https://doi.org/10.18093/0869-0189-2020-30-5-553-560

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COVID-19 in individuals adapted to aerobic exercise

Andrey Yu. Tret'yakov [1], *Svetlana P. Zakharchenko* [1], *Lyubov' V. Romasenko* [2], *Alena V. Dyatlova* [3], *Aleksandra V. Zhabskaya* [1, 4], *Oleg V. Ermilov* [1, 5, ✉], *Mikhail A. Tret'yakov* [1], *Dar'ya D. Chentsova* [6]

1 Federal Belgorod National Research University, Ministry of Education and Science of Russia: ul. Pobedy 85, Belgorod, 308015, Russia

2 V.P.Serbskiy National Medical Research Center of Psychiatry and Narcology, Healthcare Ministry of Russia: Kropotkinsky per. 23, Moscow, 119034, Russia

3 State Institution "City Clinic No.212", Moscow Healthcare Department: Solntsevsky Prospekt 11a, Moscow, 119620, Russia

4 Belgorod City Municipal Hospital No.2: ul. Gubkina 46, Belgorod, 308036, Russia

5 Saint Ioasaf Belgorod Region Clinical Hospital: ul. Nekrasova 8/9, Belgorod, 308007, Russia

6 The Peoples' Friendship University of Russia: ul. Miklukho-Maklaya 6, Moscow, 117198, Russia

Abstract

Analysis of COVID-19 features in individuals who regularly practice aerobic training. **Methods.** Asymptomatic persons and patients with COVID-19 older than 30 years, 293 people (180 men and 113 women), 214 of them – inhabitants of the Moscow region (the beginning of the sampling – 2nd decade of April 2020) and 79 – inhabitants of the Belgorod region (the beginning of the sampling – 2nd decade of May 2020), adapted (27 people – 1st group) and unadapted (266 – control group) to aerobic training (AT). Computer tomography of the chest, RNA test for SARS-CoV-2 in smears from the nasopharynx-oropharynx, the clinical blood sample and level of antibodies to SARS-CoV-2 were studied. The criterion for adaptation to aerobic loads was considered compliance with the rules of the American Heart Association, 2008. **Results.** Adapted to AT individuals, in contrast to the control group, characterized with the prevalence of asymptomatic ($p = 0.045$) and absence of severe forms of COVID-19, limited cataral simptoms of the disease ($p < 0.001$), rare pneumonia with absence (1) or presence (2) of acute respiratory failure ($p_1 = 0{,}028$; $p_2 = 0{,}034$), along with lower prevalence of diseases, potentiating this infection ($p = 0.03$). **Conclusion.** Patients adapted to AT have less severe course of COVID-19.

Key words: COVID-19, adaptation, aerobic exercise.

Conflict of interests. The authors declare the absence of conflict of interests.

For citation: Tret'yakov A.Yu., Zakharchenko S.P., Romasenko L.V., Dyatlova A.V., Zhabskaya A.V., Ermilov O.V., Tret'yakov M.A., Chentsova D.D. COVID-19 in individuals adapted to aerobic exercise. *Pul'monologiya*. 2020; 30 (5): 553–560 (in Russian). DOI: 10.18093/0869-0189-2020-30-5-553-560

COVID-19 у лиц, адаптированных к аэробной нагрузке

А.Ю.Третьяков [1], *С.П.Захарченко* [1], *Л.В.Ромасенко* [2], *А.В.Дятлова* [3], *А.В.Жабская* [1, 4], *О.В.Ермилов* [1, 5, ✉], *М.А.Третьяков* [1], *Д.Д.Ченцова* [6]

1 Федеральное государственное автономное образовательное учреждение высшего образования «Белгородский государственный национальный исследовательский университет» Министерства науки и высшего образования Российской Федерации: 308015, Россия, Белгород, ул. Победы, 85

2 Федеральное государственное бюджетное учреждение «Национальный медицинский исследовательский центр психиатрии и наркологии имени В.П.Сербского» Министерства здравоохранения Российской Федерации: 119034, Россия, Москва, Кропоткинский пер., д. 23

3 Государственное бюджетное учреждение здравоохранения города Москвы «Городская поликлиника № 212 Департамента здравоохранения города Москвы»: 119620, Россия, Москва, Солнцевский просп., 11а, стр. 1

4 Областное государственное бюджетное учреждение здравоохранения «Городская больница № 2 г. Белгорода»: 308036, Россия, Белгород, ул. Губкина, 46

5 Областное государственное бюджетное учреждение здравоохранения «Белгородская областная клиническая больница Святителя Иоасафа»: 308007, Россия, Белгород, ул. Некрасова, 8 / 9

6 Федеральное государственное автономное образовательное учреждение высшего образования «Российский университет дружбы народов»: 117198, Россия, Москва, ул. Миклухо-Маклая, 6

