УДК 61 (091)+613.693

КОРИФЕЙ МИРОВОЙ ТРАНСЛЯЦИОННОЙ МЕДИЦИНЫ НИКОЛАЙ НИКОЛАЕВИЧ СИРОТИНИН: К 120-ЛЕТИЮ СО ДНЯ РОЖДЕНИЯ

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РЕЗЮМЕ. Историко-биографическая статья о жизни и творческих достижениях выдающегося советского патофизиолога Николая Николаевича Сиротинина (1896–1977) к 120-летию со дня его рождения. В статье обсуждается его фундаментальный и прикладной вклад в космические исследования, физиологию и патофизиологию адаптации, высотную медицину и учение о реактивности и резистентности, а также в изучение гипоксии. Из-за тесной связи его фундаментальных исследований с практическими потребностями экстремальной медицины и широкого прикладного внедрения его открытий и изобретений, Н. Н. Сиротинина по праву можно считать ярким ранним представителем трансляционной медицины [3 рис., библиография — 12 ист.].

КЛЮЧЕВЫЕ СЛОВА: Сиротинин Н. Н., правило Сиротинина, гипоксия, реактивность, резистентность, экстремальная медицина, аэрокосмическая медицина, анафилаксия, высотная болезнь, ступенчатая акклиматизация, кислородный коктейль.

CORYPHAEUS OF WORLD TRANSLATIONAL MEDICINE NIKOLAY NIKOLAEVICH SIROTININ: A 120TH ANNIVERSARY

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ABSTRACT: Historical and biographical paper about life and creative achievements of eminent Soviet pathophysiologist, Nikolay Nikolaevich Sirotinin (1896–1977) to his 120th anniversary. An article discusses his fundamental and applied contribution into space research, Physiology and Pathophysiology of adaptation, high altitude Medicine, and doctrine of reactivity and resistance as well as into research of hypoxia. Because of tight linkage of his fundamental studies to practical needs of Extreme Medicine and broad applied inculcation of his discoveries, Sirotinin is regarded as bright early representative of Translational Medicine [3 figs, bibliography — 12 refs].

KEY WORDS: Sirotinin N. N., Sirotinin's rule, hypoxia, reactivity, resistance, Extreme Medicine, Aerospace Medicine, anaphylaxis, high altitude disease, stepwise acclimatization principle, oxygen cocktail.

The only pathophysiologist in the whole history of this basic medical discipline to be awarded the prestigious "K. E. Tsiolkovsky's Gold Medal" for outstanding contribution into space research and Cosmonautics was the renowned Soviet scientist Nikolay Nikolaevich Sirotinin (fig. 1). N. N. Sirotinin was born on the 26th of November, 1896 in the city of Saratov, on the Volga River. His mother, Maria Alekseevna worked in municipal administration. His father, also Nikolay Nikolaevich Sirotinin (1856–1921), was a mathematician, specializing in Statistics. He worked as a municipal official (secretary of Saratov City Duma, later — speaker of City Duma) and was a person of leftist views combined with great energy: In his youth Sirotinin-senior was an active socialist revolutionary, follower of N. G. Chernyshevskiy, moved from Odessa to Saratov in 1889 to be closer

Fig. 1. N. N. Sirotinin (1896–1977) [2]

to his political leader; in elderly years he became well-known for his progressive social projects. It was thanks to his enthusiastic initiative, supported by Prime Minister P. A. Stolypin (former governer of Saratov) that the Nikolaevsky University of Saratov was established in 1909. Previously this city had never had a university. New educational establishment began with a single faculty — the medical one. In 1921 Sirotinin-senior, who worked after revolution in regional office of statistics, died of cholera. The Sirotinins had five children; all of them graduated from the newly established higher school of Saratov and dedicated their careers to Biology and Medicine. Nikolay Sirotinin-junior was a third child, single son in family. His sisters Olga and Lyubov' became biologists, Elena and Galina — specialized in Preventive Medicine, all contributed greatly in regional sanitary service and education. Nikolay graduated from gymnasium in 1915 with gold medal and entered Emperor's Saratov University the same year. Since 1919 young man started his practical scientific work in "Microb" Research Institute, recently transferred to Saratov from Petrograd. In 1919 he graduated from the Faculty of Medicine, Saratov State University, where he was a disciple of an outstanding pathophysiologist, to that moment — the youngest professor of Medicine in Russia — Aleksandr Aleksandrovich Bogomolets (1881–1946), who belonged to scientific

