

**Transfusion of cadaveric blood:
an outstanding achievement of Russian transplantation, and transfusion
medicine (to the 85th anniversary since the method establishment)**

**M.Sh. Khubutiya¹, S.A. Kabanova¹, P.M. Bogopol'skiy¹,
S.P. Glyantsev², V.A. Gulyaev¹**

*¹N.V. Sklifosovsky Research Institute for Emergency Medicine of
Moscow Healthcare Department, Moscow*

²Bakoulev Scientific Center for Cardiovascular Surgery, Moscow

Contact: Pavel M. Bogopol'skiy, bogopolsky_med@mail.ru

The article reveals some little known facts of the idea origin, the issue development, and specifically, the implementation of the cadaveric blood transfusion method into clinical practice and the history of its development since the 20s of the XX century to nowadays.

Keywords: cadaver blood, transplantation, hemotransfusion, history of method development.

"The fibrinolysis (cadaveric) blood transfusion undertaken in experiment by V.N. Shamov and in clinical practice by S.S. Yudin, ... made it possible to most clearly show that organs and tissues outlive the death of the whole organism ...".

D.A. Arapov, K.S. Simonyan, 1960¹

¹ Arapov D.A., Simonyan K.S. Preface // Tsurinova E.G. *Perelivanie fibrinoliznoy krovi* [Transfusion of fibrinolysis blood]. Moscow: Medgiz Publ., 1960. p. 3. (In Russian).

"The implementation of the idea "the deceased for service of the alive" was not without certain difficulties and hesitation ... However, to dispel medical fears was much easier than to overcome the criticisms, sarcasm, and prejudice having nothing in common with scientific objections"

E.G. Tsurinova, 1960

In 1962, Professor V.N. Shamov (1882-1962), the Director of Leningrad Institute for Blood Transfusion (LIBT), the Head of the Hospital Surgery Department in the Military Medical Academy named after S.M. Kirov, Lieutenant General of Medical Service, Active Member of the USSR Academy of Medical Sciences (USSR AMS), and Professor S.S. Yudin (1891-1954), the Chief Surgeon of the N.V. Sklifosovsky Institute for Emergency Medicine, Active Member of the USSR AMS were awarded the Lenin Prize of the USSR (posthumously) "For developing and implementing the method of fibrinolysis blood preparation and use".

This fact is well known and needs no proof. However, the events of the past often have many blank spots that become clearer in the process of studying the issue or after the discovery of new facts and documents. Our article dedicated to 85-th anniversary since implementation of the cadaveric blood transfusion method reveals some hardly known facts related to the idea, the development of the method, and particularly, its introduction in clinical practice, and its history since the 20s of the XX century to our days.

Background

The theoretical basis of cadaveric blood transfusion methodology was the established fact that organs and tissues of a warm-blooded organism retrieved from the body after death are able to continue functioning,

provided they restore blood circulation and metabolism. The study of this issue was greatly contributed by physiologists from many countries: C. Ludwig and M. Hoffa (1849), C. Ludwig and E. Cyon (1866), H.N. Martin (1881), J.-V. Laborde (1885), N.Ya. Chistovich (1887), E. Hendon and P. Gilis (1892), Ch. Brown-Sequard (1895), O. Langendorff (1895), F.S. Locke (1901), A.A. Kulyabko (1902), A. Carrel (1905), F.A. Andreyev (1916).

Thus, in 1902, an outstanding Russian physiologist A.A.Kulyabko managed to revive the heart of a 3-month-old baby at 20 hours after death from pneumonia, by the perfusion of coronary vessels with oxygenated Locke's fluid. That gave the grounds for A.A. Kulyabko to conclude that "*... the death of the body is not at all a sheer transition from the living to non-living state*" [1, p. 21].

In 1913-1915, a Russian physiologist F.A.Andreev published the results of a large experimental study performed in 1907 on reviving the cardiac, respiratory, and central nervous system functions. Concluding his work, he wrote: "*Death, therefore, is not an instant phenomenon: it is a more or less slowly progressing process reaching the end in different organs and tissues at different rates*" [2, p.35].