Резюме

Целью исследования явился анализ особенностей течения COVID-19 у лиц, регулярно практикующих аэробный тренинг. **Материалы и методы.** В исследовании принимали участие лица старше 30 лет с бессимптомной формой и больные COVID-19 ($n = 293$: 180 мужчин, 113 женщин), жители ($n = 214$) Московского региона (начало формирования выборки – 2-я декада апреля 2020) и жители ($n = 79$) Белгородской области (начало формирования выборки – 2-я декада мая 2020), адаптированные (1-я группа; $n = 27$) и неадаптированные (контрольная группа; $n = 266$) к аэробным нагрузкам. У всех пациентов проводились компьютерная томография органов грудной клетки, тест на РНК SARS-CoV-2 в мазках из носо-, ротоглотки, общий анализ крови, определение антител к SARS-CoV-2. Критерием адаптации к аэробным нагрузкам считалось соответствие правилам *American Heart Association* (2008). **Результаты.** У адаптированных к аэробным нагрузкам лиц, в отличие от контрольной группы, отмечены преобладание бессимптомной ($p = 0{,}045$) и отсутствие тяжелой формы COVID-19, ограниченная острая респираторная вирусная инфекция, клинический вариант болезни ($p < 0{,}001$), низкая частота случаев пневмонии с отсутствием (1) или наличием (2) острой дыхательной недостаточности ($p_1 = 0{,}028$; $p_2 = 0{,}034$) наряду с меньшей распространенностью заболеваний, потенцирующих данную инфекцию ($p = 0{,}03$). **Заключение.** Пациентов, адаптированных к аэробным нагрузкам, отличает менее тяжелое течение COVID-19.

Ключевые слова: COVID-19, адаптация, аэробные нагрузки.
Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

Для цитирования: Третьяков А.Ю., Захарченко С.П., Ромасенко Л.В., Дятлова А.В., Жабская А.В., Ермилов О.В., Третьяков М.А., Ченцова Д.Д. COVID-19 у лиц, адаптированных к аэробной нагрузке. *Пульмонология*. 2020; 30 (5): 553–560. DOI: 10.18093/0869-0189-2020-30-5-553-560

The significant results of adaptation are improved reliability of biological systems and body as well as increased resistance to external disturbances [1]. In this regard, the search for clinical inhomogeneity patterns of COVID-19 should focus on characterisation on initial respiratory system fitness, more specifically – adaptation to aerobic exercise (AE). However, the issue "CoV-2 – adaptation to AE" is wider than the issue "CoV-2 – sports", even when the question is about the so-called cyclic sports (field-and-track athletics, rowing, swimming, cycling). This limitation, especially in case of professional sports, is due not only to the age (sportspeople are relatively young), but also to the influence of key elements of a sports process affecting harmonious development: immunomodulating competitive stress, infection-promoting crowding during workouts and competitions, and highly commercialised nature of sports. Therefore, a few researches on the specifics of COVID-19-pathology in physically trained individuals, specifically in sportspeople, are not able to resolve the issue of natural sanitation mechanisms, resulting, in some cases, in asymptomatic disease and, in some cases, in severe pneumonia associated with corona virus infection [2, 3].

This paper, initiated during the period of higher uncertainty and mysteriousness of the new disease for the Russian healthcare system, is aimed at assessment of COVID-19 characteristics in individuals adapted to AE. At the same time, the initial knowledge about the lower incidence and relatively good outcomes in younger population was a prerequisite for sampling patients over 30 years old only.

Materials and methods

The study included asymptomatic individuals and COVID-19 patients over 30 years old, 293 individuals (180 men and 113 women), with the median and interquartile age of 54.5 (44 – 65) years old, 214 of them were citizens of Moscow and Moscow region (sampling initiation: 2nd decade of April 2020) and 79 citizens of Belgorod region (sampling initiation: 2nd decade of May 2020). 56 subjects (21.1%) previously visited endemic regions abroad (including 49 citizens of Moscow and Moscow Region). COVID-19 was diagnosed in accordance with The Temporary Guidelines for Prevention, Diagnosis and Management of a Novel Corona Virus Infection of the Ministry of Health of the Russian Federation (revision 4 dated March 27, 2020 and revision 5 dated April 08, 2020), where 3 severity levels (mild: 146 individuals, moderate: 63 individuals, and severe: 53 individuals) and 6 clinical patterns are identified; only 4 of them were recorded in the study: ARVI, pneumonia without respiratory distress (RD), pneumonia with severe RD, acute respiratory distress syndrome (no sepsis and septic shock cases were recorded). Due to uneven capability (especially in outpatient settings) to perform a full set of diagnostic procedures, assessment was based on computer-aided chest tomography (CT), SARS-CoV-2 RNA smears from the nasopharynx – oropharynx, clinical blood assay with differential white blood cell count, and antibody levels (IgG and IgM).

Asymptomatic cases included cases (31 patients if the incubation stage of the disease is excluded) limited to positive SARS-CoV-2 RNA smear PCR tests and/or increased IgG (over 10 U/mL) and IgM (over 2 U/mL) titre against SARS-CoV-2 (ELISA). Any other medical history data, excluding asymptomatic cases, were obtained only from COVID-19 survivors.

In order to characterise "adaptation to AE", the modified American Heart Association criteria (AHA, 2008) were used, where an individual had highly intensive aerobic physical exercises during previous 12 months (min. 150 minutes/week) or combined intensive exercises (min. 75 minutes/week) with moderate exercises (min. 150 minutes/week). Intensity levels corresponded to AHA classification, based on the heart rate (HR) during exercises: moderate intensive exercises if the HR was 50 – 70% of the maximum value ($HR_{max.}$ = 220 – age), intensive exercises if the HR was > 70% – ⩽ $85\%_{max}$. However, such an estimation precision of exercises duration and HR in clinical settings is rather an aim, not a real possibility, recorded only in patients who were aware of and used the principles of self-control. All other subjects were included into the group with adaptation to AE if during the previous 12 months they regularly (at least 5 times weekly) went running outside or on a treadmill (min. 30 minutes), stationary bike exercises (min. 40 minutes), stair stepper exercises (with an overall duration of 30 min.) or intensive nordic walking (60 – 90 minutes). In AHA guidelines (2008), such aerobic exercises are included into "intensive exercises". Eventually, these criteria were met by 27 individual (17 men, 10 women), with the median and interquartile age of 54 (42 – 67) years old (group 1). The remaining 266 individuals from the main group not adapted to AE (163 men and 103 women aged 55 (43 – 66) years) were controls (group 2). As there were no individuals with markedly depressed immunity (administration of system glucocorticosteroids, cytostatic agents, exhaustion, etc.) or persons from close communities (orphanages, retirement homes) in group 1, these characteristics were exclusion criteria in controls as well.

