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Towards 125th anniversary of the outstanding pathophysiologist and bright star of Russian science — Leonid Ruvimovich Perelman

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ABSTRACT

The article is devoted to the study of the life and activities of the outstanding scientist pathophysiologist Professor Leonid Ruvimovich Perelman, whose researh and pedagogical activity had a significant impact on the development of Pathophysiology and Medicine not only in Russia, but also in the world. The main attention is paid to the key stages of his biography — his family, the early stages of the researcher's development, his contribution to the development of experimental and clinical pathophysiology, his numerous discoveries that influenced some key areas of modern medicine, as well as his role in the formation of scientific schools. A special place is given to the analysis of scientific publications of Leonid Ruvimovich Perelman, experimental and theoretical works that made a significant contribution to the understanding of the mechanisms of the most important pathological processes and the development of new approaches to diagnosis and therapy, which have found application nowadays in neuroimmunoendocrinology, regenerative medicine, oncology, surgery and other fields. Leonid Ruvimovich's teaching methods, his scientific guidance of countless undergraduate and postgraduate papers, and his influence on the training of highly qualified specialists in pathological physiology, who worked in many educational institutions in Russia, including the St. Petersburg State Paediatric Medical University, are discussed. The conclusion emphasises the significance of Perelman's legacy for modern medical science, as well as the relevance of his ideas in planning new research for their further implementation in clinical practice.

Keywords: pathophysiology, biography, Leonid Ruvimovich Perelman, permissive action of hormones

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К 125-летию выдающегося патофизиолога — яркой звезды российской науки — Леонида Рувимовича Перельмана

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АННОТАЦИЯ

Статья посвящена описанию жизни и деятельности выдающегося ученого-патофизиолога профессора Леонида Рувимовича Перельмана, чьи научные труды и педагогическая работа оказали значительное влияние на развитие не только отечественной патофизиологии и медицины, но и на мировую науку. Основное внимание уделяется ключевым этапам его биографии — семье, раннему периоду становления исследователя, вкладу в развитие экспериментальной и клинической патофизиологии, многочисленным открытиям, повлиявшим на ключевые области современной медицины, а также его роли в формировании научных школ. Особое место занимает анализ научных публикаций Леонида Рувимовича Перельмана, экспериментальных и теоретических работ, внесших существенный вклад в понимание механизмов важнейших патологических процессов и разработку новых подходов к диагностике и терапии, что нашло применение в настоящее время в нейроиммуноэндокринологии, регенеративной медицине, онкологии, хирургии и других областях медицинской науки. Рассматриваются методики преподавания Леонида Рувимовича, его научное руководство бесчисленными работами студентов и аспирантов, а также влияние на подготовку высококвалифицированных специалистов в области патологической физиологии, которые работали во многих учебных заведениях России, в том числе в Санкт-Петербургском государственном педиатрическом медицинском университете. В заключении подчеркивается значимость наследия Перельмана для современной медицинской науки, а также актуальность его идей в планировании новых исследований для их дальнейшего внедрения в клиническую практику.

Ключевые слова: патофизиология, биография, Леонид Рувимович Перельман, пермиссивное действие гормонов

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INTRODUCTION

The history of Russian medicine contains names that, like bright stars, illuminate the path for many generations of scientists. Leonid Ruvimovich Perelman (1900–1969) (Fig. 1) is one of these famous names. He was an outstanding pathophysiologist whose discoveries in the fields of endocrinology, immunology, and phthisiopulmonology were decades ahead of their time. His scientific career, which began during the turbulent years of revolution and civil war, spanned all the tragic vicissitudes of the Soviet era, from Stalin's repressions to the blockade of Leningrad. Despite all the obstacles, he managed not only to remain faithful to science, but also to make groundbreaking discoveries that are still relevant in modern medicine.

THE FORMATION OF A SCIENTIST (1900–1920 YEARS)

Leonid Ruvimovich Perelman was born on July 6, 1900, in Kazan, in a family of doctors. Intellectual atmosphere at home, where the cult of knowledge and respect for science reigned, largely determined his future path. As his contemporaries recalled, even in his high school years, he showed an extraordinary breadth of interests. He was fond of philosophy, literature, music, and natural sciences [18].