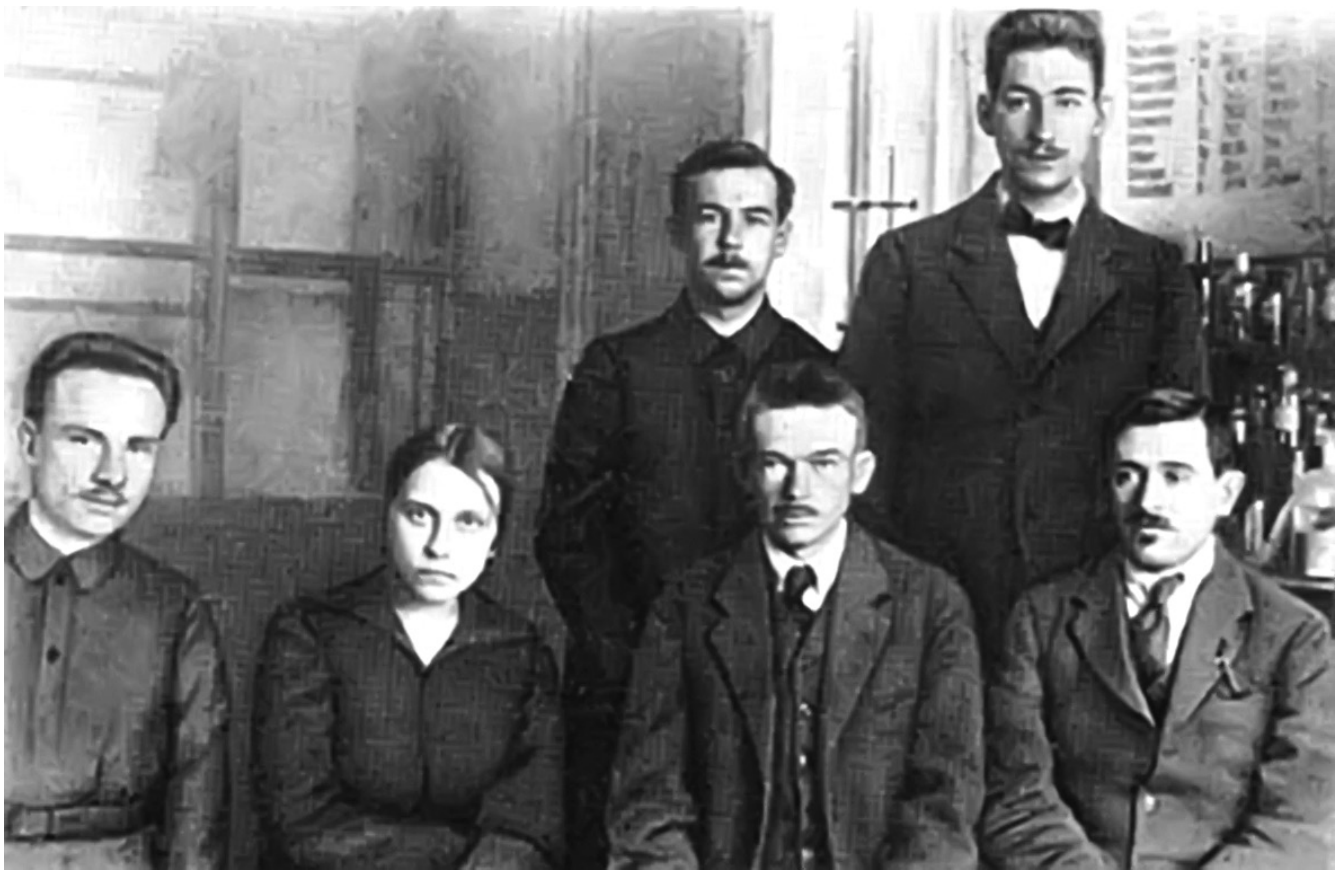

Fig. 2. The pupils and teacher in 1923 at Saratov University. First row, left to right: N. N. Sirotin in, N. B. Medvedeva, A. A. Bogomolets, E. N. Kogan. Second row: B. M. Schmidt, L. R. Perel'man. (URL: http://www.sgmu.ru/info/str/depts/patphys/index.html)

school of I. I. Mechnikov and V. V. Podvysotskiy (fig. 2). At the same time in "Microb" Research Institute, his supervisor was another bright representative of Mechnikov's school, an eminent epidemiologist Daniil Kirillovich Zabolotnyi (1866–1929). After graduation, the young scholar worked at alma mater under the guidance of A. A. Bogomolets until 1925. He studied the production and use of anti-diphtheria sera (1921) and maintained a movable anti-malaria laboratory of the regional railroad (1923). That period was full of epidemics, related to social cataclysms of 1914–1921. Because of constant practical involvement in huge work for prevention of infectious diseases, young graduate passed conclusive exams and obtained M. D. Diploma only in 1924 [1–3].

Later N. N. Sirotinin moved to Moscow following prof. A. A. Bogomolets, who accepted a position there. The career of young scientist in following post-revolutionary years developed rapidly. In 1925–1929 N. N. Sirotinin subsequently held the positions of Assistant Professor and Associate Professor at the 2nd Moscow Medical Institute. In parallel, he was research scientist in the Institute of Brain, where the brains of outstanding persons (including that of V. I. Lenin and A. A. Bogdanov) were preserved and studied [3]. The Brain Institute shared the building with Institute of Blood Transfusion, unique research facility, earlier established by A. A. Bogdanov, where A. A. Bogomolets headed the experimental department [4]. In 1929 at Kazan State Medical Institute N. N. Sirotinin became the Chairman of Pathophysiology Department (the oldest in Russia), thus returning to Volga River, and headed this department until 1938. Main subject of N. N. Sirotinin's