Regular intensive exercises are one of the endurance and stamina features of an individual – determination, adding to other endurance and stamina features: bravery, independence, self-command, etc. For additional characterisation of patient personality and determination specification, we used the "persistence" scale from the Willed Self-Regulation questionnaire by *A.V.Zverkov — E.V.Eidman* [4]. Of note, the objectivity of results in such an analysis is greatly dependent on trusted relations between the patients and his/her physician; and the formal nature of tests with filling out questionnaires sometimes compromises the method. This is especially true with COVID-19 patients who had a psychological trauma. Therefore, in order to maintain the principles of medical paternalism, the 16 questions (where pronouns "I", "My", "Me" were replaced with "You", "Yours", "For you") were distributed along the conversation with the patient, and the operator calculated the final result after listening to the recorded dialogue. The results were processed using variation statistical methods in Statistica 6.0 (StatSoft, Inc., USA) and Biostatistics for Windows 4,03.

Results and discussion

In the groups of COVID-19 patients from Moscow, Moscow Region and Belgorod Region, the share of individuals who regularly do aerobic exercises was 9.2% (27 individuals). There were 3 patients over 80 years old: 2 men of 81 and 83 years old and a 80-year old woman who went for 5 — 7 km of nordic walking every day. As far as disease severity is concerned, individuals adapted to AE did not have severe pathology; they were mostly asymptomatic ($p < 0.05$), only 1 patient had a moderate disease (see Table 1). It is worth mentioning that this regularity was identified during provisional analysis, when the groups were formed, during the period of the highest uncertainly as to the correct search direction, when in addition to very limited amount of information about the infection and lack of experience in COVID-19 patient management, we have already had some references to severe course of COVID-19 in an individual highly adapted to AE. It was a 38-year old Italian marathon runner who spent over 2 weeks on mechanical ventilation, and on 27 February the Daily Mail named him a super-spreader of the infection in Lombardy [5].

The rate of mild cases in group 1 (excluding asymptomatic cases) was 95%, whereas in group 2 it was 66.5%; the rate of moderate and severe cases in group 2 was 11.6% and 21.9%, respectively. This severity ratio is quite different from the currently accepted values for COVID-19 (81, 14 and 5%); this is probably due to a small sample number, age limitations (individuals under 30 years old were excluded) and the criterion of no marked immune depression.

In individuals adapted to AE, very often the disease was limited to ARVI only ($p < 0.001$), while pneumonia with severe RD was diagnosed only in 1 patient (a 57-year old man) who had moderately severe disease. In controls, pneumonia with severe RD was diagnosed in 42.9% ($p < 0.05$), and the rate of pneumonia without severe RD was a bit lower (44.7%). Also, the unadapted group of patients included 3 men and 1 woman who suffered from ARDS.

Analysis of individual signs in COVID-19 patients (20 individuals in group 1 and 242 individuals in group 2) demonstrates fewer symptoms of respiratory abnormalities in patients adapted to AE: they had caught, dyspnea and chest X-ray abnormalities less frequently (see Table 2). When all symptomatic cases were excluded, this group included only 6 individuals with typical CT pattern: 1 man with right unilateral "ground glass" areas in S6 and 10 (CT stage: I), 4 patients had bilateral pneumonia stage, and one patient had a bilateral disease with CT stage II. In controls, CT changes were recorded in 234 individuals ($p < 0.05$), including 22.4% (53 individuals) with stage 3 and 3 — 4 ($p = 0.087$).

Table 1
Severity structure and clinical variants of COVID-19 in individuals adapted (group 1) and unadapted (group 2) to aerobic training; n (%)
Таблица 1
Структура тяжести и клинические варианты COVID-19 у лиц, адаптированных (1-я группа) и неадаптированных (2-я группа) к аэробной нагрузке; n (%)

Characteristics	Group 1 *n* = 27	Group 2 *n* = 266	*p*
Mild disease	19 (70.4)	161 (60.5)	N/a
Moderate disease	1 (3.7)	28 (10.5)	N/a
Severe disease	–	53 (19.9)	0,042
Asymptomatic disease	7 (25.9)	24 (9.0)	0,045
ARVI	14 (51.9)	8 (3.0)	< 0,001
Pneumonia without RD	5 (18.5)	153 (57.5)	0,028
Pneumonia with RD	1 (3.7)	77 (28.9)	0,034
ARDS	–	4 (1.5)	N/a

Note: ARVI, acute respiratory viral infection; RD, acute respiratory distress; ARDS, acute respiratory distress syndrome; *p* confidence for χ^2; N/a, no data available.
Примечание: достоверность *p* по критерию χ^2.

Because of a variable conception of the disease duration by patients (whether presence of symptoms or duration of hospitalisation or sick leave), we used fever duration as a criterion, taking into account that the majority of patients remembered quite a unique, usually two-phase ARVI. In adapted patients, the median duration was 2 days shorter than in controls ($p < 0.01$); the maximum fever duration in group 1 was 12 days, while in group 2 it was 27 days.

