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# Efim Semionovich London (1868–1939) – coryphaeus of Immunology and Pathology, alumnus of Warsaw University

The period between 1890 and 1917 in the history of Russian science and culture is known as the "Silver Age". Within the terms of Cultural Studies, it was defined as archeo-modern, when Russian society went into modernity, still keeping many cultural archetypes which survived from the pre-modern past [1]. It was a time of rapid progress and vanguard contradictory innovations not only in industry and economics, but also in domestic fine arts, literature, and science as well. It brought global fame to many Russian intellectuals, beginning from Nobel Prize winners in Physiology or Medicine: Ivan Petrovich Pavlov (1849–1936) and Ilya Il'ich Mechnikov (1945–1916) and ending with coryphaei of Russian literature, music and ballet or forerunners of the world visual arts and theatre. These were not only ethnic Russians, but representatives of many nations of multinational Russian civilization.

The passionate overheating of that epoch resulted in three Russian revolutions. Finally, World War I and Civil War in Russia have stopped or redirected this rise of Russian thought, crushed the Russian Empire, and gave birth to the Soviet Republic and 5 other independent states of Europe. For many creative intellectuals these events were fatal and the ones that stayed alive focused mostly on surviving, so after a very bright and early debut in creative work their footprints were later lost in history, and sometimes the world knows only their surnames, if it remembers them at all. At the same time, they hold undoubted global priority in many areas, including medicine [2]. A few of them, however, inherited the creative passion of the Silver Age and brought it further into the 20th century, already being citizens of the new Soviet Russia. They found their place and pathway in new life, although

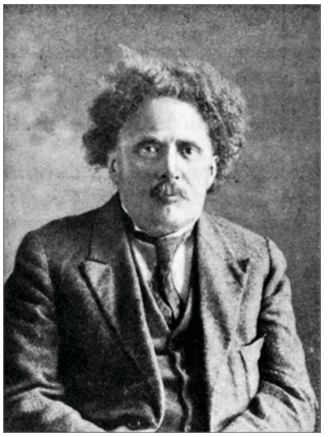

FIGURE 1.
E. S. London

in many aspects the coming century looked like the Iron Age, and not Silver… . This article describes life and creative achievements of one of the brightest persons among these Soviet heirs of the Russian "Silver Age" and is dedicated to the 150th anniversary of his birth.

An outstanding pathophysiologist, biochemist and immunologist, founder of Radiobiology – Efim Semionovich (Efraim Abel Shmuelovich) London (fig. 1) was born 28 December 1868 – to a Litvak family in a small town of Kalvarija, Kalvarija County, Suwałki Governorate, Polish Kingdom of the Russian Empire. There were two other children in the family: Emmanuel and Bluma in. Kalvarija was located on the highway joining Saint Petersburg and Warsaw and was known for its military outpatient clinic and a factory distilling medical ethanol. The young man decided to be a medical doctor and after graduating from the 3rd Gymnasium in Suwałki went to Warsaw.

During 1888–94 he was a medical student at Emperor's Warsaw University (he was accepted at the second attempt), a pupil of the renown Russian pathologist: Professor Sergei Mikhailovich Lukyanov (1855–1935), and inherited from his first teacher (fig. 2) a deep interest in pathology of metabolism. S. M. Lukyanov was a prominent figure among pathologists, broadly known in Europe, member of Florence Academy of Physics and Medicine. E.S. London later called him "the teacher of teachers of General Pathology – both domestically and abroad".

A graduate of Saint Petersburg Emperor's Military Medical Academy (where he studied in 1874–79) (fig. 3), Professor Lukyanov was one

FIGURE 2.
S. M. Lukyanov

of the global leaders in the studies of starvation, which he characterized as "typical pathologic process of endogenous nutrition". He is considered to be one of the pioneers of Pathochemistry, emphasizing that "behind the morphological structure always is lurking physical and chemical structure determining the pathological process". It was S.M. Lukyanov who established in 1890 in Warsaw the first ever course of Cytopathology in world academic practice and published there over 60 academic papers, including the textbooks of Cytopathology and Cardiovascular Pathology translated into German (1891) and French (1895). Another his pupil of that period was Ludwig von Aschoff (1866–1942). S. M. Lukyanov influenced E. S. London greatly, and the pupil inherited an interest in Pathochemistry of starvation, nutrition and metabolism from the teacher, as well as in the physical backgroundof pathologic phenomena. S. M. Lukyanov was born in an Orthodox family, studied at Lutheran gymnasium in Saint Petersburg and became one of the key faculty members at the University of Warsaw in Catholic Poland (since 1886). (fig. 4).

Needless to say, London's teacher was a man of very broad ecumenicity and progressive humanitarian views, close friend and bio-

FIGURE 3.
S. M. Lukyanov (2nd from the left) as a cadet of Emperor's Military Medical Academy during laboratory classes

grapher of the famous Russian religious philosopher – cosmist Vladimir S. Solov'ev (1853–1900), and hence he contributed not only to Experimental Medicine, but also to Philosophy and Art History He characterized Philosophy as "a bridge between Science and Faith". Later, in the Saint Petersburg period of his career, he became a statesman. For several years, by the Tsar's edict, S. M. Lukyanov was the Chief Procurator of the Holy Synod of the Russian Orthodox Church (the supreme official supervisor for the largest confession of the Empire), being an experimental pathologist at the same time. That was a unique case in the new clergy history [3].