In the 1920s, the clinical practice in Russia was enriched with allogenic transplantations of certain organs and tissues. For example, in Russia, the following investigators became known: V.P. Filatov for successful transplantation of cadaveric cornea, D.A. Arapov for transplantation of cadaver testicles, E.Yu. Kramarenko for transplantation of cadaveric bladder mucosa, N.A. Bogoraz for transplantation of thyroid lobe on a vascular pedicle from a living donor. [3]

Start of experiments on cadaveric blood transfusion

In September 1928, at the III All-Ukrainian Congress of Surgeons in Dnepropetrovsk, Professor V.N. Shamov², the Head of Surgery Department of Kharkov Medical Training Institute reported the results of his experimental work in collaboration with his colleague M.Kh.Kostyukov on reviving the exsanguinated dogs using massive transfusions of cadaveric blood. The investigators set out the task to answer two questions in their experiment: 1) whether the cadaveric blood carries toxicity; and 2) whether the blood is a vital tissue that can function adequately in a recipient body. Experiments were carried out as follows: after removing 70% of the circulating blood volume, the bloodstream of an experimental dog was washed with warm saline and thereby the extent of exsanguination was brought to 90%. Then the experimental dog in a state of agony received the cadaveric blood transfused from another dog killed 11 hours before the experiment. After the transfusion of allogenic cadaveric blood, the experimental animal rapidly returned to life [3-5]. These first world's experiments convincingly demonstrated the feasibility of using a cadaveric tissue, the blood in that case, for saving a body being on the verge of life and death. Based on the conducted studies, V.N.Shamov made the conclusion: *"The corpse should no longer be considered dead in the first hours after death, it not only continues living in some of its parts, but also can give to those still living the gifts of great value: quite viable tissues and organs"* [4, p. 188] .

Doctor S.S. Yudin took part in the III All-Ukrainian Congress of

² In 1919 for the first time in Russia, V.N. Shamov transfused the group-matched blood in the clinic of S.P. Fedorov.

Surgeons shortly after he had become the Head of the Surgical Department at the N.V. Sklifosovsky Institute for Emergency Medicine. Having heard the presentation of V.N. Shamov and M.Kh. Kostyukov on fundamental issues of transplantation, S.S. Yudin immediately appreciated the method of cadaveric blood transfusion and its potential practical benefits that it could bring to emergency surgery and transfusion. Having obtained a principal consent from V.N. Shamov to joint research in that field, S.S. Yudin planned the study to investigate the feasibility of using cadaveric blood in the clinical practice of the N.V. Sklifosovsky Institute.

Start of using the method in clinical practice

In 1929, the Journal "New Surgical Archive" (*Nov. Khir. Arkhiv*) published an article by V.N. Shamov and M.Kh. Kostyukov entitled "By studying the homoplasty from a corpse - a blood transfusion from a corpse" [7]. A year later, on March 23, 1930, S.S. Yudin and his colleague R.G.Sakayan³ were the first in the world who made a successful cadaveric blood transfusion to a man dying from a massive blood loss in the Surgical Department of the N.V. Sklifosovsky Institute [3, 6, 8, 9].

In September 1930, at the IV All-Ukrainian Congress of Surgeons, S.S.Yudin and R.G.Sakayan reported as many as 7 clinical cadaveric blood transfusions [3, 6]. Since then, the cadaveric blood was comprehensively studied, and further introduced in the clinical practice of N.V.Sklifosovsky Institute as a full-value transfusion media [3, 9].

After the first clinical transfusion of cadaveric blood, S.S. Yudin,

³ Apparently, S.S. Yudin became acquainted with R.G. Sakayan in Serpukhov where the latter worked as a surgeon at a Serpukhov Public Hospital in early 1920s.

apparently, entrusted his colleague R.G. Sakayan with subsequent development of the method. We believe that this was the cause of the arousal and discussion of some controversial issues related to the author's priority of cadaveric blood transfusion method in experiment and in clinic. The first such discussion took place at the 193rd Meeting of Moscow and Moscow Region Surgical Society in October 1930, where R.G.Sakayan spoke on "The experience of a blood transfusion from a cadaver" [10]. Having reported the first case, and the subsequent 6 cases in which the patients received cadaveric blood transfusion in the amount from 300 to 450 cm³ as preoperative preparation, R.G. Sakayan concluded his report with the words, "*We have shown that cadaver blood collected within 4 hours after the death, can be used without a risk to patient's life. The question is about the practical use of [cadaveric] blood. This issue is under development in the 2nd Surgical Department of the 1st MMI*"⁴ [10, p.169].

