Experience of Military Medicine in the Fight against the New Coronavirus Infection

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Abstract—The results achieved by the medical service of the Armed Forces of the Russian Federation to overcome the new coronavirus infection are presented. The high efficiency of the established unified system of biological safety and strict ranking of the priorities of anti-epidemic measures is shown. The experience of organizing traveling medical and nursing teams, as well as temporary military medical units on the territory of Russia, as well as in foreign countries, is demonstrated. Among the priority scientific results of military doctors, especially noteworthy is the study of the world’s first COVID-19 vaccine Sputnik V, its immunogenicity, the effectiveness of its use in previously ill patients and revaccination, as well as the use of immune plasma from those who have been ill and vaccinated. By the examples of organized military groups and the general population, the features of the formation of herd immunity have been studied. Military doctors were the first in the country to show the effectiveness of hormone therapy in the treatment of coronavirus infection and to study its effects. They carried out ultrastructural studies of the life cycle of the virus. It is shown that the system of comprehensive measures implemented by military medicine determined a lower incidence of new coronavirus infection among the personnel of the Ministry of Defense of Russia and a lower mortality among the military.

Keywords: new coronavirus infection, military medicine, glucocorticoid therapy, immune plasma, vaccination, revaccination, herd immunity

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According to the website стопкоронавирус.рф and the MMA freelance Research Institute of Novel Coronavirus Infection Problems [1, 2], the recorded number of people infected with SARS-CoV-2 around the world continues to increase; the number relative to the population of the country is, for example, about 14% in the United States, about 10% in Brazil, and no more than 5% in Russia, while in the Armed Forces of the Russian Federation this figure is about 1% and is associated primarily with replacements 2 times a year.

More than 6 million people have died of SARS-CoV-2 infection across the world, including about 5% of cases in the United States, about 7% in Brazil, and about 1% in Russia, and in the Armed Forces of the Russian Federation this indicator totals tenths of a percent. The achievement of such low rates of morbidity and mortality in the Armed Forces of the Russian Federation became possible owing to the identification of seven main areas of activity as priorities, which formed the basis of a unified concept of biological safety and organization of medical care for infectious patients in conditions of their mass admission:

• a single vertical of medical support management for attached contingents;
• a standardized approach to the construction of multipurpose medical centers;
...formation of mobile medical service units of constant readiness;

- implementation of sanitary and anti-epidemic measures and vaccination of personnel;

- maintenance of medical equipment and emergency stock in medical warehouses in medical organizations;

- determination of a unified methodological approach to the training of doctors and regular updating of methodological recommendations;

- scientific study of the pathogenesis of the infection and substantiation of diagnosis, treatment tactics, and disease prevention.

Competent organizational, medical, and preventive decisions, as well as the scientific rationale for the tactics of treating the infection with account for the form, severity, and period of the disease and comorbidities, saved the lives of tens of thousands of patients.

In pursuance of the instructions of the President of the Russian Federation, in the interests of the Ministry of Defense of the Russian Federation, the military construction complex in the shortest possible time erected 32 multifunctional medical centers (MFMCs) with a total capacity of 2945 beds in the military districts. They are equipped with the most state-of-the-art high-tech equipment, which allows them to provide medical care in the required volume and at a high technological level, with the possibility of using telemedicine technologies for real-time consultations with leading specialists from military hospitals. During the pandemic, more than 36000 patients with COVID-19 were treated at the MFMCs.

With the use of technological solutions developed and tested in the Russian Ministry of Defense, the military construction complex built and put into operation 11 multifunctional centers for 1120 beds in the interests of civil health care (Fig. 1).

Solving the tasks posed by the new challenge, the Ministry of Defense actively strengthened interstate cooperation and took measures to strengthen military cooperation with partner states in the fight against the new coronavirus infection. At the request of the heads of foreign states and in accordance with the decision of the Supreme Commander of the Armed Forces of the Russian Federation V.V. Putin, consolidated detachments were formed in the shortest possible time to provide practical assistance in the foci of the pandemic in Italy, Serbia, Kyrgyzstan, Kazakhstan, Abkhazia, South Ossetia, and Nagorno-Karabakh [3]. From the beginning of the pandemic, over 2000 citizens of foreign countries received medical assistance from mobile units of the Russian Armed Forces.

More than 2000 patients in the republics of Dagestan, Khakassia, and Tyva and Krasnoyarsk and Trans-Baikal krais received medical care from mobile multipurpose hospitals of the Russian Ministry of Defense. In addition, at the request of the heads of subjects of the Russian Federation, medical and nursing teams of the Russian Defense Ministry were sent to civilian medical organizations in Moscow, Kurgan oblast, the Komi Republic, and the Republic of Crimea, as well as Sverdlovsk, Tula, and Irkutsk oblasts. In total, more than 30000 patients received assistance in the mobile units of the medical service of the Armed Forces of the Russian Federation.
In accordance with the appeal of the Governor of Moscow oblast, a temporary infectious disease center with 1420 beds for the treatment of patients with COVID-19 was deployed on the basis of the Patriot Military Patriotic Park of Culture and Recreation of the Armed Forces of the Russian Federation. During its operation, military doctors treated more than 15000 patients in total. The operation of the center was provided by more than 3000 associates of the Military Medical Academy.