E. S. London took from his polymath teacher the broad spectrum of creative activities, as well as the teacher's versatile cognitive style, and never limited himself within the borders of Pathology only. He appeared to be a very grateful and faithful disciple and in the next century did a lot to look after his old teacher, who experienced serious problems with new powers of Soviet Russia. Their relations through the whole life were exemplary mutual attitudes of teacher and pupil. Under the guidance of such a unique intellectual as Prof. S. M. Lukyanov,

FIGURE 4.
Emperor's Warsaw University in the period of Lukyanov's professorship and London's studentship there, source: https://www.uw.edu.pl/uniwersytet/historia/ accessed: 18.11.2018

young Efim started his research career very early, while still being a student. He suggested a mathematical method for evaluation of bacterial growth and was awarded a silver medal for his first course research paper. It was published on 9 pages in "Proceedings of Warsaw University" (1893) and dedicated to cardiac effects of atropine [4]. After graduation "cum laude" from Warsaw University (1894) E. S. London worked as a rural Zemstvo physician in a village at Marijampole volost, Lithuania, close to his home town.

The Russian Empire of that period had neither a Health Ministry, nor any centrally driven system of health care. Instead, there was the Zemstvo Medicine, quite an effective system of mass available health care in rural and provincial areas, self-ruled by local elected organs (Zemstvos) and guided by all-Russia's Congresses of Physicians. It was financed from the local property tax distributed by Zemstvo deputies, hence the salary of a Zemstvo doctor was quite attractive, and such

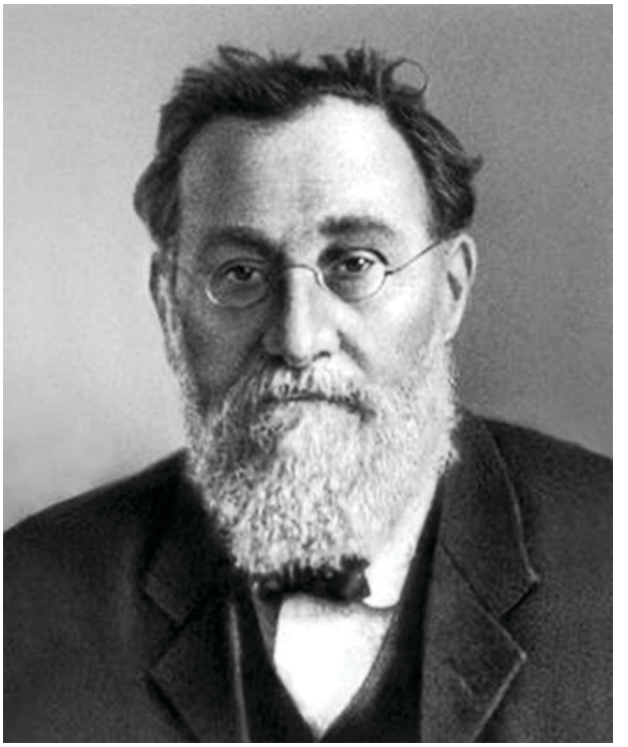

FIGURE 5.
I. I. Mechnikov

positions in many regions of the Empire were highly competitive [5]. The young physician, however, was firmly intended to become an experimental scientist. As many Zemstvo physicians, he combined medical practice with research based on local material. The result was an excellent paper in Forensic Medicine (which was the second major field of Lukyanov's activities) – on comparative biological characteristics of human and animal hair as an object of forensic investigation, later published as a separate article [6]. His graduation paper was awarded a gold medal by the decision of Warsaw University Academic Board of 16 May 1895. Later he even taught Forensic Medicine part time at the Saint Petersburg Law School (1899/1900).

As an excellent young scholar later, in 1900 E. S. London by recommendation of his teacher was sent to postgraduate studies, at the expense of the state, to Ilya I. Mechnikov's lab at Pasteur Institute, Paris, where he took from his second teacher I. I. Mechnikov (fig. 5)