In 1917, after graduating from high school, Perelman entered the medical faculty of Saratov University. This was a turning point in his life. Here he met his main teacher, Alexander Alexandrovich Bogomolets, who headed the Department of General Pathology. Bogomolets, a student of Ilya Ilyich Mechnikov himself, created one of the strongest schools of pathophysiology in the country in Saratov.

In November 1919, during his second year of studies, Leonid Ruvimovich began working as a laboratory assistant in the department, where, under Bogomolets' guidance, he learned the basics of experimental medicine. During these years, his unique style of thinking took shape, that was a combination of depth of theoretical analysis and mastery of experimental techniques.

Fig. 1. Leonid Ruvymovych Perelman (50-es of the XX century)
Рис. 1. Леонид Рувимович Перельман (50-е годы XX века)

The year 1920 was a test for the young scientist. Like many students, he voluntarily joined the Red Army, where he served as a medical orderly on the South-Eastern Front. Here, while undergoing cavalry training, Leonid Ruvimovich developed a lifelong love of horse riding, a passion that remained with him into his mature years. According to his colleagues' recollections, even after becoming a professor, he still found time to train in a riding arena [18].

SCIENTIFIC BREAKTHROUGH (1920–1930 YEARS)

After demobilization, the young scientist returned to university to continue his studies, and upon graduation in 1922, he was appointed assistant prosector at the Department of General Pathology and Bacteriology. Already in 1924, while still being an intern, he made a discovery that forever inscribed his name in the history of endocrinology. In a short work published by the provincial publishing house Sargublit, he was the first in the world to describe a permissive effect of hormones, namely their ability to modulate the effects of other biologically active substances. During Leonid Ruvimovich's first three years at the department under the guidance of Professor A.A. Bogomolets, five experimental scientific papers were completed and published, two of which concerned endocrinology [6]. One of them was the article "On the functional relationship between the parathyroid and male sex glands", published in the journal "Archive of Clinical and Experimental Medicine" in 1924. This work was pioneering and had a significant impact on the development of both domestic and global endocrinology, demonstrating the permissive effect of hormones on a model of parathyroid tetany [9]. Only in 1949 did Americans D. Ingle and J. Engel come to the same conclusions, unaware of the priority of their Soviet colleague [20, 21].

In 1925, his second work, "On the relationship between the parathyroid glands and adrenal glands in the pathogenesis of tetaniae parathyreoprival", was published. The discovery of the permissive action of hormones, made on a model of parathyroid tetany, was many years ahead of similar research by Western scientists [19].

In 1925, following Bogomolets, Perelman moved to the Second Moscow University, where he worked as a lecturer for a year. However, in 1926, he returned to Saratov, where, after defending his dissertation in 1928, he became a private lecturer. These years were extremely fruitful. He developed his famous method of chronic parabiosis, which allowed him to clearly distinguish between humoral and nervous regulatory mechanisms [4].

The turning point in Perelman's scientific career came in 1929, when he was elected professor and head of the Department of Pathophysiology at the Leningrad Sanitary and Hygienic Medical Institute (now the I.I. Mechnikov North-Western State Medical University). He held this position for an unprecedented 38 years, until 1967.

For 21 years, L.R. Perelman headed the Department of Experimental Pathology at the Leningrad Tuberculosis Institute, where he studied the way this pathology depended on metabolic processes and hormonal dynamics [10].

MAIN SCIENTIFIC ACHIEVEMENTS

In the early 1930s, L.R. Perelman headed the Department of Pathological Physiology at the Leningrad Pediatric Medical Institute, taking over this position from Professor Efim Semenovich London, who entrusted the department to a young but very talented scientist. Professor Perelman headed this department at the Pediatric Institute for a long time. Here, in the 1930s and 1940s, he made significant contributions to the development of important theoretical and practical problems in pathophysiology and medicine.

