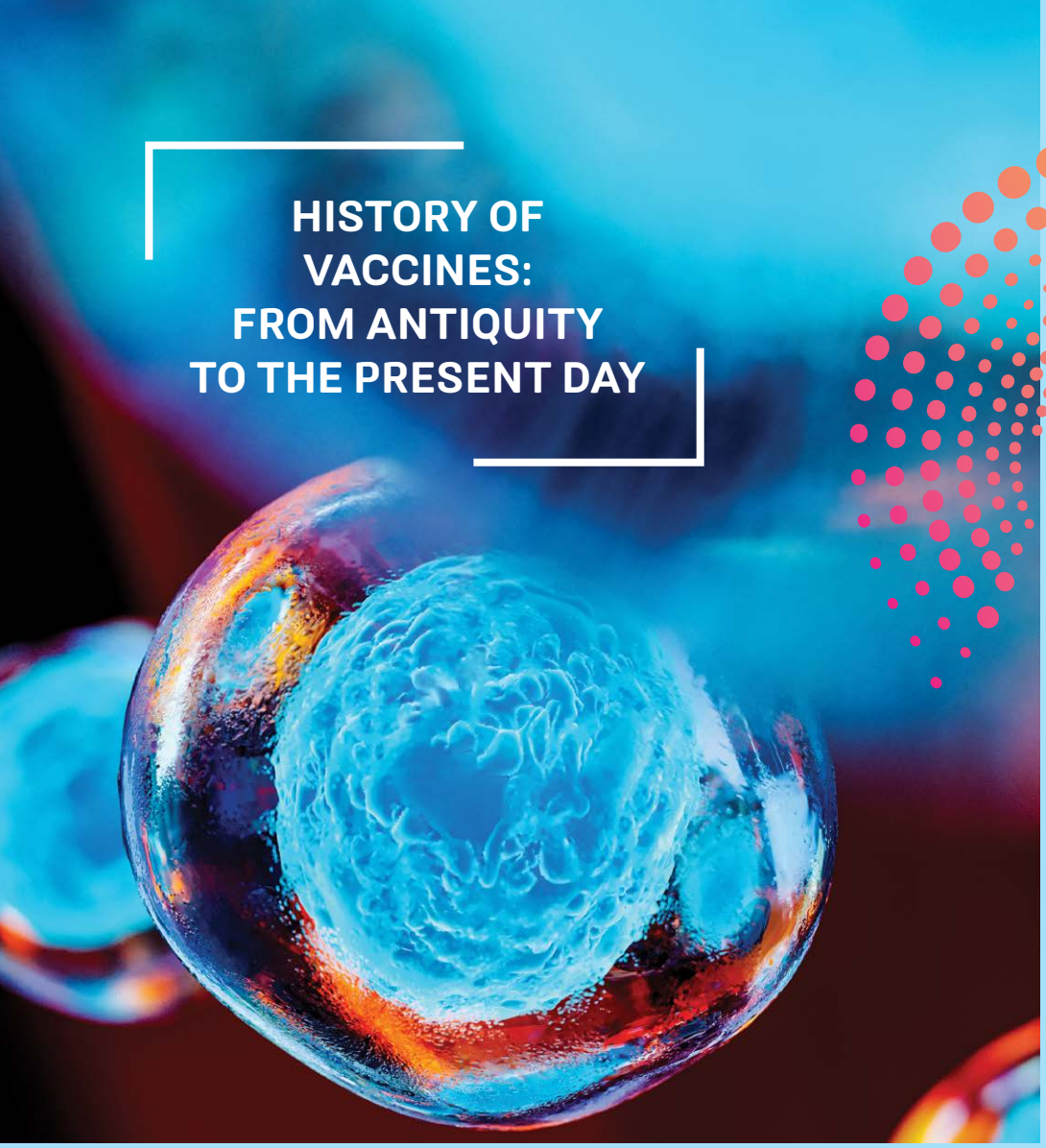

HISTORY OF VACCINES: FROM ANTIQUITY TO THE PRESENT DAY

95

Top 5 inventions of Ukrainian scientists

Overcome pain: the latest methods in Ukraine

Farmak

4 / 2020

SCIENCE INSIDE

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ELF-TREATMENT MAY BE HARMFUL FOR YOUR HEALTH

Dear friends!

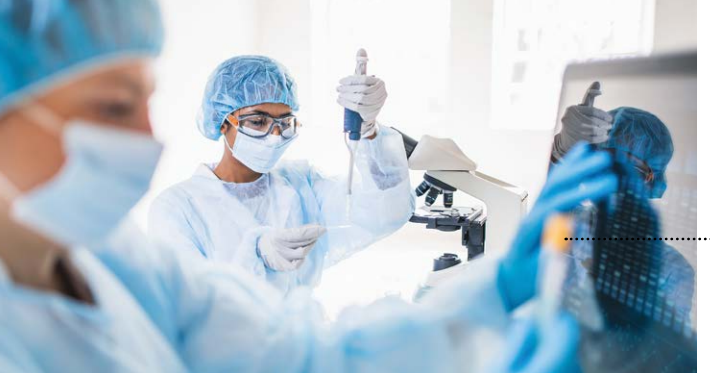
This issue of our magazine is dedicated to science as a fundamental component that makes it possible for the state and society to develop. The government should strategically focus on increasing the scientific potential in Ukraine: the development of science needs state support, grant system, ecosystem. Business should also make its own contribution to science.

Investing in development, our Company aims not only to track innovations, but also to localize and adapt them in Ukraine. Taking into account the global trends, Farmak is developing a biotechnology area. However, our investments go beyond the Company, as we consider it our duty to invest in projects designed to improve the situation in the scientific environment as a whole. Our goal is to support the scientific community, invest in theoretical and practical research and applied developments. This will contribute to the development of the scientific process in the country and will prevent a brain drain of Ukrainian scientists. We are convinced that if the proper policy of the domestic science support is implemented, our country has real opportunities to become one of the world's R&D centres.

Despite all difficulties faced by the domestic science today, Ukrainian scientists still have what to be proud of. Due to their persistence, enthusiasm and engagement, they have achieved and continue to achieve the significant results. The scientific activity undoubtedly requires tremendous efforts and dedication. That is one of the reasons why science has always been "not for everyone". As we know from the history, many researchers and inventors, whose contributions cannot be underestimated today, faced significant obstacles in their life. Upholding their ideas, they resisted the conventional views, false stereotypes, and sometimes plain ignorance. Therefore, in order to leave behind such occurrences, we must make every effort to promote scientific activity.

That is why Farmak initiates and invests in projects aimed at finding talented young people and supporting young scientists to show the society: science is important, noble and interesting. And if the state and business can unite, get their priorities right and create the necessary conditions for the scientific environment development, we can also say in the near future that science is prestigious and profitable.

Best regards,
Volodymyr KOSTIUK,
Executive Director of JSC Farmak



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“WE STRIVE TO COVER THE FULL RANGE OF RESEARCHES”

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NOBEL HEROES

119 years of struggle for health

SCIENCE INSIDE
“Farmak JSC” CORPORATE MAGAZINE

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History of vaccines: from

THE HISTORICALLY HIGH EXPECTATIONS ASSOCIATED WITH THE DEVELOPMENT OF VACCINES AGAINST CORONAVIRUS AND OTHER MICROWORLD "enemies" are a reason to recall the milestones in the development of vaccinology, a science that has radically changed the fate of mankind for the better.

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PROTECTION THROUGH DISEASE

It is known that smallpox was the first disease that was overcome with vaccination which was developed during the fight against this disease as a saving method. Smallpox was epidemic in ancient times and became so widespread in the Middle Ages in Europe that it was considered as a constant companion through life, at least for those who managed to survive. Because the disease annually caused the death of 1.5 million Europeans. The skin of those who overcame the disease remained scarred for ever. The fact that in the 18th century the French police called the absence of scars on the face a special sign shows how severely people suffered from smallpox.

antiquity to the present day

The attempts to protect against the disaster with artificial infection, i.e. the instillation of biomaterial of the infected to healthy people, were made in ancient times as well. This gave a chance for a mild course of the disease. Such practices were recorded in India, China, Persia, Africa, and the Caucasus. Obviously, such medical procedures were risky, but it was the only known method of protection. It is worthy of note that it was more common in areas where the slave trading flourished or beauty was considered a commodity. So it is not surprising that variolation, i.e. subcutaneous instillation of the contents of a vaccinial vesicle to a healthy person, became known in Europe from the eastern countries with a culture of harems. This procedure was promoted by the wife of the British ambassador, Lady Montagu, who learned about the method in Turkey, caused her children vaccinated and began to promote variolation among the aristocracy. The procedure did not give a 100% guarantee, and 2% of its consequences were fatal. However, this is not 40% which could die of the natural course of smallpox!

AN ATTENUATED "RELATIVE" IS A SAVIOUR

Variolation was quite actively applied in practice until English physician Edward Jenner marked a place for himself in the history of medicine. At the same time, remembering the "father of vaccination", we should pay tribute to him not only for inventiveness but also for observation skills because the instillation of not human, but cow, much less dangerous smallpox virus, which gave a reliable immunity, was a known method of protection. The enthusiast's main contribution was that he tried to prove the efficacy of the new method and to bring information about the results of his experiments (well-known now) to the general public. And he did not succeed immediately: the report to the British Royal Society was rejected with the advice "not to publish such a preposterous idea that would harm his stable reputation", so the brochure "An Inquiry into the Causes and Effects of the Variolae Vaccinae" remained unnoticed. The book published at his own expense and describing successful examples of vaccination drew much criticism. It took him several years to convince other doctors of the efficacy of vaccinations. Later, some of them tried to steal the credit for the new method. But he was finally recognized, contemporaries began to call Jenner a "do-gooder", and cowpox vaccination spread throughout Europe and worldwide. In 1980, the WHO declared victory over smallpox.

That smallpox was the first disease that was overcome with vaccination which was developed during the fight against this disease as a saving method.

In addition, smallpox was a "convenient" disease for empirical experiments – its pathogen was contained in vesicles on the patients' skin. Edward Jenner did a lot to give a theoretical explanation of the effect of vaccination: to describe the substance produced by cowpox, Jenner used the rarely used term "virus". But too little was known about the triggers of other infectious diseases, as

well as ways to treat them. We owe the detection of many invisible enemies of mankind and the fight against them to the scientists of the 19th century such as Louis Pasteur, Robert Koch and others.

IN SEARCH OF APPROACHES TO AGGRESSORS

After studying Koch's etiology of anthrax, Pasteur focused on immunological experiments and made a real breakthrough by finding a way to prevent infectious diseases by instilling attenuated pathogens. As often happens, a discovery was made by a fluke. At that time, the scientist studied bacteria that caused chicken cholera. When instilling bacterial concentrate, birds died after even the lowest doses. Once a portion was forgotten for a week, and after its instillation, the chickens with only mild symptoms of the disease survived. After instillation of another unspoiled portion

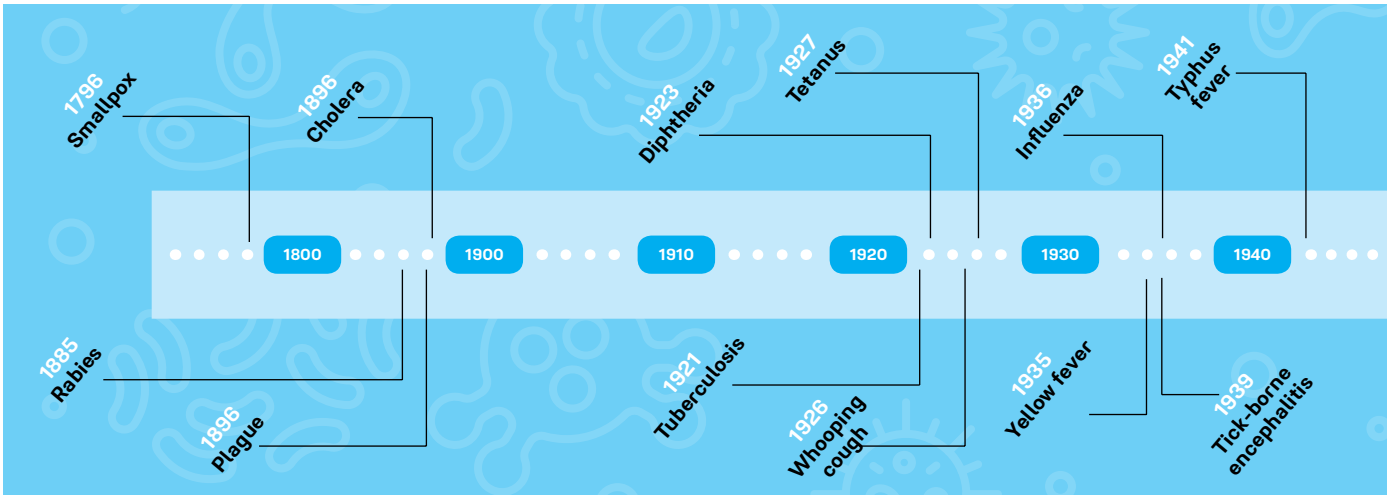
After studying Koch's etiology of anthrax, Pasteur focused on immunological experiments and made a real breakthrough by finding a way to prevent infectious diseases by instilling attenuated pathogens.

of the medicinal product, the subjects also recovered. It was clear: infection with attenuated bacteria formed a defensive mechanism against highly virulent microorganisms.

Due to this discovery, Pasteur and his colleagues were able to develop cholera and anthrax vaccines used for animals. Pasteur also worked on rabies but the methods were not effective because the disease pathogen was not a bacterium but a virus. It took him years of trial and error to find the relevant tissue with virus and a method to attenuate it. The incredible effort was finally rewarded in the form of the saved lives. Pasteur was recognized as a national hero of France and at the same time he was subjected to attacks. All cases that were unsuccessful due to late treatment and other reasons were declared the result of the vaccination. Over time, as the rabies vaccine underwent a lot of improvements, Pasteur's theoretical assumptions were completely confirmed.

"FRAGILE" BACILLUS AND A PERNICIOUS RESORT

Not immediately and not all the desired results were achieved by Pasteur's contemporary Robert Koch, which, however, in no way diminishes his colossal contribution to the development of vaccinology, including Koch's postulates which provided criteria establish a causal relationship between a microorganism and a disease; the development of microbiological research methods, in particular bacteria growing on agar or gelatin substrates which were well studied in anthrax, cholera and other pathogens. As one of Koch's assistants said later, the method was so successful that the researcher "he shook the marvellous tree, and discoveries rained into his lap". However, to study the tuberculosis pathogen was not so easy. In order for capricious tuberculosis bacilli to reproduce themselves, researchers had to create special conditions as close as possible to the body's environment. But even after they were put to the serum taken from the slaughterhouse, the research lasted for a long time because Mycobacterium tuberculosis is naturally slow in reproduction. After many months of experiments, Koch managed to identify the aggressor and later was awarded the Nobel Prize. But the scientist did not manage to develop a tuberculosis vaccine: the tuberculin,



an aqueous glycerol solution with molecular fragments of bacteria, he obtained, had no prophylactic effect and caused allergic reactions. However, tuberculin still took over: it was used to diagnose tuberculosis and the test was named after French physician Charles Mantoux.

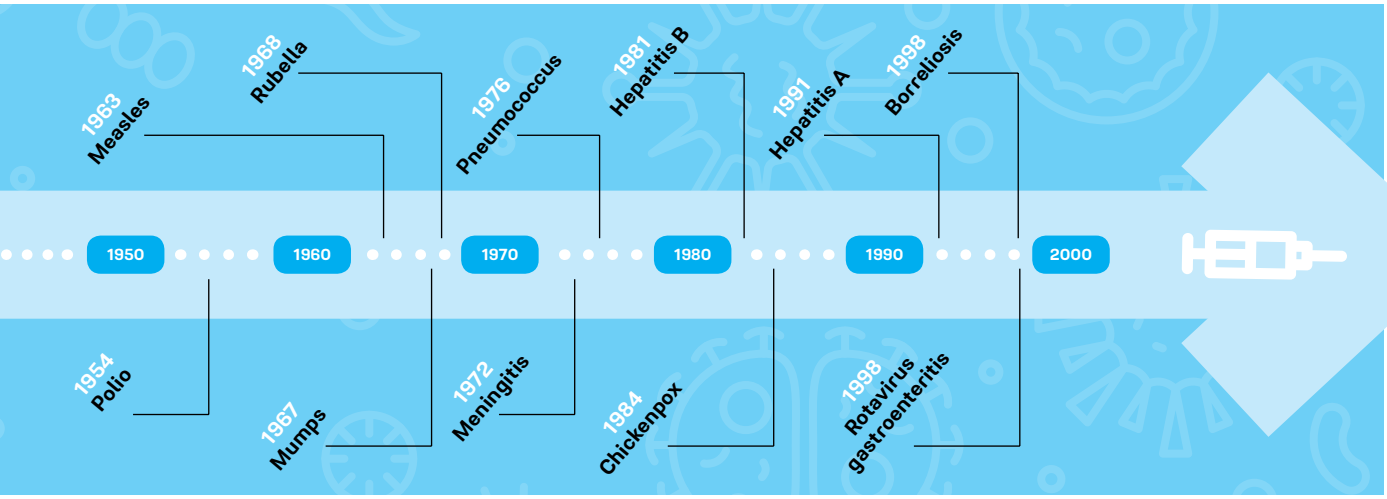
Later, a vaccine was invented based on the tuberculosis pathogen in cattle. Unlike cowpox which can cause mild illness, Mycobacterium bovis is dangerous for humans. To attenuate the bacterium, microbiologist Albert Calmette and veterinarian Camille Guérin used a method of attenuation developed by Norwegian researcher Kristian Feyer Andvord. It was observed that the medium of potato starch, glycerine and bile was perfect for bacilli. After Mycobacterium bovis spent 13 (!) years at such a "resort", they lost their virulence due to evolutionary patterns. The attenuated microorganism was named Bacillus Calmette–Guérin after its "tamers". BCG vaccine is known in Ukraine as «BTsZh» since translator's transcribed the name Guérin as «zhiuren». It was first introduced in 1921 and still remains the only vaccination recommended by the WHO, as tests of other modern options are still ongoing.