The spread of the new coronavirus infection in the Armed Forces of the Russian Federation required a change in the tactics of evacuation measures. During the pandemic period, 59 sorties were performed, and 91 seriously ill patients were evacuated [4] (Fig. 2).

To ensure a high level of training of medical specialists in the diagnosis, treatment, and prevention of COVID-19, 9 educational programs for professional retraining and advanced training were organized on the basis of the Military Medical Academy and its branch in Moscow, as well as at regional courses. The training was completed by 27000 doctors and paramedical personnel, including those representing the civil healthcare system of Pskov oblast and the republics of Dagestan and Tyva.

For the purpose of international exchange of experience, the format of international teleconferences was repeatedly used, and teleconsultation on difficult cases in remote regions was conducted. For the first time in modern history, a command and staff exercise of military specialists from the Council of Defense Ministers of the ASEAN (Association of Southeast Asian Nations) member states was held via videoconferencing. Within the framework of the IX Moscow Conference on International Security in June 2021, a plenary meeting “The Role of Military Departments in the Fight against the New Coronavirus Infection COVID-19” was held with the participation of the defense ministers of the participating countries. Moderation was entrusted to the medical service of the Russian Armed Forces as the most successful in this field [5].

The Kirov Military Medical Academy and central hospitals are conducting extensive scientific work on the study of SARS-CoV-2 and the issues of optimizing its diagnosis, treatment, and prevention. Risk factors for predisposition to COVID-19 disease were assessed, and the results of this study have been put into practice [6]. For the first time, based on laboratory markers, the main criteria for the effectiveness of the treatment of patients with the new coronavirus infection were determined [7]. The ventilation and gas exchange functions of the lungs were studied in patients who had recovered from the new coronavirus infection [8]. Highly effective methods of rehabilitation of patients directly in the red zone were developed, including the activation of patients in resuscitation and intensive care units, as well as a comprehensive system of rehabilitation after the infection [9] (Fig. 3). For the first time, a decision was made to revaccinate six months after the primary vaccination, and satisfactory tolerability to revaccination was established in all reporting panels [10].

Based on foreign experience and our own data, risk factors for predisposition to the new coronavirus infection were assessed, which allowed us for the first time to develop and implement a domestic algorithm in the form of a computer program for screening large groups of people in situations where speed and a high degree (100% if possible) of survey coverage are desirable to make an adequate management decision promptly. The total score obtained as a result of the assessment according to the algorithm can be correlated with recommendations regarding the volume of preventive and antiepidemic measures [5]. A complex multivariate statistical analysis made it possible to divide clearly the military who had undergone COVID-19 into groups. The greatest risk of getting sick with COVID-19 was found in young males and females in organized teams.

The study of biopsy specimens of the nasopharyngeal mucosa by electron microscopy first revealed changes in the life cycle of the SARS-CoV-2 virus
depending on the phase of the infectious process and the clinical form of the disease. Thus, in the inapparent (asymptomatic) form, no viral particles were detected in the cells. With ARVI, the virus was determined in the initial period, in the peak period, and during convalescence (recovery). In the case of viral damage to the lungs, the virus was detected only in the initial period; however, it was in this form of the disease that the highest concentration of SARS-CoV-2 viral particles was visualized in vesicles and in cells as a whole [11] (Fig. 4).

A high degree of immunological activity of the disease already at its onset, with a relatively rapid decrease in the role of direct viral damage to the lungs, serves as an argument in favor of the use of anti-inflammatory drugs and, above all, glucocorticoids (GCs). For the first time in world and Russian practice, methods for treating moderate and severe forms of COVID-19 using methylprednisolone pulse therapy were developed and successfully applied, making it possible to form and file a patent application with the Federal Service for Intellectual Property (Rospatent). In severe forms of the disease, the body’s immunological reaction becomes excessive, pathological, constituting a damage factor. A lot of experience has been accumulated in terminating the “cytokine storm” using GCs in combination with anticytokine drugs [12].

