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# HIRUDOTHERAPY. HISTORY AND MODERNITY (Literature review)

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✓ ***Resume***

***The article presents the main stages of development and theoretical substantiation of hirudotherapy from ancient times to the present. The historical and empirical basis of the use of hirudotherapy in world practice has been studied. The features of the use of hirudotherapy in different countries (USA, Europe, Russia) at the present time. The therapeutic effects of hirudotherapy in clinical practice are explained by the composition of the saliva of the medicinal leech and the reflex effect on the body at the local and general levels, which occurs at the time of blood sucking and hemorrhage, which is well studied to date. The pathogenetic mechanisms of hirudotherapy action are analyzed. Hirudotherapy is able to reduce the processes of ischemia, hypoxia and normalize microcirculation. An overview of the effective use of hirudotherapy in different groups of patients with cerebrovascular, cardiovascular diseases. The evidence base for the effectiveness of hirudotherapy in cerebrovascular accidents seems to be sufficient to use hirudotherapy as a method of complementary medicine in the complex treatment of cerebrovascular diseases and for the prevention of acute cerebrovascular accidents.***

***Key words: hirudotherapy; history; hypertonic disease; cerebrovascular disease***

# ГИРУДОТЕРАПИЯ. ИСТОРИЯ И СОВРЕМЕННОСТЬ

(литературный обзор)

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✓ ***Резюме***

***В статье представлены основные этапы развития и теоретического обоснования гирудотерапии от древних времен до современности. Изучена историко-эмпирическая база применения гирудотерапии в мировой практике. Изучены особенности применения гирудотерапии в разных странах (США, Европа, Россия) в настоящее время. Терапевтические эффекты гирудотерапии в клинической практике объясняются хорошо изученным на сегодняшний день составом слюны медицинской пиявки и рефлекторным воздействием на организм на местном и общем уровнях, возникающим в момент кровососания и кровоизвлечения. Проанализированы патогенетические механизмы действия гирудотерапии. Гирудотерапия способна уменьшать процессы ишемии, гипоксии и нормализовать микроциркуляцию. Дан обзор эффективного применения гирудотерапии в разных группах больных с цереброваскулярными, сердечно-сосудистыми заболеваниями. Доказательная база эффективности гирудотерапии при нарушениях мозгового кровообращения представляется достаточной для того, чтобы использовать гирудотерапию как метод комплементарной медицины в комплексном лечении цереброваскулярных заболеваний и для профилактики острых нарушений мозгового кровообращения.***

***Ключевые слова: гирудотерапия, история, современное обоснование, применение, гипертоническая болезнь, цереброваскулярные заболевания***

# HIRUDOTERAPIYA TARIX VA ZAMONAVIY HOLATI

(Adabiyotlar sharhi)

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Tibbiyot xodimlari kasbiy rivojlantirish markazi

✓ ***Rezyume***

***Maqolada hirudoterapiyaning qadim zamonlardan to hozirgi kungacha bo'lgan rivojlanishining asosiy bosqichlari va nazariy asoslari keltirilgan. Jirudoterapiyani jahon amaliyotida qo'llashning tarixiy va empirik asoslari o'rganildi. Hozirgi vaqtda turli mamlakatlarda (AQSh, Evropa, Rossiya) hirudoterapiyani qo'llash xususiyatlari o'rganildi. Klinik amaliyotda hirudoterapiyaning terapevtik ta'siri, dorivor sulukning tupurik tarkibi va organizmga mahalliy va umumiy darajadagi refleks ta'siri bilan izohlanadi, bu qonni so'rish va qon ketish vaqtida yaxshi o'rganiladi. sana. Hirudoterapiya ta'sirining patogenetik mexanizmlari tahlil qilinadi. Hirudoterapiya ishemiya, gipoksiya jarayonlarini kamaytirishga va mikrosirkulyatsiyani normallashtirishga qodir. Serebrovaskulyar va yurak-qon tomir kasalliklari bilan og'rigan bemorlarning turli guruhlarida hirudoterapiyadan samarali foydalanishga umumiy nuqtai berilgan. Serebrovaskulyar baxtsiz hodisalarda hirudoterapiya samaradorligi uchun dalillar bazasi serebrovaskulyar kasalliklarni kompleks davolashda va o'tkir miyovaskulyar falokatlarni oldini olishda qo'shimcha tibbiyot usuli sifatida hirudoterapiyadan foydalanish uchun etarli ko'rinadi.***