Regular aerobic exercises did not prevent group 1 patients from having diseases that potentiate COVID-19; however, this group included only 7 patients with obesity, arterial hypertension (AH) and diabetes mellitus (DM), whereas in controls these conditions were recorded in approx. 70% ($p < 0.05$, see Table 3). Intergroup differences in comorbidity were caused by various combinations of obesity and DM ($p < 0.05$), but not AH. Of note, among individuals adapted to AE there was one individual with obesity, DM and AH (a 54-year old man). We have been following this patient up for 2 years; his hyperglycemia is corrected with a combination of antihyperglycemic agents

Table 2
Frequency of individual signs* COVID-19 in patients adapted (group 1) and unadapted (group 2) to aerobic training; n (%)
Таблица 2
Частота отдельных признаков* COVID-19 у больных, адаптированных (1-я группа) и неадаптированных (2-я группа) к аэробной нагрузке; n (%)

Characteristics	Group 1 *n* = 19	Group 2 *n* = 242	*p*
Fever	16 (84.2)	241 (99.6)	N/a
Fever duration, days, *Me* (*Q1* – *Q2*)	3 (3–5)	5 (3–14)	0,001**
Cough	3 (15.8)	227 (93.8)	0,003
Dyspnoe	1 (5.2)	112 (46.3)	0,023
Runny nose	18 (94.7)	181 (74.8)	N/a
Impaired olfaction	17 (89.5)	231 (95.5)	N/a
Headache	5 (26.3)	107 (44.2)	– " –
Impaired sense of taste	1 (5.2)	60 (24.8)	– " –
Diarrhea	–	18 (7.4)	– " –
Myalgia, arthralgia	6 (31.6)	148 (61.2)	– " –
All CT positive cases	6 (31.6)	234 (96.7)	0,025
Severe CT positive cases:			
• I	5 (26.3)	134 (55.4)	N/a
• II	1 (5.2)	39 (16.1)	N/a
• II – III	–	8 (3.3)	– " –
• III	–	50 (20.7)	– " –
• III – IV	–	3 (1.2)	– " –
Lymphocyte depletion (lymphocyte count < 20%)	–	28 (11.6)	

Note: CT, computered tomography; p confidence for χ^2; *, for paraclinic signs, when the test was repeated, we used a result with the highest deviation; **, *p* confidence for Mann – Whitney test; *Me* (*Q1* – *Q2*) – median, quartile 25 – 75%; N/a, no data available.

Примечание: * – для параклинических признаков при неоднократности выполнения исследования использован результат с наибольшим отклонением; ** – достоверность *p* по критерию Т Манна–Уитни; *Me* (*Q1*–*Q2*) – медиана, квартиль 25–75 %.

and a two-component antihypertensive regime, including ACE inhibitors; also, he has been regularly exercising on a stationary bike for 14 months (45 – 90 min/day); his disease was a 5-day ARVI without impaired olfaction.

Analysis of mean values for "persistence", modified Willed Self-Regulation questionnaire did not allow revealing a significant difference between patients who regularly exercise and those who do not use aerobic exercises in their daily life. In group 1, the value was 12 (7 – 13) points, whereas in group 2 it was 10 (6 – 12) points, with the difference of 16.7%, just trending towards confidence ($p = 0.093$), without any statistically significant difference. A probable reason might be both inadequate specificity of the method used and a small number of subjects in the test and control groups.

Without getting into details of effects from adaptation to AE, three mechanisms should be named that can contribute to favourable COVID-19 course in patients adapted to physical exercises. On the one hand, long-term adaptation to AE (or stamina training) has a very important characteristic: it results in sparing use of regulatory respiration elements during regular stress and enhanced reserves of the respiratory system, together with the ability to mobilise more efficiently when required. Favourable cross effects from such adaptation for antioxidant and immune systems are well known as well [1]. A typical inflammation manifestation is energy deficit in the inflamed site; frequent sympathicotonia and resulting phospholipase activation and lipide peroxidation are associated with cytopathy. On the contrary, in adaptation to AE, with increase in antioxidant enzyme levels in tissues (superoxide dismutase and glutathione peroxidase) and mitochondria genesis, this effect significantly reduces [6, 7]. Also, aerobic exercises promote improved density and adrenoreceptor affinity in breathing muscles, bronchi smooth muscle cells, bronchial arteries, glands and epithelium. First, it allows improving the rate and amplitude of inhale and exhale muscle contraction (their strength) in response to significantly lower (non-toxic) adrenaline concentrations, synchronising their activity with other skeletal muscles participating in locomotor behaviour; second, it efficiently reduces resistance in the bronchial tree as a result of more marked bronchodilation; and third, it improves the quality of bronchi mucosa sanitation due to ciliary activity stimulation and less viscous secretion passage [1, 6].

Most prominent changes in COVID-19 are found in the alveolar-capillary membrane (ACM), and the virus enters the cell through membrane protein – angiotensin converting enzyme 2 (ACE II) [8]. In addition to the growth in the pulmonary capacity, AE are known to modify the ACM structure and to improve its diffusion capacity. During overall diffusion capacity tests with carbon monoxide (DL_{CO}), trained subjects demonstrated significantly higher values *vs* untrained individuals not only at rest, but specifically during exercises; a similar difference was noted for blood volume in pulmonary capillaries (V_c) and diffusion capacity of membrane ($D_м$) [9]. In our study, untrained patients were distinguished for a large number of cases with high body mass index and DM. Obesity and DM significantly disturb the ACM structure and function [10]. For an experimental model, increased thickness, reduced elasticity and diffusion capacity both in normal state and in hypoxic events were proven. Also, in obesity associated with hypoxia, the number of type II alveolar epithelial cells and alveolar macrophage are significantly reduced; oxidised defective DNA are more numerous, thus promoting impaired overall resistivity of ACM [11]. Now it is difficult to give an unambiguous answer to the question: is it only the training of the respiratory system that increases the level of its resistance to coronovirus, or the small number of comorbid diseases – obesity and diabetes mellitus – is also important here, presented in this work in the group of persons adapted to AN. Most likely today, both factors should be taken into account, but the degree of signifi-

