Many new facts and theories have appeared in physiology. The solution of complex physiological problems required collaboration of physiologists, pathologists, biochemists, biophysicists, mathematicians, and other specialists. That was possible due to the rapid development of new technologies as well as the robust foundation laid by the outstanding physiologists of the 19th century.

This article describes the activities of outstanding Russian and Ukrainian physiologists of the 19th and the early 20th centuries. Among them were Ivan Sechenov, Nikolai Vvedenskii, Aleksei Ukhtomskii, Alexandr Samoilov and Ivan Pavlov in Russia, Ivan Shchelkov, Vasyl Danylevskyi, Adolf Beck, Bronislaw Verigo, Alexander Walter, Vasyl Chahovets, and Volodymyr Pravdych-Neminskyi in Ukraine.

Keywords: Ivan Sechenov, Nikolai Vvedenskii, Aleksei Ukhtomskii, Alexandr Samoilov, Ivan Pavlov, Ivan Shchelkov, Vasyl Danylevskyi, Adolf Beck, Bronislaw Verigo, Alexander Walter, Vasyl Chahovets, Volodymyr Pravdych-Neminskyi.

Background

In the 19th century, Russian physiology occupied a leading position in the world of science. This was connected to a variety of economic and political circumstances. In the middle of the 19th century, Russia went from a feudal serfdom society to a bourgeois-capitalist system. Foremost among these reforms was the abolition of serfdom in 1861. Then followed the transformation of higher education, the introduction of territorial self-government in 1864, and legislative and military reform [1]. At that time, achievements of natural science and physiology, primarily as the basis of the scientific worldview, were distributed and promoted actively in democratic circles of Russian society.

Ivan Sechenov and his talented disciples had determined the beginning of successful study of physiology in Russia. Most outstanding of them were Nikolai Vvedenskii, Aleksei Ukhtomskii, and Alexandr Samoilov. A great contribution to Russian and world physiology made Ivan Pavlov and his disciples. At the same time, the outstanding physiologists, such as Ivan Shchelkov, Vasyl Danylevskyi, Adolf Beck, Bronislaw Verigo, Alexander Walter, Vasyl Chahovets and Volodymyr Pravdych-Neminskyi have been working in Ukraine.

Ivan Sechenov

In the second half of the 19th century, the development of physiology in Russia is associated with the activity of Ivan Sechenov (1829–1905), who was considered a father of this science, as named by Ivan Pavlov. The latter wrote, «Before him, a professor of physiology was only a teacher who transmitted the results of European physiologists. Ivan Sechenov primarily became an eminent scientist. Sechenov became the initiator of physiological work on a large piece worldwide. He not only started Russian physiology but immediately won it a place of honor” [2].

Ivan Sechenov was born in Simbirsk province. He studied at the School of Military Engineers and later served in Kiev. Soon he left military service and entered the Medical Faculty of Moscow University [3].

He became interested in physiology, which he then studied in Berlin and Paris. He worked for a long time in the laboratory of the Viennese physiologist Karl Ludwig. For his work «On the influence of alcohol on the body», he made the device called an absorptiometer that could determine the distribution of gases and changes in their composition. Sechenov formulated the law of constant composition of alveolar air [4,5]. Under this law, the partial pressure of gases in alveolar air can be identified. These works of Sechenov contributed greatly to the understanding of gas exchange in the human body when flying at altitude and when working at great depths underwater. Sechenov first showed the role...
of carbon dioxide in the regulation of breathing. Sechenov returned to Russia in 1860, defended his doctoral thesis, and began working at the Department of Physiology at the St. Petersburg Medical-Surgical Academy [6].

This department was headed by professor Nikolai Yakubovich, who graduated from Kharkiv University in 1836. He was the author of works pertaining to the structure of the brain and spinal cord, for which he won an award of the Paris Academy of Sciences. The main scientific discovery of Sechenov was experimental confirmation of the central inhibition of reflex activity. In the years 1862–1863, Sechenov published in Russian, French and German his work regarding the presence of braking centers in the brain. This work made him famous in the world of science [3]. Sechenov first attempted to learn the laws of the brain, otherwise known as mental activity. Before Sechenov, no physiologist dared to look into the physiology of thought processes. Sechenov made a bold attempt to unravel the principle of the brain as an experimentalist, a physiologist. His work «Reflexes of the Brain» (1866) is a result of years of research. In the first part of the book, he analyzes involuntary movements. In the second one, he explores voluntary movements [7].