While answering the questions, R.G. Sakayan said: "*There is evidence, as if such transfusions [of the blood] from the dead were made in German War*" [10, p.169]. And further, "*Answering [the question] who owns the idea to transfuse the blood from a cadaver, I am reporting that the speaker himself proposed the procedure 3 years ago, and S.S.Yudin helped to put this idea into practice*" [10, p.170]. Worthwhile to note that Dr. V.V. Lebedenko, while speaking in the debate on R.G.Sakayan's presentation, reminded the audience about the experiments made in Voronezh University by N.N.Burdenko in 1922 where they studied the characteristics of the blood transfused to the dogs from their dead congeners. According to

⁴ At that time, R.G. Sakayan left his position at the N.V. Sklifosovsky Institute and started working in the 1st Moscow Medical Institute (MMI).

V.V. Lebedenko, these studies had shown that blood collected from dogs at 7 hours postmortem and transfused to another dog caused no hemolysis and had no effect on the blood morphology [10].

Thus, the question of the priority in the development of the cadaveric blood transfusion method in experiment and in clinic remained open [11]. In 1932, the Journal "Soviet Surgery" (*Sov. Khirurgiya*) published the article by R.G.Sakayan entitled "Experiments on a blood transfusion from a corpse" [12]. The article implied that for the period of his work in N.V.Sklifosovsky Institute, the transfusions were made to 88 patients⁵. R.G.Sakayan wrote about the cadaveric blood transfusion, "*Working in the Surgical Department of the Sklifosovsky Institute <...> I made cadaveric blood transfusions in 7 cases. Developing this subject, I met the full support and assistance from Dr. S.S.Yudin, the Head of the Surgical Department, and A.V.Rusakov, the Dissector of the Institute who had long been working on the issues of tissue transplantation*" [12, p.95]. And further, "*Burdenko made a similar experiment for the first time in 1921. Blood was collected from the dog's corpse at 7 hours from death and was kept in citrate and liquid petrolatum for up to 24 hours*⁶, and was transfused to a live dog without any complications" [12, p.95]. We will also mention that R.G.Sakayan tried to assert his priority abroad by publishing the article "A trial blood transfusion from a corpse" in the Journal "Zentralblatt für Chirurgie" in 1931 [13].

Thus, the following three questions arose from the aforementioned: 1) who was the first to express the idea of cadaveric blood transfusion? 2) who

⁵ No hemotransfusions had been made in N.V. Sklifosovsky Institute for Emergency Medicine until 1928 [8].

⁶ One of the methods of blood preservation that was used in the 1920s.

first performed the procedure in experiment? and 3) who first made it in clinic?

We have no answer to the first question, besides R.G. Sakayan's mentioning of the experiments that were allegedly conducted during World War I⁷.

The answer to the second question is obvious: there were no reports of N.N.Burdenko's experiments in the scientific medical literature before publications by V.N. Shamov, so the priority of developing an experimental method of cadaveric blood transfusion should still belong to V.N. Shamov and M.Kh. Kostyukov. We can only suppose that the idea to investigate the properties of cadaveric blood as a transplant tissue and transfusion media in animal experiments came to N.N.Burdenko and V.N.Shamov independently from each other; but this has not been proved anyway.

With regard to clinical use of the method, S.S.Yudin wrote that it was he who personally initiated the procedure that was undertaken on March 23, 1930, under his full responsibility, in the presence of many staff employees, and he performed the most important part of the procedure by making a blood exfusion of 420 cm³ from the inferior vena cava of the cadaver⁸ [14]. Thus, S.S.Yudin used the cadaveric blood transfusion to the patient with a massive blood loss, and R.G.Sakayan further used this method to prepare patients for a forthcoming surgery. However, it remains unclear why R.G. Sakayan published the experience of the first seven transfusions without

⁷ Information on other priorities is not available in literature.

⁸ In his presentation at the Meeting of the Moscow Surgical Society on October 3, 1930, R.G. Sakayan reported that 360 cm³ of citrated blood taken from the cadaver were transfused in that case. [10]

mentioning his boss as a co-author. We do not undertake to judge whether it was justified from the ethic point of view, but we shall remind that the report on the first 7 cadaveric blood transfusions was presented at the IV All-Ukrainian Congress of Surgeons still by two authors: S.S.Yudin and R.G.Sakayan [3, 6], though the presentation was made by the latter⁹.