Neuroimmunoendocrinology: foresight into the future. One of the most prophetic areas of Perelman's work was the study of interaction between the nervous, immune, and endocrine systems. When many people around the world thought that these systems did not interact with each other, Leonid Ruvimovich was able to discern many common mechanisms between them. He was one of the first to understand the significance of cytotoxins that are antibodies to cellular structures. The scientist predicted that these molecules could be applied for therapy of autoimmune, oncological, and neurodegenerative diseases. In his research, Perelman determined that stress factors modulate the immune response through the hypothalamic-pituitary-adrenal axis, and inflammatory processes disrupt neuroendocrine regulation [12]. Today, these ideas form the basis of an entire field of study — neuroimmunoendocrinology. It has been discovered that neurotransmitters and hormones modulate the immune system by influencing the proliferation of immunocompetent cells and their production of cytokines [14].

Physiology of breathing: a revolution in phthisiology. For more than 20 years, Perelman studied mechanisms of respiratory regulation. One of his discoveries was active lung tone since lung tissue is capable of independently maintaining an optimal level of tension thanks to neuro-reflex regulation, rather than following the movements of the chest. Leonid Ruvimovich also studied the pleuropulmonary reflex, in which irritation of this serous membrane affects its tone and participation in the act of breathing. These discoveries are still used in phthisiopulmonology today and are the "gold standard" in diagnosing certain diseases [15, 19].

Parabiosis method: a unique experimental model. The chronic parabiosis technique (surgical connection of two organisms) developed by Perelman made it possible to establish a humoral nature of transmission from one organism to another. Thanks to this research, many fundamental discoveries were made in immunology, transplantology, and oncology. They included the discovery that donor blood coagulation factors can influence regeneration of recipient tissues, methods for suppressing transplant rejection, and the influence of systemic factors on tumor growth. Another significant discovery was the stimulation of tissue regeneration in an old organism through blood transfusions from a young organism. Thus, it can be concluded that Perelman laid foundations for aging research, regenerative medicine, and cancer therapy through this method [8, 17].

Blockaded Leningrad: working in catastrophic conditions and scientific achievements in studying the pathology of starvation. When the blockade ring closed around Leningrad in September 1941, Leonid Ruvimovich Perelman was one of a few prominent scientists who remained in the city. Unlike many of his colleagues who were evacuated to Kazan or Tomsk, he consciously remained at his post, considering it was his duty to continue working in these inhuman conditions and taking on the management of three departments of pathophysiology at once — at the Leningrad Pediatric Medical Institute (LPMI), the 1st Medical Institute, and the Leningrad Sanitary and Hygienic Medical Institute (LSHMI).

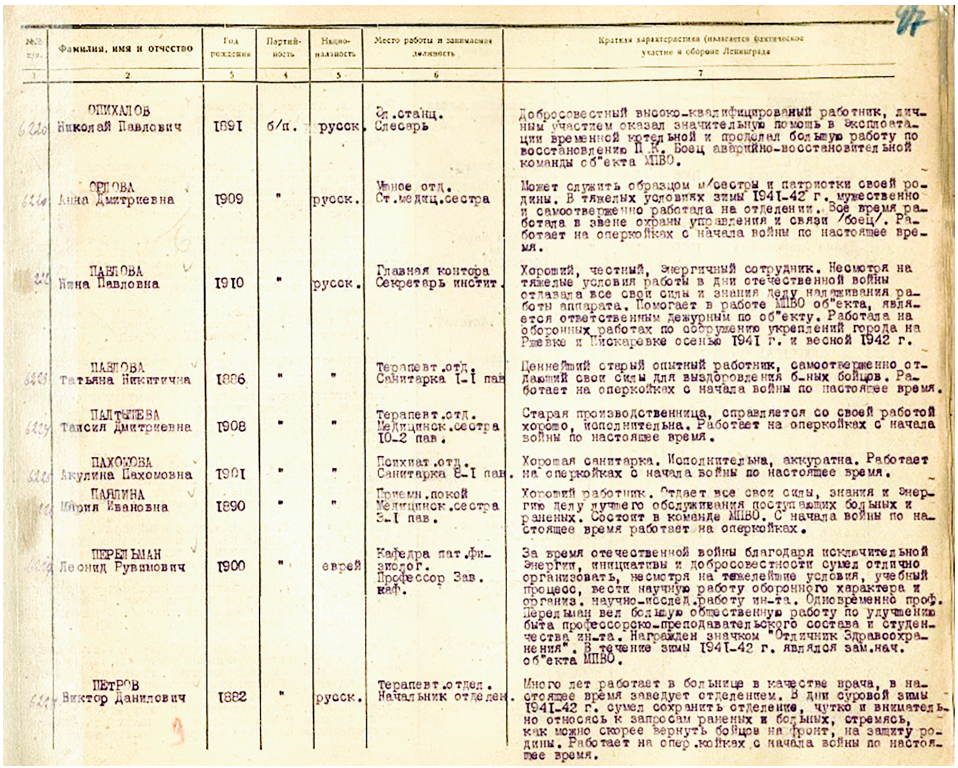
The Department of Pathophysiology at LSHMI, which he headed, continued to operate in a dilapidated building. The temperature in laboratories rarely rose above zero degrees during the winter of 1941–1942. There was a shortage of everything from reagents to firewood. In these conditions, Perelman organized unique research on the effects of starvation, which he conducted... on himself and his colleagues[1].