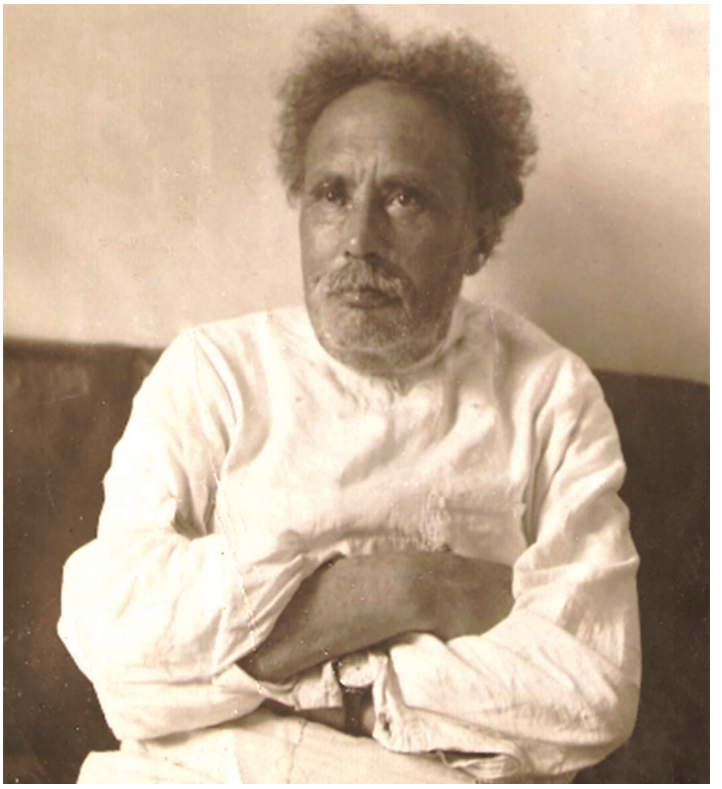

FIGURE 6.
E. S. London in IEM (circa 1935)

a deep interest in a recently born science of Immunology and in items of Immunopathology. Mechikov's lab in Paris was a frontier of translational immunological and microbiological studies, leading in the medical world of that time, a school for many international trainees [7].

I.I. Mechnikov during that period inspired E. S. London on several pioneering works in neuroimmunology and in animal modeling of autoimmune diseases. Thus, it was E. S. London (together with another Mechnikov's disciple – Ivan G. Savchenko (1862–1932) who has first demonstrated influence of CNS over immune response and showed that dove decortication cancels its inborn anti-anthrax immunity, which was a pioneering step in Neuroimmunology (1896) [8]. He also described (in 1900) together with Aleksandr M. Besredka (1870–1940) true anti-haemolysins – which were in fact first anti--idiotypic autoantibodies [9]. E. S. London demonstrated (1901) the

presence of natural autoantibodies in healthy young adults (these were antibodies against self sperm antigens or anti-spermolysins), thus refuting the "horror autotoxicus" principle, recently proclaimed by an opponent of Mechnikov's school – Paul Ehrlich [10, 11]. Jointly with another Mechnikov's disciple, Sergei I. Metal'nikov (1870–1946), E. S. London created the first model of autoimmune orchitis and was the first to obtain artificial antibody-mediated contraception (1900–01) [10]. The phenomenon of stress-induced immunodepression was also discovered by E. S. London during chronic experiments with electric stimulation of n. ischiadicus of a rabbit (1896–97), long before the term "stress" was used in psychology and the stress reaction described [12]. In this research he measured complement system activity, which was the first study on complement in Russia.

In 1895 he was invited by his former teacher S. M. Lukyanov, who from 1894 was the head of the Emperor's Institute of Experimental Medicine (IEM) – to the capital of Russia as a Deputy Chief of the General Pathology Department, where E. S. London worked continuously from 1895 till his last day – for more than 43 years (fig. 6).

The IEM, recently (1890) established in Saint Petersburg, was an excellent complex research facility, designed under the supervision of I. P. Pavlov. It was to the moment the largest institution of this kind in the world. The position offered was very honorable for such a young scientist and, for sure, E. S. London was obliged to S. M. Lukyanov, who invited him remembering his exceptional scientific potential from their previous work together in Warsaw. It was a really fortunate choice.

Director of IEM S. M. Lukyanov set in front of his pupil the ambitious task of bringing the laboratory to the most advanced methodological level. The globally hottest areas of medical research in that period were Immunology and Radiology. S. M. Lukyanov funded the purchase of the modern equipment for E. S. London's lab. And the pupil did not disappoint his teacher regarding both of these trends. He displayed the excellence of both experimentalist and theoretician.

In 1900 E. S. London defended his doctoral thesis, *On the doctrine of haemolysins* [9], where he described not only autoantibodies to red blood cells, but also antihaemolysins or the first anti-idiotypic antibodies ever recognized. He postulated the physiologic regulatory role for both anti-sperm antibodies and their anti-idiotypes, which was an absolutely revolutionary thought for that time, when autoimmunity related exclusively to disease. As early as in 1900–01, when contra-

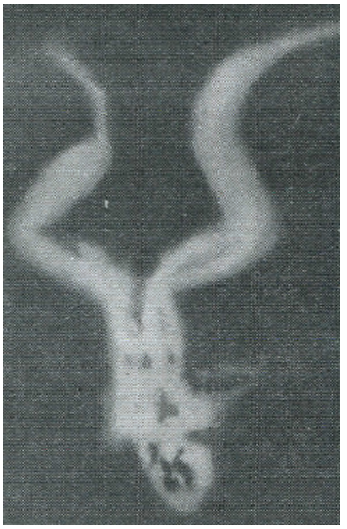

FIGURE 7.
First radioautograph in the history of biomedicine: a frog after inhalation of radon, preparation by E. S. London (1904) [17, p. 174]

dictions between adepts of cellular and humoral concepts of immunity seemed absolutely irreconcilable, he pointed out that both theories should merge into one, because humoral and cellular phenomena of immunity most probably have the same cell origin [9]. As Head of Pathology lab in IEM (since 1903), he contributed greatly to the doctrine of physiologic (natural) autoimmunity, discovered natural anti-sperm autoantibodies in healthy individuals and suggested the first autoimmune model of infertility and a successful experimental immunological contraception method [10].