KILL OR ATTENUATE?

It became clear during Pasteur's experiments that viruses required different approaches than bacteria. Methods of virus growing in tissue cultures resulted in active work aimed at overcoming many viral diseases including poliomyelitis. The first results were obtained in the 1930s, but in 1935 the consideration of their efficacy ended in scandal. Professor John Kolmer obtained an attenuated live vaccine and had to admit that several children had poliomyelitis symptoms after instillation. Outbreaks were also reported in the cities where the pharmaceutical product was tested. So after the report, the professor had to leave the department with the crowd screaming: "Killer!".

The next speaker was a young researcher, Maurice Brodie, who represented studies conducted with a vaccine based on a virus killed with formaldehyde. There were incomparably fewer problems caused by vaccination. However, the report's future was already determined in advance: an angry audience told Brodie the same epithets as his colleague which completely ruined his career. After this public outburst of discontent, the research was paused.

However, the number of poliomyelitis cases was growing, and in the 1950s the fight against the disease became more intense. The first commercial pharmaceutical product was Jonas Salk's "killed-virus" vaccine. It proved its safety, and the Americans wholeheartedly rejoiced because they feared poliomyelitis more than nuclear war. Specialists worldwide, including representatives of the Soviet Union, Mykhailo Chumakov, director of the Poliomyelitis Research Institute, and his wife, Maryna Voroshylova, arrived to the United States. Later they assisted in the production of Salk's vaccine in the USSR. However, as opponents of this pharmaceutical product predicted, post-vaccination immunity was unstable and booster injections were required. That was when another pharmaceutical product was developed under the leadership of Albert Sabin. He noticed: when viruses are cultured at low temperature, only non-pathogenic strains survive. And if swallowed, the "mutants" reproduce themselves in the gastrointestinal tract and facilitate producing antibodies that are effective against wild poliovirus. And this is not the only bonus: children, infecting each other with non-patho-



genic "mutants", actually immunize those who were not vaccinated.

Because the United States did not see the point of abandoning Salk's vaccine, Sabin gave the strain developed by him to Chumakov. After getting approval from the Kremlin, Chumakov started vaccinations, and the latest method became effective. Due to the new live vaccine, the poliomyelitis epidemic was overcome worldwide. Today, to combine the advantages of both approaches, the "killed" virus is first instilled and then attenuated one is used for protection with minimal side effects.

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FROM NEUTRALIZATION TO BIOENGINEERING

Since methods for the sustained attenuation of microorganisms or their inactivation were developed in the 20th century, as well as the use of neutralized bacterial toxins for vaccination became possible, hundreds of pharmaceutical products to treat dozens of diseases were developed. However, with the development of molecular biology, it became clear that the immune system was able to detect even fragments of the pathogen, and to obtain these compounds that have a protein or polysaccharide structure, it is not necessary to "de-compound" pathogens, they could be synthesized using biotechnological methods. The first recombinant vaccine was aimed at protecting against hepatitis B. The advantages of pharmaceutical products of this type include the fact that they cannot cause vaccination-associated disease, because the key structures of the pathogen have never been part of a live pathogen. However, it was found that some recombinant pharmaceutical products may give a weak immune response and require additional adjuvants that stimulate antigenic activity.

PREVENT AND TREAT

It got better and better. Genetic immunization is one of the most promising areas of vaccinology. It involves instillation of not a protein-antigen but a sequence of nucleic acids (DNA or RNA) which encode information about the protein. A plasmid known as a ring of DNA, or a safe virus is used to deliver nucleic acids to tissues. Such a carrier, or vector, penetrates the cell and begins to synthesize the necessary proteins, and the "vaccine" is synthesized directly inside the body. Numerous studies are currently ongoing to combat infectious and non-infectious diseases (including cancer).

The areas which are just emerging include the so-called reverse vaccinology. It involves the study from the genome to its products while earlier researchers began their studies moving from the whole microorganism to its components. Computer analysis makes it possible to analyse all protein components of the pathogen and determine which of them are suitable for vaccine development. Further, due to recombinant methods the gene responsible for virulence is removed from the virus but does not affect reproduction and the ability to form an immune response. The first achievement of this area was the development of a meningococcal B vaccine, later – a vaccine against some streptococci, Staphylococcus aureus and some other pathogens.

Along with prevention, the efforts of scientists are aimed at developing therapeutic vaccines that induce an immune response in the patient and facilitate recovery or improvement. Such pharmaceutical products are targeted at chronic diseases caused by bacteria or viruses (including HIV), oncopathology, allergic and autoimmune diseases. The available therapeutic vaccines are obtained using classical methods. The modern areas include the development of dendritic vaccines based on special white blood cells specializing in the search for potentially dangerous microorganisms. Dendritic vaccines are likely to prove their efficacy in the fight against cancer.

“WE STRIVE TO COVER THE FULL RANGE OF RESEARCHES”

VICTORIA ZADOROZHNA, KEY NATIONAL SPECIALIST IN EPIDEMIOLOGY, PROFESSOR, DOCTOR OF MEDICAL SCIENCES, CORRESPONDING MEMBER OF THE NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE – about the fight against the pandemic and the role of domestic specialists.

Victoria Ivanivna, now great hopes are placed on scientists. Of course, they are not omnipotent but they make a powerful contribution to studying the situation and developing an action plan. Please tell us which of the tasks are currently priority for the Institute of L.V. Gromashevsky Institute of Epidemiology and Infectious Disease headed by you?

Our Institute has always been the main institution that identified the main biological hazards and ways to combat them since its founding in 1896. And despite all the difficulties that have arisen in the process of medical reform in Ukraine, we do not stop working. Since the beginning of the pandemic, we have been actively involved in the work of headquarters at all levels, including the Ministry of Health and the Government. We also promptly respond to all inquiries in order to provide scientifically sound recommendations in a timely manner. And most important – this is our routine research aimed at a comprehensive study of current infectious diseases, which in modern conditions are evolving very quickly, changing their “face” in order to prevent and treat them effectively.

■ ***The development of fundamentally new drugs requires unrealistic (unfortunately!) funds for Ukrainian scientific, government and non-government institutions. But, do our experts have the opportunity for scientific researches?***

We immediately began to study and experiment on how effective domestic antiviral drugs available in Ukraine are against Coronavirus – because we can make certain conclusions only on the basis of research. And some of the results impressed us literally, we did not even expect such a significant impact! Later, our results were confirmed in leading foreign institutes. In addition to drug therapy, we are also experimentally investigating the potential of stem cells to confront the latest threat.

■ ***So, now it is advisable to study all the treatments that are in the arsenal of physicians?***

Yes. As an example, we can mention the drugs of indirect antiviral action. Cuba's experience, where they are widely used, has shown: in this country the number of people who fell ill is almost 20 times less than, say, in the neighbouring Dominican Republic!

We can say that the results of our observations are quite reliable and completely coincide with the conclusions of world experts.

■ ***Does your team have the opportunity to help patients directly?***

We always work with doctors and hold consultations, especially when it comes to serious cases. The institute has prepared 30 sickbeds for COVID-19 infected, and as soon as we get permission, we will be able to participate in the rescue of patients directly. At the same time, we will be able to learn more about the pathogenesis and course of the disease, its treatment, stability and duration of the formed immunity, and so on.

In general, we strive to cover the full range of researches. Of course, we do not have such modern equipment as some foreign leading medical and research centres abroad, but we can say that the results of our observations are quite reliable and completely coincide with the conclusions of world experts.

■ ***What are the conclusions of Institute's monitoring of virus circulation?***

Among the results of study conducted within Gostomel – about 4% of the population who have not been diagnosed with Covid were detected, but they had antibodies to the virus. This means that part of the population have an illness in a mild or even asymptomatic form. The further away, this percentage will be higher.

■ ***Is it possible to single out certain points that indicate the national features of the pandemic?***

In fact, this is an extremely difficult question, as we are dealing with quite contradictory data. The reason for this is, inter alia, the specifics of the disease itself – it does not fit into the classical schemes of epidemiology. However, it is safe to say that Ukraine has a relatively low mortality rate, which reached 2% and has now declined slightly to 1.9%. For example, in some Western European countries (Sweden, Belgium) this indicator is up to 10%.

As for the risks for different age groups, here the data are almost the same as those recorded at the beginning of the pandemic in China. It is well known that the elderly people, patients with cardiovascular problems, diabetes, respiratory diseases

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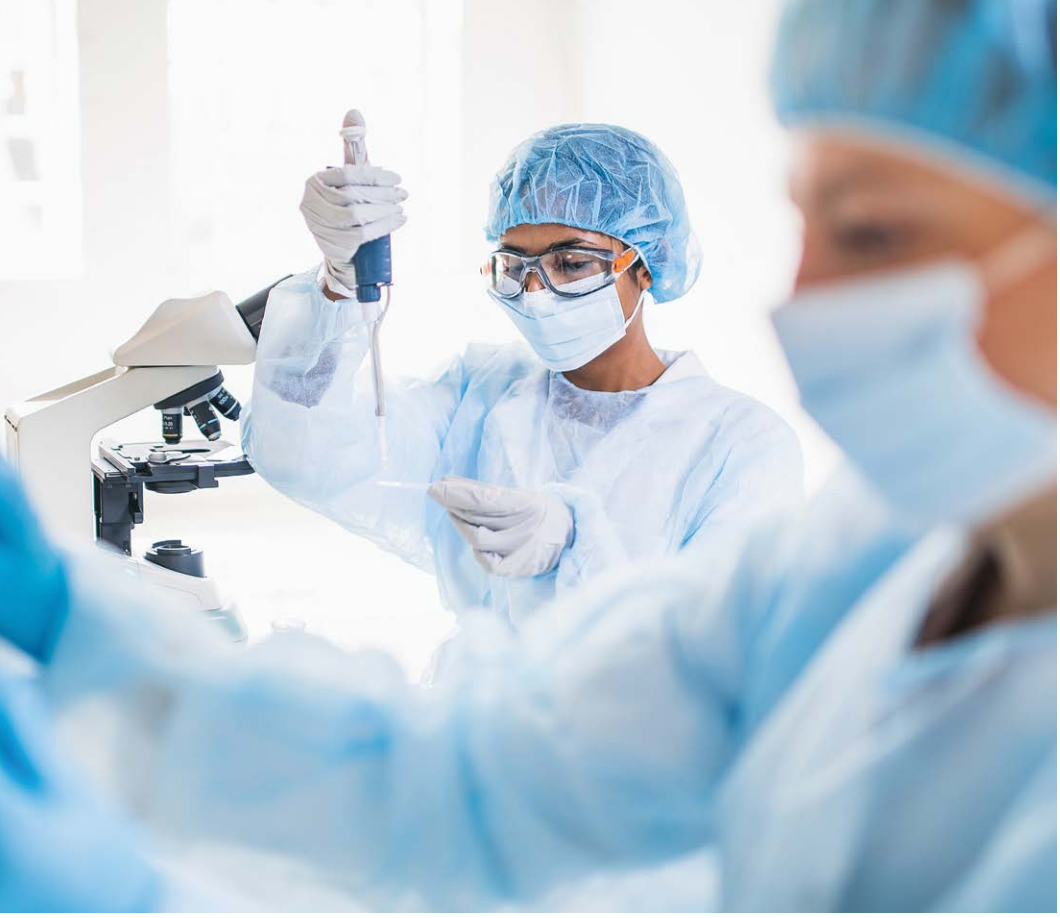


and other chronic diseases should be extremely careful.

Looking to the future, hopes are pinned on both breakthroughs in medicine and change in the behaviour of the virus itself. It has been suggested that the pathogen, which is zoogenic in nature, adapts to the human body and becomes less aggressive eventually – for its own survival.

By the time the causer of the pandemic was identified, it appeared to be fully adapted to being in human population. Observations have shown that the virus lives according to its own laws which have not yet been fully studied. However, radical changes in genetic properties were not detected: certain "modifications" of the virus disappear, others still remain. Thus, D614G mutation of SARS-CoV-2 virus has virtually supplanted the previous version, common in Europe and America. The virus in the "updated version", unfortunately, became more contagious – it began to bind more effectively to specific receptors and penetrate into cells. But, fortunately, it did not become more pathogenic.

■ ***Does the fact that the evolution of the virus takes place without special "jumps" inspire hope that vaccines will still be effective?***

Now, without exaggeration, all the forces of the world community have been addressed into the development of vaccines. More than 150 manufacturers have joined the search and attempts are being made to apply all known methods of manufacturing such drugs (there are six of them). There are also high expectations for RNA and DNA vaccines. Theoretical justification for the effectiveness of such vaccines is not new, but we do not yet have commercial drugs that would be widely used. If the plan succeeds, it could be a breakthrough. In the meantime, we have to wait. Dozens of developments are already at the stage of clinical trials, but it takes time, and rescue is an urgent issue today and now.

In addition to drug therapy, we are also experimentally investigating the potential of stem cells to confront the latest threat.

■ ***While there is no vaccine, probably no one wants to participate in the formation of collective immunity at the expense of own health. So, how to protect yourself?***

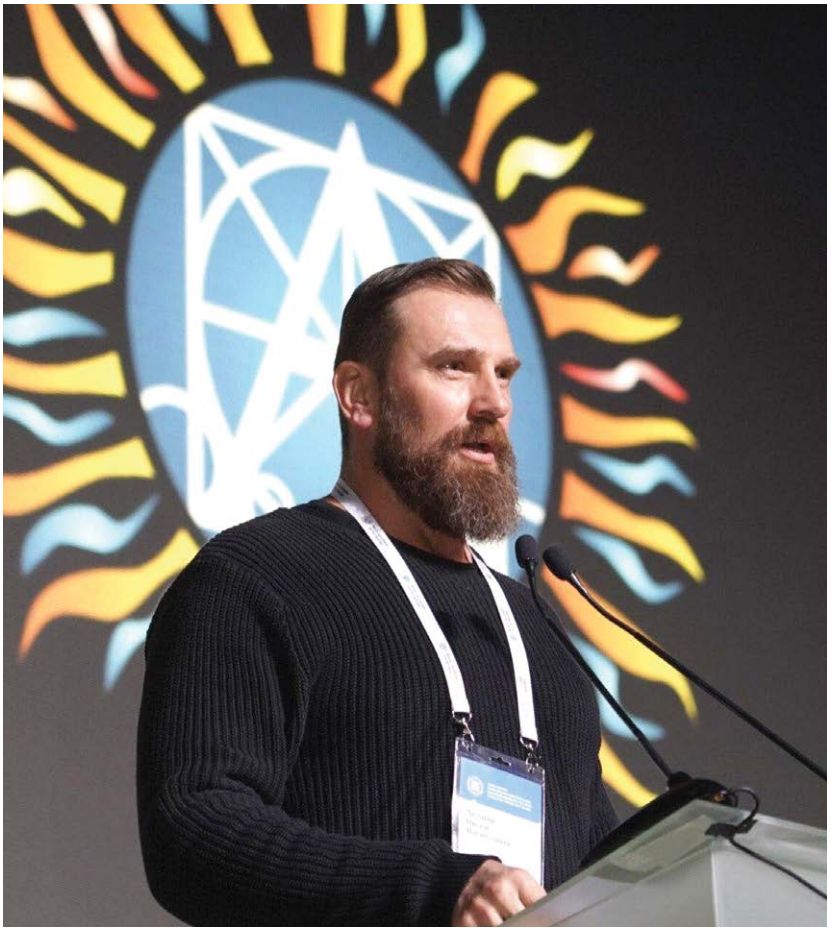
The main tips have become everyday: if possible, avoid crowds, use sanitizers and to wear a mask in public obligatory. And this is not only an issue of personal safety, but also responsibility to others. It is no coincidence that 80 years ago academician Lev Vasylovych Gromashevskyi, whose name our Institute has, emphasized: if everyone wore protective masks during the SARS season, there would be no seasonal outbreaks. Also, for all, and especially for those who are at risk, to vaccinate against influenza is rationally – it will facilitate the diagnosis in case of illness and allow to avoid a mixed infection in which the disease becomes extremely severe.

