



Mini-Review/Systematic Review

People with asthma: care during the COVID-19 pandemic and the importance of regular exercise for the immune system

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Abstract - Aim: To show the possible immunologic pathways of protection for asthmatics against infection of Covid-19 through the capacity of recognition and cytotoxicity to eliminate pathogens improved by regular exercise aerobic. **Methods:** The bibliographic search was conducted on the following databases: Pubmed/Medline, Scielo, and Scholar Google from 2020 to 2021. The following keywords and Boolean operators were used: asthma, aerobic training (AT), immune system, and Covid-19. **Results:** After the screening, 349 were initially found, after evaluation only 20 studies had all criteria. Twelve studies showed that AT induces changes in the immune system with a reduction of inflammation. In complement, the literature showed an innate pathway that improves immune function against COVID-19 by reducing angiotensin-converting enzyme 2 (ACE2) in the lung, which seems to hinder the multiplication of the COVID-19 virus in the lung. Apparently, asthmatics patients are less susceptible to respiratory infection caused by COVID-19 because they have low levels of ACE2. Furthermore, trained asthmatics showed a lower risk of infection for SARS-CoV-2. **Conclusion:** The findings reported that asthmatics people can benefit from AT, and these individuals seem not to be a risk group for covid-19 because they have low levels of ACE2 protein. Taken together, this review reinforces the importance of asthmatic patients be physically active throughout their lifetime, but specially during the pandemic to prevent contamination by SARS-CoV-2.

Keywords: asthmatic, infection, virus, epidemic, inflammation.

Introduction

Asthma is a disease characterized by symptoms such as difficulty in breathing, wheezing, a feeling of tightness in the chest, cough, limitation of pulmonary expiratory flow, and chronic inflammation in the airways¹. In complement, studies have shown that there appear to be several types of asthma phenotypes, such as allergic with features that describe the outward manifestation of an individual's airway inflammation and that may be useful for predicting responsiveness to specific treatments². Asthma with features of severe allergic inflammation in the airways presents an important predominance of immune response T2³. The T2 cells expressed the cytokines IL-4, IL-5, IL-9, and IL-13, which play a central role in the inflammatory process directed against helminths and extracellular bacteria, and participate in the asthma pathophysiology^{2,3}.

The allergic asthma physiopathology presents an important inflammatory component, so it is necessary to use inhaled corticosteroids with or without beta-2 agonists short and long term, in cases of severe asthma is the common use of oral corticosteroids for treatment¹. In addition,

more actions must induce a better asthma control such as avoiding environmental exposures¹ and performing the regular physical exercise with aerobic training (AT) predominance⁴, a type of exercise that requires the ability of pulmonary, cardiovascular, and muscular system response to increase rapidly the flux of O₂ from the atmosphere to muscle mitochondria allowing aerobic ATP production for prolonged periods of physical exercise⁵. The AT enhances asthma control by reducing daily symptoms, anxiety, and depression^{4,6}. Exercises over 30 min (2 x week; 40 min per session; moderate intensity) can improve cardiorespiratory fitness⁶ and induces the reduction of airway inflammation⁷. The possible pathways induced by exercise in asthma lung inflammation, for example, involve the capacity of regular exercise in modulating the immune allergic response of T2^{7,8}, and the T reg cell⁸. Effects induced by AT seem to reduce the airway inflammation^{4,7,10}, inducing an increase in asthma clinical control^{4,6,10}.

The evidence suggests that the asthmatics' maintenance of clinical drug treatment¹, and the association with regular aerobic training for better asthma clinical

control^{4,6}. Despite this, due to the Covid-19 pandemic, asthmatics had part of their disease control treatment impaired in relation to performed regular performance, since the World Health Association (WHO) recommendation was the social distance to reduce the chance of contamination¹¹, which also suggests staying away from hospital centers to avoid increasing the risk of contamination by Covid-19¹².

The Covid-19 (SARS-CoV-2) pandemic began in December 2019 in China¹³. The contagious disease mainly causes a severe acute respiratory syndrome (SARS)¹⁴, which is much more serious than it was in the beginning. Recently, the evidence showed that infected people who had a greater worsening of SARS had a series of conditions such as pneumonia¹³, blood clotting problems^{15,16}, cardiac changes¹⁷, injuries in the liver¹⁸, and the cerebral cortex¹⁹.

At the beginning of the pandemic, asthmatics were considered to be an important risk group for Covid-19. Interestingly, the evidence has motivated that the Covid-19 appears to be less lethal for asthmatics²⁰, based on studies that showed low mortality²¹⁻²⁴. A recent review showed that among 36,072 patients diagnosed with COVID-19 only 655 presented asthma²⁵. Despite the evidence, asthmatics need to strictly follow international recommendations on combating covid-19 and proper use of asthma control medications to keep asthmatics away from hospital emergency centers avoiding the contagion risk of Covid-19²⁶.

Aim

The objective of the mini-review is to describe possible protective immunologic pathways which could induce protection against Covid-19 infections in people with asthma that performed AT.

Methods

The present mini-review was done with an analysis the methodological design was carried out with a search and analysis of studies that related the effects of regular physical exercise on the improvement of the immune system of people with moderate or severe asthma through a review, guided by the bibliographic search in the databases: Pubmed/Medline, Scielo, and Scholar Google databases. The keywords and Boolean operators used were “asthma OR asthmatics, AND “exercise training OR physical training OR physical activity OR physical exercise”. Studies in Portuguese and English were sought. In addition, the search restricted the search to controlled and uncontrolled clinical trials, eliminating review studies, with animal models and congress abstracts. The search was performed between January 2020 to October 2021 and the selection of studies following criteria:

- To present the features of the asthmatics
- Longitudinal studies controlled or uncontrolled, and randomized or unrandomized
- Have performed an intervention with regular AT
- Description of the workload, week frequency, amount of time of each session, and total duration of the protocol of intervention
- Have evaluated and shown the effects of AT on the immune system or in inflammatory parameters associated with the immune response of asthmatics
- After searching the database, the studies found were evaluated. They were excluded when they were not related to the theme and objective proposed by the study.

