DOI: 10.20514/2226-6704-2020-10-6-407-413

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# ЖИЗНЬ И ДЕЯТЕЛЬНОСТЬ РОБЕРТА КОХА

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# Robert Koch's Professional and Personal Life

## Резюме

Пожалуй, всех творческих людей, чьи фамилии мы помним, объединяет такая черта характера, как увлеченность. И область творчества здесь не так уж важна — и в искусстве, и в технических науках, и в медицине для достижения результата необходимо полное погружение в исследование, некая одержимость.

Роберт Кох (1843–1910 гг) — великий исследователь, немецкий врач, микробиолог и гигиенист, примером своей жизни доказал, что четкая цель, сила духа и работоспособность побеждают все неблагоприятные обстоятельства. В нашей работе была рассмотрена жизнь и деятельность Роберта Коха на значительном отрезке времени — с окончания учебы до открытия туберкулина, анонсирования его как средства лечения туберкулеза и признания ошибочности этого утверждения. С точки зрения авторов работы, этот отрезок времени представляет огромный интерес. Мы видим Роберта Коха — ученого, обладающего незаурядными способностями и уникальным сочетанием свойств характера. Трудолюбие и высочайшая трудоспособность, требовательность к себе, четкая организация работы, умение не останавливаться при сложностях — предопределили успех его исследований.

***Ключевые слова:*** *Роберт Кох, туберкулез, туберкулин, Эмми Фраац*

## Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

## Источники финансирования

Авторы заявляют об отсутствии финансирования при проведении исследования

Статья получена 14.08.2020 г.

Принята к публикации 26.10.2020 г.

**Для цитирования:** Максимов Г.В., Лушина О.В., Павлова М.В. и др. ЖИЗНЬ И ДЕЯТЕЛЬНОСТЬ РОБЕРТА КОХА. Архивъ внутренней медицины. 2020; 10(6): 407-413. DOI: 10.20514/2226-6704-2020-10-6-407-413

## Abstract

All creative people, whose names we remember, are united by such a character trait as passion. And the field of creativity is not so important here — both in art, and in technical sciences, and in medicine, to achieve a result, complete immersion in research, some kind of obsession is necessary.

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Robert Koch (1843-1910) — a great researcher, a German physician, microbiologist and hygienist, proved by his own example that a clear goal, fortitude and efficiency overcome all unfavorable circumstances.
This work examined the life and work of Robert Koch over a significant period of time — from graduation to the discovery of tuberculin, its announcement as a treatment for tuberculosis and the recognition of the fallacy of this statement. From the point of view of the authors of the work, this period of time is of great interest. We see Robert Koch — a scientist with extraordinary abilities and a unique combination of character traits. Diligence and the highest ability to work, exactingness towards himself, a clear organization of work, the ability not to stop in the face of difficulties — predetermined the success of his research.

***Key words:*** *Robert Koch, tuberculosis, tuberculin, Emmy Fraaz*

### Conflict of interests
The authors declare that this study, its theme, subject and content do not affect competing interests

### Sources of funding
The authors declare no funding for this study

Article received on 14.08.2020
Accepted for publication on 26.10.2020

**For citation:** Maksimov G.V., Lushina O.V., Pavlova M.V. et al. Robert Koch's Professional and Personal Life. The Russian Archives of Internal Medicine. 2020; 10(6): 407-413. DOI: 10.20514/2226-6704-2020-10-6-407-413