■ ***You and your colleagues now have a huge responsibility, because you have to keep track of huge amounts of information…***

And not just to track, but also to analyse, conduct their own epidemiological, virological, clinical studies aimed at determining the epidemiological characteristics of this infection, obtaining effective domestic drugs, means of prevention, diagnosis, treatment regimens! That's why we work day and night, during breaks, on the road… – so that, what is known today about the threatening virus should be put into a single puzzle and we understand in which direction we need to move.

Oksen LISOVYI: “A comprehensive support program for young researchers should be implemented in Ukraine”

Domestic science needs a comprehensive reform, one of the main components of which is the involvement of talented Ukrainian youth in research. **AN IMPORTANT STEP IN THIS DIRECTION IS THE COOPERATION OF BUSINESSES AND OUT-OF-SCHOOL EDUCATIONAL INSTITUTIONS. OKSEN LISOVYI, CANDIDATE OF PHILOSOPHICAL SCIENCES, DIRECTOR OF THE NATIONAL CENTER “JUNIOR ACADEMY OF SCIENCES OF UKRAINE”, TOLD ABOUT THE IMPORTANCE OF SUCH PARTNERSHIP.**



■ ***Oksen Vasyliovych, how would you describe the state of Ukrainian science today?***

It is difficult to evaluate science in general, because each industry has its own peculiarities. However, distinguishing the common peculiarities, I can mention the phenomenon of "ageing" of our science. We see how talented young scientists are often forced to stop their research and seek self-realization in other fields of activities, or even go abroad to build a successful scientific career. This problem caused by the declined research prestige, the lack of decent funding and support programs for young scientists has a negative effect on the ability to produce modern, innovative ideas.

■ ***What should be the strategy for involving young people in science?***

In my opinion, a comprehensive approach which will be implemented in three areas will be effective. First, it is necessary to cultivate love of research in future scientists from the cradle. The success of reforming various fields of domestic science directly depends on the timely involvement of talented youth. The state should allocate sufficient funds for the implementation of extracurricular education programs. Second, scientists who are just beginning to build a career should be able to meet a number of their needs: from basic – for example, housing and decent wages – to the possibility of networking with world research centres. A support program for young researchers should be implemented in Ukraine. Another important thing is the concept of Citizen science which, in particular, consists of involving amateur scientists in research who do not necessarily have a specialized education. Such measures contribute to a better understanding of the importance of sufficient funding for research by society and government. After all, almost all aspects of everyday life of a man of today are somehow connected with the results of the professional activity of scientists – we use their developments every day.

■ ***Regarding the first aspect – when, in your opinion, is it better to start encouraging a child in research?***

I think the sooner the better. The optimal period when a child should be interested in science is primary school. You should not postpone familiarization with research to adolescence: at the age of 13-14, a teenager is usually interested in entertainment and is guided by the need for socialization or self-affirmation among peers, rather than craving for scientific knowledge. Therefore, it is important to encourage a talented child before this stage of adulthood.

■ ***What is the role of the Junior Academy of Sciences of Ukraine in the context of reforming Ukrainian science?***

The Junior Academy of Sciences of Ukraine which is subordinated to the National Academy of Sciences of Ukraine and the Ministry of Education and Science of Ukraine provides students with conditions for productive research and assists them in professional identity. In this way, we partially solve the problem of "ageing" of science, contributing to the early replenishment of the research staff with talented young people.

However, unfortunately, we lack knowledge-intensive business support. Our students quite often spend lot of time and effort on research that has no prospects due to many reasons: first, the niche for the project may be already occupied. Sometimes the solutions proposed by the student seem theoretically good but cannot be practically useful etc. Mentors of the business sector are able to give a young researcher guidance in the relevance of projects and create development that will be demanded.

■ ***Why do you think the Ukrainian companies do not pay enough attention to working with children?***

The problem of domestic knowledge-intensive business is the lack of understanding of what "field sowing" is – the key to replenishing the company's staff with qualified specialists in the future. Most companies primarily recruit already trained specialists – university graduates. At the same time, students in 10-11 grades actually blindly choose EIT (external independent testing) subjects. In contrast, we observe the experience of successful foreign companies: for example, Bayer or Volkswagen which create special "children's" laboratories for talented students. This experience should be taken as an example by representatives of knowledge-intensive business in Ukraine. In this way, they will prepare motivated, enthusiastic employees in advance, while facilitating to strengthen the scientific potential of the whole country.

■ ***The signing of the Memorandum of Cooperation between JSC Farmak and National Centre "Junior Academy of Sciences of Ukraine" was a significant event in the Ukrainian pharmaceutical industry. Why was the pharmaceutical company chosen as a partner and how is this cooperation maintained?***

JSC Farmak is one of the few Ukrainian companies willing to invest in the scientific future – both the Company and the state as a whole. Our cooperation involves the following areas: examination, career guidance and joint implementation of educational projects in pharmacology, medicine and chemistry. We hope that such partnership will be useful for the students of our Academy and for Farmak.

Pharmaceutical industry is a driver of scientific developments, and Farmak, confirming its leadership, allocates funds and focus its efforts on own developments, the creation of educational projects and support of the scientific industry as a whole. **WHAT IS NEEDED FOR UKRAINE TO STRENGTHEN ITS POTENTIAL?**

FARMAK INVESTS IN SCIENCE

IMPLEMENTING INNOVATIONS

Pharmaceutical industry and biotechnology are the most high-tech industries and rank first in the world in terms of absolute and relative costs. These sectors account for 70% of all investments in the medicine – more than USD 1 trillion. The lion's share of these funds are spent on research. Farmak acts the same way, spending most of its profits on development. The Company annually invests about USD 15 million in R&D. A team of high-qualified specialists, including 150 scientists, is launching about 20 new medicinal products to the market a year, and about 100 complex-component effective medicines are now under development.

Taking into account how promising the biotechnology is becoming in medicine and pharmaceutical industry, Farmak is confidently building up its competencies in this area. To date, the Company has equipped a biotechnological laboratory that makes it possible to simulate the process of obtaining active substance as the main component of a medicinal product that has therapeutic properties. The amount of investment in this project is UAH 60 million. We are actively working on obtaining our own genetically engineered therapeutic proteins. We plan to thoroughly characterize these substances, make finished dosage forms from them, conduct non-clinical and clinical studies Then we will be able to plan the construction of a biotechnology manufacturing site. This prospect will take at least five years.

In JSC Farmak

The Company annually invests about USD

~15

million in R&D.

RESPONDING TO CHALLENGES

A systemic crisis caused by the pandemic inevitably makes adjustments to the previous plans for the Company's long-term development. It noticeably strengthens the course of most states towards self-sufficiency. A special responsibility is imposed by this circumstance on the leaders of the Ukrainian pharmaceutical market for providing people with the necessary medicines. Other important steps included a number of necessary procedures regarding medicinal products which could be effective in fighting the Coronavirus infection. For example, dexamethasone phosphate, solution for injection, was re-registered. In addition to its main indication, this pharmaceutical product was also included in the list of medicinal products used in the treatment of complications caused by COVID-19. Today, the phase III of multicenter randomized, double-blind, placebo-controlled study of enisamium iodide in patients with COVID-19 is being carried out in Ukraine, with the participation of international companies. It's too early, though, to talk about results, the proven anti-influenza efficacy of enisamium iodide gives reason to hope for success.

SUPPORTING SCIENTISTS

To meet domestic needs and increase the export of medicines, our country must preserve and increase its own intellectual capital. "Ukraine can become one of the world's leading R&D centres," says Filya ZHEBROVSKA, Chairman of the Supervisory Board of JSC Farmak. "We do not need to involve foreign scientists – we have our own, who only need proper conditions for their research work. Today we are looking for Ukrainian scientists who have gone abroad, and we want to bring them back home. Farmak is ready to provide grants to such researchers. We are looking for startups to facilitate implementing these developments. In particular, we are ready to support scientific developments in pharmaceutical products to treat cancer, and vaccines."

Socially responsible business should not be aloof from the development of science. We are talking both about the present: creating jobs or providing grants, and about the future: providing conditions that will encourage the younger generation to become interested in science.

TAKING CARE OF YOUTH

Farmak realizes that young talents need support and works closely with leading Ukrainian universities. The Company has been holding the "School of Young Scientists" for seven consecutive years in order to revive the scientific potential of our country. Over the years, this project has reached an international level and has become a notable platform for learning and exchange of views.

The Memorandum of Cooperation between Farmak and the Junior Academy of Sciences (JAS) is an important step in supporting young people. Its goal is to consolidate the efforts of business and scientific institutions to support talented students and strengthen the intellectual potential of our state. "One of the ambitious goals of this cooperation between Farmak and the JAS is to strengthen the prevention and response to the outflow of talented youth abroad. We also want to support the desire of the JAS members to develop the Ukrainian science. I am sure that each of them will be able to break into the world,

Visit of students to JSC Farmak

making more than one sensational and important breakthrough," said Volodymyr Kostiuk, Executive Director of JSC Farmak.

"Every developed country that cares about its future has strong views on training specialists for science and high technology. In order to become professionals in these industries, the present-day teenagers should obtain thorough business education, learn how to generate new ideas, create original products and solutions. Therefore, the Junior Academy of Sciences of Ukraine finds it important to cooperate with such tech giants as Farmak. And today we are excited to join forces to help the Ukrainian students to acquire the necessary skills in order to implement their abilities and talents," stressed Oksen Lisovyi, Director of the National Center "Junior Academy of Sciences of Ukraine".

IMPLEMENTING VARIOUS PROJECTS

The cooperation between Farmak and the JAS will open the new opportunities for talented youth, who will be awarded at the all-Ukrainian contests where they will present their research works, will make it possible for them to be consulted by the best experts of Farmak. The members of the JAS will be able to gain knowledge by working in the laboratories at the R&D site of the Company, to participate in Farmak's educational projects: School of Young Scientist, Farmak_lab and others.

The development of scientific potential in Ukraine should be a strategic task for the government. What is required is state support, the system of grants, the comfortable environment for the science development. Socially responsible business should also participate in supporting science.

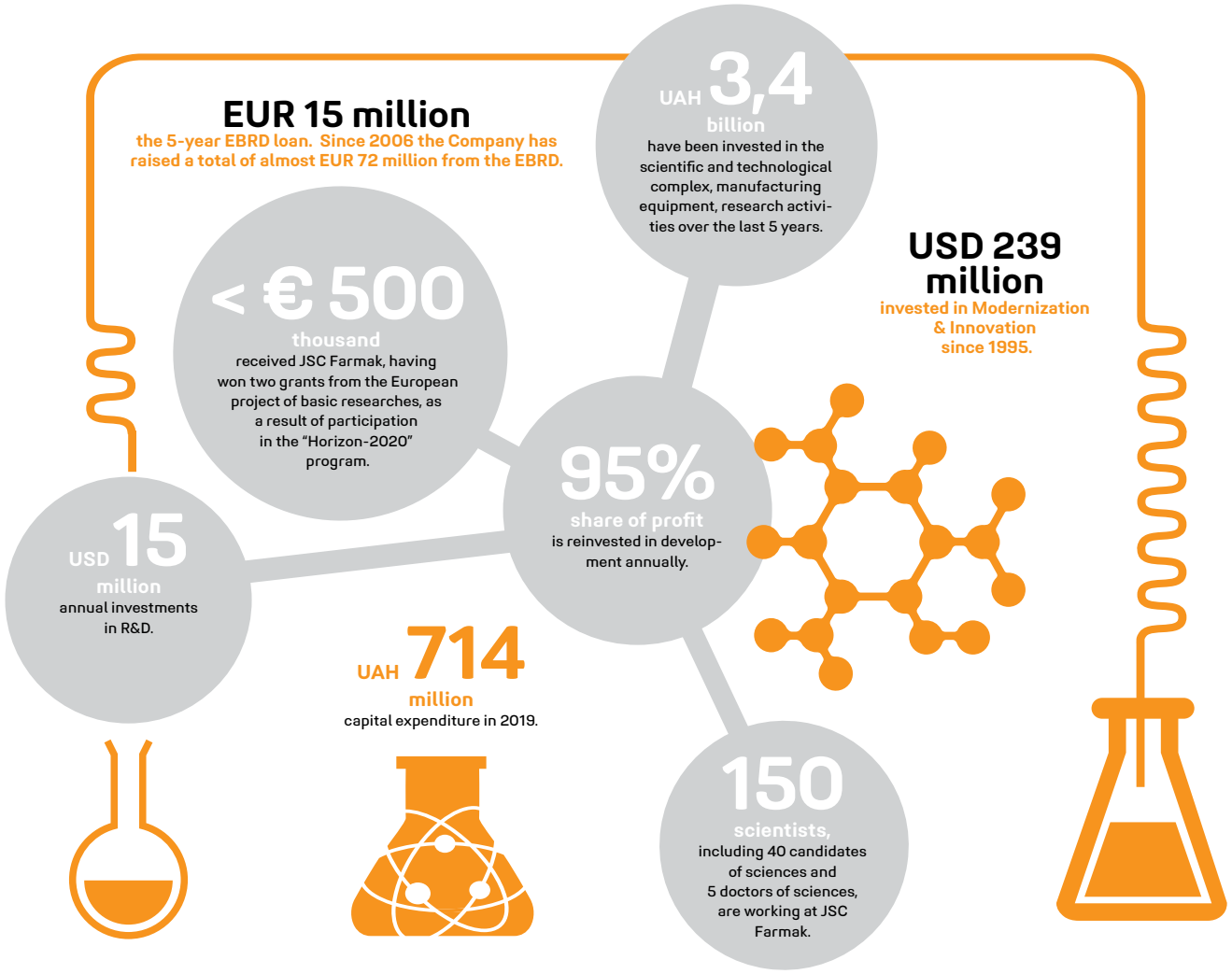
Efforts should be aimed not only at supporting those who have already chosen science as their

future profession, but also at increasing general science knowledge, in particular of those young people who have not yet decided on their future path. To this end, the JAS, with the support of the Ministry of Education and Science of Ukraine, created the Science Museum, located in the new Science pavilion at the VDNKh (Exhibition of Achievements of National Economy). Within the framework of the partnership project, JSC Farmak presented in the museum its installation of an enlarged copy of a human cell.

POPULARIZING THE ACHIEVEMENTS OF SCIENTISTS

Ukrainian scientists are working on the Hadron Collider, developing matrix polymers, studying neural connections, space weather... And this is only a small part of the directions in which our compatriots make their discoveries. The book «Bude tobi nauka" ("That's science for you") tells more details about the achievements of Ukrainian scientists, and was issued by Farmak on the occasion of its 95th anniversary. It contains 30 biographical sketches about modern Ukrainian scientists, including physicists, biochemists, genetics, immunologists, neurophysiologists, nanotechnology specialists, IT specialists and representatives of other fields of science.

By initiating this publication, Farmak seeks to popularize science among all Ukrainians and, first of all, among young people who choose their own path, as well as to show that you can be successful in your own country too – after all, there are companies interested in developing Ukraine's scientific potential.



TABLET'S

TABLETS ARE ABSOLUTE LEADERS AMONG DOZENS OF DOSAGE FORMS BECAUSE THEY ARE SO EASY TO STORE, DOSE AND USE. However, the most convenient form for taking requires nearly the greatest effort from developers of medicinal products.

YULIIA KONDRATOVA
Head of the Analytical Development Department of JSC Farmak

When taking medicinal products, we do not usually care too much about what happens further with them in the body because the result is important for us! But before bringing relief, the pharmaceutical product undergoes difficult processes to give its targeted effect.

WHAT ARE THE PROCESSES?

There are tablets that dissolve in the oral cavity. Their local effect or absorption begins through the mucous membrane. There are medicinal products that have to «pass by» the stomach for active substances to extract in a certain part of the intestine. But in most cases, the disintegration of medicinal products and the absorption of the necessary components occur in the stomach. If the tablet does not dissolve for some reasons and travels further, its effect will not be as intended. Or it will release the active substance very quickly and its effect will be unpredictable, which will harm the body. The circulatory system distributes the active substances in the body, some of which are converted into new ones in the liver. This process is called metabolism. After biotransformation, part of the inactive metabolites will «exit», and part of the transformed active substances together with the blood will move to other organs. In order for APIs to release where and when intended during this difficult journey, many nuances need to be taken into account.

WHAT SHOULD BE CONSIDERED?

