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Scientific and pedagogical school of Professor A.A. Lebedev (commemorating the 95th anniversary of his birth)

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Abstract

August 28, 2025 marks the 95th anniversary of the birth of Aleksei A. Lebedev, the founder of the Samara Scientific and Pedagogical School of Pharmacologists, which has all-Russian and international recognition in the field of "Pharmacology of the Kidneys and Water-Salt Metabolism".

The milestones of A. A. Lebedev's biography are presented. His influence on the development of pharmacology, training of scientific and pedagogical personnel in the field of pharmacology, clinical pharmacology and clinical medicine in Russia is analyzed.

Keywords: experimental and clinical pharmacology; drugs; teaching pharmacology; scientific research.

Conflict of interest: nothing to disclose.

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Научно-педагогическая школа профессора А.А. Лебедева (к 95-летию со дня рождения)

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Аннотация

28 августа 2025 года исполнилось 95 лет со дня рождения Алексея Александровича Лебедева, основоположника Самарской научно-педагогической школы фармакологов, имеющей общероссийское и международное признание по направлению «Фармакология почек и водно-солевого обмена». В статье представлены основные этапы биографии А.А. Лебедева. Проведен анализ его влияния на развитие фармакологии, подготовку научно-педагогических кадров в области фармакологии, клинической фармакологии и клинической медицины в Российской Федерации.

Ключевые слова: экспериментальная и клиническая фармакология; лекарственные средства; преподавание фармакологии; научные исследования.

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Aleksei Aleksandrovich LEBEDEV (28.08.1930 – 09.03.2008)

A GLIMPSE INTO A REMARKABLE LIFE

Aleksei Aleksandrovich Lebedev, Honored Scientist of the Russian Federation, Doctor of Medicine, Professor Emeritus of the Ivanovo State Medical Academy and Samara State Medical University, was born on 28 August 1930, in the town of Suzdal of the Vladimir Region in a family of doctors. Having moved to the town of Ivanovo, Aleksei Aleksandrovich followed the family traditions and entered the Ivanovo State Medical University; in 1953, he graduated with honors.

He chose his field of scientific interest in the third year of studies, when he joined the students' club of the pharmacology department; he kept the interest to pharmacological science until the very end. His formation as a scientist was greatly influenced by his tutor, Georgy Mikhailovich Shpuga, who had developed the method of kidney autotransplantation to the cervical vessels as early as in 1937. The method involves anastomosing the carotid artery to the renal artery, and the jugular vein with the renal vein. It was found that the kidney transplanted to the neck functioned 30–40% worse compared to the intact kidney, which was likely due to denervation occurring during organ transplantation. The idea suggested by Prof. G.M. Shpuga, on the necessity of reinnervating the transplanted kidney to improve its function and trophicity, later formed the basis of the doctoral dissertation of A.A. Lebedev.

It proposed an original idea of restoring the innervation during surgery by anastomosing the central end of the vagus nerve with the peripheral ends of the renal nerves severed during transplantation. A brilliant experimenter, Aleksei Aleksandrovich proved that both afferent and efferent innervation of the kidneys recover after anastomosing of the nerves. Reinnervation was confirmed in the works of his students: long-term monitoring of test animals demonstrated gradual adequation of the functions of the intact and the auto-transplanted kidneys. Owing to the works of A.A. Lebedev and his students one of the debatable issues of organ physiology found its solution: the question of the role of renal nerves in the kidney physiology.