In April, 1933, S.S. Yudin wrote letters to the Editors of the journals "New Surgical Archive" and "Bulletin of Surgery and Related Issues" enclosing the Minutes of Surgeons' Conference held in the Surgical Department of the N.V. Sklifosovsky Institute on 16.04.1933, and the document contained the statement confirming S.S.Yudin's priority. As a result, the Surgical Society Board had to establish a Committee headed by Prof. V.Ya. Braytsev to handle these controversies. The Report of the Committee contained the following conclusions: "It is obvious that S.S. Yudin could not perform human cadaveric blood transfusions without R.G. Sakayan because S.S. Yudin was not engaged in blood transfusion, meanwhile, R.G. Sakayan could not make such transfusions without being authorized by S.S. Yudin as the Head of the Department... So, the Committee has come to a conclusion that the merit of implementing the method of cadaveric blood transfusion in clinic belongs inseparably to both of them" [15].

Thus, the question "who was the first to make a cadaveric blood transfusion in clinic?" apparently should be answered by the wording stated

⁹ The report of S.S. Yudin and R.G. Sakayan was not included in the Proceedings of the IV All-Ukrainian Congress of Surgeons published in Dnepropetrovsk (1931). The fact that it was R.G. Sakayan who reported on the first 7 cadaveric blood transfusions at this Congress was mentioned by Spasokukotskiy S.I., and Braytsev V.Ya. [15].

in the paper by Prof. V.B. Khvatov, the Head of Laboratory for Transfusion, Tissue Preservation and Culturing at the N.V. Sklifosovsky Research Institute for Emergency Medicine (1991), "That was S.S. Yudin himself who, using a syringe, collected cadaveric blood from the inferior vena cava through an incision in the abdomen of the male corpse, he was assisted by doctors R.G. Sakayan, and V.N. Golovinchits, an Operating Room nurse N.I. Lukyanova, doctor G.A. Kurilova, and the Head Nurse A.M. Berkevich"[9].

Further investigations of cadaveric blood as a transfusion product

The Laboratory of Blood Transfusion was established at the N.V. Sklifosovsky Research Institute for Emergency Medicine in 1930, it was headed by M.G. Skundina. Besides studying the method of blood transfusion from live donors, the Laboratory was engaged in investigating biological properties of cadaveric blood and the development of methods for its conservation. In the early stages of studying the issue, it was proved that the blood after a sudden human death remains sterile and harmless in the bloodstream of the dead body within 24 hours. Red blood cells were proven to remain intact, and the white blood cells retained their phagocytic activity; a number of studied biochemical parameters suggested a possible safe use of cadaveric blood in clinical practice [9].

An important property of the blood of a suddenly died human had a specific important capacity to lyse its own clot and then remain in a liquid state. This phenomenon was reported by M.G. Skundina, A.V. Rusakov, R.E. Ginsburg, and A.A. Bocharov in 1933, and then they used this advantage for cadaveric blood harvesting without adding any preservatives [3, 9]. Worthwhile to mention that the non-coagulation phenomenon of

cadaveric blood after a sudden death was known long before M.G. Skundina and her colleagues started their research. H. Swan and D. Schechter stated that the phenomenon was first mentioned in the works by J.Hunter dated back to 1786 [16]. According to E.G.Tsurinova (1960), the liquid state of blood after a sudden death was described by Plenk and Muller in their *Manual on Forensic Medicine* in 1802 [3]. B.A. Petrov and G.A. Pafomov (1967) noted that the fact was confirmed in 1858 by an English scientist D. Snow in the monograph "The chloroform and other anesthetics" where he wrote: "*The blood remains liquid after a chloroform death, as it always remains liquid at a sudden death*" [17, p.14].

Worldwide recognition and further development of the method

At the XXII All-Union Congress of Surgeons in May 1932, S.S. Yudin and M. Skundina reported about as many as 200 cases of cadaveric blood transfusion that had become almost a routine procedure in the N.V. Sklifosovsky Institute by that time [3]. In autumn of 1932, S.S. Yudin made a presentation "*On the transfusion of cadaveric blood*" accompanied by a scientific motion picture¹⁰ at a Meeting of the Paris Surgical Society. In December 1932, S.S. Yudin reported on the use of cadaveric blood to surgeons of Spain, speaking in Barcelona at the Meeting of the Medical Faculty and the Surgical Society of Catalonia [15]. After that, the method of cadaveric blood transfusion became world-known, and the Soviet surgeons

¹⁰ In 1933, the report was published in French as a separate brochure with a foreword by a well-known surgeon A. Gosset [18].

were recognized as its inventors. In the same year, S.S. Yudin was elected a Member of the International Surgical Society, the Paris Surgical Academy, and the Catalan Surgical Society [15, 19].