## Robert Koch, a great scientist

Today, when the whole world continues struggling against tuberculosis, the biography of Robert Koch is shown in a new light. It would seem that Koch's time is behind nowadays in so many aspects: material and technical resources of laboratories, speed of communication, a great number of deeply erroneous and imperfect theories (that, however, were common among medical professionals).
Researcher Robert Koch seemed to work from the perspective of «what can I do for science and practical medicine?» He did not make demands like «give me laboratories, assistants, and a salary, then I will start working». No. Koch embarked on a very difficult yet the only possible course for him: first work, then conditions. Koch was also able to make space for himself. His first laboratory was a fenced-off corner in his own reception room; for a long time, his laboratory was equipped with an imperfect microscope and tableware borrowed from his wife. In such imperfect conditions, Koch conducted rigorously substantiated experiments and carried out diligent work.
This is probably the only way that discoveries are made: when one does not count hours of working time; when one does not compare the result and invested efforts; when material, physical and emotional costs have no special significance for the researcher for one reason — that the researcher cannot live and work in any other way. Trying to assess a creative process with a calculator in hands is the way to failure. Such a mathematical and practical approach is no good in this situation.
Koch got his results. These results and his name are now well known. We remember this man as an outstanding scientist with great talent.
However, researchers usually live with families and work with colleagues. It is impossible to talk about the biography of the genius without mentioning his family and relatives, teachers and schoolmates, and those who influenced him, helped with work or, on the contrary, hindered the course of his career. An individual in a thousand can be so restrained that his/her immediate family does not know if he/she has succeeded or failed. It is spouses, children and parents that have the difficult task of accepting and supporting. This is much more complicated than giving up on a spouse and concluding that the person is not fit for family life. Therefore, it is better to look for happiness elsewhere.
Of course, there are individualists by nature, but every adult at a certain age clearly realizes: parents grow old, colleagues and students are busy with their own work, and it is rather hard to be alone, to return every day to your empty house with no one to share your success or failure.
Family life with such a creative person also has its peculiarities. Family members should be empathic, supportive, able to endure hardships, and without discouragement. And they also have to decide not to use the very practical «calculator» to evaluate the ratio of labor and tangible benefits: money, position, «useful contacts», etc.

Everyone knows the names of Maria Sklodowska-Curie and Helena Roerich. Both women followed their spouses and found themselves in research. We do not remember the names of the wives of talented people, and we have to look them up when we need to. Usually, these wives made no discoveries of their own, wrote no books, or created their own paintings or magnificent melodies. Therefore, to the public, they remained a «shadow» of their talented spouses. Sometimes we unfairly forget that these «shadows» worked every day, providing their husbands with the opportunity to create. The work of wives is a daily routine, not historical events.

Emmy Koch was the wife of Robert Koch, the mother of his daughter. Her name is not associated with discoveries. It is hard to tell how successful this marriage was because it is obvious that the spouses had different plans for the future and even different ideas concerning here and now. However, one simple fact is revealing: Emmy shared with Robert the beginning of his medical and scientific career. She stayed with him, living on a very modest income and in conditions that did not meet her wishes. It seems that if she wanted to, Emmy could have returned to her parents (even without filing for divorce), leaving her husband to solve all the problems on his own, and then later raise the question of a reunion. She never did that. We can assume that there was no ultimatum like «family or science!». Later, we see the collapse of many years of marriage. Robert was wrapped up in science well before this divorce.

## Robert Koch, a talented researcher

The beginning of Robert Koch's career was not trouble-free. Robert Koch started his education at the University of Goettingen (1862–1866) with lectures on natural sciences and botany. Since he had a keen interest in studying insects in childhood, his family indulged him in this hobby. In June 1865, Koch won the first prize, 80 thalers, in a student research competition. That year, he was appointed assistant to Prof. Krause, Director of the Pathology Institute. It was a great breakthrough for a student, a favorable beginning of a professional career. However, graduation was followed by a long period of instability because Koch could only apply for a teaching position. But he decided to go deeper into medicine: it was a relatable, honorable and lucrative profession.

In January 1866, Robert Koch earned his doctorate in medicine, and almost immediately, in February, he went to Berlin, to the famous Charité hospital where Rudolf Ludwig Karl Virchow worked. The name of this scientist was at that time well-known among scientists all over the world; with his theory of «cellular pathology», he was considered an authority beyond exception. This theory (later refuted by Koch) stated that diseases are caused by disorders in the normal activity of body cells. In other words, the origin and cause of diseases was sought (and found!) «inside» the body, and bacteriology as a science did not exist.

But at that time, Virchow was a legend, and Koch was travelling to Berlin to expand his knowledge. Just after four weeks, depressed and disappointed, he returned home to Clausthal. Koch could not «improve his knowledge» under the guidance of this distinguished scientist: when Virchow appeared at Charité and made patient rounds, he was always surrounded by a crowd of students, young physicians, assistants, colleagues. A personal meeting, conversation, request to explain an individual clinical case, all for what Koch came there, turned out to be impossible. Even Virchow's words were often difficult to hear in such a crowd.