Sechenov has concluded that all mental acts develop by reflexes. Mental activity, as well as reflex activity, is impossible without external stimuli of the senses. As shown by clinical observations, when sense organs cease to transmit impulses to the brain, mental activity stops. Sechenov has formulated the main provisions of this as follows: «All acts of conscious and unconscious life are reflexes in origin... The organism without the external environment that supports its existence is impossible, so the scientific definition of the organism should include the environment affecting it". Sechenov has developed these ideas in «The Elements of Thought» and «Who should and How to Develop Psychology» [8]. These works were the beginning of the materialistic interpretation of psychology. Adverse working conditions forced Sechenov to move to Odessa in 1871. There, he studied the physiology of the nervous system and blood gases. In 1876, he returned to St. Petersburg, where he worked as a visiting professor for 12 years. Sechenov has proved that nerves and nerve centers can accumulate irritation. He has discovered electrical phenomena in the central nervous system. In 1888, Sechenov arrived in Moscow. At the age of 60 years, he began to serve as a privat-docent at the Department of Physiology, which was headed by Prof. B. V. Sheremetevskyi [5]. He delivered a course of lectures, which became the basis of his work «Physiology of Nerve Centers» (1891). His assistant A.F. Samoilov wrote, «Soon, I started to attend his lectures for students for which an assistant would have to prepare the
experiments. My amazement and delight knew no bounds. And now many years later, I have to say that a lecturer of such talent I have never seen in my life, neither before nor afterward. He possessed an excellent diction. I was especially struck by the force of logic in his lectures. Sechenov’s lectures were attended by students who listened very willingly» [9].

In 1891, B.F. Sheremetevskyi died, and Sechenov became the head of the Department. It was difficult to establish a new scientific work. Medical youth had little interest in physiology because «it did not produce income.» Construction of a home for the department was completed only in 1893 [10].

Sechenov sought to inspire and motivate students. The study of gases and respiratory function of the blood continued. Sechenov devoted to these studies more than 20 years of his life. Science owes to Sechenov its modern ideas about the relationship of various gases in arterial and venous blood, changes in the gas composition of the blood at low barometric pressure and respiratory function of blood hemoglobin in connection with the transfer of carbon dioxide. He proposed a method of the complete extraction of gas from the blood by his so-called mercury pump.

His main works in this area include «Absorption of CO2 by salt solutions and by strong acids» (1888), «The blood and lymph alkalis» (1893), and «A device for rapid and accurate gas analysis» (1896). He designed together with M.N. Shaternikov a special breathing apparatus, which allowed the determination of gas exchange at rest and at work in humans («Portable Breathing Apparatus», 1900) [5].

Studies in the new field of physiology – the physiology of labor – started at the University of Moscow. In 1895, Sechenov published the paper «Physiological criteria for setting the duration of the working day» (1894). In this work, Sechenov gives scientific justification to the basic requirement of the labor movement of an eight-hour working day [3,6].

Nikolai Vvedenskii and Aleksei Ukhtomskii

A great contribution to the study of the physiology of the nerves was made by a disciple of Sechenov, professor of physiology of St. Petersburg University Nikolai Vvedenskii (1852–1922).

Using a telephone set, he showed that up to 500 waves of excitation per second may pass through the nerve, but the nerve ending can transmit no more than 100–150 pulses per second. Thus, the different parts of the nerve do not have the same functional properties. He concluded that it is
possible to excite or inhibit every nerve depending on the pulse rate. Excessive stimulation causes inhibition. Thus, inhibition arises naturally from excitation, and they have a same cause. In 1901, Vvedenskii published his main work «Excitation, Inhibition, Narcosis,» where he formulated his theory of parabiosis [11]. A huge amount of experimental material allowed him to establish that the effect of various physical and chemical stimuli always ends up with a measure of inhibition. In this case, an excitable tissue ceases to respond to the stimulus. This state of inhibition he called parabiosis. Examining this condition in detail, Vvedenskii defined the essence of parabiosis. According to him, if the stimulus continues for a long time and constantly increases in rhythm, the nervous tissue will be increasing its state of excitement more and more. In its development, this state goes through three stages: equalizing, paradoxical and braking, the dimensions which depend on the nature of the stimulus. Thus, according to Vvedenskii, parabiotic inhibition is excitement that is distinguished by resistance and instability. He cited the example of anesthesia as inhibiting of the parabiotic type – it is a state of complete insensitivity that occurs in the area of living tissue or of the whole organism under the influence of drugs. This was the first unified theory of neural process – the theory of parabiosis. His subsequent work was devoted to more detailed development of this issue [10].