He was a world pioneer in the field of Radiobiology with first studies of X-ray effects on living tissues (1897) [13], first experimental proving of radiation-induced cell death (1902–03) [14], first experimental model of radiation sickness (1903), first radioautograph – whole-body image of a frog which inhaled radon (1904) [15, 16] (fig. 7).

E. S. London is the author of the very principle of histoautoradiography (1904), a technique which is now a part of gold standard in the arsenal of any biomedical research centre [13, 14, 15, 16, 17] (fig. 8).

Also he has successfully performed first experimental cancer therapy by radiation (1902–1903). The primacy of E. S. London and co-author of this research [14], surgeon Semion Victorovich Goldberg (1873–

FIGURE 8.
Left – radioautograph of a rat's adrenal cortex, zona glomerulosa – with tritiated thymidine. The match over the premitotic nuclei witnesses for active DNA reduplication, a mitosis is observed over the matched nuclei (preparation by L.P. Churilov).
Right – creator of autoradiography method E. S. London in the beginning of XX century

–1940) in this field is globally recognized. It was the first histologically proven cure of a basal cell facial skin carcinoma in 2 patients. Later London's pupil, a lady-physician Lyubov M. Horovitz-Vlasova (1879–1941) tried radiotherapy also in kala-azar (1906) [18]. Unfortunately, cancer, presumably related to radiation exposure during scientific experiments killed S. V. Goldberg, as well as many pioneers of Radiology.

One of the brightest discoveries of E. S. London in the early history of Radiobiology was a phenomenon of greatest radio-sensitivity of gonads, bone marrow and lymphoid tissue and relative radio-resistance of the brain. He described radiation as a cause of immunodepression long before the appearance of the concept of immunodeficiency [17, 19].

First ever published monograph in Radiobiology was also authored by E. S. London (1911). It was ordered to him by Leipzig Academic Society, because of his status of current renowned leader in the field, and issued in Germany under the title "Radium in Biology and Medicine" [16]. The book is still being reprinted (8 editions), translated and cited, even nowadays [16, 17]. Earlier one could find on this topic only articles and just one chapter of a selection book written by Charles Baskerville [20].

E. S. London was a scholar with broad university education and a deep interest in Physics and Mathematics. For example, he published

later (1922) one of the first Russian popular science books on the theory of relativity, appreciated by leading physicists [21]. The scientist clearly saw the broadest prospects of nuclear research. Relying on support from S. M. Lukyanov (who by that time was a deputy and acting minister of education, later a member of the State Council, a senator and chief procurator of the Holy Synod, close to royal court), E. S. London tried to convince the Russian authorities that radium studies should be prioritized. At that moment he was already noticeable public figure. The archives of his family, now kept at the Rockefeller foundation, show that E. S. London was scientific co-editor of the most popular Russian journal "Niva", and a frequent guest of the royal family [22]. Professor E. S. London sent a letter to the Emperor in which he predicted that the "development and might of the nations in the twentieth century will depend on degree of their possession with the technology of radium". By that time in the world there were no more than 48 g of this pure metal, and in Russia – only tenths of a gram. In that period each gram of radium cost up to half a million gold rubles. The historical letter by E. S. London, together with the famous letter to the tycoon Pavel P. Ryabushinsky (1871–1924) – by another outstanding natural scientist Vladimir I. Vernadsky (1863–1945), who first realized the potential of nuclear energy, convinced the addressees and pushed both power and business in Russia to the prioritized financing of radiological research and expeditions in order to find nuclear ore in Russia [20]. These efforts later facilitated the rapid development of Russian nuclear science and technology, as it provided Russia with early purchases of radium and the priority development of nuclear science. Both the tsarist government and private businesses invested a lot of money in this new area of science under the influence of many factors, but academic and public activity of E. S. London was not the least of them. Soviet Russia made its own radium a bit later, by the efforts of a student of V. I. Vernadsky, an Assistant Professor to the Chair of Chemistry at Petrograd University (later – academician), Vitaly G. Khlopin (1890–1950). It happened on 1 December, 1921. Hence, the nuclear research in Russia was started long before the Soviet period, and E. S. London, who collaborated with Roentgen--Radiological Institute established in Petrograd in 1918 and headed by his pupil Dr. M. I. Nemenov, can be regarded as one of the most important figures in the early global and domestic history of Radiobiology and nuclear research [17, 20].


FIGURE 9.
E. S. London installing a cannula for angiostomosis

E. S. London, as well as his teacher, devoted a lot of effort to the studies of Physiology and Pathology of digestion and nutrition [23]. As early as in 1907 he obtained the first proof that not only amino acids, but also short peptides can be absorbed in the animal gut [24]. These data were highly appreciated, cited and commented by a coryphaeus of physical chemistry, Swedish Nobel Prize laureate Svante August Arrhenius (1859–1927) [25], who visited London's lab and maintained good relations with the eminent Russian scientist.