Results

After searching in the scientific database were identified 349 studies, after the screening only 21 articles presented all criteria suggested by the present review (Figure 1). Fifteen studies with adults and 6 with children or adolescents. The general data showed an age of 31.9 (± 15.5) years, a physical training program with 11.0 (± 4.20) weeks, a frequency of 2.45 (± 3.86) days/week, and a duration time of exercise sessions of 46.8 (± 18.4) min. Specifically, in children or adolescents the results showed an age of 10.7 (± 2.63) years, a physical training program of 9.0 (± 2.51) weeks, a frequency of 2.33 (± 1.46) days/week, and a duration time of exercise session with 53.6 (± 20.4) min. In adults, the findings showed the age of 41.4 (± 10.2) years, a physical training program of 11.8 (± 3.93) weeks, a frequency of 2.50 (± 3.01) days/week, and a duration time of exercise sessions of 43.9 (± 20.6) min. In general, the intensity performed was the moderate from 70 to 80%, which was difficult to quantify accurately, because each study had used different methods such as percentage of heart rate maximal (HRmax), oxygen uptake maximal (VO2max), Watts maximal (Wmax), HR of the reserve, or only described as moderate (Table 1).

A total of 12 studies (62%)^{10,27-37} showed that AT induced some change in the immune system inflammatory response, while 9 studies (38%)³⁸⁻⁴⁵ did not show any change in the immune system. In complement, other general benefits were observed such as improvements in the aerobic fitness (10 studies), health-related quality of life (7 studies), clinical control (2 studies), reduction of symptoms of asthma (6 studies), and decrease of airways hyperresponsiveness (2 studies) (Table 1).

Discussion

The previous studies showed that AT induced improvements in the clinical and aerobic fitness, in addition, some findings showed a reduction of inflammatory

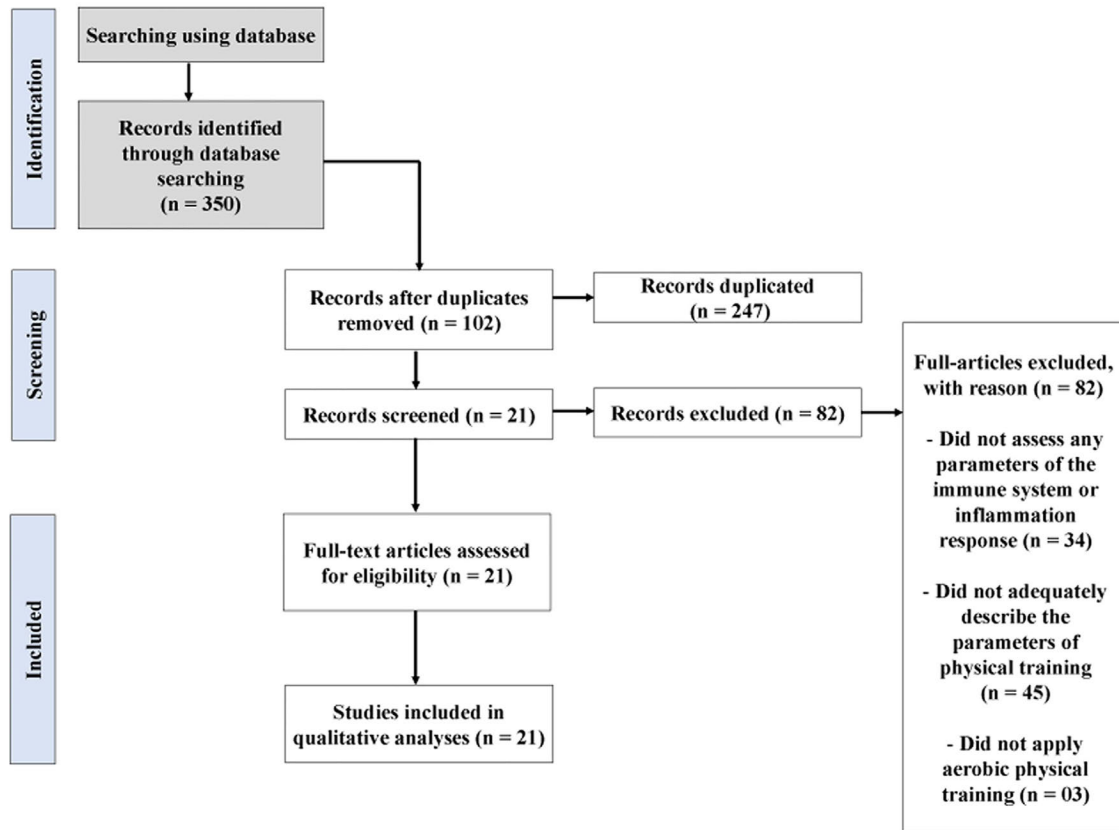


Figure 1 - Flowchart of the study (CONSORT diagram). The study was carried out by screening studies in the databases using descriptive words according to the purpose of the study. Respected studies and those that did not meet the criteria for inclusion in the study were excluded. Initially, 350 articles were found. Despite this, only 21 studies presented criteria to be included in the present study. The characteristics of the selected studies can be seen in [Table 1](#).

profile at the lung and systemic changes in the immune system function in people with asthma. To the best of our knowledge, it is not known whether asthmatics who practice AT, in addition to the clinical control and physical and immune benefits, could reduce the risk of developing infectious lung diseases such as the acute respiratory syndrome caused by Covid-19.