research was reactivity and resistance of human organism. He paid great attention to the problems of allergy and immunity and to the evolutionary interplay of these phenomena, especially as regards the mechanisms of anaphylaxis and rheumatic fever. He was the leading domestic researcher in the field of anaphylaxis and dedicated his doctoral thesis (1928) to this topic. He studied metabolic changes and role of mononuclear phagocytes in anaphylaxis [2] and published first Russian guide in the field of Allergology (1934) [5].His closest disciple at Kazan was Andrey Dmitrievich Ado (1909–1997), who later became an outstanding pathophysiologist and successfully continued the trend of teacher's studies in Allergology.

However, most valuable discoveries and inventions N. N. Sirotinin made in the field of hypoxia and anti-hypoxic resistance. In Kazan and later in Kiev, where N. N. Sirotinin worked since 1934, he organized several research expeditions in the high altitudes of Pamir, Altay and Caucausus mountains and established a permanent biomedical research station on the peak of Elbrus, the highest mountain of Europe (fig. 3). This happened for the first time in the whole world history of Medicine. N. N. Sirotinin has demonstrated that *all immature animal forms are more resistant to acute hypoxia than mature ones* (for example, puppies compared to dogs, larvae compared to insects or tadpoles in comparison to frogs) [6–8]. This phenomenon is now known as "Sirotinin's rule" [9], which has influenced even air companies safety instructions for passengers, who normally are reminded to take on oxygen masks in emergency first on themselves and only after that — on their kids. In addition, N. N. Sirotinin has discovered the protective role of hypercapnia during acute hypoxia and the aggravating influence of hypocapnia on the course of hypoxia, revealed the increase of body resistance under the combined influence of hypercapnia, hypoxia and hypothermia, and deeply explored the mechanisms of hibernation [6–8].