Vvedenskii’s work was continued and developed by his disciple Aleksei Ukhtomskii (1875–1942). In 1904, preparing for a lecture of his teacher the demonstration experience, Ukhtomski noticed that electrical stimulation of the motor points of the cerebral cortex of the dog during the act of defecation inhibits movement of the limbs and increases arousal in the centers of defecation enshrined in the lumbar segments of the spinal cord. As soon as defecation is completed, electrical stimulation of the motor cortex points begins to cause the normal movement of the limbs. This accidental observation attracted the attention of Ukhtomskii, who attempted to explain this phenomenon. A series of similar experiments confirmed his view that there is a pattern that explains the activity of central nervous system. This pattern Ukhtomskii called the dominant. The theory of the dominant was finally formulated in 1922 [12]. Since 1928, Ukhtomskii had taken up the problem of physiological lability associated with his doctrine of assimilation of rhythm. Ukhtomskii found the ability of organs and the whole organism to rebuild their rhythm of excitation in accordance with the rhythm of stimuli imposed from the outside [13].

One of his disciples, professor M.I. Vinogradov, gave apt characterization of the personality of Ukhtomskii: «Anyone who had ever met this deep and original mind, always remembered impression of tremendous mental strength and at the same time the extreme thinness and moving sincerity» [13]. The outstanding physiologist Ukhtomskii died in 1942 in Leningrad besieged by the Nazis [10].

A close disciple of Ivan Sechenov was Professor Alexandr Samoilov (1867–1930), who organized the large physiological laboratory in Kazan. Samoilov had known works in the electrophysiology of the heart and nervous system, which formed the basis of electrocardiography [9]. 15 years earlier than Henry Hallett Dale and Wilhelm Siegmund Feldberg in England, Samoilov proved that the specific chemical agents (mediators) are carried out with nerve stimulation on skeletal muscle [10].

Ivan Pavlov

The next stage of development of Russian physiology was associated with the works of the great scientist Ivan Pavlov and his disciples.
Ivan Pavlov (1849–1936) expanded and developed the reflex theory. Based on this theory, he disclosed a neural mechanism that provides the most perfect and complex forms of human and higher animal reactions to the external environment. This mechanism is a conditioned reflex. The organ of higher nervous activity is the cerebral cortex of the brain.

In 1879, Pavlov graduated from the Medical Surgical Academy and was invited to the physiology laboratory of S.P. Botkin at his clinic where Pavlov led the physiological and pharmacological studies. In Botkin’s laboratory, Ivan Pavlov completed his doctoral thesis «Centrifugal nerves of the heart» (1883) and then began research on the physiology of digestion [14,15]. In 1890, Pavlov was elected as a professor of pharmacology (and in 1895 professor of physiology) of the Medical Military Academy and as a head at the department of the Physiological Institute of Experimental Medicine in St. Petersburg. Pavlov did the first experiments on dogs when he was still a student at St. Petersburg University. He had the outstanding surgical skills that saved the lives of experimental animals many times. Most of the experiments that brought world fame to the Russian scientist, were conducted in the physiological laboratory of the Institute of Experimental Medicine [16].

Pavlov’s investigations on the physiology of the cardiovascular and digestive systems and the higher central nervous system are classical. In 1890, he published a work about the function of the stomach with sham feeding, in which for the first time he managed to take pure gastric juice from a healthy animal.

In 1894, Pavlov published his work on the small ventricle, showing communication with the general nervous apparatus of the stomach. In 1897, he published «Lectures on the work of the main digestive glands», which were generalizations of research in the field of the digestive system [15]. It was the actual creation of this section of physiology. Despite the language barrier, the works of Pavlov and his colleagues at the Institute of Experimental Medicine became known throughout the world [16].