Пульмонология • Pul'monologiya. 2020; 30 (5): 553–560. DOI: 10.18093/0869-0189-2020-30-5-553-560

Table 3
Diseases that potentiate COVID-19 in the compared groups; n (%)
Таблица 3
Заболевания, потенцирующие COVID-19 в сравниваемых группах; n (%)

Disease	Group 1 *n* = 27	Group 2 *n* = 266	*p*
Obesity + DM	–	53 (19.9)	0.043
Obesity + AH	–	16 (6.0)	N/a
AH + DM	–	3 (1.1)	N/a
Obesity + DM+ AH	1 (3.7)	22 (8.3)	– " –
Obesity	2 (7.4)	52 (19.5)	– " –
DM	–	1 (0.3)	– " –
AH	4 (14.8)	38 (14.3)	– " –
All cases with obesity	3 (11.1)	143 (53.8)	0.009
All cases with DM	1 (3.7)	79 (29.7)	0.031
All mentioned diseases that potentiate COVID-19	7 (25.9)	185 (69.5)	0.03

Note: DM, diabetes mellitus; AH, arterial hypertension; p confidence for χ^2; N/a, no data available.
Примечание: достоверность p по критерию χ^2.

cance of each of them must be specified in the course of a subsequent study with an increase in the volume of the experimental and control groups.

ACE II, an ACE homolog which differs from ACE in its physiological effects, is a component of counterregulatory axis (ACE II/AT (1 – 7)/MasR). Regular physical exercises reduce ACE II levels in tissues [12, 13]; therefore, they should have facilitated corona virus penetration to the cell and made COVID-19 more aggressive. However, clinical and experimental trials of ACE inhibitors and angiotensin II receptor blockers (their pharmacological mechanism causes increase in ACE II level) show quite another pattern: administration of medicines is associated with reduced risks of death of COVID-19 patients; during the experiment, medicines reduced mortality and prevented acute damages of lungs in mice challenged with SARS-CoV [8, 14, 15]. Other arguments for physical exercises and ACE II growth are presented in a study by *D.M.Magalhães et al.* (2020): as exemplified by physically trained men who were doing highly intensive aerobic exercises, blood and urine ACE II levels significantly rise, and in moderate exercises, renal elimination of ferment is significantly increased [16]. It is clear that they are free, unbound (solubilized) protein fractions. Therefore, it is possible that ACE II split from cell membranes is increased in AE; therefore, in adapted individuals, the probability of virus entering the cell via this receptor is reduced.

The human and animal immune system is affected by the overall physical activity and AE [17]. Adaptation to AE impacts cell and humoral elements of inborn and acquired immunity: regular exercises modify the ratio of natural killer cells increasing the number of younger (CD56-bright NK) colonies; the neutrophils/lymphocytes ratio and the density of *Toll*- and NOD-like receptors increase; Th1, Th2, Th_{reg}, secretory IgA levels change in upper respiratory tract mucosa, etc. [18, 19]. All these factors improve body resistance to respiratory infections, neoplasms, toxic and even radiation impacts [1, 6, 20, 21]. Still, there are negative cross-effects from such adaptation. They result from excessive exercises (J-effect by *D.C.Nieman*, 1994), when the risk of respiratory infections increases. It is true about long AE [22–24]. An additional condition is physical epithelium damage (bronchial and alveolar) resulting from long-term hyperventilation in case of inadequate training conditions [25]. It is likely that all these conditions were present in references, where COVID-19 in individuals adapted to AE was severe (only 2 cases were recorded among numerous marathon runners and only 1 among professional cyclists) [2, 3]. Unfavourable consequences from adaptation to AE can be prevented by following the rules established by the Russian school of physiology: “prevention... Is first of all sustainable limitation of physical exercises and adequate selection of ontogeny stage when exercises can be done (or increased); second, use of combined adaptation when the body adapts to several factors”, thermal (cold water treatment), hypoxic, etc. regimen [1].

Conclusion

In this study of physically active individuals of 30+ years old adapted to AE, as opposed to patients who are not used to aerobic exercises, COVID-19 was mostly asymptomatic or was associated with limited clinical ARVI, rare pneumonia (or CT positive cases), together with lower morbidity of rates that potentiate this infection, especially obesity and DM; the degree of their participation and the independent role of the adaptation factor to AE in changing the severity of COVID-19 is planned to be clarified in the course of a subsequent study.

References

1. Gazenko O., Meerson F., Pshennikova M. [Physiology of adaptation processes]. Moscow: Nauka; 1986 (in Russian).
2. Halabchi F., Ahmadinejad Z., Selk-Ghaffari M. COVID-19 Epidemic: exercise or not to exercise; that is the question! *Asian. J. Sports. Med.* 2020; 11 (1): e102630. DOI: 10.5812/asjsm.102630.
3. Wackerhage H., Everett R., Krüger K. et al. Sport, exercise and COVID-19, the disease caused by the SARS-CoV-2 coronavirus. *Dtsch. Z. Sportmed.* 2020; 71 (5): e1–12. DOI: 10.5960/dzsm.2020.441.
4. Pashukova T.I., Dopira A.I., D’yakonov G.V. [Psychological research: a workshop on general psychology for students of pedagogical universities]. Moscow: Institut prakticheskoy psikhologii; 1996 (in Russian).
5. Paterlini M. On the front lines of coronavirus: the Italian response to covid-19. *Br. Med. J.* 2020; 368: m1065. DOI: 10.1136/bmj.m1065.