Robert Koch was in a very difficult situation. It was almost impossible to get private practice: he was a young physician, a recent graduate, a «theoretician» with no experience of working alone. Then happenstance came to his aid — a cholera epidemic broke out. Physicians were needed urgently, and Koch was able to get a job in Hamburg. Ironically, at that time (in 1866), he was already looking at Vibrio cholerae in a microscope but considered this unimportant since he was working based on Virchow's theory. In 1884, Koch's impeccably substantiated report on the discovery of «cholera comma bacillus» would become a turning point: Virchow acknowledges bacteriology. But recognition and fame are in the distant future. The cholera epidemic is over, and Koch is jobless again.

It is only in September of 1866 that he got a position at the psychiatric hospital of Langenhagen village, near the city of Rakwitz. Honestly speaking, a position at a psychiatric hospital was very far from Koch's plans to become a physician on shipboard. However, after a long time of uncertainty, he now had a stable job and a salary. The young physician compared his dreams with reality and concluded that his long-time hopes could not be realized. He took up his duties

at the hospital and at the same time started looking for private practice. Now, when Koch's near future was clear and predictable, he could think about his own family. In 1867, Koch married Emmy Adolfine Josephine Fraatz, the daughter of a Hanoverian Superintendent General. A childhood friend, certified physician, was a «desirable alliance» for Emmy Fraatz. The spouse of a physician is a high status for a married lady, but the wedding was far from a magnificent celebration. It soon became clear that the young couple was going to live a modest life. Emmy Fraatz had expected more from her spouse.

The situation soon worsened: Koch's salary at the hospital was cut by half, income from private practice was small, and the couple was forced to return to Clausthal. Koch later found work in Niemegk. The family moved but was again in very modest financial circumstances. In 1868, their daughter Gertrude was born. Koch was confronted with reality: he had to find a stable job with a stable salary and to decide on his research work.

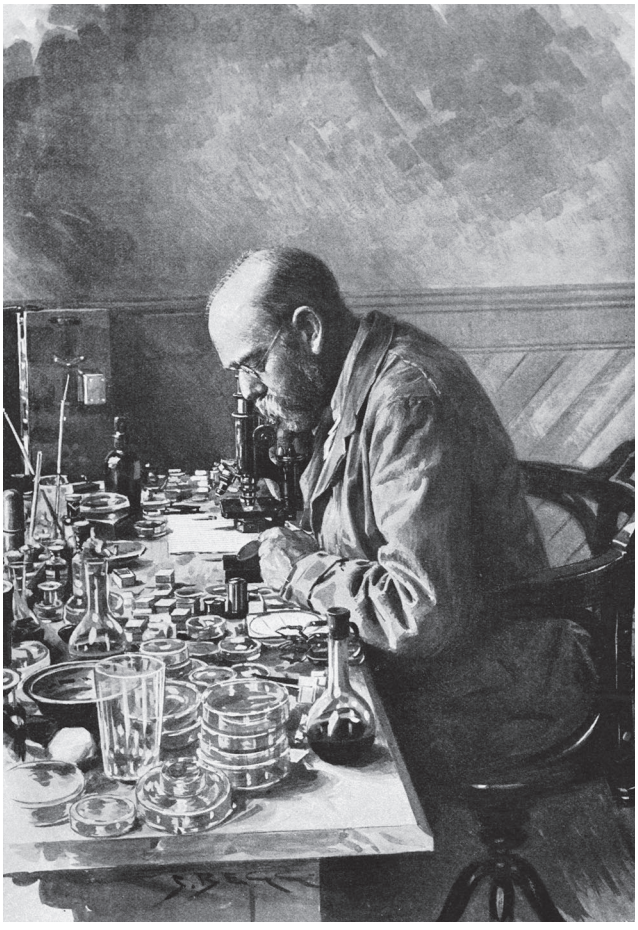

***Figure 1.*** *Robert Koch at work (Photo from Paul de Kruif's book "Microbe Hunters", Orell Füssli, Zurich, 1927)*

The young physician moved to another place in the city of Rakwitz, Poznań province. He conducted private practice, and the local population eagerly sought his services. Hard work paid off.