The AT is part of the clinical treatment of people with asthma, which is considered a therapy non-pharmacological^{1,46}. In the last years, studies have been shown the effects of AT on the immune system pathways and the inflammatory profile of the asthmatics²⁷⁻³⁹, and the findings suggest a possible protective effect of AT for these patients due to the reduction of lung^{27,30,31} and systemic inflammation^{10,32-34} which seem is associated with the increase of aerobic fitness⁴ an improvement physical that promote the increase to the clinical control and health status^{10,30,38}.

However, a few studies showed changes in the immunologic allergic response of the asthmatics that performed regular exercise as observed by the present study that identified only 20 researchers ([Table 1](#)), which is justified by the difficulty of observing changes in the inflam-

matory profile of the asthmatics⁴. Another important consideration is that at the present moment we do to know if people with asthma that performed AT could show other benefits that go beyond reducing lung inflammation or decreasing exacerbations, as well as it is not known whether asthmatics if the AT could reduce the development of the other co-morbidities as well as other acute respiratory disease induced by the virus through of some protective pathway of the immune system.

In times of viral pandemic, it is not well understood why asthmatics are not so affected by Covid-19 when compared to other patients with chronic non-transmissible inflammatory diseases such as obesity, diabetes, and hypertension. For a better understanding of the low mortality of asthmatics killed among those infected by the pandemic⁴⁷, this review suggests two important considerations to be investigated: i) mechanisms of the immune system of the asthmatic that are part of the pathophysiology of chronic disease, which could act to reduce Covid-19 contamination in T2 profile asthmatics; ii) regulatory mechanisms induced by AT in the immune system, increasing the leukocyte cytotoxicity capacity of the innate immune barrier and in the T2 response.

Table 1 - Characteristics of physical training programs performed by participants with asthma.

Authors	Age (years)	Type of physical exercise performed	Total weeks of physical training	Intensity or Workload	Weekly frequency (days)	Duration of exercise sessions (min.)	Main results
##Gonçalves et al., 2008	36.4	Aerobics; Walking and running; breathing exercises	12	70% of the VO2max	2	≈ 30	HRQoL ↑ Aerobic fitness ↑ FeNO ↓
#Moreira et al., 2008	12.9	Aerobics; Exercise circuit: calisthenics and resistance	12	Describes only Moderate	2	≈ 55	IgE ↓
#Gunay et al., 2010	9.8	Aerobics; cycling	8	80% of the HRmax	2	≈ 60	LTE4 ↓ MDA ↓ MMP9 ↓ Endothelin-1 ↓
##Mendes et al., 2011	36.9	Aerobics; Walking and running; breathing exercises	12	70% of the VO2max	2	≈ 30	Aerobic fitness ↑ Eosinophils ↓ FeNO ↓
##Boyd et al., 2012	53.0	Aerobics	12	From 60 to 75% (HR of reserve)	3	≈ 40	HRQoL ↑ Clinical control ↑ I.S. parameter ↓↑
#El-Akkary et al., 2013	9.75	Aerobics; cycling; breathing exercises	12	75% of the HRmax	2	≈ 47	AHR ↓ I.S. parameter ↓↑
#Andrade et al., 2014	11.5	Aerobics; Stretching	6	70 a 80% of the HRmax	3	≈ 70	Aerobic fitness ↑ PFE ↑ HRQoL ↑ Symptoms ↓ I.S. parameter ↓↑
##França-Pinto et al., 2015	42.0	Aerobics; Walking and running; breathing exercises	12	70% of the VO2max	2	≈ 30	HRQoL ↑ Clinical control ↑ AHR ↓ I.S. parameter ↓↑
#Gomes et al., 2015	7.50	Aerobics; Exercises performed using video games; treadmill run	8	Describes only 70%	2	≈ 40	FeNO ↓
##Tarmast et al., 2015	39.5	Aerobics; cycling	12	From 60 to 80% of the HRmax	2	≈ 60	IL-1β ↓ BMI ↓ Body fat ↓

(continued)

Table 1 - continued

Authors	Age (years)	Type of physical exercise performed	Total weeks of physical training	Intensity or Workload	Weekly frequency (days)	Duration of exercise sessions (min.)	Main results
##Abd El-Kader et al., 2016	46.7	Aerobics: Physical exercises performed on the treadmill; walk and run	24	From 60 to 80% of the HRmax	3	≈ 30	IL-2 ↓ IL-4 ↓ IL-6 ↓ TNF-α ↓ LDL ↓ Bone and mineral density ↑
##Freitas et al., 2017	47.2	Aerobics; Resistance exercises	12	From 60 to 80% of the HRmax; 50 - 75% IRM	2	≈ 80	IL-8 ↓ MCP-1 ↓ Symptoms ↓ IL-10 ↑ Aerobic fitness ↑
#Toennesen et al., 2018a	40.5	Aerobics: Interval training with cycle ergometer; High intensity shots vs active recovery	8	<30%, <60%; and >90% and 100% of the HRmax	3	≈ 50	HRQoL ↑ Symptoms ↓ I.S. parameter ↓↑
##Freitas et al., 2018	47.2	Aerobics; Resistance exercises	12	From 60 to 80% of the HRmax; 50 to 75% of 1 RM	2	≈ 80	Aerobic fitness ↑ Sleep quality ↑ Symptoms ↓ Depression ↓ I.S. parameter ↓↑
#Toennesen et al., 2018b	39.4	Aerobics: Interval training with cycle ergometer; High intensity shots vs active recovery	8	< 30%, < 60% and > 90% and 100% of the HRmax	3	≈ 15	Aerobic fitness ↑ Symptoms ↓ I.S. parameter ↓↑
##Zameshan and Gholamnejad, 2019	35.6	Aerobics: walking and running on a treadmill	12	From 60 to 80% of the HRmax	3	≈ 60	IL-4 ↓ IFN-γ ↓ Cortisol ↑
##Al-Sharif et al., 2020	38.8	Aerobics: walking and running on a treadmill	12	From 60 to 70% of the HRmax	3	≈ 45	BMI ↓ IL-6 ↓ IL-8 ↓ TNF-a ↓ CD4 and CD8 ↓