***Kalit so'zlar: hirudoterapiya, tarix, zamonaviy mantiqiy asos, qo'llanilishi, gipertoniya, serebrovaskulyar kasalliklar***

## Introduction

In recent decades, against the background of increasing allergization of the population, polypharmacy, an increase in the number of complications and side effects of pharmacotherapy, a steady increase in the number of chronic diseases, there has been an active search for the possibilities of using various non-drug methods of influencing the human body. Methods that have been successfully applied by our ancestors for millennia are again attracting special attention. One of these methods is hirudotherapy - the use of medicinal leeches for medicinal purposes.

## Historical reference

Hirudotherapy is used by mankind fortreatment of various diseases for many centuries. One of the earliest documented evidence of use is a painting in an Egyptian tomb, dating from about 1500 BC. e. It is believed that after successful treatment with leeches, the Egyptian queen Cleopatra became pregnant and gave birth to an heir to Caesar (about 50 BC), after which she ordered to depict Egyptian tombs on the walls pharaohs leech. ... The ancient Roman naturalist Pliny the Elder (1st century AD) gave a description of the leech and for the first time noted the positive changes in the human body during the setting of leeches. Following Pliny, he studied the possibilities of the medical use of bloodsucking leeches the largest Roman physician Claudius Galen (131-200 years). Another well-known physician of Ancient Rome, Aetius (335–454), also spoke positively about bloodletting by means of pond leeches. The first detailed recommendations on the use of leeches are given by Abu Ali Ibn Sino (Avicenna). In his brilliant treatise "The Canon of Medicine" in the 22nd paragraph, he writes: "Leeches are good to use for skin diseases, such as scaly, ringworm, red spots on the skin, freckles and other diseases" [1]. In the Middle Ages, during the time of the Great.

Inquisition, it was forbidden to plant leeches in large quantities.

Another increase in interest in leeches is observed during the Renaissance. This historical period includes the fundamental work of the Armenian physician and naturalist Amirdovlat Amasiatsi (15th century) [2]. Author states: “If you apply it to the scab, it will suck out the spoiled blood, and the ulcer will easily heal ... blood, it will suck it out. In the 16th century in England, doctors did not leave their homes without leeches, and these doctors were even nicknamed leeches, that is, "leeches."

The first official mention of leeches in Russia showed up in the law of the Russian Empire No. 6424 of May 29, 1733: “On the non-obstruction of the students of the Moscow State Hospital to collect herbs and roots and catch piavits in ponds, lakes and the rivers of the Moscow province ”[14]. Outstanding doctors of the Russian Empire actively treated with leeches (I.E.Dyadkovsky, M.L. Mudrov).

In 1859 A. Voskresensky published a monograph, dedicated to "medical leeches". Great Russian surgeon N.I. Pirogov (1810-1881) recommended to put up to 200 pieces in one session, which,of course, redundant, but the fact of use is important them leeches in their practice [4].