Absorption of the medicinal product depends on how it is manufactured. For example, in direct compression, when the substance and excipients are taken in the form of powders and are tableted, the medicinal

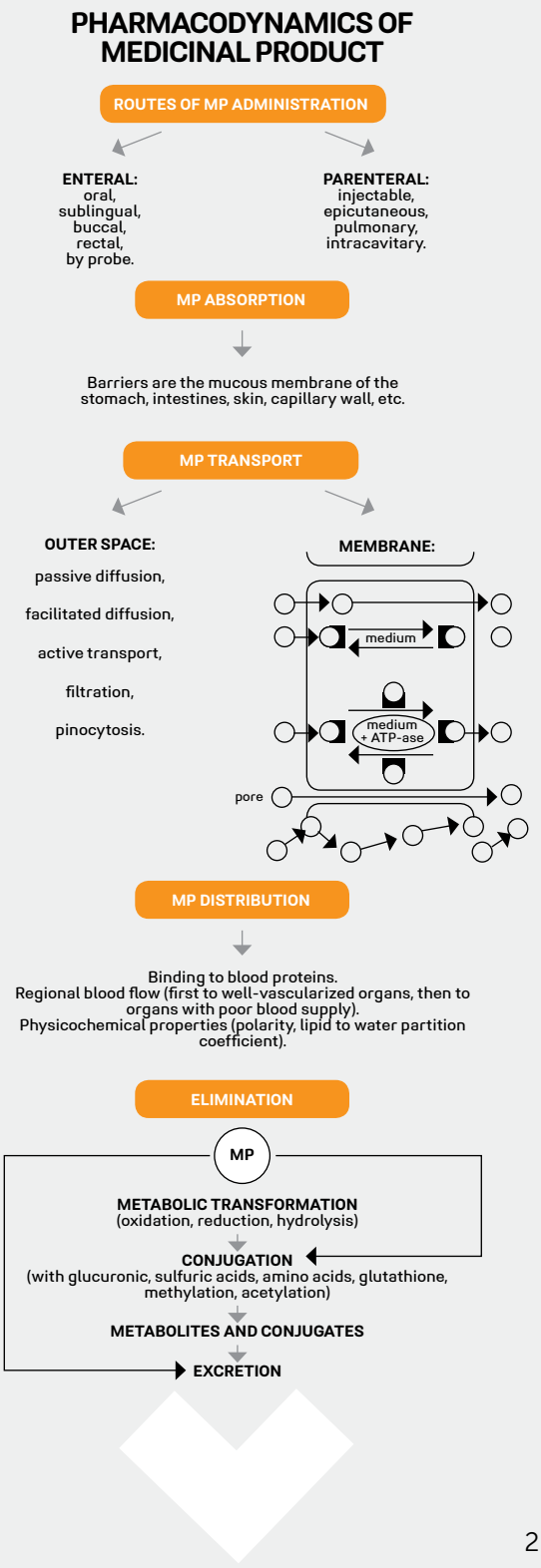
JOURNEY

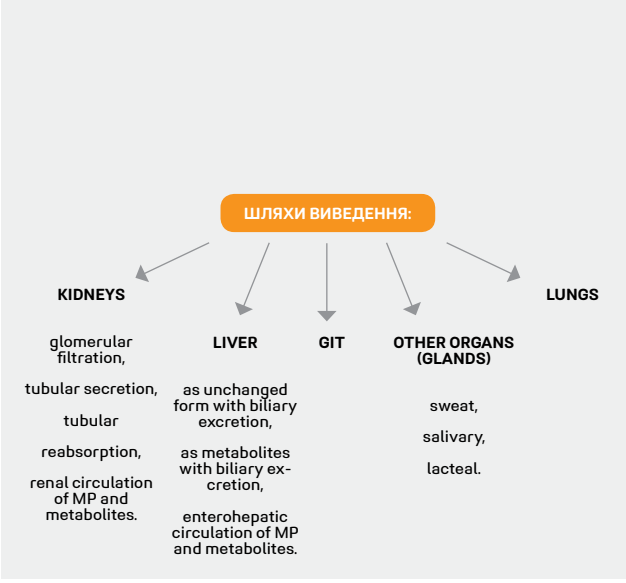
product immediately decomposes into particles of the substance. 90% of tablets are made in another way, by wet granulation. APIs are combined with excipients, and under the influence of the body's environment the product first breaks down into granules, and then into substances. This way is more complicated, but it makes it possible to vary the speed of effect: some tablets should give effects in 15 minutes; some become effective within an hour; and some need a longer period of time for APIs to release in order to give a prolonged therapeutic effect.

The concentration of API and even the shape of the active molecule crystals, the choice of excipients, the degree of grinding of the components, the tablet shape, the technology of its manufacture are only a part of aspects to be taken into account in the development process!

WHAT SHOULD BE PREDICTED?

The process of tablet disintegration may occur differently since each body has its own





peculiarities. For example, it is known that the tablet breaks down in the stomach under the action of gastric juice. It is believed that this is a mixture of hydrochloric acid with pH 1.2. But there may be people with hypoacidity or hyperacidity. It has been observed that the gastric environment is more acidic in women than in men, but the secretion of gastric juice is more intense in men. But this does not mean that the medicinal products will not be effective: manufacturers must take into account all possible situations in the process of pharmaceutical product development.

HOW TO CHECK?

The experiments take place in a quite simple but effective way. The device for studying the process of active substance releasing, which is used to study tablets and capsules, is a special container in the middle of which the temperature of the human body is maintained and mechanical elements are available to mix the contents (to simulate processes in the stomach or intestine). It is filled with artificial gastric juice or biosolution with enzymes similar to the environment of the small or large intestine. Then the medicinal product is placed in this solution in the device.

The «simplicity» ends at this stage, because during research of generic, experts need to make a huge number of measurements. According to a certain schedule, at certain points in time: sometimes every 5 minutes, sometimes up to 24 hours, samples of the solution are taken and the amount of active substance to be released is determined. According to the obtained indicators, graphs of concentration dependence on time are drawn up. They are analysed by comparing with the data obtained for the reference (original) medicinal product. The developers of generics start talking about the success of their own development only when the curves coincide by more than 50%. Sometimes, to achieve this result, at least 50 laboratory batches should be tested! The stage of research, which tests the kinetics of medicinal product, can be 80% of the entire process of its development. But only when this stage is completed, there is confidence that the final bioequivalence studies will confirm: a really quality generic is finally developed!

The tablet is not the only convenient solid medicinal product. For example, there are gelatin capsules containing pellets. Pellets have a more complex structure than powder or granules. This form is used when the API is very sensitive to external factors (e.g., light) and to simplify the pharmaceutical manufacturing, such API is pelletized at pharmaceutical synthesis plants so that it has a certain mechanism of effect.

Bronkhalyk

Farmak

COUGH LOZENGES

- antispasmodic*
- antioxidant*
- anti-inflammatory*
- antimicrobial*

TWO-PHASE LOZENGES

METHOD OF ADMINISTRATION

Adults: 1-2 lozenges several times a day, however, not more than 6 lozenges per day.

Children over 6: not more than 3 lozenges per day.

Dissolve slowly in the mouth.

* - According to prescribing information for the dietary supplement Bronchalik. Dietary supplement advertisement. It is not a medicinal product. Declaration of conformity for the product "Bronkhalyk" to the requirements of Ukrainian food legislation of June 15, 2018. Manufacturer: JSC "Farmak" 63 Kyrylivska Str., Kyiv, 04080, Ukraine +38 (044) 239-19-40 / fax: +38 (044) 485-26-86 /e-mail: info@farmak.ua /website: www.farmak.ua

Uzbekistan: integrated approach to development of science

Today, the Republic of Uzbekistan is a modern progressive state. Many aspects of its life have been determined in recent years by the new Development Strategy drawn up under the rule of President Shavkat Mirziyoyev. **DEVELOPMENT OF SCIENCE IS AN IMPORTANT PART IN THIS LARGE-SCALE AND AMBITIOUS PLAN.**

EDUCATION IS A PRIORITY

New international and private universities have been actively established in Uzbekistan for several years: education has gained a second wind. The large-scale plan for the implementation of the President's Strategy requires an integrated approach comprising several main directions. Research stimulation is one of the most important objectives: first of all, it involves the establishment of specialized scientific laboratories in universities and research institutes. For example, the renewable energy laboratory was established at the Yeoju Technical Institute in Tashkent for students' scientific research. The modern computer laboratory, where young IT specialists are engaged in programming and development of computer services, including neural networks, is operating at the Inha University (Institute of Information Technology). And at the Tashkent State Technical University, there

Photo istockphoto.com; uz.sputniknews.ru

are many physics, chemistry and mathematics laboratories equipped with innovative equipment.

QUALITY AND PERFORMANCE

The improvement of the performance of Uzbekistan's universities and research institutes should be based, in particular, on international experience. For instance, due to issue of licenses to foreign private universities which began in 2018, education sector was significantly changed: over the next three years, foreign institutions opened their doors to tens of thousands of Uzbek prospective students. For example, many private universities from South Korea have been established: YTIT, BUT, etc.

In addition, the credit based modular system that has been partially introduced in higher educational institutions in Uzbekistan since 2020, allows students to independently adjust their schedules and to choose subjects of their interest.

Photo profi-forex.org

The discovery of a dwarf planet by scientists of the Maidanak Astronomical Observatory in 2007 has become an outstanding achievement of Uzbekistan in astronomy.

Unfortunately, the program is not being implemented as quickly as wished, but there is every reason to believe that its implementation will become a milestone of the Uzbekistan's education sector, contributing to the increase in the performance and quality of all educational institutions in the country.

THE MOST IMPORTANT SECTORS

According to the recent trends, agriculture, energy and economic sectors are the priority sectors for the Government of Uzbekistan. The construction of a nuclear power plant, complexes of wind and power generators, as well as solar panels is a huge potential for the development of the country, and funding of clean and safe technologies will have a positive impact on the climate and the environment.

The discovery of a dwarf planet by scientists of the Maidanak Astronomical Observatory in 2007 has become an outstanding achievement in astronomy. This celestial object was included in the catalogue of the Harvard Minor Planet Center in 2009 under number 210271. In 2010, the new planet was named by the President as «Samarkand».

It is also important to note the developments in breeding and genetics: a team of plant breeders of the Institute of Genetics and Experimental Plant Biology of the Academy of Sciences of the Republic of Uzbekistan developed a gene-knockout cotton variety which is known for its well-developed root system and increased productivity. A joint patent is being applied for this technology with the University of Texas (USA), with the share of Uzbekistan of 70%.

INTERNATIONAL SUPPORT

In order to develop and promote scientific projects in Uzbekistan, the Science and Technology Agency was established. A list of programs related to fundamental and practical scientific research is published on its website. Young scientists are provided with comprehensive support and the opportunities to participate in joint international projects. Information on various programs and scientific internships can be also found on the website of the Academy of Sciences of Uzbekistan.

In addition, numerous cultural centres have been established in the country (Korean People's Centre, German Cultural Centre, Polish Cultural Centre), which operate with the support of foreign embassies and sponsors. Many of them also lobby for the development of science and raising the level of education in Uzbekistan. Their joint efforts help young specialists with further employment and promote scientific projects.

Undoubtedly, significant changes await Uzbekistan: the country's science and scientific communities are doomed to succeed. The necessary knowledge that is already acquired by the representatives of the younger generation will make it possible for Uzbekistan to join the ranks of world leaders in scientific sector.

State Institution "The Institute of Blood Pathology and Transfusion Medicine of the National Academy of Medical Sciences of Ukraine" in Lviv has recently celebrated the 80th anniversary of the founding. **ITS DIRECTOR VASYL NOVAK, HONOURED WORKER OF SCIENCE AND TECHNOLOGY OF UKRAINE, TELLS ABOUT WHAT ACHIEVEMENTS HAVE BEEN MADE BY THE INSTITUTE IN SCIENCE AND PRACTICE SINCE ITS FOUNDING.**

INNOVATIONS IN TREATMENT OF BLOOD PATHOLOGIES

RESEARCH BASE

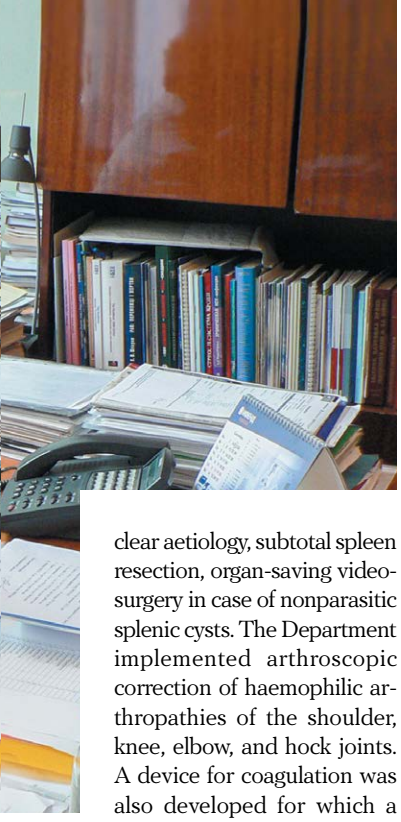
Significant progress in theoretical and practical haematology and transfusion medicine over the past decades influenced the directions of scientific developments at the State Institution "The Institute of Blood Pathology and Transfusion Medicine of NAMS of Ukraine". The ability of potential inventions to improve the indicators of patients' life duration and quality has become the selection criterion. The leading scientists of the Institute have established unique scientific schools: haematology surgical haematology, industrial and clinical transfusiology, immunology, haemostasiology and extracorporeal haematology. The scientific outlook of the current heads of the Institute's structural divisions was formed at these schools, including: I.Y. Yevstakhevych, Z.V. Masliak, B.V. Kondratskyi, O.V. Stasyshyn, T.V. Danysh, M.I. Voroniak, O.O. Shalai. 12 doctoral and 35 candidate's dissertations were defended by the Institute's staff.

The foundations of the Institute were laid by professors S.S. Lavryk, A.H. Karavanova, V.A. Monastyrskyi, M.R. Kopystianskyi, R.M. Hlants, M.V. Myndiuk, B.V. Kachorovskyi.

OUTSTANDING ACHIEVEMENTS

The structural divisions of the Institute of Blood Pathology and Transfusion Medicine are known in Ukraine for innovative diagnostic and therapeutic procedures that are performed based on them.

- ***The Department of Haematology*** is engaged in implementing a program for the treatment of patients with chronic lymphocytic leukaemia, as well as CD20-positive non-Hodgkin's lymphomas, preparing patients with multiple myeloma and malignant lymphomas for haematopoietic stem cell transplantation, international multicenter clinical trials of new anticancer pharmaceutical products.
- Over the past 25 years, the ***Department of General and Haematological Surgery*** developed and implemented videosurgery diagnostic resection of retroperitoneal lymph nodes (a patent was issued), a method of ultrasound-controlled percutaneous trephine biopsy of abdominal lymph nodes, laparoscopic spleen biopsy in splenomegaly of un-



clear aetiology, subtotal spleen resection, organ-saving video-surgery in case of nonparasitic splenic cysts. The Department implemented arthroscopic correction of haemophilic arthropathies of the shoulder, knee, elbow, and hock joints. A device for coagulation was also developed for which a patent was issued.

■ High-dose chemotherapy followed by auto-HST for patients with lymphoid neoplasia, concomitant therapy in the early and late post-transplant period, and monitoring the efficacy of HST are conducted at ***the HST Centre***. The Centre is accredited by the Ministry of Health of Ukraine and is part of the pilot project for auto- HST in haematological patients. 25 auto- HSTs were performed based on the Centre in patients with multiple myeloma and lymphomas.

■ Therapeutic plasma, cyto-, photopheresis, haemo- and plasmasorption, ultraviolet blood irradiation, He-Ne laser treatment have been implemented at ***the Department of Extracorporeal Haematology and Haematopoietic Stem Cell Transplantation and the Haemapheresis Centre.*** The research is being conducted to develop domestic plasmacytapheresis devices, refrigeration centrifuges and arrange their manufacturing. The Department is the basic site for obtaining hematopoietic stem cells.

■ Mass manufacturing of complex pharmaceutical products of multifunctional action from domestic manufacturers and their use in medical practice have been implemented at ***the Laboratory of Technology of Transfusion Pharmaceutical Products.*** Solutions have been developed for the preparation and preservation of blood and for resuspension of thawed erythrocytes. A scheme for obtaining prothrombin complex concentrate from donor plasma, and methods for cryopreservation of erythrocytes at moderately low temperatures have been developed (-20 °C and -40 °C).

■ The new methods for detecting gene mutations in chronic myeloid neoplasias developed and implemented by t***he Laboratory of Molecular Genetics*** make it possible to make diagnosis as accurately as possible and monitor the treatment progress and outcome at the level of genomic DNA/RNA using the polymerase chain reaction method. The Laboratory conducts complete molecular genetic studies in Ph-negative myeloid neoplasia, implements a method for detecting BRAF (mutations in hairy cell leukemia and melanoma), and carries out molecular genetic monitoring of thrombophilia.

■ ***The Laboratory of Immunology and Genetics of Blood Neoplasias*** is engaged in research of morphological, immunophenotypic and lectinophilic signs, as well as cytogenetic abnormalities of substrate cells, cytogenetic monitoring and analysis of cytokine production in lymphoid and myeloid neoplasias. The modern methods of studying classical cytogenetics (karyotyping) and molecular genetic method (fluorescent in situ hybridization) have been embodied in medical practice.

The specialized clinical diagnostic laboratory was established based on the Institute of Blood Pathology and Transfusion Medicine to conduct laboratory tests for all clinics of the Institute. Now COVID-19 can be diagnosed at this laboratory.