The career of the ascending young scholar in IEM was not absolutely cloudless, although it progressed quite rapidly. E. S. London was an experimental surgeon of excellent mastership. His studies of digestion were performed by method of serial cannulation of different

portions of gut conveyer, thus he was able to follow stepwise digestion of nutrients. Later he improved the cannulation method and constructed cannulae with 2 barrels, giving an option to block a portion of an empty organ. After that he invented special silver cannulae valid for installation into large blood vessels (fig. 9).

The idea was simple and revolutionary: To check and compare the biochemical content of blood from an inlet and outlet of organ circulation, sampling blood and bioptates, and thus consider the metabolic requirements and functions of a cannulated organ. He called this method "angiostomosis" (1919). The modifications with cannulation of the empty organs and brain sinuses were called by E. S. London "organostomosis" (1923, 1935) and "sinusostomosis" (1936) [17, 26–32]. These techniques gave the option to evaluate intermediate products of organ metabolism. The content of arterial blood E. S. London considered as being an invariant, standard menu offered to all organs, but the content of venous blood reflected the metabolic roles and needs of different "customers". It was advantageous to study in vivo organ as a whole, keeping all its neural and humoral regulation in comparison to in vitro studies of its cells or pieces [17]. Later this original approach, a precursor of the modern cybernetic principle of "black box", brought to E. S. London several breaking discoveries in duodenal, cerebral and hepatic metabolism, as well as in DNA structural studies; and after many publications in 4 languages came both world fame and Nobel nominations (see below). But, so far he was just a talented scientist working at imperial research centre side by side with a coryphaeus of world science – Nobel Prize winner Ivan P. Pavlov, who also studied digestion, used a prototypic cannulation method and enjoyed a global reputation of an excellent experimental surgeon. The relation between Pavlov and London's teacher Lukyanov was long existing, but not simple. Sergei and Ivan were classmates at the Military Medical Academy. Pavlov was his elder, he came to the Academy after a full course at Petersburg University (Physical and Mathematical Faculty, Natural Science Division) in order to get his second M.D. Diploma. Sergei, however, progressed more rapidly during their common experience of military medical education than his older friend Ivan, and was senior sergeant at the moment when Pavlov was still an ordinary cadet (fig. 10).

Moreover, the academic prize of 1879 for the best research also went, by unanimous decision of 16 professors, not to Ivan Pavlov, but

FIGURE 10.
Clinical studies in Emperor's Military Medical Academy, a lesson of auscultation. To the right from the teacher stand cadets: V. M. Bekhterev (with notes in his hands), S. M. Lukyanov, I. P. Pavlov (from Museum of S.M. Kirov Military Medical Academy, courtesy of Assoc. Prof. A.E. Korovin)

to Sergei Lukyanov for his graduation paper "Character of Metamorphosis in Feverish Organism". A position at Warsaw University was offered to I. P. Pavlov, but he rejected it and S. M. Lukyanov became full professor in Warsaw University. I. P. Pavlov (as well as I. I. Mechnikov) rejected the offer of Prince A. P. Oldenburgsky, key sponsor of the research facility, to be the head of the newly established IEM, and this position went to S. M. Lukyanov, who promoted E. S. London. Later Pavlov became Nobel Prize winner (1904) and S. M. Lukyanov had an excellent career of statesman (1905–1911) and ascended to Senate and Government (Chief-Procurator of the Holy Synod was a rank of minister). He had to apply many efforts to the reformation of orthodox clergy in Russia and was a categorical opponent of Grigory E. Rasputin (1869–1916), whose influence on the royal family irritated clericals. Rasputin was a strong challenger, and Lukyanov with every year had

less time for experimental science at IEM [3]. Now he was no longer director of IEM, although kept the position on the Advisory Board of this institution. Meanwhile, the attitude of I. P. Pavlov towards E. S. London worsened. Initially Pavlov appreciated London and was of very high opinion on the scientific potential of the young experimentalist. In 1902–07 London used in his experiments the technique of "Pavlov's sac" and was instructed by the Maestro of animal experimentation on how to do that [3, 17]. The reason of spoiled relations was the scandal that broke out between them in 1910 because of a disagreement over who should be the surgical instructor of a young Belgian physiologist -trainee E. van der Pűt. The trainee came with the intention to study at Pavlov's lab, but maestro postponed their meeting several times. Finally, the Belgian came across London, who misinformed him on the true desire of Pavlov to see young surgeon at his lab and in fact, "lured" the trainee to London's lab. Pavlov was infuriated and privately derided London as "insolent Yid". A guest surgeon complained to a trustee of IEM, Prince A. P. Oldenburgsky, which provoked a "court of honour". The colleagues pointed to London's unethical behaviour. The trustee was about to fire London, but Pavlov himself, in spite of his very sharp initial reaction, took him under protection and expressed the decision that "a man of such great talent shall continue to work for the benefit of the Institute and Motherland". Later Pavlov, discussing this episode with his pupil Boris P. Babkin (1877–1950), mentioned that he had to protect E. S. London from discharge, because as a Hebrew London might not have found another position appropriate for his scientific merits [33].