SCIENTIFIC SCHOOL OF A.A. LEBEDEV

In 1964, A.A. Lebedev was elected as the Chair of the Department of Pharmacology of the D.I. Ulyanov Kuybushev Medical Institute (now the Samara State Medical University). He worked in this position for 36 years. Under his guidance, there started a large-scale research in the areas of kidney physiology and salt and water metabolism. One of strategic areas that had to be developed and justified was the research of the very close connection between the kidney function and the blood circulation system. Even at the time, it was established that while performing the excretory function kidneys perform a not less important homeostatic function maintaining adequacy of the blood circulation. It meant that the obvious excretion of salt, water and metabolites from the body is appended on a not less crucial yet invisible function of retaining electrolytes and liquid in the body, which ensures the bodily homeostasis: volume of the circulating blood, its composition, arterial blood pressure and other parameters. When studying the activity of acetylcholine, nitroglycerin, benzohexonium and hygronium a decrease in the peripheral resistance of the vessels was established. Despite the different chemical structure and the mechanism of action of the substances, they cause a unidirectional reaction of keeping sodium and water in the body by increasing reabsorption of these components in the renal tubules. At the same time, the circulatory blood volume (CBV) increases. It was found that due to the effect of ephedrine, adrenaline, noradrenaline, occlusion of the common carotid arteries the peripheral resistance of vessels increases, as well does the excretion of sodium, potassium and water with a decrease of the CBV.

Manipulations with CBV also demonstrated the homeostatic function of the kidneys: volume reduction induced by phlebotomy elicits antinatriuretic and antidiuretic effects; conversely, increased blood volume produces the opposite renal response. These investigations led to the formulation of the theory of blood volume vascular capacity matching as a regulator of renal homeostatic function. Subsequent studies focused on elucidating specific

renal and extrarenal mechanisms mediating these responses, including the roles of renal nerves, the sympathoadrenal system, and the renin-angiotensin system, under both pharmacological interventions and pathological conditions. In all of these cases, excretion of sodium and water correlates more with the level of peripheral resistance of vessels than with the level of arterial blood pressure. Homeostatic reactions of the kidneys drastically change under hypertensive disease, myocardial infarction, heart failure, and under intervention of pathogenic factors into this process.

In the course of analysis of homeostatic reactions of the kidneys ensuring maintenance of the blood circulation adequacy, Prof. Lebedev clearly saw that the intricate mechanisms of kidney excretion could not be understood without an in-depth study of the nephron functions. It was necessary to study the tubule reabsorption of the principal ion of the internal medium, sodium, which determines its osmotic concentration, alkaline potential, volume of intravascular and extracellular fluid. Research in this direction assumed a large-scale character. It became necessary to re-conceptualize the transport of sodium and chloride in the nephron. The existing model of sodium transfer from the lumen to the interstitium at the start of the work stated that the ion moves passively through sodium channels in the luminal membrane of nephrocytes along the concentration gradient, while across the basolateral membrane, sodium was believed to be transported against the electrochemical gradient via an active transport mechanism. Chlorine follows the sodium ion, creates an oncotic gradient in the basal labyrinth, mediates the fluid flow in the extracellular pathways from the tubule lumen to the interstitium. In this way, cell reabsorption of water occurs due to primary reabsorption of sodium.

Aleksei Aleksandrovich made a proposition that the ion transport may fulfil not only in a transcellular way but also by transfer in the intercellular space. There appeared the theory of fixed charges of the nephron wall that explained and proved the possibility of transcellular transport. In the experiments using biomembranes performing sodium transfer from the internal surface to the external (wall of the urinary bladder of a frog), the possibility of transfer of sucrose, ions of iodide, chloride, lithium and fluoresceine in the intercellular space was demonstrated multiple times. Subsequently, it was established that cations are always transported in greater quantity from the mucosal to the serosal surface, while anions move in the opposite direction. The charge hypothesis provided an explanation for this phenomenon, attributing it to fixed charges creating flow asymmetry. It was hypothesized that within the nephron, at the entrance to the intercellular spaces on the luminal side, negative charges are present, promoting cation movement and hindering anion transport, while on the basolateral surface in the region of the intercellular spaces, positive charges exist, facilitating the opposite phenomenon. This mechanism contributes to the generation of a transepithelial potential across the nephron wall.

The theory of gate charges of cell junctions proved very useful for the interpretation of mechanism of action of some diuretics. Such diuretics as etacrynic acid, osmotic diuretics, mercurial diuretics expand the gates of the cell junctions, while the gate charges lose their role and the selectivity of ion flows decreases.

The problem of localization and tubular effect of diuretics became the center of many dissertations supervised by the professor. However, this path was full of methodological complications. The nephron, the main structural unit of the kidney, is microscopic in size, it is not possible to study it directly; therefore, model experiments were performed on epithelial structures performing directed transfer of sodium: the skin and the wall of the urinary bladder of a frog, the wall of large intestine of mammals.