■ ***The Laboratory of Blood Biochemistry*** has been developing the new methods for the isolation and purification of blood plasma proteins and their sub-fractionation products in order to develop therapeutic and diagnostic products since 1995. The developed schemes are based on modern methods of fractionation (affinity chromatography). Original macroporous silica-based sorbents are used as matrices for biospecific chromatography of various protein factors of the blood coagulation and fibrinolysis.

In addition, the only dental office in Ukraine operates at the Institute that provides dental care services to patients with coagulopathy, including patients with haemophilia.

From the archives of the Institute

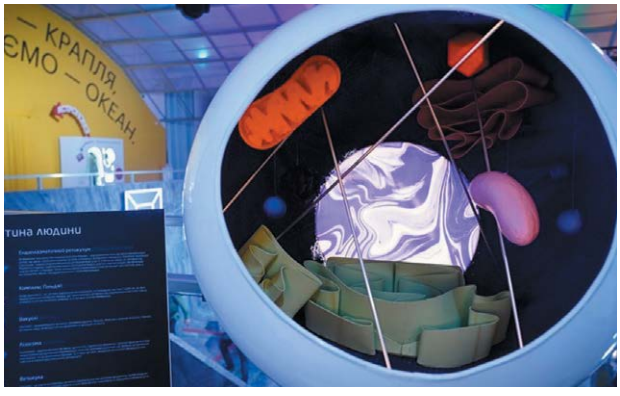
TOUCH... THE EXHIBITS

Ride a bike with square wheels, go on a space journey, hold in hand models of innards and even create a rainbow by yourself... **ALL THESE OPTIONS ARE NOW AVAILABLE TO VISITORS OF THE MUSEUM OF SCIENCE WHICH RECENTLY OPENED IN ONE OF THE PAVILIONS OF CAPITAL'S VDNG.**

@aleksbenhannun

FOR THE FIRST TIME IN UKRAINE

The unique interactive space is divided into seven thematic blocks where more than 120 exhibits and installations related to research activities are presented. These non-trivial items can be seen in "Science" – pavilion № 23 built in 1960 as a platform for scientific exhibitions. One of the main "points" of the new cultural and educational institution is that it is the first Ukrainian state museum which visitors are not only allowed but even recommended to touch the exhibits. A walk through the halls of the museum is a great way to make many of your own discoveries and get an unforgettable experience. The founders of the institution were the Junior Academy of Sciences of Ukraine and the Gres Todorchuk Agency with the assistance of the Ministry of Education and the National Academy of Sciences of Ukraine. This project is international: Specialists from Ukraine, Poland, the USA, Canada and Sweden took part in its creation.



@sciencemuseum.com.ua

Company Farmak became one of the project partners. Among the exhibits of the Museum of Science are those presented in the first mobile pharmaceutical museum created by the Company. In particular, the installation of an enlarged copy of a cell of the human body.

SCIENCE FROM AROUND THE WORLD

The Museum of Science presents a variety of developments of the researchers from many countries. For example,

Photo Aleks Benhannun; Sciencemuseum.com.ua

the exhibits "Human", "Great Inventions", "Acoustics" and «Optics» were created by the Polish company Strong Interactions. The square-wheeled tricycle, which visitors can ride on a special platform, came to Kyiv from the New York Museum of Mathematics (by the way, there are only four such bicycles in the world), one of two 2-meter holograms on the planet – from Great Britain, 3D-model of the human body – from Sweden, a unique optical illusion from Professor David Novik – from the United States of America. Interesting exhibits from different countries will not leave indifferent connoisseurs of fascinating discoveries.

FUN SCIENCE

To awaken in children a love for research, to convince that the work of a scientist is extremely interesting, full of surprises and is not limited to axioms and equations – this is the goal set by the organizers of the project. The museum has everything you need to learn about science in practice and become part of the scientific world. Here you can have fun learning the principle of "knowledge through experience" – to experiment with exhibits, to engage in an exciting business all your imagination and clearly learn about the laws of nature, the principles of operation of certain mechanisms and more. For example, each visitor can safely shout into a giant plastic ear, which immediately measures and reports the volume of the scream. The organizers hope that the exciting excursions of the museum staff will encourage students to research in the future, so that in the future they will join the Junior Academy of Sciences and start working on their own projects under the guidance of experienced scientists.

Excursion to the museum will not impact your wallets. An adult ticket costs UAH 100, a children ticket – UAH 50, and for people with disabilities of groups I and II and for children of killed people during the hostilities in Donbas the entrance is free.

TERRITORY OF FREEDOM

Unlike classic museums, where it is forbidden to touch anything, in the new institution curious guests will not have to be bored, restraining their curiosity. With the installations placed here it is allowed to carry out any manipulations: twist in the hands, poke, juggle and even, if you are really want, throw some of them. An interesting exhibit which has already gained popularity among museum visitors – a bowling ball, which can hit the glass 600 thousand times – just as many blows it can withstand. Those who want to improve their accuracy can shoot an air cannon at a target on the wall. And for those who want to test their knowledge, the organizers have prepared an exciting test: you need to

@sciencemuseum.com.ua

deal with the issues listed on the special tablets. If you answer correctly, the glass ceiling in the room changes its colour. (If only exams in schools or universities were held in this way!) By the way, this chameleon ceiling is the largest interactive exhibit of the museum: its area is 400 sq. m.

WHY NOT IN THE "FLYING SAUCER"?

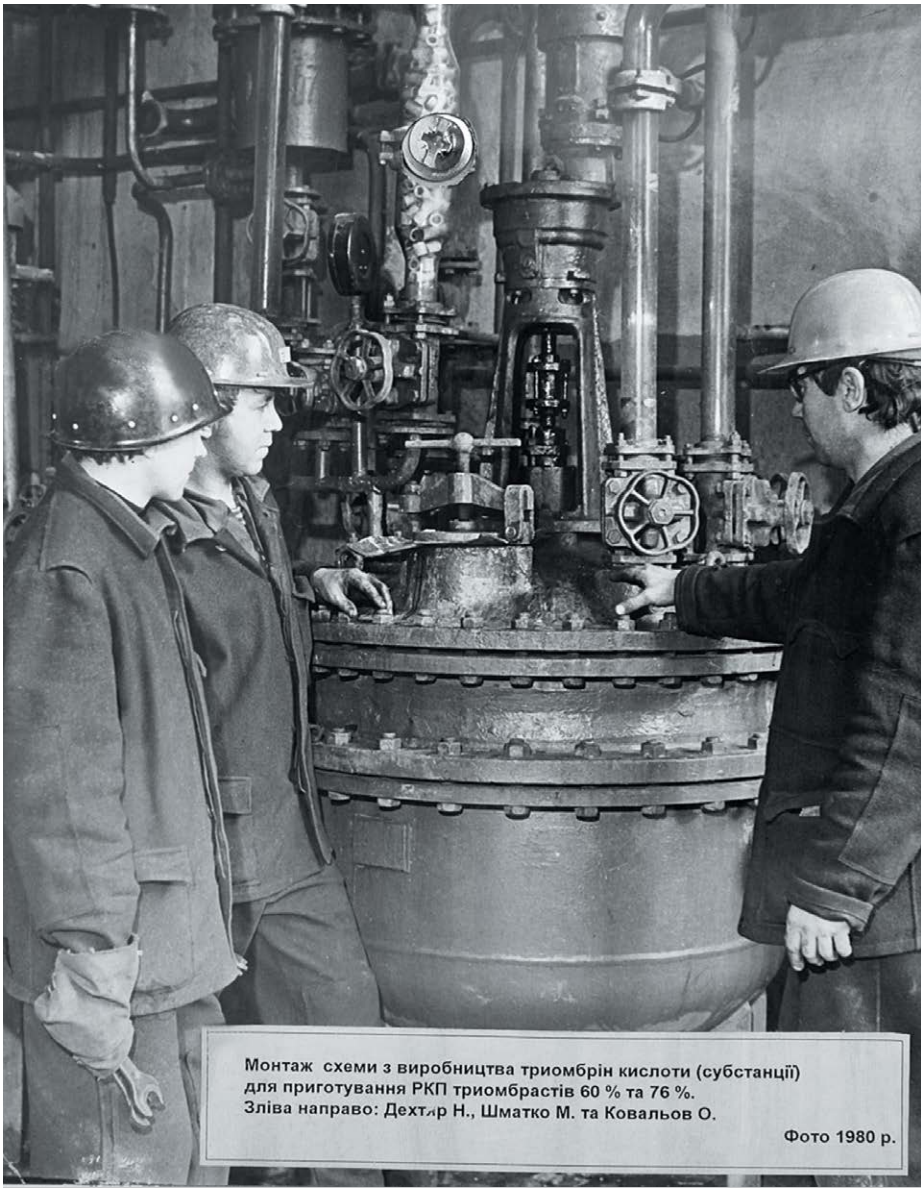
In this unique building – a monument of Soviet modernism at Lybidska metro station – where the Museum of Science was planned to be located 3 years ago when the authors received the support of the Ministry of Education and Science of Ukraine and the first funding for their project. About 7,000 sq. m. were allocated for the museum premises at that time, but the premises are still not repaired and the organizers did not want to postpone the project, so the museum settled at the VDNG temporarily. Probably, after the completion of repair works, it will still move to Lybidska metro station.

RECORD AT THE VDNG

Among the most popular installations of the Museum is a pendulum made of lamps with a length of 21 meters which claims to be mentioned in the Guinness World Records. When it is launched upwards, guests become spectators of the light show: running up the lamps paint the original patterns on the ceiling.

FARMAK.
Stress test

After getting through the tough economic challenges, the leading company of the Ukrainian pharmaceutical industry has not only gained a new leader, but also entered the new millennium with great professional achievements and ambitious plans. **THE COMPANY BEGAN TO ACTIVELY FORM A NEW PRODUCT PORTFOLIO AND MOVED TO AN INTERNATIONAL SYSTEM OF QUALITY ASSURANCE AND MANUFACTURING STANDARDS, WHICH ALLOWS FARMAK TO REMAIN AMONG LEADERS IN THE INDUSTRY RANKINGS FOR MANY YEARS.**



Монтаж схеми з виробництва триомбрін кислоти (субстанції) для приготування РКП триомбрастів 60 % та 76 %.
Зліва направо: Дехтяр Н., Шматко М. та Ковальов О.
Фото 1980 р.

INEVITABLE DEFICIT

One of the main reasons for the total shortage of finished dosage forms in the mid-1980s was the fact that the vast majority of medicines were exported, particularly from the Soviet bloc countries such as Hungary, the GDR, Poland and Czechoslovakia. Although almost all leading European pharmaceutical companies manufactured their products on the basis of finished substances supplied from the USSR, within the so-called Council for Mutual Economic Assistance. The Lomonosov Kyiv Chemical and Pharmaceutical Plant was one of the companies that had to be a raw material colony. Its product range was significantly focused on manufacturing of substances.

The shortage of finished medicinal products was artificially "speeded up" by the social obligations of the "first state of workers and peasants", which did not correspond to real economic power. As a result, 45% of medicines were provided to the population free of charge, and a discount of up to 80% was guaranteed to many beneficiaries.

ACCELERATION, RESTRUCTURING AND CHERNOBYL

Under these conditions, even self-accounting and self-government failed to bring the pharmaceutical industry to a whole new level. And the so-called acceleration announced in 1985 and the restructuring («perebudova») carried out in 1987 failed to bring the rusted ship of the Soviet industry into the open sea of the world economy. Thus, the inconsistency of the reforms, bureaucracy, lack of systematization and transparency in relations with partners did not allow the Lomonosov Kyiv Chemical and Pharmaceutical Plant to complete the construction of the premises for manufacturing of X-ray contrast agents in time and to modernize the Company.

We should not forget about the huge costs of eliminating the consequences of the man-made disaster at the Chernobyl Nuclear Power Plant, which fell upon the state budget. In the first days after the catastrophe, specialists of the Lomonosov Kyiv Chemical and Pharmaceutical Plant became immediate participants of the elimination of its consequences – in the summer of 1986, at the request of the Kyiv Civil Defence Headquarters, they began manufacturing a special reagent solution for purification of the radioactive water used at vehicles sanitation points. Nowadays Farmak manufactures several medicinal products that are successfully used as ones of therapeutic agents for treatment of the

diseases associated with the negative impact of radiation on the human body: for example, L-Thyroxine, a synthetic analogue of thyroid hormone, has been manufactured by Farmak since 1996. This large-scale project is related to the "Chernobyl Program" and was implemented jointly with the Austrian specialists of Falcon within the TACIS program («Technical Assistance for the CIS Countries") and with the participation of the European Union. L-Thyroxine, first manufactured in Ukraine through the joint work of our scientists, international experts and highly qualified staff of Farmak, now fully meets the needs of nearly 40,000 patients.

START OF A NEW MARKET ECONOMY

With independence, Ukraine began to build not only a new country but also a modern economy. However, the transition to new forms of ownership and management has become extremely painful, as it has often been introduced by shock therapy. In just one year (1989-1990), inflation in the country rose from 7.5% to 19%, and all former economic ties and supply chains were finally severed. In such difficult conditions, the oldest chemical-pharmaceutical plant in Ukraine once again proved to be a pioneer in the industry, announcing the establishment of Open Joint Stock Company Farmak.

A key event that influenced the revival of the Company was one appointment – in 1995 Filya Ivanivna Zhebrovska, whose professional career began right here, at the Lomonosov Kyiv Chemical and Pharmaceutical Plant, became the new Chairman of the Company's Board. Her energy and enthusiasm, ability to build clear tactical and strategic planning, as well as high professional competence allowed the plant not to cross the fatal point and not to stop the manufacturing process. "At that time, we had almost no competitive products," re-

Archive photo of JSC Farmak

calls the General Director of the Company. "We could only sell Corvalol, Naphtizin and glucose from what we manufactured. But even these medicines could not be properly sold: we manufactured some medicinal products, then stopped the line, then sold for a long time... As a result, almost 1,300 employees could not be paid on time. And so the employees came to me, explained the possibilities of the plant and proposed my candidacy for the Chairman of the Board at the shareholders' meeting. They trusted me!"

At the manufacturing of JSC Farmak

NEW POLICY

The former manufacturing model, focused on the manufacturing of raw materials for the pharmaceutical industry, has shown its complete failure in the conditions of open markets. The recession and the investment crisis required a radical review of the strategy. There was only one way for Farmak to reach a whole new level – the transition to finished medicinal products. The first step was the purchase and launch of a modern Bottlepack drops manufacturing line, certified in accordance with GMH requirements, and the first product was the popular Naphtizin drops, which began to be manufactured not in glass but in plastic containers. Other nasal drops – Farmazoline and Farmadex and eye drops Taufon and Pilocarpine took up the slack. In addition, in 1996, the equipment for the manufacture of ointments, gels and pastes was purchased. As a result, manufacturing volumes increased significantly and amounted to 157% compared to 1995.

STANDARDS WE CHOOSE

In the early 2000s, the Ukrainian pharmaceutical industry regained its growth – manufacturing volumes of medicinal products increased by UAH 265 million, which was the highest number in the last 10 years. At the same time, the domestic market was supplied with Ukrainian medicinal products by 40-50%, and their range has reached 1.5 thousand items. Farmak's contribution to this pharmaceutical breakthrough cannot be overestimated, as in 2001 the Company manufactured more than 100 finished medicinal products, supplying the market with 10% of domestic medicinal products. However, the Company, focused on expanding its outlets and cooperation with leading players in the global pharmaceutical market, relied in the long-term development strategy not only on the quantity but also on the quality of its products.

The final transition to quality assurance and management took place in 2001, with the release of a new version of ISO 9001:2000. At that time, Farmak quality system was fully adapted to the new requirements and was assessed as fully complied with national and international certification systems according to special audit.

INTERNATIONAL COOPERATION

The established quality management system has become a reliable foundation for the successful implementation of Farmak's strategy for technical re-equipment and development of the product portfolio. This process started in 2001, when the construction of a new workshop for the manufacturing of the finished medicinal products began. Due to the cooperation with a German design company, the project was implemented in compliance with all European GMP requirements, although this standard was not yet mandatory in Ukraine at that time.

A key event that influenced the revival of the Company was one appointment – in 1995 Filya Ivanivna Zhebrovska, whose professional career began right here, at the Lomonosov Kyiv Chemical and Pharmaceutical Plant, became the new Chairman of the Company's Board.

The next major project in terms of scale and social significance was the manufacturing of high-quality Farmasulin insulin in partnership with the American multinational corporation Eli Lilli. The infrastructure for product quality control created, as well as investments of UAH 47 million enabled the Company to

launch a full manufacturing cycle for active pharmaceutical ingredients. The result of hard work was the release of the first batch of Ukrainian genetically engineered insulins in 2006. And in 2011, after the necessary re-equipment of manufacturing facilities, Farmasulin began to be manufactured in cartridges.

UKRAINIAN MEDICINES IN THE EUROPEAN MARKET

The development of the first generic of injectable MRI contrast agent for the German company Kuragita (later AGFA) was the most important step in the Company's reputation strengthening. In 2007, Farmak was able to synthesize the substance and develop a finished dosage form of the medicinal product called Magnegita. A specially created department of the Company prepared a registration dossier in CTD format and was the first to register its generic in 22 EU countries under the decentralized procedure (DCP), and the very next day after the expiration of patent protection of the brand Farmak began to supply Ukrainian generics to Europe. Since then and to this day, no complaints have been received on this medicinal product from the EU pharmacovigilance system.