The clinical use of cadaveric blood gained further development and was one of the major issues in the Programme of the 2nd All-Union Conference on Blood Transfusion (1935). By that time the N.V. Sklifosovsky Institute had established a novel more optimal method of cadaveric blood exfusion, though, in principle, it was similar to that used in the experiments by V.N. Shamov and V.Kh. Kostyukov [4]. Cadaveric blood exfusion was performed in the Operating Room, the internal jugular vein in the neck of the corpse was exposed and glass cannulas equipped with rubber tubes having clamps on were introduced in toward-heart direction. The ends of the tubes were attached to sterile vials containing a preserving agent. The cannula connected to the system containing the solution for washing the vascular bed was introduced into the carotid artery. Thereafter, the clamps were taken off the venous tubes, the head end of the table was lowered, and the blood from the jugular vein came into vials by gravity. In this way, from 1 to 1.5 liters of cadaveric blood could be prepared from a corpse. When the free flow of blood stopped, the venous tubes were clamped, the table was converted into a horizontal position, and the glucose-saccharose solution was infused into the bloodstream of a corpse through the arterial cannula. Such "flushing" made possible to obtain additionally about 1.5-2.5 liters of blood [19, 20].

No doubt, cadaveric blood was of significant clinical value because of large amounts available (up to 3-4 liters from a single cadaveric donor), and its inherent process of fibrinolysis obviating the need of using stabilizers [3]. A high content of glucose was another property of the blood that was first

described by M.G. Skundina. Meanwhile, the tests for the duration of cadaveric blood integrity at 4-8° C demonstrated that the onset of hemolysis occurred on the 21st-24th-25th day in whole cadaveric blood, and on the 25th-26th-33rd day in the washed blood [3].

In the early 30s, the research on cadaveric blood transfusion began in the Central Institute of Blood Transfusion (CIBT) of the USSR Healthcare Department after the death of Dr. A.A. Bogdanov, the CIBT founder and first director¹¹, the Institute was headed by A.A. Bogomolets from 1928 to 1932, and by A.A. Bagdasarov after 1932. CIBT Surgical Department was then headed by S.I.Spasokukotskiy who was one of the most ardent advocates and promoters of blood transfusion. The studies conducted in CIBT demonstrated that the blood from a cadaver harvested at 2-4 hours after the death was identical by its properties to donor's blood of 5-7-day preservation, and the cadaveric erythrocytes could live in the recipient's blood for 2-3 weeks [14]. By 1935, CIBT had undertaken 52 cadaveric blood transfusions in doses ranging from 200 to 1000 cm³ with a shelf life up to 26 days [14, 19].

Importantly, the CIBT investigators significantly improved the cadaveric blood exfusion technique. By S.S.Bryukhonenko's proposal¹², they began collecting the blood directly from the heart of the cadaver. To do that, a long cannula was inserted through the right internal jugular vein in the

¹¹ One of the main areas of A.A. Bogdanov's research activities was to study the effect of an exchanged blood transfusion made for therapeutic purpose that he tested on himself. In 1928, after a similar experiment A.A. Bogdanov died.

¹² S.S. Bryukhonenko headed the Experimental Laboratory at CIBT from 1931 to 1935.

right atrium, and the air was evacuated from the receptacle. This method enabled collecting up to 2-2.5 liters of blood for 10-12 minutes at any position of the cadaver (not necessarily on the operating table, but also on the floor, for example) [14].

In parallel to the studies conducted in Moscow, the cadaveric blood transfusion began to be studied in Leningrad by Dr. A.N. Filatov. In 1932, he headed the Clinical Department of Leningrad Institute for Blood Transfusion (LIBT) (currently named the Institute of Hematology and Blood Transfusion), and in 1939 he became the Head of the Surgical Clinic in the Institute where he studied the issues of organ and tissue harvesting and transplantation, including the cadaveric blood. In 1939, the LIBT was headed by V.N. Shamov. In 1940, V.N. Shamov and A.N. Filatov published the world's first and largest "Guidelines for Blood Transfusion" where they described in-detail the indications and methods of the collection, storage, and use of cadaveric blood [21, 22].