In August 1870, Koch volunteered for the Franco-Prussian war and worked at a hospital. In March 1872, he was transferred to the position of district sanitary physician in Wollstein. It is with Wollstein that the beginning of Koch's research is associated.

The local population gave the new physician a warm reception. Robert Koch's life began to improve. Emmy gave her husband a gift that would be significant when Koch chose his future life path: on his 28th birthday, the physician received a microscope. Koch would spend many hours trying to find bacilli under this microscope.

In addition to his official duties, Koch conducted private practice and also put-up curtains in a corner in his reception room. This was his «laboratory» — a table with a microscope gifted to him by his wife and dishes from a table set (for lack of special laboratory equipment). In this «laboratory», Koch spent all his time free from his duties as a sanitary physician and private practice. The young researcher needed no leisure time. He forgot about the daily routine and did not count the hours spent looking through the microscope. He did not know what «spare time» was. All his time belonged to his work.

Emmy could hardly find her husband at home. Koch did not really seem concerned about improving the family's financial circumstances. He fulfilled his duties, but if there was a minute, he looked through his microscope. Emmy was left alone to deal with all household issues.

There was an outbreak of anthrax in the region of Wollstein. Nobody knew exactly why and how the epidemic broke out and ended. However, farmers noticed that not all of the grazing livestock was infected; part of the herd might become ill, but other animals in another part of the grazing field would be healthy. But these were just observations.

Koch took a blood sample of a sheep that had died from anthrax and placed the preparation under a microscope. The physician clearly saw mysterious «rods» and «clusters» that are absent in the blood samples of slaughtered healthy animals. The researcher transfused the blood of an infected sheep to a mouse (Koch had no syringes, so he made an injection with a sharp wooden stick). And when the mouse died, he took a sample of fluid from the spleen, placed the preparation under the microscope

and saw the same «rods» and «clusters». He tried to culture bacteria found on his plates on wet sand with a growth medium (a fragment of the spleen of the dead mouse and fluid from a bovine eye) but the experiment failed: there were too many foreign microorganisms. Koch needed a pure bacterial culture. How can one achieve that in «field conditions»? The researcher seemed to have absolutely nothing: no equipment, no conditions, and most importantly, he was alone, without assistants and colleagues. The letter would take a long time, and whom could he write? He had only one successful experiment with the mouse and one unsuccessful attempt to culture the «rods» and «clusters». There was a mysterious anthrax epidemic near his city.

Koch did not give up. His research in the «laboratory» were in full swing. To obtain a pure culture, he carried out technically exquisite work: he made a hollow in a glass, placed a growth medium and a drop of infected blood. He smeared the edges of the hollow with vaseline, covered the preparation with another glass and turned the resulting «sandwich». The drop was hanging without touching anything. Any airflow was excluded.

And the experiment was successful! Bacteria were cultured! For eight days, Koch made reinoculations to make sure.

He was once called for childbirth and forgot to remove the preparation from the microscope. Later, he returned and looked at it. The bacteria had spent several hours without food and heat and ... had formed spores. The riddle of anthrax was solved. The formation of spores explained everything: it is how bacteria exist in unfavorable conditions. While the cattle walked in infected areas of the pasture, there was no anthrax, but it «waited». In addition to describing the mechanism of spore formation, Koch also offered new methods of dealing with corpses of animals that had died from anthrax: burying them deep in the ground or burn.

Having finished his «Etiology of Anthrax», Robert Koch sought to make its presentation at the Ferdinand Cohn Institute of Plant Physiology in Breslau. Koch took to the presentation not only the preparations but also his microscope.

The scientist's speech was a huge success. Listeners were amazed by both the sensational results and the structure of the experiments: consistency, strict logic, accuracy and pedantry.

Robert Koch returned to Wollstein. This trip proved that it was necessary to look for ways of making photos of preparations because each one of them counts. While the researcher was experimenting with photos, his friends were looking for ways to transfer Koch to Breslau University. The conditions there were surely better than a corner in his own reception room.

Robert Koch found a way of making photos of preparations: the use of aniline dyes produces good photos. Therefore, there was no need to take glasses and worry about their safety because broken glasses would put the evidence base at risk. Koch would simply have nothing to demonstrate in support of his words. But now he could take photos. In addition, keeping a photo archive helped much in the organization of researches.