Early research performed in the laboratory of A.A. Lebedev in 1970s demonstrated that the inhibitors of metabolic processes, such as strophantine, directly blocked the active transfer of sodium through biological membranes, and some diuretics, such as Mercusal, Novurit, Hypothiazid caused a significant increase in the permeability of cell membranes. The effect of Novurit was confirmed in experiments with micropuncture examination of the rat nephron, and in experiments utilizing the Na24 radioactive isotope. The obtained data demonstrated the capability of diuretics to influence bypassing sodium flows in the nephron presumably traveling through intercellular spaces. This proposal was later confirmed in multiple experiments.

The doubts completely vanished when micropuncture experiments on rat nephrons with fluorescein, marker of intercellular permeability, showed that Novurit and Mannitol significantly change the paracellular transport, while Furosemide had no effect on it. Expansion of intercellular spaces increases the bypassing flow of sodium from the interstitium to the nephron lumen, which balances the active transport and leads to an increase of natriuresis. Furosemide does not affect the intercellular transport of ions, and its effect is mediated by binding to one of the enzymes of the renal epithelium and secondary effect on the Na+-2Cl--K+ cotransporter of the luminal membrane of the ascending limb of Henle's loop. Based on the obtained data, A.A. Lebedev proposed an original classification of diuretics based on the mechanism of their action.

The search for new agents with a diuretic effect has always been the focus of interest of the department of pharmacology. This involved establishment of contacts with chemists of Kuybyshev (today, the city of Samara) and other regions to study the pharmacology of heterocyclic spirans and isoindoles (Saratov State University), triazines (Leningrad Institute of Chemistry and Pharmacology), sulfamoylbenzoic acid (Research Institute of Medicinal Products of Kupavna). Active diuretics were identified for future in-depth research. It was found that the lithium and furfurylamin salts of furosemide have especially high activity surpassing the effect of Furosemide. The Department of Pharmaceutical Chemistry of the Kuybyshev Medical Institute synthesized several compounds based on etacrynic acid and bumetanide that had a marked diuretic effect. These works had very high theoretical importance for they opened ways of synthesis of new biologically active compounds.

In the late 1980s, the Department of Pharmacology of the Kuybyshev Medical Institute became the base for research of diuretic agents. The All-Union Research Institute of Chemistry and Pharmacology (Moscow) received the state order for the development of domestic diuretic agents that involved novel synthesis of Furosemide, Hypothiazid, Triamterene, Spironolactone, and the Department performed a comparative assessment of their diuretic properties. The analysis showed that the protective action of the products is not related to their structure (they belong to different chemical classes) but was determined by the diuretic effect itself. The scientists concluded that the prophylactic action of the drugs stems from the hemodynamic effect developing on the nephron level. Thus, Furosemide

increases the lumen of proximal and distal tubules, reduces the swelling and deterioration of nephrocytes, increases the tubule flow of the fluid, and increases the hydrostatic pressure in the lumen: this enables the tubules resist the ischemic stress. The similar effect of Furosemide was confirmed in the experiments with acute hemorrhagic hypotension and toxic nephropathy. It was demonstrated that the domestically produced Furosemide does not differ from the imported analogs. After that, domestic production of Furosemide started in the country. At present, diuretics are used in acute kidney failure both as prevention and treatment drugs, in the initial period of development of kidney failure, if the arterial blood pressure and the circulating blood volume are normalized. It is to be remembered that the clinical use of diuretics was justified experimentally.

The method of nephron micropuncture, biological modeling of sodium transport, methods of fluorescent analysis of individual nephrons facilitated development of a classification of diuretics described in the article "Diuretic Agents" in the Great Medical Encyclopedia. Prof. Lebedev was the editor of five monothematic collections of articles.

A.A. Lebedev is the co-author of 16 patents on biologically active substances, including those with a diuretic action. He wrote 240 scientific works, among them 4 monographs.