World War I forced many scholars to re-direct their studies to the applied sphere. E. S. London was not an exception. In 1914–18 he served in Russian Army, being responsible for bacteriological and anti-tetanus service (fig. 11). Initially in the years 1914–16 he worked as a head of bacteriology labs in military hospitals near Riga. Later he and his co-workers worked on antisera and toxoid production in a bacteriological lab, isolated on one of the island forts of Kronshtadt, a navy base of Russia in Baltic Sea (in so called "Plague Fort") [3, 17], where London developed the original most effective method of tetanus toxin purification and its titration for making of a toxoid. This work was started even earlier and completed together with another one of Mechnikov's pupils – Vyacheslav M. Aristovsky (1882–1950) [34]. In 1918 E. S. London returned to civil life.

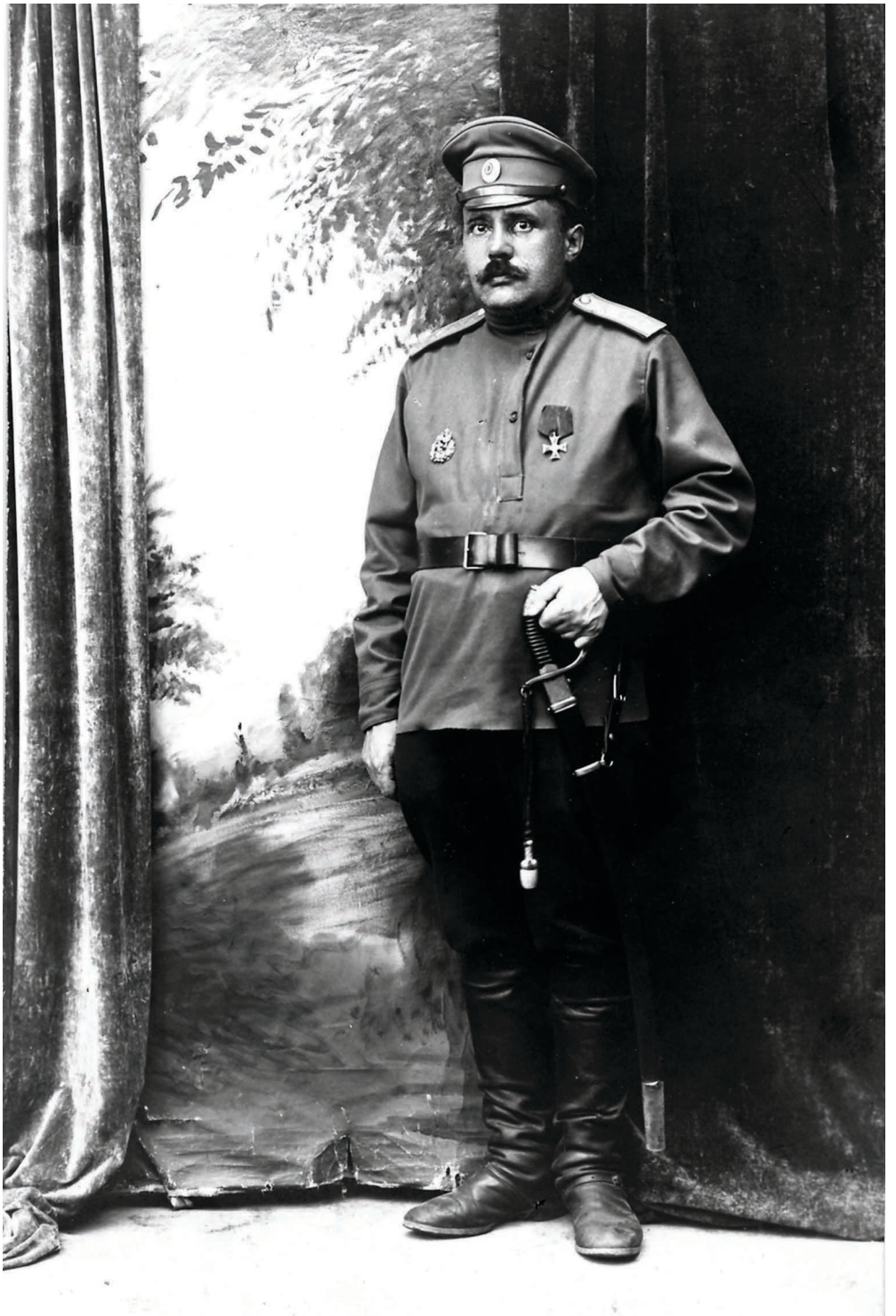

FIGURE 11.
Colonel E.S. London in Emperor's Russian Army, circa 1914 (>From Archive of IEM Museum, courtesy of Prof. Yu.A. Mazing)

He was a person of leftist, democratic views. In spite of his rapid career at the Emperor's Institute of Experimental Medicine, one of his publicist books about first Russian revolution issued in 1907 at Berlin (under nickname "Lyadov") was forbidden in Russia by censors. The heavy experience of the war years acquired in hospitals, where he witnessed a lot of suffering, strengthened his anti-tsarist position. After the revolution of 1917 E. S. London entirely supported the Soviet power, and from 1918 to his last day worked at IEM as Head of Pathology Department. The Soviet period was an acme of his academic career.

The new government proclaimed both secondary and higher education free and widely accessible to ordinary people. That is why, in spite of the economic collapse after the Civil War, many victims and millions of émigrés, to the middle of 1920s the number of secondary schools in Petrograd-Leningrad doubled as compared to 1913, and not only did all of the old universities and academies continuously function, but another 12 were established, although the total population of the city significantly decreased. Besides, many new research institutes were established.