His friends succeeded in having Koch appointed a city sanitary physician in Breslau. He could combine his new duties with research work. The family moved but was met with challenges: the official salary was too small and Koch could not find private practice. There were enough physicians in the city.

After three months, Koch's family returned to Wollstein, where the scientist continued his research. For two years, he worked on the causes of purulent inflammation of wounds (he had seen enough practical examples during the «war episode» of his career), and the result was a paper on the etiology of wound infections published in 1878. This work outlined three basic requirements (Koch – Henle postulates) on the basis of which the relationship of disease with a specific microorganism was established: 1) the microorganism should be found in all cases of this disease; 2) all manifestations of this disease should be explained by the number and distribution of microorganisms; 3) the causative agent of each infection should be found in the form of a morphologically well-defined microorganism. Koch proved that every wound disease had a specific pathogen. It was another victory. Robert Koch's name rose among medical professionals, thanks to the achieved results.

In 1880, Koch got an invitation to the Imperial Department of Health in Berlin. Robert Koch moved to Berlin with his family. Emmy's expectations finally started to come true: a big city, society, the opportunity for her daughter to attend an aristocratic school. However, the psychological dissonance between spouses increased over the years, and the marriage ended in an amicable divorce in 1893.

In Berlin, Robert Koch got absolutely new working conditions: a laboratory, equipment, experimental

animals. Koch worked with his assistants: military medics Georg Gaffky and Friedrich Loeffler. Research was conducted at the Higher Veterinary School. First of all, the task was to find a way to make pure bacteria cultures. The problem was solved: a solid growth medium based on gelatin was developed.

It was here, in this laboratory, that Koch worked on the identification of the causative agents of tuberculosis — the discovery that brought him fame and honor. Tuberculosis was previously considered a spontaneous disease promoted by poor housing and living conditions and lack of food. There was also an opinion that tuberculosis was a hereditary disease. After several years of studying tuberculosis at the Valde-Grâce hospital in Paris, physician and researcher Jean-Antoine Villemin concluded that the disease was contagious but did not find its causative agent. Research results remained unconfirmed.

Pathologist Julius Cohnheim always found tubercles from decayed tissues and pus in the organs affected by tuberculosis, but the pathogen was also not found. At the Charité hospital (where student Koch tried to practice under the watchful eye of Virchow), Robert Koch, government adviser to the Imperial Department of Health, received research material – sputum and blood of tuberculosis patients. At this time, his assistants were working on other issues: Gaffky was looking for the causative agent of typhoid fever, Loeffler — that of diphtheria. Work in the laboratory did not stop for a moment, but Koch could not find the causative agent of tuberculosis. Despite the failures, he continued his experiments.

Another TB patient, male, 36, was admitted to Charité hospital. The patient died very quickly. Koch took a sample of his lung tissue for research but again — got no results. The researcher did not give up: he put the lung tissue preparation in a bath filled with a newly invented solution of methylene blue with potassium hydroxide. A day later, Koch saw, under the microscope, a uniformly colored blue field, and nothing on the preparation. This could be anything: a happy coincidence, fair luck, or insight. We only know the fact: Koch added Vesuvin, a red-brown dye for leather, to the preparation. Destroyed lung tissue cells were stained matt brown. Bright blue tiny bacilli moved on this background. Here it was – the «invisible» microbe. Thus, tubercle bacillus was found in preparation No. 271.

But then there were several inconsistencies. Laboratory animals, rabbits and guinea pigs were not infected by the injection of «bacilli» In addition, «bacilli» do not replicate in an artificial environment (it was later established that tuberculosis bacilli replicate only in living organisms). Then another victory followed. Koch was able to grow a culture on warm serum and could prove that one could be infected with tuberculosis by inhalation of bacilli. His experiment, called Noah's Ark, confirmed that brilliantly: all animals placed in a closed box became ill after inhalation of contaminated air entering through a pipe.

Koch prepared the work «On the Etymology of Tuberculosis», but the Berlin Society of Scientific Medicine, led by Virchow, rejected it. Koch turned to the Society of Physiologists. On March 24, 1882, Robert Koch presented a report at the Physiological Institute. Virchow, who was in attendance, applauded.