(continued)

Table 1 - continued

Authors	Age (years)	Type of physical exercise performed	Total weeks of physical training	Intensity or Workload	Weekly frequency (days)	Duration of exercise sessions (min.)	Main results
^{##} Evaristo et al., 2020	50.2	aerobics; Yoga-based stretching and breathing exercises	12	60% of the HRmax	2	≈ 40	HRQoL ↑ Aerobic fitness ↑ Symptoms ↓ Anxiety ↓ Depression ↓ I.S. parameter ↓↑
[#] Elmaggar et al., 2021	12.9	Aerobics	8	From 45 to 80% of the HRmax	3	≈ 50	Aerobic fitness ↑ PeR ↓
^{##} O'Neill et al., 2021	21.4	Aerobics; HIIT: Intense workouts with 10 sprints of 1 min. and with 90% of peak power, followed by light exercises with 10 sprints of 1 min. and with 10% of peak power	6	90% (main) and 10% (recovery) of the Wmax	3	≈ 25	Aerobic fitness ↑ IP-10 ↓
^{##} Silva et al., 2022	46.7	Aerobics; HIIT: Intense workouts with 30 sprints of 30 s; or CLE; Both performed at cycle ergometer	12	HIIT with 80%-140 Watts maximal (Wmax); CLE with 60-75% of Wmax	2	≈ 40	HRQoL ↑ Aerobic fitness ↑ PAL ↑ Anxiety ↓ Depression ↓ I.S. parameter ↓↑

Legend. The symbol # represents that the study was conducted with children. The symbol ## represents that the study was conducted with adults. The symbol ↑ means increase. The symbol ↓ means reduction. The symbols mean ↓↑ without change. The symbol ≈ means approximately. Airway hyperresponsiveness (AHR); Maximal oxygen uptake (VO2max); Maximum heart rate (HRmax); Peak flow expiratory (PFE); Immunoglobulin-E (IgE); Fraction of nitric oxide exhaled (FeNO); Health-related quality of life (HRQoL); Immune system (I.S.); Low-density lipoprotein (LDL); Malnodialdehyde (MDA); High-intensity interval training (HIIT); Constant-load exercise (CLE); Matrix metalloproteinase-9 (MMP-9); Leukotriene E 4 (LTE4); Body Mass Index (BMI); Wats Maximal (Wmax); Interleukin (IL); Beta (β); Monocyte chemoattractant protein-1 (MCP-1); Tumor necrosis factor alpha (TNF-α); Minutes (min); seconds (s); Percent (%);Maximum repetition (RM); Interferon Gamma (IFN-α); "helper" or helper lymphocyte type (CD); Interferon gamma (IP-10)-induced protein 10; Protein c Reactive (PeR); Physical activity level (PAL).

Possible protective pathways against Covid-19 presented by subjects trained and untrained with asthma

Previous studies have shown that AT induces a modulation of the immune system^{10,27-37}. In this sense, the present study speculates on two categories of asthmatics, i) those who practice regular exercise or are trained; ii) and those who are untrained or sedentary. So, discussing whether it is worth exposing themselves and exercising in times of pandemic of Covid-19. The evidence showed the risk of contamination is reduced in places without other people such as the house itself or in open places with few people maintaining social distance and with the use of masks, the greatest risk occurs in gyms and sporting events with an agglomeration of people⁴⁹.

In subjects with asthma that performed AT it is possible to considerate three pathways that could induce some protection for this pneumopathy, such: A) previous studies showed that AT seems to promote the better capacity for the cells of the innate immune system to recognize and increased the phagocyte activity and kill invading agents⁵⁰ (Figures 2I and 2II; Squares A-B), so it is possible to speculate that macrophages⁵¹, and other granulocytes cells such as eosinophils of trained asthmatics present increase in the capacity of eliminating the virus Covid-19 with better efficiency; B) increase of Natural Killer circulation after exercise⁵², and an increase of capacity cytotoxicity⁵³, then capturing and killing virus (Figure 2II; Square D); C) at last, some studies showed that asthmatics present a reduction of the angiotensin-converting enzyme 2 (ACE2) in yours cells⁴⁷. The ACE2 is a cell receptor, a kind of protein that has been identified to have an important role in the SARS-CoV-2 viral entry, and at the lungs, the ACE2 seems to be used by Covid-19 to enter and multiply within the cells¹², and curiously the ACE2 seems to be reduced in lungs of subjects with asthma⁵⁴, which would be a unique pathways care of this pneumopathy (Figures 2I and 2II; Squares A and E). In addition, the present study speculates that the AT could induce effects that regulate the expression of ACE2 in asthmatics as suggested by others studies^{55,56}.

Possible protective pathways against Covid-19 presented by subjects untrained with asthma

Due to the lack of AT practice that helps in the clinical control of the disease^{5,24}, the asthmatic untrained still would not benefit from the protective mechanisms as shown in Figures 2I and 2II (pathways squares A and E). Despite this, the subjects untrained with asthma also present a reduction of ACE2 in the lungs⁴⁷. In addition, asthmatics present the exacerbated response T2, and a lot of cellular expression of inflammatory mediators that can increase the migration of granulocytes such as eosinophils, neutrophils, and macrophages^{7,50} contrary to subjects trained which present allergic inflammatory T2 response

reduced^{7,50,51,57}. Briefly, which could naturally act in the elimination of viruses by the innate and adaptive immune system (Figure 2II, square D).

To practice or not to practice aerobic exercises during the pandemic? Is it recommended or not for subjects with asthma?

The previous reviews showed the relevance of the asthmatics performing regular AT for induces improvements in the clinical control of asthma^{10,57}. The AT can also strengthen the immune system in fighting infections⁵⁸ helping to protect the barrier innate immune system against Covid-19. That is why Table 2 provides some important recommendations for subjects with asthma and the risk of contamination in times of pandemic when this public performed AT.