E. S. London collaborated with several old and newly-established universities and research institutes of the USSR and contributed greatly to early development of the Soviet Biomedicine. In 1928 he founded and until last day headed the Department of Biochemistry (the first ever in Russia) at Leningrad State University. He also established the Department of Pathophysiology at the Leningrad Paediatric Medical Institute (1932), first, and for many decades the only, graduate school of paediatric medicine in the world. This department was a place where the author of this article learned and later taught Pathophysiology for more than 30 years. Old faculty members who worked under London's guidance in their youth, in personal conversations (in the 1980s) with the author of this paper recalled that E. S. London had very extravagant habits. For example, when having dinner he used to mix the first, main and sweet dishes on a single plate, because "in the gut all this food anyway has to be mixed!".

The prolific scholar also collaborated with the Veterinary Institute (since 1921) and with State Institute for Refreshing of Physicians (since 1926). He lectured at the Agricultural Institute as well. It means that at least 3 Chairs of Pathophysiology, one Chair of Biochemistry and one research Department of Pathology in St. Petersburg–Petrograd––Leningrad were founded and for some periods headed by him. At the

FIGURE 12.
International group of scholars, invited by the Swiss government, during an expedition to the Alps in research of high altitude hypoxia's effect on metabolism. E. S. London sits near his experimental dog, next to the left of him standing E. Abderhalden and his pupil N. P. Kochneva (Davos, 1926). The fact of true absolute erythrocytosis during high altitude acclimatization has been proven during this expedition (from IEM Museum, courtesy of Prof. Yu.A. Mazing)

State Institute for Refreshing of Physicians he insisted on establishing a special department for his old teacher – S. M. Lukyanov (where he later was the only co-worker!). London used all his influence in order to protect the ex-statesman of Tsar from the allegations of Soviet power until Lukyanov's last days and wrote an official obituary of his teacher [35].

E. S. London was for 2 decades the "face" of Soviet biomedical science abroad. He enjoyed world fame since the pre-war period and maintained good relations with other leading scientists of the planet, regularly working in their labs (especially with those biochemists who studied proteins and nuclear acids: Albrecht Kossel (1853–1927), Hermann Emil Fischer (1852–1919) and Emil Abderhalden (1877––1950) (fig. 12). The last one, an outstanding German-Swiss biochemist

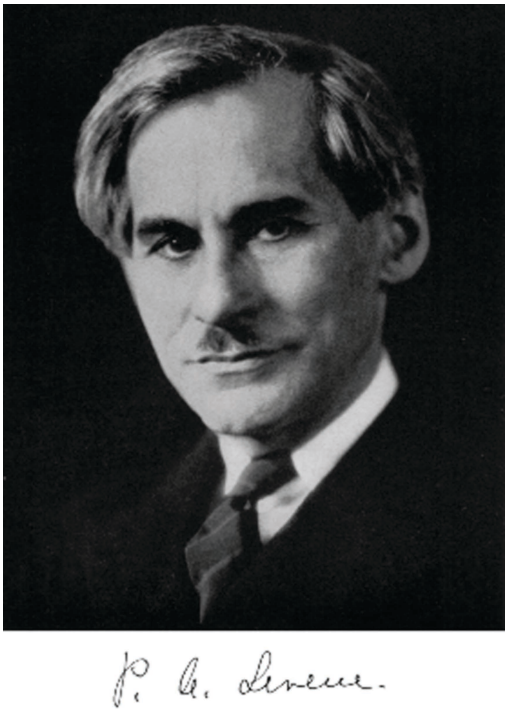

FIGURE 13.
Portrait and autograph of P. A. Levene [38]

was his close personal friend. After the revolution in Russia these relations were kept and even broadened.

London maintained intensive academic communication with Ulf Svante von Euler (1905–1983) from Sweden and Hans Krebs (1900–1981) from Germany, discussing the questions of a newly shaped area of biomedicine that was physiological chemistry. His unique method of angio-organostomosis put him in the first ranks of scholars who developed this branch of life sciences and branched Pathochemistry from the trunk of Pathophysiology. The archives of Hoppe-Seyler's Zeitschrift for 1933–34 contain a letter exchange between E. S. London, who was already a world famous Maestro of metabolic studies, and a young talent – Hans Adolf Krebs – with hot discussions and deep arguments of the two researchers about the course and intermediate metabolites of the urea cycle in liver. They could hardly put together their views based on different methods (organostomosis in vivo versus slices in vitro) [36]. It was E. S. London who discovered the priority

of glucose in brain energy supply and determined the daily energy requirements of the brain. His method of organostomosis allowed to evaluate differential requirements of various organs in various kinds of fuel substrates, as well as improve data on metabolic coefficients in different periods of starvation, in diabetes mellitus and tuberculosis [37]. The techniques of angio-organo-sinusostomosis led him to several other priority discoveries, such as: the first model of duodenal insufficiency, pioneering data on hormonal nature of specific dynamic action of food on basic metabolic rate (1936), important evidence of endocrine activity of duodenum, later confirmed by the scholars, discovery of gut hormones and disperse endocrine system [17].