Later, Koch also found a way of disinfecting tuberculosis bacteria: steam and mercuric chloride. Despite the fact that no treatment options were proposed for tuberculosis, the report on the etymology of this disease played a huge role. Until that moment, tuberculosis had appeared as a mysterious, suddenly occurring disease. Now the pathways of transmission of this pathogen were established.

Koch went further in his research. And again, circumstance set the direction of his work: in 1883, there was a cholera break out in Egypt, England and France. Pasteur (69, partially paralyzed, working on a rabies vaccine) sent physicians Roux and Thuillier to Egypt. Koch travelled there with Gaffky and Fischer (at that time, Loeffler had found diphtheria bacillus and stayed to continue this study). But in Alexandria, where the expedition arrived, the cholera outbreak had subsided. So, there were fewer preparations for research. The physicians did not give up. The death of twenty-six-year-old Thuillier from cholera came as a great shock. Probably, this fact made the researchers decide to continue their work by any means. Robert Koch and his assistants moved to India, where cholera was almost a regular disease.

Having sufficient research material, Koch proved that cholera was spread through contaminated water, food, and from person to person. At that time, India had problems with supply of clean water, so the disease was widespread.

In July 1884, at the Berlin conference, Koch presented a brilliant report about cholera. The next task was to find a way to treat tuberculosis since its infectious origin had been proven and transmission routes had been found.

In August 1890, at the Tenth International Medical Congress in Berlin, Koch announced that he had

found a drug for treating tuberculosis. He called this drug «tuberculin».

This report drew a huge response not only among medical professionals but also among the public. The number of people wishing to get tuberculin was fantastic: individuals with tuberculosis, relatives of patients, and physicians looking for a panacea for their patients. Tuberculin was widely used. Robert Koch seemed at the peak of his career, and insidious tuberculosis had been defeated forever.

But then reports of deaths after tuberculin injections started emerging. This drug did not help treat tuberculosis but improved the condition of patients with lupus. Subsequently, tuberculin was used in the diagnosis of tuberculosis, and present-day phthisiology of the 21st century is impossible without this drug discovered by the great scientist. But at that time the disappointment was comparable to the euphoria at the first reports of the wonderful properties of tuberculin. One can only guess why such a perfectionist like Koch made such a mistake. But there was still a lot of work to do. He had to admit the error and continue research, both on tuberculosis and in other areas.

Koch's ideas were still relevant to scientists and physicians even in the second half of the 20th century; tuberculin therapy was continued to be studied and used by phthisiologists E. Z. Mirzoyan in 1965 and V. A. Krylov in 1995.

If the life of the physician that was filled with painstaking work could be reduced to a list of achievements, then Robert Koch's record of accomplishments would look as follows: discovery of Bacillus anthracis and spore formation mechanism, development of anthrax vaccine; work on the etiology of wound infections, formulation of Henle – Koch postulates; development of a method for growing bacterial cultures on solid media; introduction of aniline dyes in laboratory practice; discovery of tubercule bacillus, establishment of transmission routes of tuberculosis and the infectious nature of this disease; finding Vibrio cholerae and evidence of cholera transmission routes; development and presentation of tuberculin, which is still used to this day for the diagnosis of tuberculosis; implementation of practical use of microphotography; development of a device for sterilizing growth media that cannot withstand temperatures above 100 °C (Koch apparatus); implementation of Abbe condensers; developing a pure culture of tetanus pathogen (together with Kitasato Shibasaburō); development of a vaccine against cattle plague; finding in the blood of patients with recurrent typhoid spirochetes causing this disease; identification of the mechanism of transmission of sleeping sickness.

Robert Koch is one of the founders of microbiology. His greatest discoveries are invaluable. The new methods used by Koch in his laboratory work allowed his assistants – Emil Adolf von Behring, Friedrich Loeffler, Richard Pfeiffer, Kitasato Shibasaburō, August Paul von Wasserman — to conduct their own successful research and medical practice. The highest recognition of Robert Koch as a scientist was the Nobel Prize awarded to him in 1905 for his work on the study of tuberculosis – the discovery of tuberculosis «bacillus» (Koch), mycobacteria culture on growth media and obtaining a pure culture, confirmation of the infectious nature of this disease by infection of animals and the development of tuberculosis in them.

## Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

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**M.V. Veselova:** search for literature, writing and editing the article

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