At the Karolinska Institute (Sweden), which since 1901 got the right to award the Nobel Prize in Physiology or Medicine, Pavlov’s name was often mentioned in the lists of candidates for laureates. However, one thing had caused a question. Pavlov himself rarely appeared as a collaborator in the work of his employees, and the Karolinska Institute sent to St. Petersburg its representative, Professor R. Tigershted, to find out who headed the fruitful scientific activity of this group. As a result, in 1904, Pavlov was awarded the Nobel Prize in Physiology or Medicine «in recognition of his work on the physiology of digestion, which allowed our knowledge in this field to change and expand» [10,16].

Fig. 9. Ivan Pavlov (1849–1936)

Fig. 10. Experience of “sham feeding” the dog (by Pavlov): 1 – outputted outward segment of the esophagus, 2 – stomach fistula. For his research on the nervous regulation of the digestive glands Pavlov was awarded the Nobel Prize (1904)

Fig. 11. In the yard of the house on the Academic Pavlov street 12, there is a monument to the dog – a faithful friend of man and a nameless victim of science. It was installed near the Institute of Experimental Medicine at the initiative of Ivan Pavlov, who personally developed the project
The method of chronic experimenting that was designed by Pavlov allowed him to prove the principle of nervism – the idea of the decisive role of the nervous system in the regulation of the functional condition and activities of all body organs and systems. Three main principles were the basis of his conception: the unity of structure and function, determinism, and analysis and synthesis.

Studying the behavior of animals, Pavlov discovered new types of reflexes, which are formed and fixed under certain environmental conditions. Pavlov called them conditional, unlike the known inborn reflexes that exist from birth in all animals of this species (Pavlov called them unconditional). He also showed that conditional reflexes are developed in the cerebral cortex of the brain, which made possible the experimental study of the activity of the cerebral cortex in normal and pathological conditions. Resulting of this study, the doctrine of higher nervous activity appeared – one of the greatest achievements of natural science of the 20th century. Elucidation of the laws of the higher nervous activity of animals allowed a closer approach to the discovery of the laws of human brain activity. The result was the doctrine of the two signaling systems. The second was associated with the speech and abstract thinking that only a human possesses. In 1903, Pavlov presented the first report on conditional reflexes at the International Physiological Congress in Madrid. His generalizing work «Twenty Years of Objective Study of the Higher Nervous Activity (Behavior) of Animals» was published 20 years later (13) [17]. At the 15th International Physiological Congress in Leningrad in 1935, Pavlov was recognized by elder world physiologists [10,16,18].

**Physiology in territory of Ukraine**

Ukrainian scientists have worked very closely with the luminaries of Russian physiology.

Ivan Shchelkov (1833–1909) was the founder of experimental physiology at the University of Kharkiv. After graduating from the university in 1855, he specialized in the laboratories of Rudolf Virchow and Karl Ludwig (Vienna). In Ukraine, he was first to organize an experimental laboratory of comparative physiology. His main work was devoted to the study of gas exchange. He first established the difference in gas exchange between muscles during tetanic contraction and muscles at rest. He perfected the method for spectrophotometric studies of hemoglobin in the blood of horses and humans. The researcher founded the Kharkiv school of physiologists and was the author of a textbook on physiology (1871) [19].

In Shchelkov's laboratory, the first scientific work of Vasyl Danylevskyi was performed.

In the mid-70s Danylevskyi began his research activities at the University of Kharkiv. During these years, he established the influence of the striatum and frontal lobes of the cerebral hemispheres on respiration and the heart (1874, 1876). Danylevskyi was one of the first in 1876 to discover electrical phenomena in the brain. He first made a galvanometric study of the electrical activity of the cerebral cortex and showed that this activity was associated with brain activity. Fifteen years later he wrote, «The study of electrical phenomena in the brain enables us to investigate the objective material processes, which are the substrate for subjective mental phenomena» [20]. Danylevskyi expanded on the issues of psychomotor centers of electrical stimulation of various nerves and described the phenomenon of summation for the vagus nerves. He made original papers on the origin of humans and animals hypnotism, visual sensations in an alternating magnetic field, an electric pseudo-irritability of dead matter. In 1904, he first discovered the vagus nerve excitability of rabbit heart 24 hours after death. Danylevskyi was a prominent physiologist and endocrinologist. Under his guidance in 1923, domestic insulin was made [10,19].

Lviv University, the oldest in Ukraine, was founded in 1784. The first anatomical and physiological school was headed by Y. Kostrzhevskyi and T. Sedei. Since 1895, Adolf Beck (1863–1942) headed the Department of Physiology [21].