Scientists and clinicians of the leading medical institutions of the military medical service of the Ministry of Defense of the Russian Federation were among the first to publish works on the assessment of the role of biological markers of the inflammatory response in the management of patients with COVID-19. It has been shown that a patient with lung injury needs constant monitoring of both the level of the C-reactive protein and procalcitonin. It has been found that these laboratory indicators characterize different aspects of the course of COVID-19: the former reflects the activity of the systemic process, improving the objective assessment of anti-inflammatory therapy, while the latter demonstrates the presence of nosocomial bacterial complications requiring the prescription of antibacterial drugs. The formulated provisions became the basis for determining the general strategy of anti-inflammatory therapy in the treatment of patients with moderate and severe forms of the disease. One of the most important results of these studies is the elimination of the need for antibacterial agents in patients with COVID-19 for any severity of
infection at the onset of the disease. Antibacterial drugs are prescribed only when strict clinical and laboratory markers of bacterial infection are found. Recall that the violation of this postulate leads to an increase in the risks of antibiotic-associated complications, the addition of fungal flora, and the formation of antibiotic-resistant microflora in the future [13].

The problem of the correction, substitution, and prosthetics of respiratory function in patients with COVID-19 is an urgent and complex issue. For the first time, the results of a study of the ventilation and gas exchange functions of the lungs in those who underwent the new coronavirus infection have been published. It has been shown that an impaired diffusive capacity of the lungs is the most common functional disorder of external respiration after COVID-19 since a decrease in the transfer factor of carbon monoxide (CO) was found in 56% of patients [14]. An inverse correlation was established between the volume of lung tissue damage and indicators of the vital capacity of the lungs, their forced vital capacity, forced expiratory volume in 1 s, the total lung capacity, and the CO transfer factor. On the contrary, most patients (84.4%) had no ventilation disorders. This is of extreme practical importance to individualize observation and rehabilitation programs aimed at correcting disorders of the gas exchange function of the lungs [14].

The effect of inhaling an oxygen—helium mixture and nitric oxide on the course and results of treatment of lung tissue damage in COVID-19 has been studied and tested. It has been found that inhalation with heliox (70% helium and 30% oxygen) leads to a more rapid recovery of hemoglobin oxygen saturation—SpO₂, which contributed to a reduction in the diffusive surface of the lungs, their forced vital capacity, forced expiratory volume in 1 s, the total lung capacity, and the CO transfer factor. On the contrary, most patients (84.4%) had no ventilation disorders. This is of extreme practical importance to individualize observation and rehabilitation programs aimed at correcting disorders of the gas exchange function of the lungs [14].

Techniques have been developed for the rehabilitation of patients directly in the red zone, including the activation of patients in the conditions of resuscitation and intensive care units. Recommendations for the physical recovery of patients have been published. Together with the National Society for Clinical Nutrition and Metabolism, methodological recommendations for nutritional support (clinical nutrition) for patients with COVID-19 have been developed and published [9, 16].

In the treatment of patients with the new coronavirus infection, inhaled forms of prostacyclins were used for the first time, demonstrating anti-inflammatory activity, vasodilation, and an antiplatelet effect. It was found that when using the drug iloprost, the concentration of proinflammatory cytokines in the blood decreased and the clinical improvement in the condition of patients occurred significantly faster [17].

For the first time, the efficacy and safety of immune plasma obtained from those vaccinated against COVID-19 has been evaluated. It has been found that the average stay in the hospital among patients with moderate severity of the disease who received immune plasma from vaccinated donors decreased by six bed-days compared with the control group receiving standard therapy without the use of immune plasma, and the rate of elimination of the virus after transfusion of the first dose of immune plasma increased by 2 times [18].

Risk factors for thrombotic complications have been established in patients with COVID-19, and obesity, the presence of varicose and hypertension, and hyperglycemia turned out to be statistically significant [6]. A study of the prevalence and nature of carbohydrate metabolism disorders in patients with COVID-19 showed a very high incidence of hyperglycemia (67% of cases among hospitalized patients). The use of systemic glucocorticoids in the treatment of COVID-19 led primarily to the formation of steroid-induced hyperglycemia, mainly in elderly patients. Normalization of carbohydrate metabolism six months after the end of treatment was observed in 93% of patients, which in most cases indicates the transient nature of newly diagnosed hyperglycemia in inpatients with COVID-19 [19].

Patients who had undergone the disease in a mild or asymptomatic form were characterized by the obligatory formation of postinfectious humoral immunity starting from the 30th day, which persisted for at least six months; older age was associated with a more pronounced production of IgG to the SARS-CoV-2 S-protein, reaching the highest values in the group of elderly women in the period from 45 to 180 days. Thus, in the group of patients with a mild and asymptomatic course of the disease, the older age group is a protective factor in the development of a more pronounced immune response. The moderate or severe course of the disease leads to the formation of a higher level of IgG to the SARS-CoV-2 S-protein than its mild and asymptomatic course. At the same time, a high titer of virus-neutralizing antibodies persists for 90 days after COVID-19, followed by a gradual decrease by the 180th day with a trend towards higher serum concentrations in elderly patients, mainly in women. The level of anti-S-SARS-CoV-2-IgG in patients of moderate course (CT-2) who received moderate doses of glucocorticoids was significantly higher (2 times) than in patients who had not received GCs during the observation period from 14 to 90 days. By the end of the study on day 180, this difference had leveled out [20] (Fig. 5).