Until the middle of the nineteenth century, an extraordinary development of hirudotherapy in Europe and Russia. So, more than 100 million leeches were exported from Russia annually, and the income from this trade was correlated with the state's profit from the grain trade as: 1. Poaching and speculation began to flourish in this area, and the export of leeches abroad became so great that in Russia the price of leeches has risen tremendously,

up to 50 kopecks in silver for 1 piece. In France, where hirudotherapy was especially popular, used by up to 50 million leeches annually. It is known from Napoleon's notes that from Hungary alone, 6 million leeches were imported within a year to treat his soldiersarmy. In the structure of Russian exports, leeches occupied a place equal to cereals, being an important source of income for the state treasury. At the end of the nineteenth century, J. Highcraft (1884) received from the head end of the leech is an active extract that prevents blood clotting, which is called hirudin [20]. Professor G.A.Zakharyin described hirudotherapy as a kind of distracting bloodletting. I.V.Murashev in 1912 discovered hemostatic effect of leeches and recommended hirudotherapy as an "energetic hemostatic agent." Until the 50s The twentieth century saw a rise in interest in hirudotherapy. Research work was carried out in different directions - saliva composition, treatment technique, hirudin was studied. In the USSR over the problem hirudotherapy worked I.L.Blumenthal - in the treatment of embolic processes, P.I. Mlagoblishvili and co-authors - in the treatment of skin diseases, V.V. Orlov - in obstetric and gynecological practice, E.M. Tareev, G.F. Lang - for hypertension and others.

After another decline in interest since the 1980s years, a new stage in the history of hirudotherapy began. In 1985, I.P. Baskova and co-authors discovered the enzyme destabilase in the saliva of a leech and studied in detail the mechanisms of regulation hemostasis and fibrinolysis by salivary secretion the glands of the medicinal leech [6, 7]. In 1984 the medical leech was included in the Red Book, and since 1997, a ban has been introduced on catching these animals from natural reservoirs for the purpose of mass sales. In 1990-1991, the antiseptic effect of medicinal leech saliva was discovered. It turned out that saliva extract is in many ways is similar to antibiotics and at the same time does not have the side effects of the latter.

Scientists from different countries (the largest researchers of hirudotherapy as a non-drug method of treatment are currently A.V. Chernukh, G.I. Nikonov, A.G. Abuladze, S.L. Zaslavskaya, I.N. Shishkina, V.V. Savinova, I.P. Baskov, G.R. Iskhanyan, O. Yu. Kamenev, Yu. Ya. Kamenev, etc.) established: the range of application of hirudotherapy in medicine provides "the content of leeches in saliva, in addition to hirudin, trypsin inhibitors and plasmin, inhibitors of alpha-chymotrypsin, chymosin, subtilisin and neutral proteases of granulocytes - elastase and cathepsin C, an inhibitor of blood coagulation factor Xa and kallikrein blood plasma, highly specific enzymes: hyaluronidase, destabilase, apyrase, collagenase, as well as a number of compounds of a still unexplored nature, such as leech prostanoids, histamine-like substances and a number of others "(V.A.Savinov, 2002). Interpretation of their biological action is extremely difficult already because each of these substances taken separately, "is able to induce a cascade of events in the system of the internal environment organism and maintain its constancy (homeostasis), and above all at the level of the vascular wall, in hemostatic and immune systems "[17].

Modern research has proven that the leech should be seen as one living, very complex and peculiar nonspecific irritant to the human body in general, and not just a local method of mechanical extraction of blood from capillaries above the corresponding "problem" organ [17].

It is now recognized that leeches are the only means of bloodletting at the level microcircular bed (a term introduced in physiology in 1954 thanks to the work of a prominent Soviet scientist A. Chernukh and his school), violations in which underlie tissue damage and organs, their diseases and further the body as a whole, and not just one problem organ. Exactly here important metabolic processes take place processes: delivery of nutrients to cells and tissues through capillaries, arterioles, lymphatic vessels and venules. To this at the end of the XIX and the beginning of the XX century. pointed out physiologists K. Bernard and E. Starling, and our contemporary A.S. Zalmanov he devoted most of his life to the study of microcirculation, considering its disorders "an epiphenomenon of various pictures of diseases, one of the main elements of deep dysfunctions of a sick organism." He first introduced the term "capillaropathy", and for methods of its correction - "capillarotherapy".