TRAINING OF SCIENTIFIC AND PEDAGOGICAL STAFF

A.A. Lebedev gave great attention to training of scientific research and pedagogical staff; he initiated and pioneered the Pharmaceutical Faculty of the Kuybyshev Medical Institute. He was the tutor of 11 doctors of science and 28 candidates of science. In the course of his work in Samara, he created a scientific school of pharmacologists within a single scientific field, "Pharmacology of the kidneys and salt and water metabolism". To date, this school shapes the development of this area of research in the country. In 1964, A.A. Lebedev organized the Regional Society of Pharmacologists and chaired its work for many years. He was also a member of the Russian Society of Pharmacologists, and a member of the editorial board of the "Journal of Experimental and Clinical Pharmacology". In the Scientific Council on Pharmacology and Pharmacy, A.A. Lebedev supervised the "Pharmacology of the Kidneys" branch. Aleksei Aleksandrovich spared no effort and energy in working with aspiring specialists: for 35 years, he was the academic advisor of the Students' Scientific Society of the Samara State Medical University. Under his leadership, five national conferences on kidney pharmacology and salt and water metabolism, and one national symposium. For his constructive academic and pedagogical activity, training of academic staff A.A. Lebedev was awarded with the Order of Peoples' Friendship, second-class Medal of the Order of "Merit for the Motherland", signs of the "Expert of Healthcare", "Foe Exceptional Achievement in the Work", and the Medal of "Veteran of Labor". Cambridge International Bibliographic Database awarded him with a prize for exceptional contributions to science. In 1978, for his merit in the development of Soviet pharmacology, the Academic Council of the Institute of Pharmacology of the Academy of Medical Sciences of the USSR awarded A.A. Lebedev with the medal of the founder of Russian pharmacology, Nikolay Pavlovich Kravkov.

A.A. Lebedev was Professor emeritus of the Samara State Medical University and Ivanovo State Medical Academy. He was elected as a Fellow of the Eurasia International Academy of Sciences. In 1999, the American Biographical Institute, following the recommendation of Academy Fellow D.A. Kharkevich, listed A.A. Lebedev on the International Directory of Distinguished Leadership.

Aleksei Aleksansrovich Lebedev passed away on 9 March, 2008 at the age of 78 years. The cherished memory of him stays in our hearts.

CONCLUSION

In 2008, the Rectorate of the Samara State Medical University gave the name of the Honored Scientist of the Russian Federation Prof. A.A. Lebedev to the Department of Pharmacology. The staff and faculty of the Department of Pharmacology, students of Prof. Lebedev, continue developing the lines of science pioneered by Aleksei Aleksandrovich, and, inspired by the vigor and the range of thought of the scientist, they blaze new trails. The contribution of A.A. Lebedev in the national medicine constitutes a solid foundation of ongoing research in the area of pharmacology of the kidneys and related fields of experimental pharmacology.

ADDITIONAL INFORMATION	ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ
Provenance and peer review. This paper was commissioned by the journal's Editorial Board and underwent prioritized internal peer review.	***Рассмотрение и рецензирование.*** Настоящая работа подготовлена по просьбе редакции журнала, была рассмотрена во внеочередном порядке без участия внешних рецензентов.
Study funding. The study was without external funding.	***Источник финансирования.*** Работа выполнена без привлечения финансирования.
Conflict of interest. The authors declare that there are no obvious or potential conflicts of interest associated with the content of this article.	***Конфликт интересов.*** Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с содержанием настоящей статьи.
Contribution of individual authors. Dubishchev A.V.: definition of the concept, editing of the manuscript. Zaitseva E.N., Avdeeva E.V.: collection and processing of materials, writing of the original text, editing of the manuscript. The authors gave their final approval of the manuscript for submission, and agreed to be accountable for all aspects of the work, implying proper study and resolution of issues related to the accuracy or integrity of any part of the work.	***Участие авторов.*** Дубищев А.В. – определение концепции, редактирование рукописи. Зайцева Е.Н., Авдеева Е.В. – сбор и обработка материалов, написание оригинального текста, редактирование рукописи. Все авторы одобрили финальную версию статьи перед публикацией, выразили согласие нести ответственность за все аспекты работы, подразумевающую надлежащее изучение и решение вопросов, связанных с точностью или добросовестностью любой части работы.