularly develops with this operation results in a significant thinning of the ventricular wall in only a small number of animals. This may be explained by the fact that the anterior descending branch of the left coronary artery is the one usually ligated, the exclusion of which in animals is rarely accompanied by such widespread and extensive infarction of the myocardium as in man.

In experiments on rabbits we employ a method producing a well-developed aneurysm of the left ventricle in all animals without exception. For this purpose we ligate not the anterior but the posterior descending barnch of the left coronary artery. Under thiopental anesthesia, with the animals on the right side, we perform a left-sided thoracotomy in the fifth intercostal space. From the time of injection of the narcotic, the animal breathes oxygen throughout the procedure. The pericardium is opened and a silk suture is placed in the left auricle, following which the auricle is retracted upward. Due to this, the left anterolateral surface of the heart, with the vessels coursing over it, is completely exposed. On the lateral surface of the left ventricle one easily discerns the large vein which passes from the apex to the base. At an angle, or approximately parallel to it, and slightly in front of it, passes the posterior descending branch of the left coronary artery. This is the large vessel supplying the posterolateral wall of the left ventricle. The position of the artery is distinguished by a marked constancy, of which we have become convinced on occasions when animals, during the course of the operation, have not been given oxygen, with the result that the developing hypoxemia of the artery caused a clearly visible bluish trabeculation beneath the epicardium. With the aid of an atraumatic needle, a suture is placed in a portion of the myocardium two to three mm in width in one of the sites indicated in Fig. 1 (depending upon the desired size of the aneurysm. The vein may be taken in the ligature or left alone. In order better to examine the artery, oxygen is witheld from the animal briefly at this time. The pericardium is not closed.

Penicillin is introduced into the pleural cavity, following which the thoracic cage is closed in layers without drainage. Air is removed from the pleural cavities with a syringe,

Infarction of the myocardium, accompanied by corresponding changes in the electrocardiogram (Fig. 3), was observed in all 50 animals operated upon for various purposes. The aneurysm was ordinarily situated on the posterolateral wall of the left ventricle, at the apex of the heart, and only rarely anteriorly. The rabbits tolerated the procedure well. The dimensions of the infract and of the aneurysm may readily be varied by simply ligating the artery at one or another site. The advantages of the method consist in the fact that, having carried out the operations, the experiments may be continued along one or another line de pending upon the final purposes, being completely assured of the presence of a large aneurysm of the ventricular wall.

Proteins of tissues and blood serum	Specific activity of the protein (No. imp./min/mg protein)					
	first series		second series		third series	
	rats not exposed to action [control]	rats treated twice with hydrolysate	rats treated twice with hydrolysate	rats with damaged myocardium treated twice with hydrolysate	rats treated seven times with hydrolysate	rats with damaged myocardium treated seven times with hydrolysate
Muscles of thigh	5.2	?.9	10.3	8.5	7.6	8.1
Brain	7.5	4.8	6.8	7.1	9.9	11.2
Heart	8.4	7.5	14.0	12.5	16.9	18.3
Liver	27.3	19.8	28.8	27.0	46.0	42.9
Kidney	38.6	43.9	35.6	38.1	38.8	71.6
Serum	24.0	32.4	36.4	49.7	63.8	51.6

Fig. 1. Schematic representation of the topography of the posterior descending branch of the left coronary artery of the rabbit heart, and the sites of ligation.

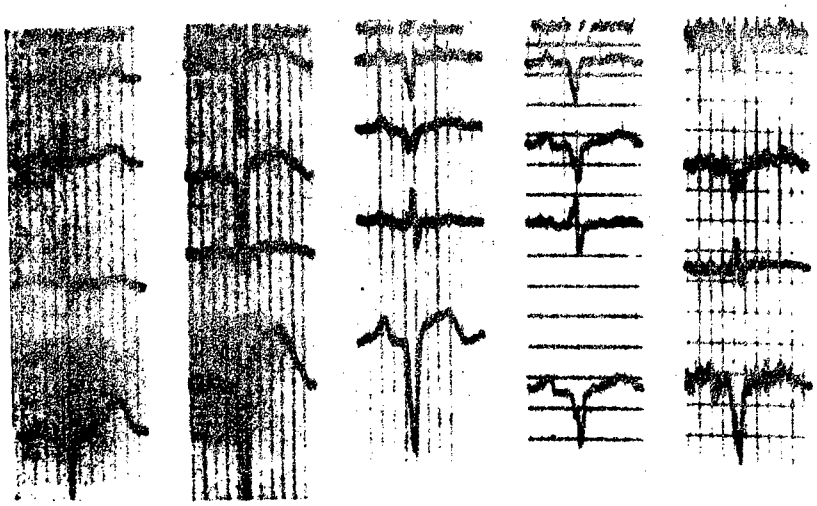

Fig. 2. Changes in the ECG following ligation of the posterior descending branch of the left coronary artery. The ECG, taken a day after the operation, shows changes characteristic of acute myocardial infarction: deep QS wave in leads I, II, and chest lead (V_6), and displacement of the RST segment upward in all leads.

After a month the RST displacement has disappeared; the QS wabe remains. After 4 months, there is a small R wave in leads I, II, and V_6. The downward deflection of the principal component of the QRS complex is retained in their leads.

Fig. 3. Large aneurysm of posterolateral surface of left ventricle of heart.

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