In the USA and Europe, leeches are officially used as effective remedy for improving local microcirculation, in microsurgery for transplantation of organs and their parts, skin flaps and with autologous transplantation of traumatically amputated fingers, ears and other parts of the face, since the leech with its enzymes promotes the preservation of the capillaries in a fresh state, preparing them for splicing with capillaries body, and at the same time kills the pathogenic flora that multiplies in the injured area [18,26].

Hirudotherapy is also used in the treatment of osteoarthritis knee joint, providing analgesic effect and improving locomotor function [21].

In China, leeches have been treated since time immemorial patients with atherosclerosis and many other diseases. In Russia, hirudotherapy is most often is a method of treating various somatic diseases of a non-infectious nature.

Hirudotherapy in the treatment of cerebrovascular Noah pathology. The first doctor to investigate the effectiveness of hirudotherapy for concussions brain, was a legendary military field surgeon N.I. Pirogov. In his work "The Beginning of General Military Surgery" he wrote: "How soon it seemed a little paint in the patient's face and the pulse rose, now I am putting leeches behind my ears "[4].

Currently, hirudotherapy is a complementary medicine method. According to the methodological recommendations "Using the method hirudotherapy in practical health care ", indications for the use of hirudotherapy are ischemic heart disease, heart insufficiency of 1-2 degrees, atherosclerotic cardiosclerosis, postinfarction cardiosclerosis, cardialgia, discirculatory atherosclerotic encephalopathy, hypertension 1–3 degrees [7]. In recent years, there has been a gradual increase in interest in this method of treatment, which has a large empirical base of use, and a number of scientifically based works, confirming the effectiveness of this method of treatment. Thus, when reviewing the evidence bases of the effectiveness of hirudotherapy in cerebrovascular diseases, using sources from international databases Scopus, PubMed, Web of Science and the Russian base of scientific publications E-library, base of abstracts published in the Russian Federation, and the patent database of the Russian Federation, a small number of works were found on the use of hirudotherapy in the treatment of hypertension, hypertensive and atherosclerotic encephalopathy, prevention of primary and repeated ischemic stroke, post-stroke rehabilitation.

The therapeutic effects of hirudotherapy in clinical practice are explained by well-studied to date, the composition of medical saliva leeches. So, in addition to hirudin, the saliva of leeches contains inhibitors of trypsin and plasmin, inhibitors of alpha-chemotrypsin, chymazin, subtilisin and neutral proteases of granulocytes – elastase and cathepsin C, inhibitors of blood coagulation factor Xa and plasma kallikrein. In the saliva highly specific enzymes have also been found: hyaluronidase, destabilase, apyrase, collagenase, triglyceridase, cholesterol esterase, as well as a number of compounds of not yet studied nature, such as leech prostanoids, histamine-like substances and a number of others [8].

Inclusion of hirudotherapy in treatment regimens patients with arterial hypertension has antihypertensive, antiatherosclerotic action, improves heart function, affects rheological parameters of blood plasma, and most importantly, hirudotherapy is able to reduce the processes of ischemia, hypoxia and normalize microcirculation [5, 18]. In review papers by foreign authors positive clinical results are described hirudotherapy in patients with arterial hypertension [22, 25].

Similar effects can be explained from a biological point of view. So, for food the leech itself needs increased blood flow, which achieved by the ingress of histamine-like substances and acetylcholine, which cause vasodilation and enhancing vascular permeability [10].

Of interest is an open controlled study conducted at the Russian State Medical University, which evaluated the effectiveness of the inclusion of a course of hirudotherapy (10 sessions) in 110 patients with chronic heart failure (CHF) II-III functional class (FC) with or without arterial hypertension. Patients primary groups (70 people) on the background of basic therapy, which was not changed in the course of treatment, hirudotherapy sessions took place. In patient groups with CHF III FC and normal arterial pressure and with CHF II – III FC and an increased level arterial pressure receiving hirudotherapy showed a statistically significant increase in the 6-minute walk distance. In patients in the control group (in subgroups with arterial hypertension and without it) significant changes did not have. After a course of hirudotherapy in patients with arterial hypertension, a significant decrease in diastolic pressure. There were no such changes in the control group [9].