The first identified positive effect of GCs on the immune response allows us to interpret their action as bimodal: suppressive in the acute phase of inflamm-
tion according to the “dose−effect” principle and stimulating (with the same “dose dependence”) in relation to the IgG level in the early and late period after COVID-19. Such a multidirectional action of glucocorticoids in an evolutionary sense gives an advantage in survival. This advantage manifests itself in the form of controlling the severity of the inflammatory response with a simultaneous subsequent strengthening of protective immunity against infection, which created a direct threat to the life of the organism [19].

In the 1980s and the first half of the 1990s, under the guidance of Academician of the Academy of Medical Sciences V.D. Belyakov, the Kirov Military Medical Academy developed and substantiated a scientific paradigm of the epidemic process—the theory of self-regulation of parasitic systems. The provisions of the theory fully explain the wavelike course of the COVID-19 epidemic process with periods of ups and downs in the incidence. It is based on the interaction of phenotypically and genotypically heterogeneous populations of people and pathogens, which is displayed by the development of asymptomatic or manifest forms of the disease. At the same time, the epidemic process has a phasic flow depending on the changes occurring in populations of the pathogen (changes in biological properties as a result of multiple passages through human organisms and the emergence of new strains with properties modified at the genetic level) and people (the formation of herd immunity owing to recovered and vaccinated individuals). A decrease in the intensity of the epidemic process occurs as a result of the emergence and spread of reservation strains of the pathogen that do not have pronounced pathogenicity, with a high level of herd immunity.

The epidemic process of the new coronavirus infection in military collectives began to develop in the spring of 2020 and had a cyclic nature. An effective set of measures to combat COVID-19 was developed and applied for the first time in the Armed Forces, which made it possible to stabilize the epidemiological situation (prevaccination period) at the initial stage of the development of the epidemic (April–September 2020). The intensive increase in the incidence starting from October 2020 was not only stopped but also reduced to the seasonal threshold level of the incidence of acute respiratory infections due to almost 100% coverage of military personnel with Gam-COVID-Vac vaccination (postvaccination period). After the large-scale vaccination, predominantly mild and asymptomatic forms of COVID-19 disease have been detected. Constant monitoring of the incidence made it possible to predict its rise in 6 months, which coincided with the expected period for a decrease in the level of herd immunity. The first revaccination of military personnel, carried out 6 months later, made it possible to prevent an increase in the incidence of COVID-19 in the Armed Forces (revaccination period). Analysis of the results of vaccination and revaccination confirms the safety and high epidemiological and immunological efficiency. There were no cases of postvaccination complications in the vaccinated. For the first time, good tolerability and high immunogenicity of the Gam-COVID-Vac (Sputnik-V) vaccine was established after its use in recovered patients.

**Fig. 5.** Dynamics of the level of IgG to the SARS-CoV-2 S-protein within 180 days from the onset of the disease.
In accordance with the decisions of the Defense Minister of the Russian Federation, from July 1, 2021, planned revaccination against the new coronavirus infection was organized in the military medical organizations of the Russian Ministry of Defense. At the beginning of 2022, more than 550,000 volunteers have passed it, i.e., more than 95% of the military personnel. The herd immunity formed in the military contingents is characterized as quite intense and amounts to more than 90%. During the pandemic, a total of 161 cases of severe disease were registered [10, 21]. Thus, all the prerequisites have been created in the Armed Forces of the Russian Federation for the new coronavirus infection to acquire the features of a seasonal acute respiratory disease.

Based on the results of the studies, methodological materials on the diagnosis, treatment, and prevention of COVID-19 have been prepared and are constantly being updated for the training of medical personnel at medical institutions of the Ministry of Defense of the Russian Federation.

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The system of comprehensive measures implemented by military medicine is effective and determines a lower incidence of the new coronavirus infection and mortality among the personnel of the Russian Ministry of Defense.

The most significant measures include the rapid deployment of new multipurpose medical centers, large-scale training of medical personnel, the effective implementation of sanitary and anti-epidemic measures, and the priority of the fastest and most comprehensive vaccination of personnel.

Conducting scientific work on studying the pathogenesis of the infection and optimizing the diagnosti c, tactics of treatment, and prevention of diseases often makes it possible to stay ahead of national recommendations and quickly integrate the results into the practice of medical institutions of the Ministry of Defense of the Russian Federation.

The accumulated experience of military medicine convincingly proves the importance of the prompt implementation of original and modern medical solutions to improve the prevention, diagnosis, and treatment of infection caused by the SARS-CoV-2 virus not only among military personnel but also in civilian health care.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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