N.V. Sklifosovsky Institute's contribution in the field of cadaveric blood transfusion and the research abroad

Despite the fact that V.N. Shamov and A.N. Filatov in Leningrad, and A.A. Bogomolets and S.I. Spasokukotskiy in Moscow actively studied the subject of cadaveric blood, this issue was developed most widely and consistently in the N.V. Sklifosovsky Research Institute for Emergency Medicine by S.S. Yudin, his disciples, and colleagues: D.A. Arapov, S.I. Barenboim, A.A. Bocharov, R.E. Ginzburg, V.N. Golovinchits, K.P. Gutiontova, B.A. Petrov, A.V. Rusakov, K.S. Simonyan, M.G. Skundina, Z.N. Stupina, E.G. Tsurinova, and Z.A. Shpanova. E.G. Tsurinova (1960) wrote that attempts to use cadaveric blood were made in different cities of

the Soviet Union, but the only Cadaveric Blood Station that justified its existence was the Blood Transfusion Department in the Sklifosovsky Research Institute for Emergency Medicine [3]. Ongoing researches conducted in the Institute were reported in a number of publications in domestic and foreign medical literature. In the period of 1934-1937, S.S. Yudin's cadaveric blood transfusion experience of over 1000 cases was published in foreign journals [23-25].

In that period, the studies on the feasibility of cadaveric blood transfusion were initiated in other countries, as well. Thus, according to H.Swan and D.Schechter (1962), cadaveric blood transfusions were made by Farmer in Chicago (USA) in the period between 1936 and 1938. His first patient was a young woman with severe postpartum uterine bleeding whose life was saved thanks to such transfusion. Soon, the establishment of Donor Blood Banks in the USA made the practice of cadaveric blood transfusion redundant. Nevertheless, in 1959 an American scientist J.W.Ferrebee was the first in the USA to make the procurement and transfusion of cadaveric bone marrow [16].

In 1940, M.G. Skundina defended her doctoral thesis on "Transfusion of cadaveric blood" where she had analyzed the clinical cases and experimental observations generated for over 10 years in the N.V. Sklifosovsky Institute for Emergency Medicine [26].

Transfusion of cadaveric blood in military field surgery

In the discussion of the report by V.N. Shamov on the 3rd All-Ukrainian Congress of Surgeons (1928), a surgeon from Odessa E.Yu. Kramarenko expressed the thought: "The idea of getting blood from the dead ... can be used in time of war" [4, p. 189]. V.N. Shamov agreed with his

remark and commented on it as follows, "... *in conditions of war, when there are huge numbers of corpses of just killed people from whom whole barrels of viable blood can be definitely gained, the question of its use for transfusion to the exsanguinated wounded is of vital importance*" [4, p.189].

During the Great Patriotic War, however, the method of cadaveric blood transfusion was not implemented in the practice of the Red Army Medical Service. At the Scientific Meeting on *Transfusion of Blood and Some Issues of Cadaver Homoplasty* held at the N.V.Sklifosovsky Research Institute for Emergency Medicine in April 1965, Prof. D.A. Arapov, the Chairman at the Meeting said in his concluding remarks, "*The greatest dream of Sergei [Yudin] was the use of cadaveric blood during warfare. Everyone knows that during World War II we did not manage to implement that*" [27, p.146-147].

Nevertheless, S.S. Yudin's method was used in combat, and even before World War II, namely, during the Spanish Civil War of 1936-1939. At that time the Blood Transfusion Service in Madrid was exemplary managed by a Canadian doctor, communist N. Bethune. Shortly before the outbreak of war, namely in 1935, N. Bethune visited Moscow to attend the International Physiological Congress and apparently studied the works on cadaveric blood transfusion carried out in the Soviet Union. In spring of 1937, N. Bethune began his own research on this issue in Madrid and his works gained a keen interest of an English communist, Doctor R. Saxton. In September, 1937, R. Saxton published his article in *Lancet* Journal where he said that the use of cadaveric blood "*by S.S.Yudin's method*" was the only way to save lives of huge numbers of wounded in the combat during the war. Soon, an American geneticist, H. Muller, a future Nobel Laureate, joined N. Bethune's research. Being a Member of the US Communist Party, H. Muller

visited the Soviet Union in 1934 at the invitation of the Academy of Sciences, and in 1937 he went to Spain to fight as a volunteer. Trying to adapt S.S. Yudin's method to war conditions, H. Muller worked in N. Bethune's Laboratory to develop the techniques of harvesting blood from dead combatants. After a series of experiments, H. Muller obtained the evidence of the efficacy of cadaveric blood transfusion method and tested it on himself. Thus, in 1937, N. Bethune and H. Muller were the first to use S.S. Yudin's innovative ideas in active combat operations [28].