Fig. 3. N. N. Sirotinin during research on the Elbrus Mountain [2]

The *stepwise method of high mountain acclimatization* and a special mixture for the adaptation of the mountain climbers ("*sirotinovka*") were invented and inculcated by him as well. N. N. Sirotinin studied experimentally the possibilities of blood oxygenation via gut. He is credited for invention of so called "oxygen cocktail" or a foamy substance containing a beverage drink (juice, milk, etc.) enriched in gaseous oxygen (1963) [6]. All these discoveries and innovations were of great practical significance and soon their broad application started in Aerospace, Navy, Military and Sports Medicine.

In Kiev N. N. Sirotinin worked at the Institute of Physiology since 1934 for all the rest of his life. In 1939 he was elected corresponding member of the Ukrainian Academy of Sciences.

During World War II Kiev was temporarily occupied by Nazi troops and N. N. Sirotinin was captured by the Nazis. Since he already was a scholar of European fame, they suggested him to be the director of some research institute in Reich. Sirotinin categorically rejected the collaboration, although it was a fatally dangerous act, and limited his activity with production of antiserum against spotty typhus, which he considered necessary for prevention of epidemics in occupied city [10, 12]. The Nazis tried to spoil his good reputation. In order to defame him, they spread misinformation about his "collaboration" with new administration, but finally the truth about the patriotic position of N. N. Sirotinin was revealed. After the war Nikolay Nikolaevich became one of the main experts in the biomedical part of Soviet space research program [11]. In 1955–1960 he was the Chairman of Pathophysiology Department in Kiev State Medical Institute. In 1957 he became a member of the Soviet Academy of Medical Sciences. N. N. Sirotinin was in charge of the training of Soviet cosmonaut Aleksei Arkhipovich Leonov before his first heroic trip to open Cosmos (1965). He was worldwide leading specialist in pathogenesis and treatment of high altitude disease [1–3]. Some of his early gerontological ideas had predicted the dependence of senescence on oxygen metabolism, which later was proven [13]. Sirotinin's great contribution into Pathophysiology brought him A. A. Bogomolets Prize of 1976. Nikolay Nikolaevich Sirotinin died in Kiev, 4 April 1977.

His works in comparative Physiology and Pathology of hypoxia and in reactivity of organism are still actual; they belong to classical milestones of Pathophysiology. Because hypoxia always accompany death of human organism, regardless of its primary reason, the meaning of Sirotinin's discoveries is (and always will be) very broad, including impacts on Resuscitation and Emergency Medicine, hyperbaric oxygenation, Stressology and Radiation Medicine. For example, a phenomenon well known since the beginning of XX century: Bergonié-Tribondeau law stating that the radiosensitivity of a tissue depends on the number of undifferentiated cells in the tissue, their mitotic activity, and the length of time they are actively proliferating [9], in fact is "reverse Sirotinin's rule", because radiation damage of cells depends of free oxygen radicals, obligatory agents of hyperoxia, so the more resistant to acute hypoxia said tissues should be less resistant to hyperoxia.

On 26 November 2016, domestic pathophysiologic community will celebrate the 120th jubilee of N. N. Sirotinin. Unfortunately, due to long-term informational separation between Soviet and Western cultures and to secrecy of many applied works by N. N. Sirotinin and his pupils, a lot of foreign pathophysiologists do not still know the glorious name of this Soviet scientist; and his legacy still waits for global appreciation. The article was written in order to fill this gap.

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