Leonid Ruvimovich's work on alimentary dystrophy has become a classic in world medicine. He meticulously recorded daily changes in basal metabolism (a decrease of 35–40% from normal), the dynamics of protein breakdown (up to 120–150 g per day in late stages of starvation), features of water-salt metabolism, and changes in endocrine regulation.

This data, collected literally at the cost of his own health, formed the basis of his monograph Pathological Physiology of Alimentary Dystrophy (1947), which is still cited in nutrition manuals [7, 11, 16].

Despite hunger and constant shelling, Perelman continued to give lectures. His students recalled how the professor, himself suffering from dystrophy, in a worn but

[1] Archive of the FSB of the Leningrad Region. F. 21/12. Op. 2. P. n. 56. D. 1. L. 18-22. Document No. 26.



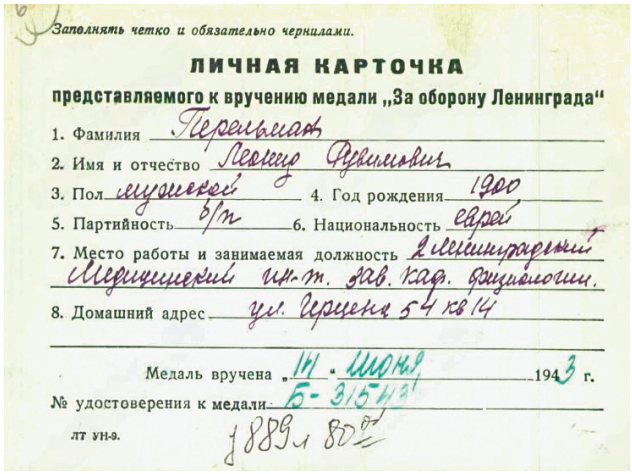
№ п/п	Фамилия, имя и отчество	Год рождения	Партийность	Национальность	Место работы и занимаемая должность	Краткая характеристика (излагается фактическое участие в обороне Ленинграда)
1	2	3	4	5	6	7
	ОПИХАЛОВ Николай Павлович	1891	б/п.	русск.	Ст.станц. Слесарь	Добросовестный высоко-квалифицированный работник, личным участием оказал значительную помощь в эксплоатации временной котельной и проделал большую работу по восстановлению П.Р. Боец аварийно-восстановительной команды об"екта МПВО.
	ОРЛОВА Анна Дмитриевна	1909	"	русск.	Мясное отд. Ст.медиц.сестра	Может служить образцом м/сестры и патриотки своей родины. В тяжелых условиях зимы 1941-42 г. мужественно и самоотверженно работала на отделении. Все время работала в звене охраны управления и связи /боец/. Работает на оперкойках с начала войны по настоящее время.
	ПАВЛОВА Нина Павловна	1910	"	русск.	Главная контора Секретарь институт.	Хороший, честный, энергичный сотрудник. Несмотря на тяжелые условия работы в дни отечественной войны отдавала все свои силы и знания делу налаживания работы аппарата. Помогает в работе МПВО об"екта, является ответственным дежурным по об"екту. Работала на оборонных работах по оборудованию укреплений города на Ржевке и Пискаровке осенью 1941 г. и весной 1942 г.
	ПАНОВА Татьяна Никитична	1886	"	"	Терапевт.отд. Санитарка I-I пав.	Ценнейший старый опытный работник, самоотверженно отдавший свои силы для выздоровления б-ных бойцов. Работает на оперкойках с начала войны по настоящее время.
	ПАПТЫЕВА Таисия Дмитриевна	1908	"	"	Терапевт.отд. Медицинск.сестра IO-2 пав.	Старая производственница, справляется со своей работой хорошо, исполнительна. Работает на оперкойках с начала войны по настоящее время.
	ПАХОМОВА Акулина Пахомовна	1901	"	"	Психиат.отд. Санитарка С-I пав.	Хорошая санитарка. Исполнительна, аккуратна. Работает на оперкойках с начала войны по настоящее время.