6. Meerson F.Z., Pshennikova M.G. [Adaptation to stressful situations and physical exertion]. M.: Meditsina; 1988 (in Russian).
7. Toledo A.C., Magalhaes R.M., Hizume D.C. et al. Aerobic exercise attenuates pulmonary injury induced by exposure to cigarette smoke. *Eur. Respir. J.* 2012; 39 (2): 254–264. DOI: 10.1183/09031936.00003411.
8. Yan T., Xiao R., Lin G. Angiotensin-converting enzyme 2 in severe acute respiratory syndrome coronavirus and SARS-CoV-2: A double-edged sword? *FASEB J.* 2020; 34 (5): 6017–6026. DOI: 10.1096/fj.202000782.
9. Tedjasaputra V., Bouwsema M.M., Stickland M.K. Effect of aerobic fitness on capillary blood volume and diffusing membrane capacity responses to exercise. *J. Physiol.* 2016; 594 (15): 4359–4370. DOI: 10.1113/JP272037.
10. Foster D.J., Ravikumar P., Bellotto D.J. et al. Fatty diabetic lung: altered alveolar structure and surfactant protein expression. *Am. J. Lung Cell. Mol. Physiol.* 2010; 298 (3): L392–403. DOI: 10.1152/ajplung.00041.2009.
11. Yilmaz C., Ravikumar P., Gyawali D. et al. Alveolar-capillary adaptation to chronic hypoxia in the fatty lung. *Acta Physiol.* 2015; 213 (4): 933–946. DOI: 10.1111/apha.12419.
12. Dizon L.A., Seo D.Y., Kim H.K. et al. Exercise perspective on common cardiac medications. *Integr. Med. Res.* 2013; 2 (2): 49–55. DOI: 10.1016/j.imr.2013.04.006.
13. Agarwal D., Welsch M.A., Keller J.N., Francis J. Chronic exercise modulates RAS components and improves balance between pro-and anti-inflammatory cytokines in the brain of SHR. *Basic Res. Cardiol.* 2011; 106 (6): 1069–1085. DOI: 10.1007/s00395-011-0231-7.
14. Zhang P., Zhu L., Cai J. Association of inpatient use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. *Circ. Res.* 2020; 126 (12): 1671–1681. DOI: 10.1161/CIRCRESAHA.120.317134.
15. Kai H., Kai M. Interactions of coronaviruses with ACE2, angiotensin II, and RAS inhibitors – lessons from available evidence and insights into COVID-19. *Hypertens. Res.* 2020; 43 (7): 648–654. DOI: 10.1038/s41440-020-0455-8.
16. Magalhães D.M., Nunes-Silva A., Rocha G.C. et al. Two protocols of aerobic exercise modulate the counter-regulatory axis of the renin-angiotensin system. *Heliyon*. 2020; 6 (1): e03208. DOI: 10.1016/j.heliyon.2020.e03208.
17. Poos M.I., Costello R., Carlson-Newberry S.J. Military strategies for sustainment of nutrition and immune function in the field. Washington, DC: The National Academies Press, Institute of Medicine; 1999. DOI: 10.17226/6450.
18. Timmons B.W., Cieslak T. Human natural killer cell subsets and acute exercise: a brief review. *Exerc. Immunol. Rev.* 2008; 14: 8–23.
19. Nieman D.C., Wentz L.M. The compelling link between physical activity and the body's defense system. *J. Sport Health Sci.* 2019; 8 (3): 201–217. DOI: 10.1016/j.jshs.2018.09.009.
20. Campbell J.P. Infekt nach Marathon? Mythos widerlegt! *Dtsch. Med. Wochensch.* 2018; 143 (12): 853–853. DOI: 10.1055/a-0598-1219.
21. Gleeson M., Pyne D.B., Austin J.P. et al. Epstein–Barr virus reactivation and upper-respiratory illness in elite swimmers. *Med. Sci. Sports Exerc.* 2002; 34 (3): 411–417. DOI: 10.1097/00005768-200203000-00005.
22. Nieman D.C. Exercise, upper respiratory tract infection, and the immune system. *Med. Sci. Sports Exerc*. 1994; 26 (2): 128–139. DOI: 10.1249/00005768-199402000-00002.
23. Campbell J.P., Turner J.E. There is limited existing evidence to support the common assumption that strenuous endurance exercise bouts impair immune competency. *Expert Rev. Clin. Immunol.* 2019; 15 (2): 105–109. DOI: 10.1080/1744666X.2019.1548933.
24. Estruel-Amades S., Camps-Bossacoma M., Massot-Cladera M. et al. Alterations in the innate immune system due to exhausting exercise in intensively trained rats. *Sci. Rep.* 2020; 10 (1): 967. DOI: 10.1038/s41598-020-57783-4.
25. Combes A., Dekerle J., Dumont X. et al. Continuous exercise induces airway epithelium damage while a matched-intensity and volume intermittent exercise does not. *Respir. Res.* 2019; 20 (1): 12. DOI: 10.1186/s12931-019-0978-1.