NEW MANUFACTURING SITE IN SHOSTKA

Having completed the full technical re-equipment of manufacturing facilities in 2013, Farmak launched a new manufacturing of active pharmaceutical ingredients (APIs). And that was spot on! The modern complex built in Shostka makes it possible to manufacture substances of European quality. Its planned capacity is 100 tons. The environmental standards for wastewater and air emissions treatment are strictly complied with at this site as well as at the main manufacturing site in Kyiv. In addition, the Company takes part in the local community life, initiating a number of socio-economic, infrastructural and cultural projects.

At the insulin production department

THE MOST INNOVATIVE COMPANY

In 2015, Farmak opened a laboratory and technological complex equipped with the state-of-the-art equipment, which makes it possible to implement the best scientific technologies in the development of new medicinal products. Today, this research complex consists of 4 analytical laboratories, 2 laboratories with biotechnological and synthetic APIs, 3 technical laboratories for finished forms and 4 pilot R&D sites. Innovative solutions are searched for by 150 scientists, including 42 candidates of sciences and 5 doctors of sciences. This allows the Company to launch 20 new medicinal products in the market annually and at the same time to work on the development of more than 100 promising medicinal products. In the last 5 years alone, UAH 3.4 billion has been invested in our own scientific and technological complex and research activities, and in 2020 investments in R&D amounted to USD 40 million. Therefore, it is quite expected that in 2020 Farmak is included in the national TOP 25 most innovative companies (according to the «Vlast deneg" (The Power of Money) magazine).

AMONG LEADERS OF PHARMACEUTICAL EXPORTERS

Expanding presence in international markets is not only the focus of Company's foreign economic strategy, but also the result of overall increase in sales. Thus, during 2000-2015, it increased by more than 35 times. Therefore, in 2013 a special department of globalization was created the goal of which was to activate the export potential of the Company. And in 2019, export sales accounted for 24.2% of total revenue. Farmak products are bought in 28 countries around the world: CIS countries, the EU, Southeast Asia, the Middle East, North Africa, Australia, New Zealand, as well as Israel and the United States. Currently, the international demand for the Company's medicinal products used in the complex therapy of COVID-19 patients has significantly increased. And this is only a portion of medicinal products amongst 14 therapeutic groups and 220 items, which are currently available in Farmak's portfolio.

Well-planned and balanced long-term development strategy allows the Company, celebrating its 95th anniversary, not only to maintain a leading position in the domestic pharmaceutical market (where Farmak's share is currently 5.9%)*, providing the population of Ukraine with modern high-quality and affordable medicines, but also to expand its presence globally, reaffirming its reputation as a trusted European exporter.

Archive photo of JSC Farmak

* according to Proxima Research International.

Digitalization, globalization and science: friends or enemies

DIGITAL SOLUTIONS ARE CHANGING THE WORLD BEFORE OUR EYES, AND WE ARE WITNESSING RADICAL CHANGES IN MEDICINE AND PHARMACEUTICALS. But do all trends have only a positive effect? And how in the modern conditions not to be on the margins of progress?

IN THE NEW CONDITIONS

The emergence and improvement of digital technologies made it possible to accumulate theoretical knowledge and practical experience at the level which was a dream before. This allowed introducing purely scientific approaches to the art of healing. The global community has strongly supported the positions of evidence-based medicine, putting a line under an approach based on trust in individual luminaries and their schools. Undoubtedly, the departure from the «medicine of authority» does not completely undo the respect we pay to the leading doctors of our times. But hardly anyone can clearly name the outstanding pharmacists who are our contemporaries because we know about the achievements of corporations rather than about specific individuals. The development of innovative pharmaceutical products has long ceased to be a matter of single geniuses, it is a task for huge teams. Such trend in the globalization of the pharmaceutical market as the consolidation of large corporations into even larger structures is also caused by the increasing cost of research and the need to consolidate global efforts in R&D.

Photo istockphoto.com

IN THE FUTURE PERSPECTIVE

What will be the consequences of digital technologies development and the overall globalization process for medicine? There are pessimistic opinions along with the conviction that the progress of science will make it possible to find revolutionary methods of treatment, and with the hope that future benefits will be fairly distributed due to prudent political decisions. Thus, considering globalization as a certain cultural paradigm, McDonaldization (a term introduced by the American sociologist George Ritzer, which describes such an organization of activities that is aimed at obtaining the fastest result through efficiency, calculability, predictability and use of "nonhuman" technology) is deemed to be its component. On the one hand, it may seem: what's wrong with getting the medical care needed as quickly as order at fast-food restaurant? It's not all as easy as it sounds: calculability can shift the emphasis from quality to quantity; predictability can lead to inappropriate unification of the approach, and control through digital solutions can result in dehumanization of the relationship between doctor and patient.

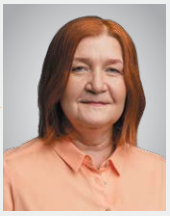
Although such warnings sound fairly valid, they are no reason to disparage digital technology as such. Since the digital innovations such as intelligent diagnostic devices, devices that facilitate communication between patients and doctors, the latest individualized medicinal products developed using intelligent systems, biotechnological pills developed in modern laboratories are the toolkit that will help doctors to raise medicine to a new, incomparably higher level, which will involve a much more individualized approach.

In practice

Today, digitalization is an integral part of the development of any pharmaceutical manufacturer. However, it should not be an end in itself. Electronic tools are effective only when they serve for a specific task.

For example, when it comes to choosing a potential original pharmaceutical product to develop a generic, it is not enough to use only software to track the stages of clinical trials of molecules, study the evidence base and verify the patent validity; it is also necessary to conduct a thorough marketing research to forecast market demand and identify key trends, says **Taras YAKOVENKO**, Head of Strategic Development Department of JSC Farmak.

In addition, digital technologies must be integrated into all processes without exception, from procurement to manufacturing and storage and delivery of finished medicinal products. Electronic accounting of raw materials, optimization of warehouses, installation of GPS trackers on vehicles to track a number of parameters, up to compliance with the temperature regime... These and dozens of other solutions significantly improve performance, says **Maryna STRIGANOVA**, Logistics and Procurement Director of JSC Farmak.



IN MARKET CONDITIONS

The market entry of most of the innovative original medicinal products is today the prerogative of multinational corporations. Even when the latest biotechnologies are developed by a small laboratory, without assistance of pharmaceutical giants in conducting clinical trials, arranging manufacturing, providing legal and marketing support, the product market entry is very problematic.

Obviously, the activities of domestic manufacturers are significantly complicated by the situation when the lion's share of manufacturing facilities is concentrated in the multinational corporations. To survive in the fierce competition on the part of market leaders, pharmaceutical companies are forming an alliance with the giants. Cooperating with world leaders without merger is also possible: mutually beneficial exchanging technologies, using manufacturing sites, involving research centres. Direct competition is also possible. In any case, whichever model of interaction with the Big Pharma is chosen, domestic manufacturers, if they do not want to give up their interests, must be as close as possible to the level of leaders. And the extent to which information and research results exchange technologies are becoming more developed today significantly increases the chances of equality between pharmaceutical market players.

The experience of Farmak shows: each of the projects was implemented by the IT Support Department of the Company in accordance with the principles of efficiency, calculability, predictability... And such steps will result in not dehumanization, but in emancipation, i.e. release of people from the oppressive routine processes, which will allow them to focus on creative processes and decision-making that no artificial intelligence can make.

TOP 5
inventions of Ukrainian scientists

Speaking about inventions that have changed the world, we usually make extensive historical journeys, proud of the names which are familiar to everyone for at least the last three hundred years. However, now we want to pay tribute to our contemporaries. **WE WOULD LIKE TO BRING TO YOUR ATTENTION THE LATEST DEVELOPMENTS OF UKRAINIAN RESEARCHERS WHICH CURRENTLY HELP DOCTORS SAVE PEOPLE'S LIVES AND TREAT SERIOUS DISEASES.**

1 WATER-JET SCALPEL

Professor Viktor Bocharov, a former designer of Antonov Design Bureau, has dedicated his scientific career to the development of hydraulic jet tools for the aviation industry. A team of scientists from the Aerospace Institute and the National Aviation University led by Bocharov applied aerospace technology in medicine and developed a liquid jet scalpel which is indispensable during operations on the internal organs. According to the inventors, the Ukrainian scalpel is better than its foreign analogues because it is more reliable, cheaper, and long-life.

The device resembles a dental drill and is equipped with two scalpels for different types of tissues, larger and smaller in diameter. A thin stream of water flowing out of the scalpel under high pressure does not damage the surrounding tissues and large blood vessels leaving a clean cut, the depth of which can be adjusted by changing the liquid pressure.

The invention was patented in 2014 having passed all stages of testing, and is now used by Ukrainian surgeons for extremely complex operations. For example, previously, in order to remove liver metastases, it required to excise part of liver. Using a jet scalpel, surgeons can save this organ as much as possible, removing tumours with the least haemorrhage.

Surgeons of Kyiv Clinical Hospital No. 1 were one of the first to use this invention for surgical operations. This technology is usually used in complex cases when the use of traditional tools is impossible. Doctors say that the new device helps not only to reduce the surgical operation duration but also significantly reduce the period of post-operative recovery.

2 CARDIOMO

Engineer Roman Bielkin, who led a young team of cardiologists, engineers

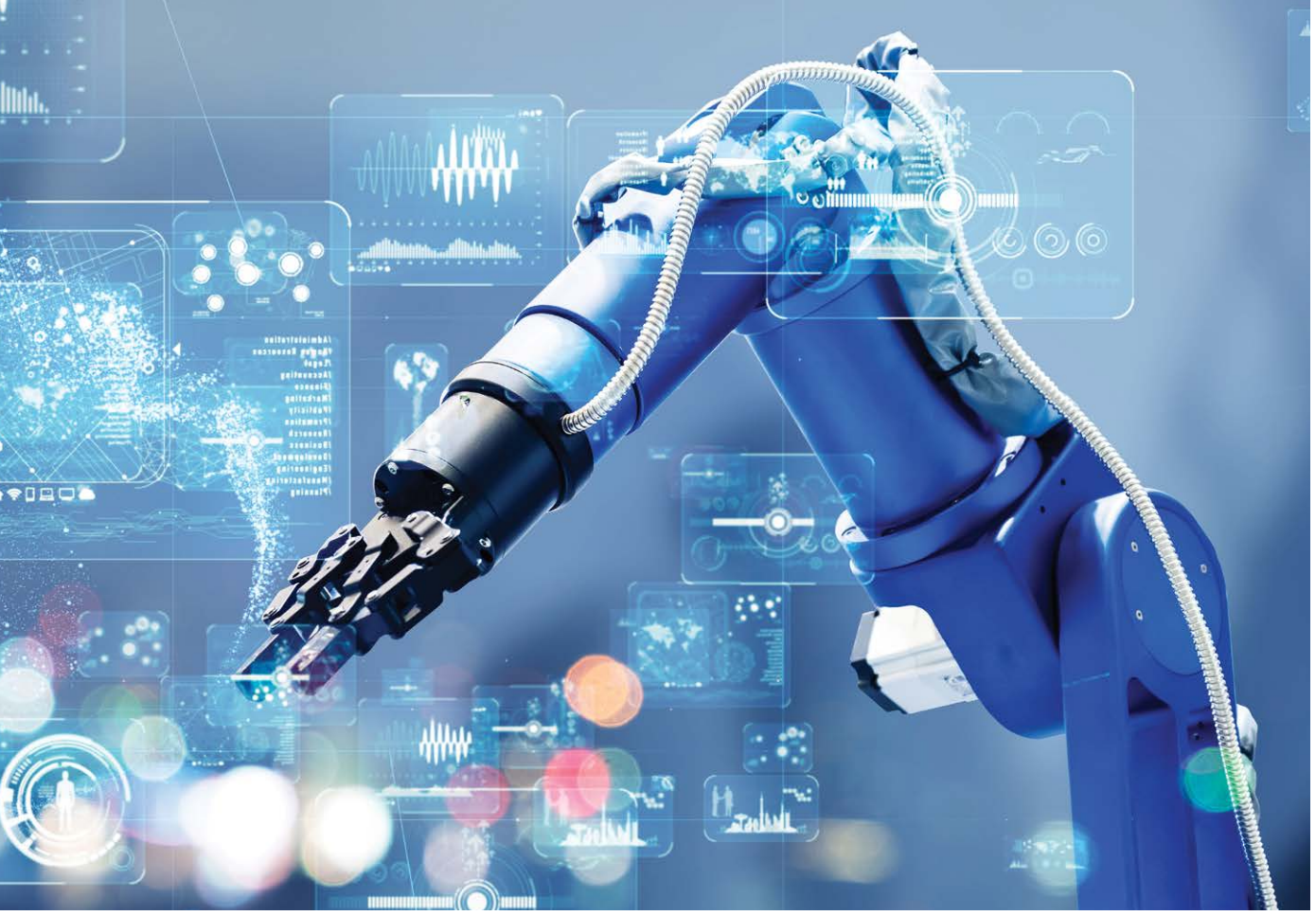


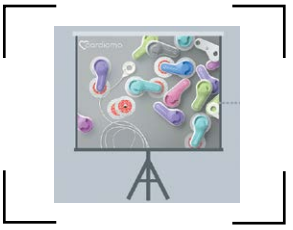
Photo istockphoto.com

and designers, developed a portable device that monitors the basic parameters of the human body, transmits the analysed data to a smartphone, and informs the user, his/her family or doctor about possible abnormalities. Many diseases turned out to give signs that can be diagnosed at an early stage and thus avoid fatal consequences.

The new device will be especially useful for the elderly who are used to ignore the symptoms and "not bother" children once again with their health problems. The monitor is attached under the heart with adhesive electrodes and reads data by analysing ECG and heart rate, lung function and respiration rate, body temperature, taking into account possible falls, body position, sleep quality, activity during the day, etc. The device operates around the clock, needs recharging every 10 days and is moisture-resistant, so a user does not need to remove it while taking a shower.

The Ukrainian start-up was met with great interest both in Ukraine and worldwide. In Ukraine, Cardiomo monitors have already been pre-ordered by M.D. Strazhesko Institute of Cardiology, Children's Clinical Hospital "Okhmadyt", Oleksandrivska Clinical Hospital, Boris Clinic. Specialists from the USA, the EU and some South American countries were interested in the device at specialized exhibitions. The Michigan Technological University ordered 40 devices for the Department of Cardiology, and the developers received many orders from European residential homes for elderly people and nursing services. The inventors calculated: after arranging the large-scale production of the device, it will be able to save the lives of 16 million people each year.

EVERY YEAR UKRAINIAN SCIENTISTS CREATE ABOUT 15 THOUSAND INVENTIONS. WE HAVE PREPARED A SELECTION OF DEVELOPMENTS AND INVENTIONS OF OUR TALENTED COMPETITORS.



3 KROVOSPAS

Krovospas haemostatic agents are haemostatic bandages, napkins, swabs and medical patches including a unique haemostatic composition developed by researchers from the Institute of Physical Chemistry, the Institute of Traumatology and Orthopedics of the National Academy of Medical Sciences (NAMS) of Ukraine and M.D. Strazhesko Institute of Cardiology, of the NAMS of Ukraine. They united in volunteer Borei Research and Development Centre and set out to develop a product to stop heavy bleeding in order to reduce the casualties of our soldiers on the front lines.

In May 2016, the Ukrainian Medical Centre of Certification of the Ministry of Health of Ukraine officially registered Krovospas, thus enabling its mass production. Its features are not worse than those of the world-popular CELOX (UK) and QuikClot Combat Gauz (USA), and in some aspects are even better.

Krovospas quickly comes into contact with blood, fills the wound cavity and begins to form a clot at 30-40 seconds, conveniently, quickly and securely swabs the wound and is easily removed. It costs much less than foreign analogues: the cost of Krovospas is about USD 5. It is indispensable on-site since it does not require special medical knowledge, so each serviceman can use it after a short-course training to provide self- and mutual assistance. Krovospas will also be useful in peacetime, in particular, in disaster medicine, ambulance, traumatology and surgery.

4 SURGICAL ZIPPER

Poltava engineer Vitalii Zapeka, once in the hospital with a leg injury, experienced first-hand that the traditional way of suturing wounds with catgut has quite unpleasant side effects. "When suturing wounds or incisions with threads," the inventor said in an interview, "the tissues are stretched and the skin is forcedly connected with the subcutaneous layer. The latter is connected with the fat layer, and the fat layer – with the muscles. As a result, an untidy scar is formed, and the suture sometimes suppurates. "

In 2002, Vitalii Zapeka received a declaratory patent for his invention "Overlaid surgical suture SAPEK" which he had developed for 10 years. The suture consists of silicone and plastic parts and an adhesive perforated surgical film. It is glued to the wound edges which are then joined and fastened with a zipper keeping the tissues connected without threads. At the same time materials do not contact with the wound suture and allow it to breathe.