The recommendations are based on five main points

i) Follow Covid-19 guidelines and precautions. Asthmatics during the pandemic need to follow all recommendations, respect social distancing and hygiene sanitary rules such as correct use of masks, washing hands with soap constantly, using 70% alcohol gel for hand cleaning when returning from the street removing clothes and shoes before entering the house, respect for the distance between people, seek medical attention when presenting signs and symptoms such as high fever and respiratory distress, care that avoids contamination and discrimination of the Covid-19 among others¹¹.

ii) Maintenance of clinical treatment and care with asthma management. Asthmatics need to properly use control and/or recovery medications as prescribed by the responsible physician and maintain the hygiene conditions of the home and work by not exposing themselves to crisis-triggering agents such as fungi, smoke, dust, and chemicals such as chlorine, among others. In order to keep the disease under control and prevent crises, thus minimizing the chance of going to a hospital²⁶.

iii) AT enhances the reduction of symptoms and crises, but is complementary and does not suspend clinical treatment, asthmatics need to follow all recommendations and care during the pandemic, to stay away from crises and hospital centers. It is important to highlight that continuous aerobic exercises^{4,30} or high-intensity interval training⁵⁷ are safe for asthmatics under clinical treatment, that is, with optimized medication and controlled asthma without an exacerbation or crises^{4,6,10}.

iv) Attending closed environments such as gyms, clubs, closed swimming pools, and martial arts mats are risky places for anyone, as it is a non-exceptional service they can be closed. The best option is to practice exercises at home or in the open, reducing the chance of encountering an environment that has a concentration of viruses due to the crowding of people or inadequate hygiene conditions⁴⁹.

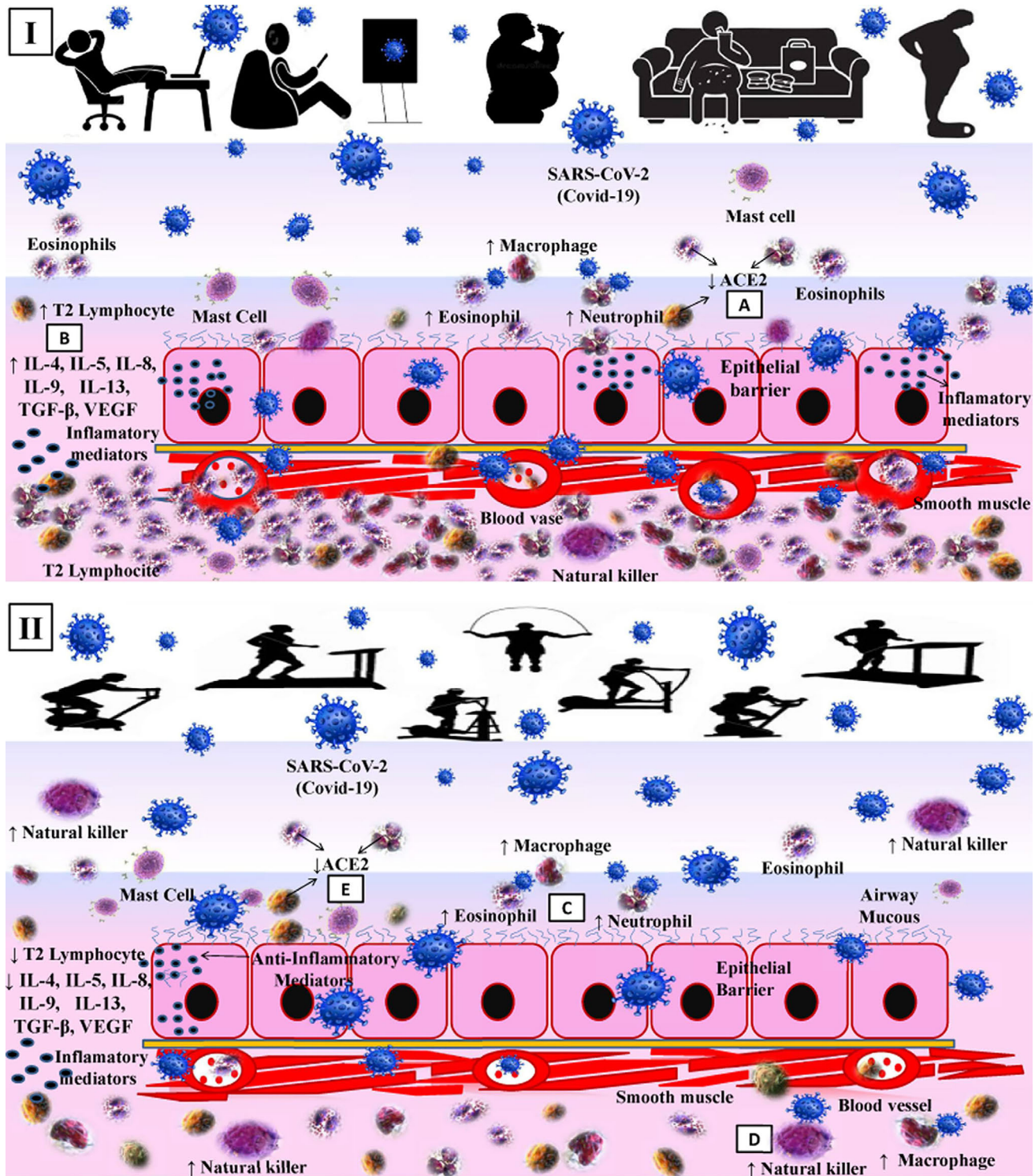


Figure 2 - Inflammatory mechanisms in the asthmatics sedentary and physically active. The **Figure 2I** represents the changes in the immune response of sedentary asthmatics. The square A means the allergic immune response recognizing, eliminating, and signaling about the infection and showing the possible pathway present in asthmatic allergies by the present reduction of the receptor of Covid-19 (ACE2) as an innate pathway. The square B means the protection based on the exacerbated response T2 by expression of inflammatory mediator as an innate pathway. The **Figure 2II** represents the changes in the immune response of asthmatics that performed aerobic training (AT). The square C means the allergic immune response recognizing, eliminating, and signaling about the infection and showing the possible pathway present in asthmatic allergies by the present reduction of the receptor of Covid-19 (ACE2) as an innate pathway. The square D means the increase of circulation of Natural Killer induced by regular aerobic exercise; The square E shows the possible pathway present in asthmatic allergies by the present reduction of receptor ACE2 to Covid-19.