In 1890, Beck published the paper «Die Bestimmung der Localisation des Gehirn und
Rückenmarksfunctionen vermittelst der elektrischen Erscheinungen» in the journal «Centralblatt für Physiologie», which was devoted to the description of spontaneous and induced electrical activity of the cortex of dogs and rabbits. In this work, Beck studied the phenomenon now known in physiology as desynchronization [22].

The University in Odessa was glorified by the Nobel Prize winner (for 1908) Illia Mechnykov as the author of the cellular (phagocytic) theory of immunity. The outstanding physiologist Bronisław Verigo (1860–1925), who also worked there, is known as the author of the «cathodic depression of Verigo» and the «Verigo effect».

Cathodic depression of Verigo is a prolonged decrease in excitability, which develops secondarily after its increase in the zone of application of the cathode. Verigo effect shows how the degree of dissociation of oxyhemoglobin depends on the partial pressure of carbon dioxide in the alveolar air and blood. With a decrease in the partial pressure of carbon dioxide, the affinity of oxygen for hemoglobin increases, and this makes it difficult to transfer oxygen from the capillaries to the tissues. Verigo also dealt with other research areas, such as protective reactions of the organism, respiratory mechanisms, physiology of digestion and immunity. In particular, after studying the effect of cold, he proposed cooling as a means to reduce bleeding in animals during vivisection. Some conclusions from these works were used in the development of therapeutic hypothermia [24].

The outstanding Ukrainian physiologist Vasyl Chahovets (1873–1941) worked in Kyiv since 1910.

His main scientific works were devoted to the study of electrical potential of the body tissues. Chahovets was the first to prove experimentally that electric current causes polarization in the nerve and living tissues. His greatest achievement was the ionic theory of the origin of bioelectric potentials (1896). Chahovets developed a condenser theory of electrical irritation in living tissues (1906). Studying electrical phenomena in the stomach, Chahovets in 1935 proposed electrogastrogram as a method of studying the secretory activity of the stomach. Among other works of the scientist, it is of interest to study the electrical anesthesia, which clarified the nature of this phenomenon. Chahovets initiated the production of domestic electro-physiological equipment and the
application of mathematical methods in biology [21].

Great contribution to the development of neurophysiology was made by Volodymyr Pravdych-Neminskyi.

Working in Kyiv in 1913, Pravdych-Neminskyi recorded the total electrical activity of the brain using electrodes placed on the surface of the dog’s brain (not in the depths of the brain as previous researchers did). He discovered that the electrical activity of the brain had two main components: first-order waves of 12–14 Hz and faster waves of up to 35 Hz [25]. His method had been improved by Hans Berger in 1924 and tested on humans. Now electroencephalography is the most informative method in epileptology.

**Conclusion**

In hindsight, the achievements of outstanding physiologists in the 19th century, including Russia and Ukraine, seem obvious. In the last hundred years, physiology evolved at a startling pace. Discoveries in chemistry and physics and continuous improvement of physical and chemical methods of research created opportunity for a new approach to the study of many biological problems. Beyond doubt, in order to move forward, we must remember the past.

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Запорожець Т. М., Санік О. В.

НАРИСИ ІСТОРІЇ
РОСІЙСЬКОЇ ТА УКРАЇНСЬКОЇ ФІЗІОЛОГІЇ
XIX ТА ПОЧАТКУ XX СТОЛІТЬ

У фізіології з'явилося багато нових фактів і теорій. Вирішення складних фізіологічних проблем вимагало співпраці фізіологів, патологів, біохіміків, біофізиків, математиків та інших фахівців. Це стало можливим завдяки швидкому розвитку нових технологій, а також надійної основи, закладеної видатними фізіологами XIX століття. Ця стаття описує діяльність видатних російських і українських фізіологів XIX і початку XX століття. Серед них: Іван Сеченов, Микола Введенський, Олексій Ухтомський, Олександр Самойлов та Іван Павлов у Росії, Іван Щелков, Василь Данилевський, Адольф Бек, Броніслав Веріго, Олександр Вальтер, Василь Чаговець та Володимир Правдич-Немінський в Україні.

Ключові слова: Іван Сеченов, Микола Введенський, Олексій Ухтомський, Олександр Самойлов, Іван Павлов, Іван Щелков, Василь Данилевський, Адольф Бек, Броніслав Веріго, Олександр Вальтер, Василь Чаговець, Володимир Правдич-Немінський.

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