If a wounded patient is brought to the hospital with a suture overlaid to stop the haemorrhage, the surgeon unfastens it, without removing it, makes an operation or other manipulations on the wound, and re-fastens the suture. It is possible to process a wound, without pulling out threads and without removing clamps. The suture is easy to use and can be applied even by the injured person before the ambulance arrives.

The invention arouses great interest both abroad and in Ukraine, but, unfortunately, mass production is pending. However, so far the inventor has already received a positive feedback from O.O. Shalimov National Institute of Surgery and Transplantology and expects investors.

5 ENABLETALK GLOVES FOR DISABLED PEOPLE

EnableTalk gloves make it possible to establish language contact between people with special needs and those who do not understand sign language. They were developed in 2012 by a team of Ukrainian students from Donetsk QuadSquad: Anton Pasternykov, Maksym Osyka, Anton Stepanov and Valeriia Yasakova. At Microsoft Imagine Cup-2012, this project took the first place, thereafter EnableTalk was short-listed in the American version of Time as one of the best inventions of 2012.

Each glove has 15 touch sensors that recognize sign language and transform it into text on a mobile device. The connection is established via Bluetooth, and the gloves are solar-powered.

In 2014, the work on the project was interrupted since young researchers moved from occupied Donetsk to various cities, and it took them several years to find new housing and work. But recently EnableTalk has restarted. The developers currently work to further improve their know-how, make contacts with schools and societies for hearing-impaired people worldwide, and work on an international patent for their technology.

Today, Max LEVCHIN is a well-known American entrepreneur, co-founder and chief engineer of PayPal, vice president of development at Google. **THE INITIAL FAILURES AND FURTHER GREAT EARNINGS OF PROGRAMMER ARE DISCUSSED IN THE NEW STORY OF THE BOOK "YOU WILL LEARN" PUBLISHED BY FARMAK COMPANY.**

From startups to giant companies

FIRST ATTEMPTS

The future successful programmer Maximilian Levchin was born in 1974 in Kyiv. His mother devoted herself to Physics and Programming and his father wrote poetry and prose. So from early age the guy was fascinated by technology and with his father he even belonged to the Kyiv sci-fi fans club "Star Trek".

At the beginning of 1990s, when he was 16, the family moved to the United States of America. Overseas he attended school in Chicago and then studied Computer Science at the University (Illinois). Already in his student years, Levchin started his own business creating four companies, among which was a service for developers and an advertising platform. These attempts were not very successful, but they gave Maximilian an understanding of what he wanted to do – to create new successful products and develop them.

CONQUER SILICON VALLEY

In 1997 young immigrant moved to Silicon Valley, where he met an avid start-up businessman Peter Thiel. Together, they founded Confinity company to provide technology financial services. And within a year they merged with a competitor – the company X.com which belonged to not very well-known at that time businessman Elon Musk. That's how PayPal established, which means "friend who helps to pay".

Max Levchin became not only the co-founder, but also the chief engineer of the start-up. It was he who developed the unique PayPal security system. At the time, this was a matter of question number 1, as all their predecessors and competitors were victims of hackers who found loopholes and robbed companies. Thanks to the extremely high level of security PayPalwon the trust of leading financial institutions immediately: it conquered the market and reached the international level in a very short time.

As the inventor recalls, the work on the project was so exciting that he even spent the night in the office so as not to waste time on the road. By the way, in everyday life he was not too demanding – in his apartment there was only a computer desk, which was also a dining room, and boxes for items.

Despite the success and achievements of Max Levchin abroad, he never forgot his roots. In 2015, he founded a scientific award and named it Frima Lukatskaya Scholarship in Computer Science – in honour of his grandmother who was a famous astrophysicist.

RECOGNITION

The titanic work of Ukrainian was not in vain – in 2002 the jury of the prestigious rating MIT Technology Review (Massachusetts Institute of Technology) recognized him as the main innovator of the year. That same year, eBay bought PayPal for $ 1.5 billion. As Levchin, as one of the co-founders, owned 2.3% of the shares, 27-year-old man received about $ 34 million from the sale. Now PayPal is a company worth tens of billion dollars with tens of thousands of employees.

NEW PROJECTS

Maximilian Levchin never stopped at what he had achieved: quickly he founded a new start-up Slide – a service for working with a large number of photos. Then, the company refocused on creating services for social networks MySpace and Facebook. In 2010, the company was bought by Google for $ 182 million, and the inventor himself became vice president of the Internet giant.

All these years, the entrepreneur continues to invest in other start-ups actively and help them with his own expertise. For example, in 2014, he became the first Yelp investor to become a popular business evaluation service gradually. Levchin has also collaborated with other successful companies: Yahoo, Enerton. Maximilian considers himself a team player because he is convinced that a group of like-minded people is always stronger and can achieve more. The main thing is that the team must have common goal, vision and values.

OVERCOME PAIN: the

Vadym BILOSHYTSKYI, Deputy Director for Research at the State Institution "Romodanov Neurosurgery Institute of NAMS of Ukraine", neurosurgeon of superior category, Doctor of Medical Sciences, Executive Director of the Public Scientific Organization "Ukrainian Institute of Pain Research", **TELLS HOW A RELEASE FROM CHRONIC PAIN THAT IS NOT PROTECTIVE AND DOES NOT MEET BIOLOGICAL GOALS CAME TO A FOCUS AND WHAT THERAPEUTIC STRATEGIES SAVE PATIENTS.**

Vadym Vasyliovych, you became one of the first domestic specialists to start working in pain medicine. How did you become interested in this area?

This happened during my internship abroad. Observing the application of modern technologies there, I discovered a new specialty. I started reading English literature... And I saw that I could offer effective ways to release from pain to many patients who I had advised to visit neurologists or other doctors.

The knowledge about such methods was spread largely due to Roman Cregg, a Lviver who built a scientific career in Great Britain but never forgot about Ukraine. In 2010, he began organizing British-Ukrainian symposia on anaesthesiology and the study of pain, implementing educational projects, and promoting internship for Ukrainian doctors abroad. The Public Organization "Ukrainian Institute of Pain Research" was founded by joint efforts. We also appreciate the hard work of the Ukrainian Association for the Study of Pain and participate in its educational activities. In fact, the main achievements in the study of pain became known in Ukraine due to the enthusiasm of not indifferent people.

The dream of releasing from pain is as old as the history of mankind, but pain medicine has emerged relatively recently as a special area. Were enthusiasts also engaged?

American doctor of Italian origin John Bonica, a man with an extraordinary life, is considered to be a founder of modern pain medicine as an independent medical specialty. To go in for the medicine, he earned his living by wrestling in tent show. For a long time, the young man lived in parallel worlds – in the ring, where he was known as Johnny Bull, he wore a wrestling mask so that he would not be recognized as a medical student. And in the hospital, he sometimes did not remove a surgical mask to hide battle injury. After entering the internship, John did not leave his sports career, although he performed in more prestigious arenas and even won the title of world light-heavyweight champion.

In one life, he caused people pain and got injured that resulted in severe pain. In another life, he saved people from pain. Pain became the main area of his professional interest. John Bonica invented epidural anaesthesia. The search for a new method of anaesthesia was prompted by the fact that he had to make great efforts to save his wife after an overdose of ether during her first childbirth. He improved the regional blocking methods while working in a military hospital during

latest methods in Ukraine

From the archives of the Institute

The world-view of pain medicine is that the doctor must thoroughly understand the causes of pain and be able to release from it. The phrase "You are not our patient" should simply be banned.

World War II. He showed the importance of a multidisciplinary approach. He founded the first Pain Center in the USA... And his main work – The Management of Pain – is considered a bible for the pain treatment.

■ ***But it's not only individuals who make history. What contributed to the actualization of a new area, e.g. a change in the attitude to the patient, a new degree of understanding a pain signal, or all these taken collectively?***

First of all, pain medicine arose in response to need. Chronic pain is extremely common in modern society. According to the WHO, up to 37% of people in developed countries have diseases and conditions associated with chronic pain. European studies have shown that one in five persons report moderate or high chronic pain. 90% of them suffer from pain for more than two years and in a third of cases pain is not reduces as a result of treatment.

The statistics are highly likely to be similar in Ukraine. This situation prompted to search and implement new technologies and methods of pain management.

■ ***But before choosing a therapeutic strategy, it is necessary to clearly determine the cause of pain. What is the specificity of the pain medicine approach?***

One of the basic principles is an individual approach which involves overcoming the traditional narrow medicine specializations. I was already a doctor of medical sciences when I started learning to find the causes of pain in the joints and spine. It was a great discovery for me when I learned how to conduct a physical examination, to check the patient's physical condition! There is a list of tests with a certain neuromuscular and skeletal loading which allow assessing the situation comprehensively. However, assessment in terms of neurology or orthopedics still prevails in our country. And the doctor assessing the situation in terms of his/her specialization often says: "You are not our patient." Therefore, a person often has to visit various doctors.

■ ***The painful conditions that require a long search for an answer include a headache that can be caused by hundreds of reasons…***

Today, the International Headache Society has developed a classification of conditions and diagnostic criteria that allow determining the root cause of ailment.

■ ***How often is migraine such cause? And how accurately is this condition diagnosed in our country?***

Migraine is a very widespread disease. According to various estimates, almost one in five or even one in four women suffers from severe headaches. Migraine is less common among men but still it affects approximately one in twenty persons.

Unfortunately, awareness of modern methods of the treatment of this disease is low in Ukraine. Problems arise at the level of diagnosis, medical records often state "vegetative-vascular dystonia", "dyscirculatory encephalopathy", "cerebral arachnoiditis". Although modern diagnostic approaches make it possible to avoid errors. When I had the opportunity to observe the work of Giorgio Lambru, a leading cephalgologist specialized in headache treatment in London, I was amazed at how masterfully he communicated and asked the right questions. We do not have such a school yet.

However, it should be noted that the effective methods for treatment of migraine, from which humanity has always suffered, have emerged recently. As one of the speakers mentioned at the Congress of the International Headache Society in Dublin last year, almost all of them were invented in our era. Even the oldest, the first medicinal product for migraine attacks, ergotamine, is less than 100 years old. Triptans began to be used as early as decades ago, and medicinal products preventing migraine belong to later developments. Now we observe a kind of a boom since we can use botulinum toxin therapy, we already have registered medicinal products based on monoclonal antibodies.

■ ***The chronic pain treatment team led by you at the Neurosurgery Institute was the first in Ukraine to start using monoclonal antibodies in migraine treatment. What is their impact aimed at?***

Recently, in 2018, after clinical trials, 4 medicinal products containing monoclonal antibodies for migraine treatment were registered and approved for clinical use in the world. In 2020, the medicinal product with the internatio-

PRINCIPLES OF PAIN MEDICINE

- **Individual approach including the search for the source of pain in terms of neurology, orthopedics, anaesthesiology and neurosurgery.**
- **Multidisciplinary treatment involving physical therapists, psychologists and other specialists, because pain is a biopsychosocial phenomenon.**
- **The use of percutaneous (injection) methods for accurate targeted medicinal product delivery or destruction of the sensory sensitive nervous system, such as the sensitive nerve.**

nal non-proprietary name fremanezumab was registered and officially imported in Ukraine. This medicinal product contains antibodies that block a substance called CGRP, calcitonin gene-related peptide.

After the discovery of this protein compound in 1982, research has shown that it is a key in migraine pathogenesis. Migraine patients show a significant release of CGRP during the attack. In addition to the amplified pain signal, this molecule activates mast cells in the meninges which emit other bioactive substances such as histamine, bradykinin, etc. CGRP, together with such substances, causes dilation and paralysis of blood vessels, an inflammatory reaction in the meninges, and further irritation of pain nerve endings, particularly in the vascular wall. All this violent reaction in the meninges during a migraine attack is called "neurogenic inflammation". It is accompanied by intense throbbing headache, nausea and/or vomiting, increased light and sound sensitivity. In chronic migraine, the concentration of CGRP in the nervous system is consistently elevated.

The role of CGRP in the development of migraine is also confirmed by the therapeutic effects of medicinal products preventing its release (traditional triptans, botulinum toxin) or blocking the peptide or its receptor (these are mentioned monoclonal antibodies and a new class of medicinal products – gepants, small molecule CGRP antagonists which are simpler molecules compared to the protein structures of monoclonal antibodies).

■ ***Therefore, the main trigger of migraine as well as the ways to affect it are known. However, innovative medicinal products including monoclonal antibodies are not first-line drugs. Is it due to their high cost?***

Not least. A few years ago, developers announced that estimated cost of developing and clinical trials of new medicinal products was billion dollars, now they are talking about larger amounts. Therefore, undoubtedly, new medicinal products are always expensive, and before using them, other more affordable and effective products are offered.

■ ***Billion-dollar costs for a fundamentally new development are not yet available to our pharmaceutical companies. Will they be able to reproduce innovative approaches after the patent expiration?***

I am convinced that this is possible since we have powerful facilitates that manufacture high-quality generics within a short time.

■ ***The search for new ways to use already known medicinal products is as important as the development of new products. As an example, the efficacy of botulinum toxin therapy in migraines was accidentally discovered in the 1990s. When is this substance also used?***

Today, our institution offers the widest list of indications for the use of this method which has no analogues in Ukraine. In addition to headaches, today botulinum toxin therapy helps to achieve positive results in the treatment of cervical dystonia, blepharospasm, chronic pelvic pain, hemifacial spasms, post-stroke spasticity of the hand.

■ ***Is the development of methods for accurate targeted medicinal product delivery among the achievements of modern medicine?***

In particular, we can mention the intrathecal administration of medicinal products involving the implantation of a pump with adjustable infusion rate and different tank volumes. The undeniable advantage of this method is the use of lower doses of analgesics.

■ ***In fact, do all the modern injection and interventional methods for pain management – radiofrequency denervation and radiofrequency neurotomy, blockades and epidural steroid injections, and trigger point effects require surgical precision?***

Certainly. For example, the procedures we have implemented in the treatment of chronic pelvic pain such as blockades and radiofrequency of the genital nerves, botulinum toxin injections into the pelvic muscles and prostate under computed tomography navigation are not currently performed in Eastern countries. Europe and the Russian Federation, and Western countries use them only in expert clinics. Similarly, only the leading Western clinics use all three possible types of navigation – X-ray, computed tomography and ultrasound.

■ ***The achievements of your team also include the successful overcoming pain by spinal cord neurostimulation.***

The theoretical foundations of neurostimulation in the pain management were laid by the gate control theory half a century ago, when it was noticed: if the intensity of the sensory impulse exceeds the intensity of the pain, the "gate" in the spinal cord closes preventing the entry of pain impulses into the brain. Today, by installing high-technology neurostimulants, we can release patients from severe pain. And the possibilities of this method are being studied. Due to meeting Ukrainians from Minneapolis who work on the fundamental issues of pain, and the head of this area, Professor Donald Simone, we formulated the idea ofthe study and won a grant: Romodanov Neurosurgery Institute, Bogomoletz Institute of Physiology and University of Minnesota will work on a detailed study of spinal cord stimulation.

■ ***Therefore, in order not to get left behind, our scientists and doctors need to enter the international arena, don't they?***

Beyond all doubt: read, study, join educational programs, seek acquaintances, find opportunities for internship. The main thing is not to be indifferent, because the doors will be opened to those who are bold enough to knock!

NOBEL HEROES 119 years of struggle for health

Pharmacy specialists along with other prominent scientists are among the Nobel Laureates: they are traditionally awarded in Physiology and Medicine. **WE TELL ABOUT THE MOST SIGNIFICANT PHARMACEUTICAL DISCOVERIES FOR OVER 100 YEARS OF NOBEL TRIUMPHS.**

WHO SAVED NOBEL?

Alfred Nobel had great respect for representatives of pharmaceutical industry. No wonder, because the development by one of them, chemist Ascanio Sobrero, saved the life of the world-famous inventor of dynamite. In 1846, the Italian scientist discovered nitroglycerin which later saved the future founder of the prestigious award during an angina attack. It is suggested that this fact prompted Nobel to regularly award the authors of major scientific discoveries.

Outstanding scientists have been awarded the Nobel Prize in Physiology or Medicine since 1901. In this period, 17 prominent pharmacologists worldwide became its laureates. Due to their research, humanity has been able to cope with many serious diseases that were previously considered untreatable. Every discovery that will be discussed below is a real victory in the eternal confrontation of life and death. So let's start our retrospective journey into the history.

ANTI-DIPHTHERIA SERUM

Emil von Behring is a physiologist who received the first-ever Nobel Prize in Physiology or Medicine. He began his career as a military

surgeon: due to low income, his father could not afford a medical education for his son, so Behring chose the Friedrich Wilhelm Medical Institute in Berlin where education was free. However, the graduates had to work as military doctors for 10 years, so Behring served in the Prussian Army until 1889. He never aspired to engage in clinical practice – he preferred research. Therefore, he later joined the Koch research group where he studied treatment methods against diphtheria. Just then the scientist made his ingenious discovery: he developed a treatment method with serum from the blood of people who had already suffered from this disease. Behring's serum saved the lives of many children. Behring's friend Paul Ehrlich

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later helped him to improve the development. Emil von Behring received his Nobel Prize for the invention of anti-diphtheria serum in 1901.