Table 2 - Comparison of the level of risk in different environments.

At home contamination risk: low	
<p>Positive points</p> <ul style="list-style-type: none"> • Exercises were not prohibited by WHO • Can be done under the supervision of a distance physical education professional using technology (applications, for example) • Improvements in the asthma control • Helps to reduce daily symptoms • Decreases psychological distress (anxiety and depression) • Reduces visits to the emergency room • Strengthens the immune barrier • On cold days, it reduces the chance of seizures, as prolonged exposure to cold air can cause seizures when exercise is intense or long-lasting (> 60 min) • Can be done together with the family and increase interpersonal interaction • Choose the day and time of the workout • Interval the duration of sessions on each day • Avoids contact with external people and reduces the chance of contamination • Increases the level of weekly physical activity • Have the rescue medication (bronchodilator) always close, in case a crisis occurs during the exercise session 	<p>Negative points</p> <ul style="list-style-type: none"> • Lack of guidance from the physical education professional worsens the intensity control and may not help in improving the cardiovascular system • If done without professional guidance, musculoskeletal injuries can occur • Discourages and reduces the weekly frequency of exercises • Lack of space or equipment can impair the practice of exercises • House environment chosen for exercise may have fungi and cause exacerbation or crisis leading to the emergency room increasing the chance of contamination by Covid-19 • Some people like to do group exercises and doing it alone can be demotivating • Lack of time due to home office, family care
Open air contamination risk: medium	
<p>Positive points</p> <ul style="list-style-type: none"> • Extends the execution time of aerobic exercise sessions such as running and cycling, for example • Can be done under the supervision of a distance physical education professional using technology (applications, for example) • Increases the level of physical activity and exercise of those who do not have space at home • Outdoor exercises induce greater energy expenditure helping to control weight and reducing obesity, diabetes and hypertension • Increase the moment of distraction by reducing negative thoughts • Improves the psychological state when having contact with the external world • It can be a moment of contact with nature bringing psychological benefits • Can be done at alternative times in isolated locations with or with few people • Can be done on public streets or spaces maintaining isolation and social distance • Use of a mask reduces the chance of contamination • Have rescue medication always nearby 	<p>Negative points</p> <ul style="list-style-type: none"> • Increases the risk of contamination by exercising alone or in a group like anyone else • Disrespects WHO recommendations on social distance • Asthmatic person may forget to take rescue medication (bronchodilator) and have a crisis during the exercise session • May cause anxiety attacks because of fear of contamination • Against the law in some cities or states • If done at high or low temperatures it can be harmful to the immune system • On cold days, exposure to cold air can potentiate crises needing to be referred to the hospital emergency room • Exercising in an isolated area can make a person the target of theft • There is no consensus in science about safe distance between people who exercise outdoors • Wearing a mask is mandatory in several cities and states, but people may not have access due to the cost or lack of material
At Gyms contamination risk: high	
<p>Positive points</p> <ul style="list-style-type: none"> • Performed under the supervision of a physical education professional • Expands access to equipment such as a treadmill, cycle ergometers, among others that favor the practice of aerobic exercises • Access to resistance exercise equipment • Improvements in the asthma control • Helps to reduce daily symptoms • Decreases psychological distress • Reduces visits to the emergency room • Strengthens the immune barrier • On cold days, it reduces the chance of seizures, as prolonged exposure to cold air can cause seizures when exercise is intense or long-lasting (> 60 min) • Choose the day and time of the workout • Interval the duration of sessions on each day • Increases the level of weekly physical activity • Have rescue medication always nearby 	<p>Negative points</p> <ul style="list-style-type: none"> • Closed environment • Chance to increase the circulation of the virus in the environment less ventilation compared to the outside area • Use of collective exercise' devices • Possibility of lack of cleaning and proper hygiene of the floor, exercise' devices and bathroom • Risk of exercise' devices contaminated • Closed changing rooms are poorly ventilated environments and can accumulate viruses • Risk of not having adequate maintenance on air conditioning filters, which can increase the risk with increased virus circulation • Crowding of people in the entry lines • Little space between exercise' devices • Increased virus circulation in areas with treadmill, cycle ergometer and elliptic • Stimulates the presence of pairs and people talking in the same environment

v) Regardless of the level of risk for the practice of AT indoor or outdoor, it is very important to emphasize that some kind of exercise can be performed by asthmatics when the disease is controlled, on contrary in cases of clinically uncontrolled asthma, the asthmatic patient must first undergo individual pulmonary rehabilitation with a physiotherapy team until acquiring this control so that he can perform exercises at home or gym^{1,46}.

Final considerations

The asthmatic patients need to perform the aerobic training with moderate intensity, at least 2 times per week to induce changes in the immune system response, and maintain clinical treatment to avoid exacerbations, look for safer places, and follow hygiene rules, reducing the chances of crises will help prevent Covid-19. Other variants of SARS-CoV-2 can emerge, and the pandemic can again cause thousands of deaths and collapse of the health system, as well as new viruses, can cause a new pandemic, so asthmatics need adjuvant treatment with regular physical exercise, which helps to reduce symptoms, crises and makes the immune system more efficient in eliminating viruses.