A number of authors consider it expedient to use a course of treatment with medical leeches for the prevention of primary and recurrent stroke in patients with progressive cerebrospinal lesions on the background of hypertensive disease and accompanied by a hypercoagulable state [23, 24]. In 2010, a controlled study of the effectiveness of the course of hirudotherapy in the prevention of ischemic stroke in patients with transient ischemic attacks. The study included 120 patients, admitted to a neurological hospital with a diagnosis of transient ischemic attack, 58 of them against the background of basic therapy, which excluded antiplatelet agents and anticoagulants, three hirudotherapy procedures were performed. After a year of observation, it was noted from the presence of ischemic strokes and a significantly smaller number of repeated transient ischemic attacks in the group of patients who underwent hirudotherapy [23]. Ukrainian scientists conducted a controlled study of the feasibility of using hirudotherapy in the complex treatment of cardioembolic stroke in the acute period. In the main group in which complex treatment included hirudotherapy, on days 1–2 and 14–16 of the disease there was a significant decrease in the activity of coagulation in comparison with the control group, with this did not result in depletion of the physiological anticoagulant system and

inhibition of fibrinolysis. The authors stated a more effective recovery of neurological deficits and subjective improvement in the well-being of patients against the background of hirudotherapy [10].

The presence of lipase cholesterol esterase activity of the secret leech saliva predetermines its use for correction of the lipid spectrum of blood, directed for the prevention of cardiovascular and cerebral catastrophes.

Assessment of the effect of hirudotherapy on the lipid spectrum The patient's blood was carried out in a controlled study, the results of which were published in 2013 by researchers from the Peoples' Friendship University of Russia (Moscow) [6]. During In this work, 63 patients aged (69.3 ± 1.7) years were examined, of whom 57 had coronary heart disease, angina pectoris II FC, arterial hypertension, postinfarction cardiosclerosis, and 45 patients had diabetes mellitus.

The patients were divided into two groups: 35 patients the main group received as part of a complex treatment of cardiovascular pathology, hirudotherapy, and 26 patients of the control group received in as part of the complex treatment of statins.

By the 20th day of treatment, patients of the main group were carried out on average 6 sessions of hirudotherapy, and after the course of treatment the level of cholesterol decreased from (8.5 ± 0.87) to (4.6 ± 1.1) mmol / L, and triglycerides - from (6.2 ± 0.83) to (1.5 ± 0.1) mmol / l. In patients of the control group, the level of cholesterol decreased from (8.4 ± 0.79) to (4.53 ± 0.85) mmol / L, and triglyceride level - from (6.3 ± 0.75) to (1.3 ± 0.3) mmol / L.

In order to identify the optimal conservative methods of rehabilitation treatment for small-volume stroke, a controlled comparative study was carried out in 62 patients with acute violation of cerebral circulation, 30 of which during the rehabilitation period were carried out additional treatment with medical leeches. On the 3rd day of hirudotherapy, noticeable stabilization of blood pressure, improvement of neurological and general condition patients [10]. It should be noted that in most of the works devoted to the use of hirudotherapy, no significant side effects of this method were noted. The method was applied both in combination with the standard drug therapy, and with its partial cancellation. Adding hirudotherapy against the background of antiplatelet therapy did not lead to any hemorrhagic events.

Of course, large-scale randomized controlled studies of the application of the hirudotherapy method are of interest in the clinic. But the possibility of such research is still difficult to implement in practice due to for a number of reasons: hirudotherapy is carried out most often in commercial centers, which leads to the impossibility holding a control group without including hirudotherapy; each doctor using hirudotherapy conducts it individually, based on on my own experience.

Thus, there is currently a scientifically grounded theoretical and practical the basis for the use of hirudotherapy in different groups of patients with an angioneurological profile (chronic cerebrovascular accident, acute period of ischemic stroke, post-stroke rehabilitation and other), which appears sufficient to use this complementary medicine method in complex treatment of cerebrovascular diseases.

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