Development of the issue in 1940-1950

Total over 5,000 cadaveric blood transfusions were made in the Sklifosovsky Institute for Emergency Medicine in the period from 1932 to 1944 [19], and for the period from 1933 to 1947, 6,000 liters of such blood were transfused to patients with surgical diseases [19]. In 1947, the Laboratory of Blood Transfusion of the Sklifosovsky Institute was headed by E.G.Tsurinova. At the end of 1948, S.S. Yudin was subjected to repressions and arrested, but in 1952, in exile in Novosibirsk, he again became an unofficial supervisor of the scientific research carried in the Sklifosovsky Institute. In his letters to B.S. Rozanov, P.I. Androsov [29], and K.S. Simonyan [19], S.S. Yudin expressed a new idea of cadaveric blood *fractionation*. Having returned to his work at the Institute in 1953, he continued to insist on the introduction in clinical practice the methods of using fractionated elements of cadaver blood, specifically, washed red blood cells, and plasma [30]. Later, shortly before his death, S.S. Yudin proved another original concept of creating a "super-universal" fibrinolysis blood; the hypothesis was as follows: if a "universal" plasma of IV (AB) group is added to "universal" red blood cells of I (O) group, then the resulted whole

blood would not agglutinate any other red blood cells and such blood could be transfused in emergencies without prior determination of the blood group of the recipient. The idea was implemented in January 16, 1956, when K.S. Simonyan, S.S. Yudin's follower, made the first world's successful "super-universal" blood transfusion of 500 mL without determining the recipient's blood group. Later, the patient was successfully operated on and received an additional "super-universal" blood transfusion of 500 mL intraoperatively. In the same year, the Moscow Blood Transfusion Station headed by A.I. Uspenskaya started working on the creation of such super-universal blood from living donors based on the concept proposed by S.S. Yudin [19].

In 1956, E.G. Tsurinova successfully defended her Doctoral Thesis on the basis of the many-year experience gained in the Sklifosovsky Institute for Emergency Medicine [31], and in 1960, she published the USSR's first monograph on fibrinolysis blood transfusion [3], thereby completely proving the priority of N.V. Sklifosovsky Research Institute for Emergency Medicine in the development of this subject.

After S.S. Yudin's death on June 12, 1954, his ideas in the field of blood transfusion were developed further. For example, total blood transfusions undertaken in the Sklifosovsky Institute in 1960, accounted for 1277 liters of cadaveric blood and only 307 liters of live donor blood. By 1960, K.S. Simonyan had performed 263 successful transfusions of super-universal blood, including 38 cases of blood transfusion made without a prior determination of the recipient's blood group [19]. In 1960, the Blood Transfusion Laboratory of the Sklifosovsky Institute started preparing dry plasma from cadaveric blood. The clinics of the Institute began such plasma transfusions that amounted from 140 to 200 liters annually. In 1960, on the base of the Blood Transfusion Laboratory, a Tissue Bank was established for

harvesting and procurement of skin, bones, cartilage, joints, fascia, tendons, glands, etc. [17].

An important fact that in 1960s the method of cadaveric blood transfusion was implemented in Kiev, Lvov, Donetsk, Odessa, Minsk, Tashkent, Gorky, Novosibirsk, Irkutsk, Kemerovo, Kirov, Novokuznetsk, Khabarovsk, and other cities of the country [9, 19]. Numerous studies proved that cadaver blood produced a pronounced therapeutic effect in massive hemorrhage and shock, but its use also appeared useful in the treatment of extensive burns, severe poisoning, and radiation damage [9, 17, 32].

Further improvement of the method in 1960-1970s

In 1962, the Laboratory of Tissue Preservation and Transfusion was headed by G.A. Pafomov. Under his leadership, comprehensive studies were conducted to investigate hemocoagulating, fibrinolytic, antiprotein, electrophoretic, gel-chromatografic, and immunological properties of blood proteins from suddenly died people. The studies resulted in obtaining strong evidence of possible using cadaveric blood plasma for the development of targeted-effect drugs. Importantly, in the 1960s, the method of harvesting dry and native frozen plasma from cadaveric blood was developed, post-transfusion adverse effects reduced to 1%, a new solution enabling the blood preservation for up to 25 days was offered [9].