ANTIBACTERIAL EFFECT OF PRONTOSIL

The World War II dramatically changed the life of the scientific community. Gerhard Domagk, a German pharmacologist who won the Nobel Prize in 1939, was forced to decline the award. The Third Reich did not recognize any

contacts between German scientists and scholars from other countries, so the researcher was arrested by the Gestapo for a week instead of recognition and fame.

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE IS AWARDED ANNUALLY, WITH THE EXCEPTION OF 1915-1918, 1921, 1925, AND 1940-1942.

Domagk discovered the antibacterial effect of prontosil, which was successfully used against streptococcus. For a long time, before discovery of penicillin, this medicinal product was "a frontliner" in combating bacterial threats. Among others, Gerhard Domagk's research laid the foundation for the development of anti-tuberculosis medicines.

FLEMING, CHAIN, FLOREY: ANTIBIOTIC THERAPY

The discovery of penicillin was one of the most famous Nobel Prize-winning research. The first antibiotic was discovered by three scientists: microbiologist Alexander Fleming,

biochemist Ernst Chain and pharmacologist Walter Florey. Fleming isolated penicillin, and Chain and Florey developed a method for treatment of patients with infectious diseases with a new medicinal product.

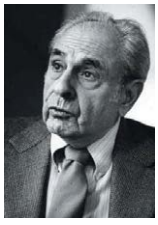
Given the losses caused by bacterial complications during the World War II, this antibiotic became a real salvation for many people. In addition, the discovery of penicillin enabled to develop all modern antibiotics. The scientists received their Nobel Prize in 1945.

YELLOW FEVER VACCINE

The 1951 Nobel Prize laureate Max Theiler is known worldwide as the "author" of the yellow fever vaccine. It is a viral disease that affects human blood and is now considered very dangerous, and in the 1950s it was a real disaster for Africa and South America. Theiler was born and raised in Pretoria, South Africa, in the family of a veterinarian, so the future scientist knew yellow fever very well. After a lot of research on mice and monkeys, Theiler was able to develop an effective vaccine in 1937. Its clinical trials in Brazil were completed in three years, and then the medicinal product became widely used as a reliable protection against dangerous disease. A representative of the Nobel Committee considered that Theiler's research was not only salvation from yellow fever, but also hope for a successful fight against other viruses that threatened humanity.

FIGHT AGAINST TUBERCULOSIS

Almost simultaneously with Theiler, but in another part of the world, microbiologist Selman Waksman, who was our compatriot, worked on discovering an effective cure for tuberculosis. He was born in Nova Pryluka (former Kyiv province) and graduated from the gymnasium in Odesa. In 1910, Selman emigrated to the United States, where he acquired education of microbiologist, but not medical: he studied soil microbiology at the College of Agriculture. His revolutionary discovery started after request from the American Tuberculosis Association. The staff of the organization requested Waksman to investigate the destruction of tuberculosis bacteria in soil. The works of the scientist and his research group to develop an antibiotic that is effective in combating the disease were based on the conclusion about the destruction of the tuberculosis pathogen by other microorganisms. In 1942, streptomycin as precursor to streptomycin isolated a year later by Albert Schatz, a member of the Waksman Group, became such medicinal product. Streptomycin became an effective weapon of mankind against tuberculosis and leprosy. Selman Waksman's contribution to the fight against these diseases was recognized through the award of the Nobel Prize in Physiology and Medicine in 1952.



SALVATION FROM ALLERGY

Another pharmacologist whose research was awarded the Nobel Prize was Daniel Bovet, a representative in fact of three countries. The scientist who is an Italian by origin was born in Switzerland and acquired his scientific education in France. He continued and developed Domagk's works on the study of prontosil. Based on this substance oxidation mechanism, Bovet developed sulfonamide medicines that became effective antibacterial agents. Undertaking the study of allergic processes in the human body, he invented the first antihistamine medicine – thymoxydiethylamine which laid the foundation for the whole further development of allergy therapy in 1937.

The study of curare was another contribution of Daniel Bovet to pharmacology. The researcher found that this substance relaxed muscles, so it can be safely used for the body, for example, to relieve seizures. Bovet developed a synthetic analogue of curare – gallamine which is still used in medicine as a muscle relaxant.

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Daniel Bovet was awarded the Nobel Prize in 1957 for all his achievements in pharmacology.

DETERMINING THE ROLE OF PROSTAGLANDINS

In 1982, the Nobel Prize for the study of prostaglandins and other biologically active compounds was awarded to three pharmacologists: British Professor of Experimental Pharmacology John Wayne and Swedish biochemists:

Bengt Samuelsson and Sune Bergström. In particular, Wayne found that aspirin affects prostaglandins as an inhibitor, and suggested its use for the treatment and prevention of thrombosis. The studies by Bergström and Samuelsson enabled to study the effects of prostaglandins on the human body and their use in the treatment of cardiovascular and gynaecological diseases, as well as to prevent gastrointestinal ulcers.

PRINCIPLES OF MEDICAL THERAPY: NEW ROUND

The Nobel Prize Laureates are often people with difficult destinies. These include Gertrude Elion who, along with James Black and George Hitchings, received an honorary award in 1988 and became the world's second Nobel Laureate in Physiology and Medicine. It

is interesting that Elion did not have a doctorate degree. However, it was not her fault: at that time, women had no access to postgraduate education. But this misfortune did not prevent Gertrude from becoming an outstanding biochemist and pharmacologist and successfully managing the experimental therapy department at Burroughs Wellcome (North Carolina). As a result of the hard work of Gertrude Elion and her colleagues, many medicines were developed: for example, mercaptopurine used to treat leukemia; immunosuppressant azathioprine and allopurinol used to treat gout; antimalarial medicinal product pyrimethamine, as well as acyclovir widely known as an antiherpes product.

THE 21ST CENTURY: "FOLLOW THE EXAMPLE" OF NATURE

In the early third decade of the new millennium, pharmacological research is still at the forefront of science. Scientists who have dedicated their lives to the fight against annoying diseases, regularly make new discoveries, which receive the most prestigious prize.

In 2015, two areas of pharmacological research were the focus of the Nobel Committee. Japanese biochemist Satoshi Ōmura and American biochemist William Campbell were awarded for developing a new group of medicinal products

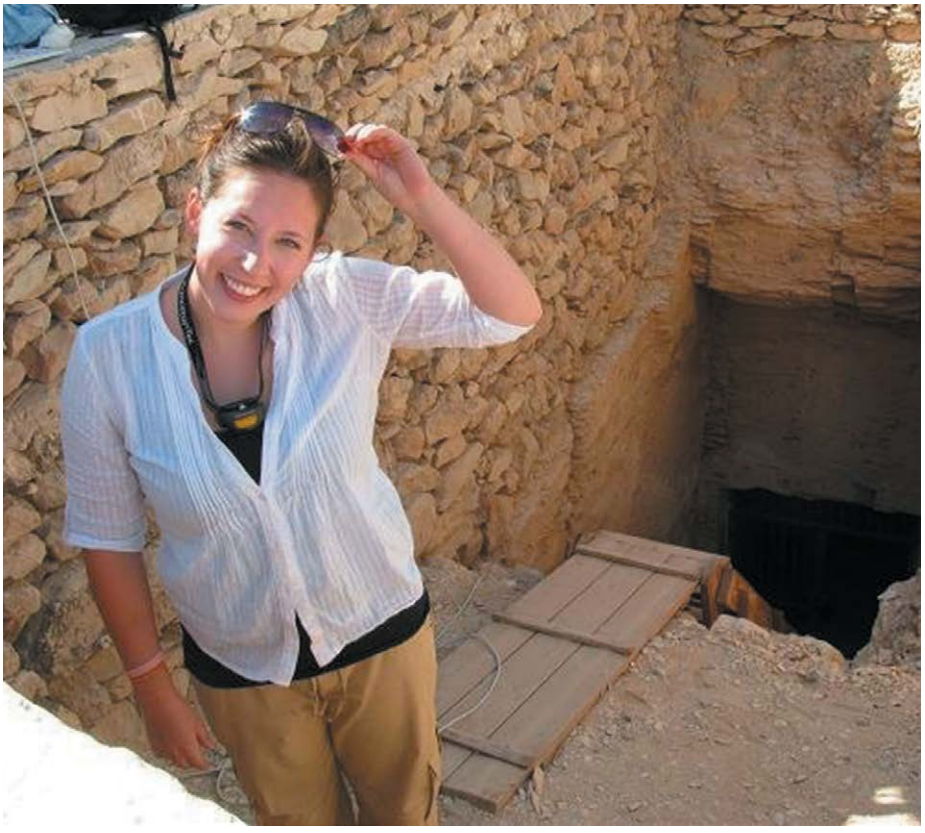
to combat roundworm infestations that cause diseases such as onchocerciasis and elephantiasis. These diseases lead to connective tissue pathologies. Avermectins produced by streptomyces fungi were used to develop these medicinal products.

The 2015 Nobel Prize was also awarded to Chinese female pharmacologist Tu Youyou. A specialist in traditional Chinese medicine, she worked on antimalarial medicines in the 1960s. She used Chinese wormwood extract to develop artemisinin. The research was under the direct control of the Chinese Communist Party and was completely secret. That is why Tu Youyou was awarded the Nobel Prize for her victory over malaria only at the age of 84, more than 30 years after completing her work. She became one of the first Asian women to receive the most prestigious scientific award.

OVERCOME CANCER

In 2018, another step towards victory over cancer was made. Immunologists Tasuku Honjo and James Allison were recognized for developing an effective treatment method of cancer. They developed a medicinal product that inhibits the negative immune response of the human body allowing the human immune system to destroy cancer cells on its own. The main danger of cancer is the rapid suppression of the body's immune system, as a result of which the disease is not counteracted. The medicinal product helps to open the human body's own resources forcing it to fight cancer cells. Former US President James Carter was one of those who survived due to the new medicines. Melanoma already metastasised to the brain, and doctors were convinced that the former head of state had no chance to survive. However, the use of the new medicinal product helped Carter fully recover. And the scientists were awarded the most prestigious scientific award and gratitude from the whole mankind.

Kathrin Hunt: “Humanity is not guilty for having cancer”



HOW HAVE ONCOLOGY CHANGED OVER THE MILLENNIA?
The American scientist, one of the founders of the Paleo-Oncological Research Organization, a community of archaeologists, oncologists and other researchers, is looking to answer this question to develop strict standards and methods for detecting cancer in ancient skeletal remains.

TO SEE AND UNDERSTAND

Kathrin Hunt, 27, is an Egyptologist, archaeologist and paleooncologist. The choice of such an extraordinary field of activity was caused by girl’s personal life drama – at the age of 22 Kathrin, an student-archaeologist, who had already signed up for excavations in the Egyptian Valley of the Kings, was diagnosed with a malignant swelling. Long-term consumptive treatment did not force the young scientist to give up her favourite profession, but adjusted the course of her further research – the detection of changes caused by cancer in bones of ancient burials.

“The main methodology used to detect cancer in ancient remains is visual analysis: search for skeletal anomalies, – says Hunt. – It often looks like “broken” cavities in the bones, even if the cancer started in the soft tissues. For example, if lung cancer metastasizes, it causes

Photo femiscience.com

characteristic affections of the ribs and scapula, or clavicle, joints of the humerus, and sometimes the skull; for example, bone cancer, such as osteosarcoma and osteochondroma cause uncontrolled bone growth".

As soon as researchers detect an abnormality, they should perform an X-ray or microscopic analysis by examining cross-sections of the bones under a scanning electronic microscope. It is also necessary to do CT or X-ray of the bone to better understand what is happening around the affection. Next, a biomolecular method for detecting mutations in ancient DNA is being developed. "Researchers are also working on protein analysis to evaluate compounds associated with cancer biomarkers", says Hunt. – It can help us understand a little bit what was going on in the immune system of an ancient cancer patient".

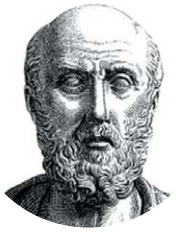
IN WRITTEN SOURCES

Kathrin, who had been dreaming of archeology since childhood, was not going to give up and stop her scientific work because of her illness, so after the last course of chemotherapy she flew to the Valley of the Kings for excavations. "I was bald then, leaning on a cane and almost staggered from the wind," – she recalls. Because of this, she was looked at with fear or pity. "Have people always responded that way to cancer?" – Kathrin became interested and began research, finding and analysing mentions of cancer in ancient texts, the oldest of which is the Egyptian Ebers papyrus which dates from about 1500 BC.

"Ancient doctors not only noted the signs of the disease, but also prescribed treatment: surgery, cauterization, starvation – and treated patients with phytogenic drugs, including, for example, distaff thistle flowers soaked in wine, preparations based on spurge or squirting cucumbers", says Hunt, noting that some elements of the ancient pharmacopoeia are still used in modern chemotherapy.

In addition to the Ebers Papyrus, cancer was mentioned in the Edwin Smith Papyrus dating to 1600 BC. But while the Ebers Papyrus pays more attention to pharmacological and magical treatments, the Smith Papyrus focuses only on surgery. It also states that this disease is incurable.

"After learning that cancer was in the beginning of human existence and people even tried to treat it, I decided to continue researching the disease from a paleooncology point of view," says Kathrin. – After all, if we can read about it in ancient literature, we can find physical evidence of its existence during archaeological excavations".



THE CONTRIBUTION OF ANCIENT DOCTORS

Even when ancient Egyptian papyri were not discovered, European physicians knew about the existence of cancer from ancient Greek texts. Even Hippocrates introduced the term carcinoma" (from καρκίνος – cancer, or crab, and ωμα, abbreviated from ὄγκωμα – tumor, because the unwanted tumor resembled the shape of arthropods). Another prominent doctor of antiquity, Galen, also treated cancer. He used the word ὄγκος to describe all tumors which gave the modern root of the word "oncology".

In the first century BC Roman doctor Aulus Cornelius Celsus suggested to treat cancer by removing the tumor at the early stages, and not to treat at all -at the later stages. He translated the Greek word καρκίνος into Latin, and under this name the disease entered many European languages (cancer).

THE SEARCHES ARE NOT STOPPED

Today, Kathrin Hunt is a co-founder of two organizations: Ancient Cancer Foundation and its research branch – Paleo-Oncology Research Organization. As part of this project, archaeologists and oncologists are creating an open database of archaeological finds from different eras and regions of the world that contain oncology signs and developing a methodology for detecting traces of malignant tumors in fossils.

Kathrin does not leave field works. She worked as an osteologist at excavation in the Israel Valley in Israel and collaborated with the Transylvanian Bioarchaeological Project, researching a late Roman necropolis in the Romanian village of Jucu de Sus. Today, she holds the position of archaeologist at the "Group 106" organization in Minnesota.

AGAINST FALSE STEREOTYPES

In addition to purely scientific value, Kathrin's researches have a humanistic perspec-

the current way of life is, so to speak, half-true, because paleooncology shows that the disease has always been a companion of humanity.

The data obtained by paleooncologists can be applied in practice and a fuller picture of cancer, formed on the basis of archaeological research, helps humanity to understand better the causes of its occurrence. This will allow us to develop methods for more effective prevention, diagnosis and treatment of this serious disease. For example, understanding how a mutation that causes cancer has changed over the millennia will make it possible to predict how it may change in the future and possibly even slow it down.

tive. There are many rumours and legends about the origin of cancer and the factors that cause this fatal disease in the age of the Internet – from half-truth generalizations to outright harmful insinuations.

For example, the belief that cancer is contagious, or the myths that the appearance of malignant tumor is a punishment for bad deeds or thoughts, the result of evil eye or jinx – are narrow mindedness that stigmatize cancer patients and add suffering to people who are already forced to overcome considerable difficulties in the fight against a serious disease.

The notion that cancer is exclusively a modern disease caused by environmental pollution, bad habits and

THE MOST ANCIENT OF THE WITNESSES

The first bone abnormalities, which indicate the presence of cancer, were discovered in the days before the dinosaur era. Confirmed traces of tumors have been found on the skeleton of the North American fossil fish Phanerosteon mirabile which lived almost 300 million years ago. Currently, there are about a dozen skeletal remains of dinosaurs, according to which researchers can unequivocally say about the presence of tumors in these ancient reptiles. For example, in 1999, the Lancet published an article of American paleopathologists Rothschild, Witzke, and Gershkovich on pathologies caused by metastases in the bones of hadrosaurs – duck-billed herbivorous dinosaurs that inhabited territory of the present Alberta province (Canada) about 150 million years ago. The height of hadrosaurs reached ten meters in length, weight - several tons and they lived in large herds, so paleopathologists find their skeletons in sufficient numbers to compare and analyse pathologies.

If we abandon reptiles and return to the problems of humanity, it should be noted that cancer became a "companion" of human before the time when Homo finally became Sapiens. The first confirmed case of the tumor was found on the jaw of Homo Erectus from Kenya, who lived about 1.5 million years ago.

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