	ПАЛИНА Мария Ивановна	1890	"	"	Приемн.покой Медицинск.сестра С-I пав.	Хороший работник. Отдает все свои силы, знания и энергию делу лучшего обслуживания поступающих больных и раненых. Состоит в команде МПВО. С начала войны по настоящее время работает на оперкойках.
	ПЕРЕЛЬМАН Леонид Рувимович	1900	"	еврей	Кафедра пат.физиолог. Профессор Зав. каф.	За время отечественной войны благодаря исключительной энергии, инициативы и добросовестности сумел отлично организовать, несмотря на тяжелейшие условия, учебный процесс, вести научную работу оборонного характера и органиа. научно-исслед.работу ин-та. Одновременно проф. Перельман вел большую общественную работу по улучшению быта профессорско-преподавательского состава и студенчества ин-та. Награжден значком "Отличник Здравоохранения". В течение зимы 1941-42 г. являлся зам.нач. об"екта МПВО.
	ПЕТРОВ Виктор Данилович	1882	"	русск.	Терапевт.отдел. Начальник отделен.	Много лет работает в больнице в качестве врача, в настоящее время заведует отделением. В дни суровой зимы 1941-42 г. сумел сохранить отделение, чутко и внимательно относясь к запросам раненых и больных, стремясь, как можно скорее вернуть бойцов на фронт, на защиту родины. Работает на опер.койках с начала войны по настоящее время.

Fig. 2. Lists of workers and employees of enterprises and institutions of Krasnogvardeysky District, awarded the medal “For the Defence of Leningrad”, Vol. 2. (Archival Committee of St. Petersburg: https://medal.spbarchives.ru/person?docId=436079)

Рис. 2. Списки рабочих и служащих предприятий и учреждений Красногвардейского района, награжденных медалью «За оборону Ленинграда», Т. 2. (Архивный комитет Санкт-Петербурга: https://medal.spbarchives.ru/person?docId=436079)

neatly cleaned suit, with his usual bow tie (which he called a “kitty”), taught classes under the light of a smoky lamp. Archives preserve notes from his lectures in 1942, written with a trembling hand on scraps of wallpaper—the last available “information carriers” in the besieged city.

Simultaneously with his scientific activities, Perelman held the position of scientific secretary of the 2nd Leningrad Medical Institute. In this position, he organized the work of hospital pathological services, coordinated research on the prevention of infections, and personally participated in creating “siege” methods of diagnosis and treatment. His diaries of this period (partially published in 2000) are a unique document of the era, where scientific observations are intertwined with reflections on the nature of human resilience [13]. Leonid Ruvimovich Perelman was awarded the Medal “For the Defense of Leningrad” (Figs. 2, 3) for his conscientious service during the Great Patriotic War in besieged Leningrad [2, 13, 19].



Заполнять четко и обязательно чернилами.