Received: July 25, 2020

Литература

1. Газенко О., Меерсон Ф., Пшенникова М. Физиология адаптационных процессов. М.: Наука; 1986.
2. Halabchi F., Ahmadinejad Z., Selk-Ghaffari M. COVID-19 Epidemic: exercise or not to exercise; that is the question! *Asian. J. Sports. Med.* 2020; 11 (1): e102630. DOI: 10.5812/asjsm.102630.
3. Wackerhage H., Everett R., Krüger K. et al. Sport, exercise and COVID-19, the disease caused by the SARS-CoV-2 coronavirus. *Dtsch. Z. Sportmed.* 2020; 71 (5): e1–12. DOI: 10.5960/dzsm.2020.441.
4. Пашукова Т.И., Допира А.И., Дьяконов Г.В. Психологические исследования: Практикум по общей психологии для студентов педагогических вузов. М.: Институт практической психологии; 1996.
5. Paterlini M. On the front lines of coronavirus: the Italian response to covid-19. *Br. Med. J.* 2020; 368: m1065. DOI: 10.1136/bmj.m1065.
6. Меерсон Ф.З., Пшенникова М.Г. Адаптация к стрессорным ситуациям и физическим нагрузкам. М.: Медицина; 1988.
7. Toledo A.C., Magalhaes R.M., Hizume D.C. et al. Aerobic exercise attenuates pulmonary injury induced by exposure to cigarette smoke. *Eur. Respir. J.* 2012; 39 (2): 254–264. DOI: 10.1183/09031936.00003411.
8. Yan T., Xiao R., Lin G. Angiotensin-converting enzyme 2 in severe acute respiratory syndrome coronavirus and SARS-CoV-2: A double-edged sword? *FASEB J.* 2020; 34 (5): 6017–6026. DOI: 10.1096/fj.202000782.
9. Tedjasaputra V., Bouwsema M.M., Stickland M.K. Effect of aerobic fitness on capillary blood volume and diffusing membrane capacity responses to exercise. *J. Physiol.* 2016; 594 (15): 4359–4370. DOI: 10.1113/JP272037.
10. Foster D.J., Ravikumar P., Bellotto D.J. et al. Fatty diabetic lung: altered alveolar structure and surfactant protein expression. *Am. J. Lung Cell. Mol. Physiol.* 2010; 298 (3): L392–403. DOI: 10.1152/ajplung.00041.2009.

11. Yilmaz C., Ravikumar P., Gyawali D. et al. Alveolar-capillary adaptation to chronic hypoxia in the fatty lung. *Acta Physiol.* 2015; 213 (4): 933–946. DOI: 10.1111/apha.12419.
12. Dizon L.A., Seo D.Y., Kim H.K. et al. Exercise perspective on common cardiac medications. *Integr. Med. Res.* 2013; 2 (2): 49–55. DOI: 10.1016/j.imr.2013.04.006.
13. Agarwal D., Welsch M.A., Keller J.N., Francis J. Chronic exercise modulates RAS components and improves balance between pro-and anti-inflammatory cytokines in the brain of SHR. *Basic Res. Cardiol.* 2011; 106 (6): 1069–1085. DOI: 10.1007/s00395-011-0231-7.
14. Zhang P., Zhu L., Cai J. Association of inpatient use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. *Circ. Res.* 2020; 126 (12): 1671–1681. DOI: 10.1161/CIRCRESAHA.120.317134.
15. Kai H., Kai M. Interactions of coronaviruses with ACE2, angiotensin II, and RAS inhibitors – lessons from available evidence and insights into COVID-19. *Hypertens. Res.* 2020; 43 (7): 648–654. DOI: 10.1038/s41440-020-0455-8.
16. Magalhães D.M., Nunes-Silva A., Rocha G.C. et al. Two protocols of aerobic exercise modulate the counter-regulatory axis of the renin-angiotensin system. *Heliyon*. 2020; 6 (1): e03208. DOI: 10.1016/j.heliyon.2020.e03208.
17. Poos M.I., Costello R., Carlson-Newberry S.J. Military strategies for sustainment of nutrition and immune function in the field. Washington, DC: The National Academies Press, Institute of Medicine; 1999. DOI: 10.17226/6450.
18. Timmons B.W., Cieslak T. Human natural killer cell subsets and acute exercise: a brief review. *Exerc. Immunol. Rev*. 2008; 14: 8–23.
19. Nieman D.C., Wentz L.M. The compelling link between physical activity and the body's defense system. *J. Sport Health Sci.* 2019; 8 (3): 201–217. DOI: 10.1016/j.jshs.2018.09.009.
20. Campbell J.P. Infekt nach Marathon? Mythos widerlegt! *Dtsch. Med. Wochensch.* 2018; 143 (12): 853–853. DOI: 10.1055/a-0598-1219.
21. Gleeson M., Pyne D.B., Austin J.P. et al. Epstein-Barr virus reactivation and upper-respiratory illness in elite swimmers. *Med. Sci. Sports Exerc.* 2002; 34 (3): 411–417. DOI: 10.1097/00005768-200203000-00005.
22. Nieman D.C. Exercise, upper respiratory tract infection, and the immune system. *Med. Sci. Sports Exerc*. 1994; 26 (2): 128–139. DOI: 10.1249/00005768-199402000-00002.
23. Campbell J.P., Turner J.E. There is limited existing evidence to support the common assumption that strenuous endurance exercise bouts impair immune competency. *Expert Rev. Clin. Immunol.* 2019; 15 (2): 105–109. DOI: 10.1080/1744666X. 2019.1548933.
24. Estruel-Amades S., Camps-Bossacoma M., Massot-Cladera M. et al. Alterations in the innate immune system due to exhausting exercise in intensively trained rats. *Sci. Rep.* 2020; 10 (1): 967. DOI: 10.1038/s41598-020-57783-4.
25. Combes A., Dekerle J., Dumont X. et al. Continuous exercise induces airway epithelium damage while a matched-intensity and volume intermittent exercise does not. *Respir. Res.* 2019; 20 (1): 12. DOI: 10.1186/s12931-019-0978-1.