E. S. London was elected full member of several academies and scholarly societies, like the Leopoldina Academy in Halle, Germany (1925), the Harvey Society in the USA (1928), and the American Academy of Arts and Sciences in New York (1929). From 1935 he was Honorary Scientist of RSFSR (supreme professional achievement for Soviet scholars). His scientific heritage includes over 300 publications and a posthumous selection of his papers, re-published by Soviet Academy of Sciences twice (1956, 1968) [17]. Among his pupils 25 became Doctors of Science, including outstanding pathologists, biochemists, oncologists, internists, radiologists, paediatricians and veterinarians.

In 1927, in spite of the absence of formal diplomatic relations between USSR and USA, the renowned Soviet scholar was invited by the Rockefeller Institute in New York to visit the United States and to do research there. The old Bolshevik, People's Commissar of Health Nikolay A. Semashko (1874–1949) facilitated this trip and twice prolonged it – by initiative of the American side. London went to USA by ship (with his own money) with his unique cannulae and 2 cannulated dogs, accompanied by his wife, Raissa Abramovna Eshman-London, a gifted piano-player and the future mother of his 3 sons.

Although his pre-operated dogs perished during the cross-ocean trip, immediately after arrival E. S. London reproduced the operations on new animals. Animal defenders were already very active in New York, which is why Professor London had to operate on dogs in Canada and travel with the prepared animals back to the USA. The new cannulae were shipped from Soviet Russia, because in the USA local workshops could not reproduce them. During London's two long academic visits to the USA, he was working together with a friend from

FIGURE 14.
Left: Musical duet of Efim and Raissa London (1938); right: Experimental operation on a dog by trio of E. S. London and his pupils. In the middle stands Nikolay N. Zaiko (1908–1991), future famous pathophysiologist, and Dr. N. P. Kochneva assists

his youth, Russo-American biochemist: Phoebus Aaron Theodore Levene (1869–1940) [aka Febus Fishelevich or Fedya Levin for short]. P. Levene (fig. 13) graduated from Emperor's Military Medical Academy in Saint Petersburg; he was a student of I. P. Pavlov and of a famous composer and medical chemist Aleksandr P. Borodin (1833–1887).

To that moment he was a globally leading researcher of nucleic acids [38]. Thymonucleic acid obtained from thymus was very difficult object for chemical analysis (as we know nowadays – because of a mixture with ribonucleic acids abundant in thymic tissue). However, experimenting with London's organostomosis-angiostomosis method (feeding hungry cannulated dogs with thymonucleic acid and checking their portal blood) London and Levene discovered in 1928–29 deoxyribose as a constituent of DNA, and offered the first ever model of DNA structure. Their articles, published in "Science" and "J. Biol. Chem." attracted attention of specialists worldwide and coined the very term "DNA" [39, 40]. That was the most important achievement in nuclear acid Biochemistry after A. Kossel and before Erwin Chargaff (1905–2002). Curiously, the restoration of Levene's ties with the scientists of Soviet Russia was facilitated by a random event. I. P. Pavlov during his visit to the United States in 1923 was robbed at the Grand Central railroad


FIGURE 15.
Monuments to E. S. London in St. Petersburg. Left: by M. G. Manizer (IEM, 1962); right – a tombstone on his grave (1949)

station by a pickpocket. His former student P. A. Levene was the only one in New York whose address the great physiologist remembered. Levene helped his teacher to restore documents and tickets. I. P. Pavlov learned more of Levene's work and hardships with nucleic acid structural analysis, suggested to use enzymatic hydrolysis in vivo and promoted Levene's relations with Soviet colleagues. In 1924 Levene visited the city of his youth and met Pavlov's colleagues, including E. S. London. Plain digestion with Pavlov's fistulas appeared to be unsuccessful, but at the end of 1920s London's modification of fistula method lead to a breakthrough [41].

During his stay in the US, E. S. London not only experimented but also had meetings with the members of local Russian-speaking community and friends of Soviet Union [42]. He delivered public lectures on physiologic effects of music based on his previous research and perspectives of musical therapy [43], and his wife concerted with great success. E. S. London also was an enthusiastic and skilful musician, a master of flute. Their family duet concerted until the last days of his

life (fig. 14). The trip gave to E. S. London a fortunate opportunity to meet his long missed brother and sister, who lived in USA.

The political terror of the late 1930s in the USSR fortunately did not affect E. S. London, always loyal to Soviet power. The organo/sinuso/angiostomosis method developed by E. S. London brought him 2 nominations for Nobel Prize (1939) and the preliminary recommendation of that year from the Nobel Foundation expert Ulf Svante von Euler, who characterized E. S. London in his official reply to Nobel Committee as "priority nominee #1" [44]. The decision which could make E. S. London the third Russian Nobel Prize winner in Medicine was never realized because of London's death from atherosclerosis and arterial hypertension on 21 March 1939.

E.S. London was buried in Leningrad at "Literatorskie mostki" of Volkovo Orthodox cemetery, traditional place of burial for the most outstanding personalities. One still can find in St. Petersburg 2 monuments (fig. 15) and a memorial board in IEM, commemorating this great alumnus of Warsaw University.

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