ЛИЧНАЯ КАРТОЧКА

представляемого к вручению медали „За оборону Ленинграда“

1. Фамилия Перельман
2. Имя и отчество Леонид Рувимович
3. Пол мужской 4. Год рождения 1900
5. Партийность б/п 6. Национальность еврей
7. Место работы и занимаемая должность 2 Ленинградский Медицинский ин-т. зав. каф. физиологии.
8. Домашний адрес ул. Герцена 54 кв 14

Медаль вручена „14“ июня 1943 г.

№ удостоверения к медали Б-315 №2

лт ун-в. 1889 г 80

Fig. 3. Personal card of the person being presented for the medal ‘For the Defence of Leningrad’ (Archival Committeeman of St. Petersburg: https://medal.spbarchives.ru/person?docId=436079)

Рис. 3. Личная карточка представляемого к вручению медали «За оборону Ленинграда» (Архивный комитент Санкт-Петербурга: https://medal.spbarchives.ru/person?docId=436079)

SCIENTIFIC SCHOOL AND PEDAGOGICAL LEGACY

Perelman’s pedagogical system was distinguished by a deep integration of theory and practice, an interdisciplinary approach, special attention to the philosophical foundations of medicine, and a cult of experimental verification of any theoretical propositions. According to his students’ recollections, his lectures were not simply a presentation of facts, but an “intellectual theater” where each concept took on flesh and blood [2, 5].

Under Perelman’s guidance, more than 50 candidates and doctors of science defended their theses.

Professor A.S. Zaychik, the founder of a new direction in immunopathology, and Professor N.N. Zaiko,

the author of classic textbooks on pathophysiology, are among his most famous students. A distinctive feature of his school was the combination of fundamental research with a clear clinical focus. His contemporaries said: “Perelman taught us that true science is always a little ahead of its time — otherwise it is not science, but craft.”

Despite the fact that Perelman never managed to publish his own textbook (due to opposition from official circles), he created a unique “Practical Guide to Pathological Physiology” (1962), participated in writing a fundamental 4-volume guide to pathophysiology (1966), and left behind a huge handwritten legacy (lectures, guidelines). His notes, written in calligraphic handwriting in seven languages, are kept as relics in the museum of the Department of Pathology at St. Petersburg State University [2, 3].

THE LAST YEARS OF HIS LIFE AND THE SIGNIFICANCE OF HIS LEGACY (1960–1969)

The 60-year-old Perelman remained remarkably productive even in the last decade of his life. His main areas of research were: the pathophysiology of peptic ulcer disease (in collaboration with the Institute of Gastroenterology), problems of gerontology (continuing Mechnikov’s ideas), and the study of cytotoxic antibodies. From 1962 to 1967, he consulted for the Department of Experimental Pathology at the Institute of Gastroenterology of the USSR Academy of Medical Sciences.

Leonid Ruvimovich’s life ended tragically and absurdly. He died in 1969 from peritonitis that developed after appendicitis. Although he was approaching his 70th birthday, he was still in his creative prime, leaving behind many unfulfilled plans.

Perelman received true recognition only after his death. In 2000, on the 100th anniversary of his birth, a two-volume guide to pathophysiology was published in his memory. His name has been given to lecture halls at medical universities in St. Petersburg. “Perelman readings” are held regularly. In 2015, a monograph was published on his contribution to world science.

Today, it is particularly evident how many of Perelman’s works were ahead of their time: his research on the permissive action of hormones formed the basis of the modern concept of hormone receptors; his work on neuroimmunoendocrinology anticipated the discovery of cytokines; and the parabiotic technique found new application in stem cell research [1–3, 5, 19].

Leonid Ruvimovich Perelman lived a life that would seem implausible if it were not documented. He was a man who retained his dignity and devotion to science during the blockade and in the camps, a scientist whose discoveries were decades ahead of Western science, and a teacher who trained a whole galaxy of outstanding researchers.

His legacy is not only specific scientific achievements, but also an example of how one can remain devoted to science even in the most inhuman conditions. In this sense, his life truly became the embodiment of victory over those social and historical circumstances that, it would seem, should have stopped any scientific development. When we read his works from the 1920s and 1940s, we are struck not only by their scientific depth, but also by the astonishing modernity of his thinking. Perhaps, the ability to think decades ahead is the main lesson that this outstanding scientist and courageous man left us.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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