Поступила 25.07.20

Author Information / Информация об авторах

Andrey Yu. Tret'yakov – Doctor of Medicine, Professor, Medical Institute, Federal Belgorod National Research University, Ministry of Education and Science of Russia; tel.: (4722) 30-12-11; e-mail: opensource2007@yandex.ru
Третьяков Андрей Юрьевич – д. м. н., профессор Медицинского института Федерального государственного автономного образовательного учреждения высшего образования «Белгородский государственный национальный исследовательский университет» Министерства науки и высшего образования Российской Федерации; тел.: (4722) 30-12-11; e-mail: opensource2007@yandex.ru

Svetlana P. Zakharchenko – Candidate of Medicine, Senior Researcher, Medical Institute, Federal Belgorod National Research University, Ministry of Education and Science of Russia; tel.: (4722) 30-12-11; e-mail: openbox.2013@yandex.ru
Захарченко Светлана Петровна – к. м. н., старший научный сотрудник Медицинского института Федерального государственного автономного образовательного учреждения высшего образования «Белгородский государственный национальный исследовательский университет» Министерства науки и высшего образования Российской Федерации; тел.: (4722) 30-12-11; e-mail: openbox.2013@yandex.ru

Lyubov' V. Romasenko – Doctor of Medicine, Professor, Head of Psychosomatic Disorders Department, Borderline Psychiatry Department, V.P.Serbskiy National Medical Research Center of Psychiatry and Narcology, Healthcare Ministry of Russia; tel.: (499) 248-75-96; e-mail: lromasenko@mail.ru
Ромасенко Любовь Владимировна – д. м. н., профессор, руководитель отделения психосоматических расстройств, отдел пограничной психиатрии Федерального государственного бюджетного учреждения «Национальный медицинский исследовательский центр психиатрии и наркологии имени В.П.Сербского» Министерства здравоохранения Российской Федерации; тел.: (499) 248-75-96; e-mail: lromasenko@mail.ru

Alena V. Dyatlova – Physician, Department of Therapy No.1, State Institution "City Clinic No.212", Moscow Healthcare Department; tel.: (903) 673-50-95; e-mail: dr.al-vasilchenko@yandex.ru
Дятлова Алена Владиславовна – врач-терапевт Государственного бюджетного учреждения здравоохранения города Москвы «Городская поликлиника № 212 Департамента здравоохранения города Москвы»; тел.: (903) 673-50-95; e-mail: dr.al-vasilchenko@yandex.ru

Aleksandra V. Zhabskaya – Postgraduate Student, Medical Institute, Federal Belgorod National Research University, Ministry of Education and Science of Russia; Radiologist, Belgorod City Municipal Hospital No.2; tel.: (4722) 30-12-11; e-mail: zhabskaya.sasha@yandex.ru
Жабская Александра Васильевна – аспирант Медицинского института Федерального государственного автономного образовательного учреждения высшего образования «Белгородский государственный национальный исследовательский университет» Министерства науки и высшего образования Российской Федерации, врач-рентгенолог Областного государственного бюджетного учреждения здравоохранения «Городская больница № 2 г. Белгорода»; тел.: (4722) 30-12-11; e-mail: zhabskaya.sasha@yandex.ru

Oleg V. Ermilov, Assistant – Medical Institute, Federal Belgorod National Research University, Ministry of Education and Science of Russia; Pulmonologist, Department of Pulmonology, Saint Ioasaf Belgorod Region Clinical Hospital; tel.: (4722) 50-42-32; e-mail: neglect@mail.ru (ORCID: *https://orcid.org/0000-0001-8489-3851*)
Ермилов Олег Владимирович – ассистент Медицинского института Федерального государственного автономного образовательного учреждения высшего образования «Белгородский государственный национальный исследовательский университет» Министерства науки и высшего образования Российской Федерации, врач-пульмонолог пульмонологического отделения Областного государственного

бюджетного учреждения здравоохранения «Белгородская областная клиническая больница Святителя Иоасафа»; тел.: (4722) 50-42-32; e-mail: neglect@mail.ru (ORCID: *https://orcid.org/0000-0001-8489-3851*)

Mikhail A. Tret'yakov – Federal Belgorod National Research University, Ministry of Education and Science of Russia; tel.: (4722) 30-12-11; e-mail: tretyakov.mihail2012@yandex.ru
Третьяков Михаил Андреевич – сотрудник Медицинского института Федерального государственного автономного образовательного учреждения высшего образования «Белгородский государственный национальный исследовательский университет» Министерства науки и высшего образования Российской Федерации; тел.: (4722) 30-12-11; e-mail: tretyakov.mihail2012@yandex.ru

Dar'ya D. Chentsova – Physician, Clinical and Diagnostic Center, The Peoples' Friendship University of Russia; tel.: (495) 434-24-91; e-mail: dmitricu@rambler.ru
Ченцова Дарья Дмитриевна – врач-терапевт клинико-диагностического центра Федерального государственного автономного образовательного учреждения высшего образования «Российский университет дружбы народов»; тел.: (495) 434-24-91; e-mail: dmitricu@rambler.ru