H.Swan and D.Schechter wrote in 1962 that the US had no serious scientific research on fibrinolysis blood transfusion, meanwhile, the USSR had achieved a great success in that area [16]. Nevertheless, in 1961-1964, American scientists J. Kevorkian, G.W. Bylsma, J.J. Marra, N. Neal, and E.Rea published their experience of direct cadaveric blood transfusions; they

tested the method on healthy volunteers and on themselves. The authors proposed this method to be used in Military Medicine on battlefields, but the US Department of Defense gave no definite reaction to their proposal [33, 34].

In 1975, the second monograph (after the one by E.N.Tsurinova) on the clinical application of cadaveric blood was published by K.S.Simonyan who had been one of the main supporters of cadaveric blood transfusion method [6]. *"Unfortunately, the studies in the field of post-mortem blood transfusion are now facing difficulties that did not exist before"*, he complained. *"The existing regulations have set forth the conditions that essentially preclude the possibilities of post-agonal blood transfusions and gaining a broad clinical experience that is the only decisive argument, as has always been"* [6, p.22].

Nevertheless, we believe that the strict instructions on blood harvesting and transfusion (including cadaveric blood), and the severe penalties for their violations are justified, at least, because any blood transfusion is a transplantation of allogeneic tissues without the use of immunosuppression, and, therefore, one can not foresee all risks of complications.

Despite various difficulties and unsolved ethic problems, the cadaveric blood transfusion method continued its development in our country and abroad in 70-80s [35-38]. A number of important aspects of the problem were the main subjects of doctoral theses by G.A. Pafomov (1971), and V.B. Khvatov (1984) [39, 40]. In that period, the Sklifosovsky Institute faced a rapid development of therapeutic agents made of the blood plasma taken from suddenly died people, including the agents with fibrinolytic and antiproteinase effect [9].

A few words on the current state of the issue from transplantation view

One of the most important scientific stipulations in transplantation states that the death of the whole organism is not an instant event, but a more or less long process of irreversible changes occurring in organs and tissues at different rates, the brain cortex being the fastest of vital anatomical structures to die.

In accordance with the currently valid Act of the Russian Federation "On the transplantation of organs and (or) tissues" № 4180-I of December 22, 1992, (as amended on June 20, 2000, October 16, 2006, February 9, and November 29, 2007), and the issued on its basis Healthcare Ministry Regulation "On approval of the instructions on ascertaining the death of a person on the basis of the brain death diagnosis" № 460 of December 20, 2001, the brain death is considered equal to a human death, so the issue of cadaveric blood transfusion acquires a new meaning. Though the whole blood (cadaveric whole blood) transfusions has long ceased to be undertaken, the blood of a conditioned donor with brain death can be used to prepare a variety of components and products, meanwhile, their use is most appropriate for transfusion to the recipients with the same blood group who had received organs from the same donor. But then the question arises whether this blood is cadaveric or not? The answer is not as simple as it may seem ("as far as the individual has been declared dead, so his/her blood is cadaveric"). But as in a conditioned heart-beating donor, all tissues and organs, other than the brain, live, the same can be applied to blood. In such case, if the blood is "live" in the brain-dead individual, its handling should, apparently, be subjected to the rules of harvesting and use applied to the

common donor blood. Meanwhile, if the blood is regarded as cadaveric, its use as a transfusion media is regulated by the Healthcare Ministry Regulations of 10.04.62 and 14.06.72 [9]. Anyway, components and products of cadaveric blood are currently safely used in the practice of N.V. Sklifosovsky Research Institute for Emergency Medicine. Specifically, the method of obtaining a blood cellular component from brain-dead donor blood has been developed here to increase the efficacy of transfusion therapy in liver transplantation. Erythrocyte-platelet mass with bone marrow cells from brain-dead donors prepared by using a Cell-Saver machine was added to the complex of transfusion therapy that improved the blood oxygen delivery function in hemorrhage, compensated thrombocytopenia, produced an immunomodulatory effect, and reduced the sensitization degree and the risk of graft rejection in the recipient [41 -45].

Conclusion

Thus, the development of the cadaveric blood transfusion method is an absolute priority of our country, and it also a very important stage in the history of domestic and world Transplantation and Transfusion. It started with the experiments made by V.N. Shamov and M.Kh. Kostyukov in late 1920s, and clinical studies conducted by S.S.Yudin and his assistants in 1930-1950. These works provided a rich material for detailed investigations of many important aspects of cadaveric blood transfusion in the XXth century.

In connection with the rapid development of clinical transplantation observed in the XXI century, and a significant increase in the number of organ transplants from donors with brain death, the cadaveric blood

transfusion method, apparently, will have new and very important prospects, but their discussion is beyond the scope of the present study.

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