References

1. Global Initiative for Asthma (GINA). Global strategy for Asthma management and prevention. National Institutes of Health/National Heart, Lung and Blood Institute of Health. Available from: <http://www.ginasthma.org/> [Accessed 11th August 2021].
2. Robinson D, Humbert M, Buhl R, Cruz AA, Inoue H, Korom S, et al. Revisiting type 2-high and type 2-low airway inflammation in asthma: current knowledge and therapeutic implications. *Clin Exp Allergy*. 2017;47(2):161-75. doi
3. Kuruvilla ME, Lee FE, Lee GB. Understanding Asthma phenotypes, endotypes, and mechanisms of disease. *Clin Rev Allergy Immunol*. 2020;56(2):19-33. doi
4. Hansen ESH, Pitzner-Fabricsius A, Toennesen LL, Rasmussen HK, Hostrup M, Hellsten Y, et al. Effect of aerobic exercise training on asthma in adults - a systematic review and meta-analysis. *Eur Respir J*. 2020;56(1):2000146. doi
5. Poole DC, Jones AM. Oxygen uptake kinetics. *Compr Physiol*. 2012;2(2):933-96. doi
6. Carson KV, Chandratilleke MG, Picot J, Brinn MP, Esterman AJ, Smith BJ. Physical training for asthma. *Cochrane Database Syst Rev*. 2013;30(9):CD001116. doi
7. Silva RA, Almeida FM, Olivo CR, Saraiva-Romanholo BM, Perini A, Martins MA, et al. Comparison of the effects of aerobic conditioning before and after pulmonary allergic inflammation. *Inflammation*. 2015;38(3):1229-38. doi
8. Alberca-Custódio RW, Greiffo FR, MacKenzie B, Oliveira-Junior MC, Andrade-Sousa AS, Graudenz GS, et al. Aerobic exercise reduces Asthma phenotype by modulation of the leukotriene pathway. *Front Immunol*. 2016;7:237. doi
9. Lowder T, Dugger K, Deshane J, Estell K, Schwiebert LM. Repeated bouts of aerobic exercise enhance regulatory T cell responses in a murine asthma model. *Brain Behav Immun*. 2010;24(1):153-9. doi
10. Freitas PD, Ferreira PG, Silva AG, Stelmach R, Carvalho-Pinto RM, Fernandes FL, et al. The role of exercise in a weight-loss program on clinical control in obese adults with asthma. A randomized controlled trial. *Am J Respir Crit Care Med*. 2017;195(1):32-42. doi
11. World Health Organization. Interim recommendations on obligatory hand hygiene against transmission of COVID-19. Available from: <https://www.who.int/who-documents-detail/interim-recommendations-on-obligatory-hand-hygiene-against-transmission-of-covid-19> [Accessed 15th October 2021].
12. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. *Int J Antimicrob Agents*. 2020;55(3):105924. doi
13. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727-33. doi
14. Muniyappa R, Gubbi S. COVID-19 pandemic, coronaviruses, and diabetes mellitus. *Am J Physiol Endocrinol Metab*. 2020;318(5):E736-E741. doi
15. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. *Clin Chim Acta*. 2020;506:145-8. doi
16. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020;8:475-81. doi
17. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;7:811-8. doi
18. Cai Q, Chen J. Reply to: "Clinical characteristics of COVID-19 patients with abnormal liver tests". *J Hepatol*. 2020;73(3):713-4. doi
19. Zanin L, Saraceno G, Panciani PP, Renisi G, Signorini L, Migliorati K, et al. SARS-CoV-2 can induce brain and spine demyelinating lesions. *Acta Neurochir (Wien)*. 2020;162(7):1491-4. doi
20. Liciskaia C, Yangb CL, Ducharmec FM, Radhakrishnand D, Podgerse D, Ramseyf C, et al. Addressing therapeutic questions to help Canadian physicians optimize asthma management for their patients during the COVID-19 pandemic. *Can J Res Cri Car S Med*. 2020;4(2):73-6. doi
21. Kim ES, Chin BS, Kang CK, Kim NJ, Kang YM, Choi JP, et al. Korea National Committee for clinical management of COVID-19. Clinical course and outcomes of patients with severe acute respiratory syndrome Coronavirus 2 infection: a preliminary report of the first 28 patients from the Korean cohort study on COVID-19. *J Korean Med Sci*. 2020;35(13):e142. doi

22. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J Allergy Clin Immunol.* 2020;146(1):110-8. doi
23. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of Coronavirus disease 2019 in China. *N Engl J Med.* 2020;382(18):1708-20. doi
24. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy.* 2020;75(7):1730-41. doi
25. Mendes NF, Jara CP, Mansour E, Araújo EP, Velloso LA. Asthma and COVID-19: a systematic review. *Allergy Asthma Clin Immunol.* 2021;17(5):1-12. doi
26. Stanley D. Lancet. Reflecting on world Asthma day in the era of COVID-19. *Respir Med.* 2020;8(5):423. doi
27. Gonçalves RC, Nunes, MPT, Cukier A, Stelmach R, Martins MA, Carvalho CRF. Effects of an aerobic physical training program on psychosocial characteristics, quality-of-life, symptoms, and exhaled nitric oxide in individuals with moderate or severe persistent asthma. *Rev Bras Fisioter.* 2008;12(2):9.
28. Moreira A, Delgado L, Haahtela T, Fonseca J, Moreira P, Lopes C, et al. Physical training does not increase allergic inflammation in asthmatic children. *Eur Respir J.* 2008;32(6):1570-5. doi
29. Gunay O, Onur E, Yilmaz O, Dundar PE, Tikiz C, Var A, et al. Effects of physical exercise on lung injury and oxidant stress in children with asthma. *Allergol Immunopathol.* 2012;40(1):20-4. doi
30. Mendes FA, Almeida FM, Cukier A, Stelmach R, Jacob-Filho W, Martins MA, et al. Effects of aerobic training on airway inflammation in asthmatic patients. *Medicine and Science in Sports and Exercise.* 2011;43(2):197-203. doi
31. Gomes EL, Carvalho CR, Peixoto-Souza FS, Teixeira-Carvalho EF, Mendonça JF, Stibulov R, et al. Active video game exercise training improves the clinical control of Asthma in children: randomized controlled trial. *PLoS One.* 2015;10(8):e0135433. doi
32. Tarmast D, Imanipour V, Kasparast JRM, Sajedi A, Morovatnya K. Impact of two types of exercise on inflammation in patients with Asthma: endurance exercise reduces serum concentrations of interleukin-1 β . *Indian J Appl Pure Biol.* 2015;30(1):33-9.
33. Abd El-Kader SM, Al-Jiffri OH, Ashmawy EM, Gaowgzeh RA. Treadmill walking exercise modulates bone mineral status and inflammatory cytokines in obese asthmatic patients with long term intake of corticosteroids. *Afr Health Sci.* 2016;16(3):798-808. doi
34. Zarneshan A, Gholamnejad M. Moderate aerobic exercise enhances the th1/th2 ratio in women with asthma. *Tanaffos.* 2019;18(3):230-7. PMID: PMC7210570
35. Al-Sharif FM, Abd El-Kader SM, Neamatallah ZA, AlKhatteeb AM. Weight reduction improves the immune system and inflammatory cytokines in obese asthmatic patients. *Afr Health Sci.* 2020;20(2):897-902. doi
36. Elnaggar RK, Shendy MA, Elfakharany MS. Effect of 8 weeks of incremental aerobic training on inflammatory mediators, cardiorespiratory indices, and functional capacity in obese children with bronchial Asthma. *Pediatr Exerc Sci.* 2021;33(1):23-31. doi
37. O'Neill CD, Patlan I, Jeffery M, Lewis D, Jenkins M, Jones-Taggart H, et al. Effects of high-intensity interval training on cardiorespiratory fitness and salivary levels of IL-8, IL-1ra, and IP-10 in adults with asthma and non-asthma controls. *J Asthma.* 2021;28:1-10. doi
38. Boyd A, Yang CT, Estell K, Tuggle MSC, Gerald LB, Dransfield M, et al. Feasibility of exercising adults with asthma: a randomized pilot study. *Allergy Asthma Clin Immunol.* 2012;8(1):13. doi
39. El-Akkary IM, Abdel-Fatah Zel-K, El-Seweify Mel-S, El-Batouti GA, Aziz EA, Adam AI. Role of leukotrienes in exercise-induced bronchoconstriction before and after a pilot rehabilitation training program. *Int J Gen Med.* 2013;29(6):631-6. doi
40. Andrade LB, Britto MC, Lucena-Silva N, Gomes RG, Figueroa JN. The efficacy of aerobic training in improving the inflammatory component of asthmatic children. *Randomized trial. Respiratory Medicine.* 2014;108(10):1438-45. doi
41. França-Pinto A, Mendes FA, de Carvalho-Pinto RM, Agondi RC, Cukier A, Stelmach R, et al. Aerobic training decreases bronchial hyperresponsiveness and systemic inflammation in patients with moderate or severe asthma: a randomised controlled trial. *Thorax.* 2015;70(8):732-9. doi
42. Toennesen LL, Soerensen ED, Hostrup M, Porsbjerg C, Bangsbo J, Backer V. Feasibility of high-intensity training in asthma. *Eur Clin Respir J.* 2018;5(1):1468714. doi
43. Freitas PD, Silva AG, Ferreira PG, DA Silva A, Salge JM, Carvalho-Pinto RM, et al. Exercise improves physical activity and comorbidities in obese adults with Asthma. *Med Sci Sports Exerc.* 2018;50(7):1367-76. doi
44. Toennesen LL, Meteran H, Hostrup M, Wium Geiker NR, Jensen CB, Parker D, et al. Effects of exercise and diet in nonobese Asthma patients-a randomized controlled trial. *J Allergy Clin Immunol Pract.* 2018;6(3):803-11. doi
45. Evaristo KB, Mendes FAR, Saccomani MG, Cukier A, Carvalho-Pinto RM, Rodrigues MR, et al. Effects of aerobic training versus breathing exercises on Asthma control: a randomized trial. *The Journal of Allergy and Clinical Immunology.* 2020;8(9):2989-96.e4. doi
46. Pizzichini MMM, Carvalho-Pinto RM, Cançado JED, Rubin AS, Cerci Neto A, Cardoso AP, et al. Brazilian Thoracic Association recommendations for the management of asthma. *J Bras Pneumol.* 2020;46(1):e20190307. doi
47. Morais-Almeida M, Pité H, Aguiar R, Ansotegui I, Bousquet J. Asthma and the Coronavirus disease 2019 pandemic: a literature review. *Int Arch Allergy Immunol.* 2020;181(9):680-8. doi
48. Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. *J Sport Health Sci.* 2019;8(3):201-17. doi.
49. Texas Medical Association. What's more risky, going to a bar or opening the mail? Available from: <https://www.texmed.org/TexasMedicineDetail.aspx?id=53977> [Accessed 30th March 2022].
50. Olivo CR, Miyaji EN, Oliveira ML, Almeida FM, Lourenço JD, Abreu RM, et al. Aerobic exercise attenuates pulmonary

- inflammation induced by *Streptococcus pneumoniae*. *J Appl Physiol*. 2014;117(9):998-1007. doi
51. Sugiura H, Sugiura H, Nishida H, Inaba R, Mirbod SM, Iwata H. Effects of different durations of exercise on macrophage functions in mice effects of different durations of exercise on macrophage functions in mice. *J Appl Physiol*. 2001;90(3):789-94. doi
 52. Gleeson M, Bishop NC. The T cell and NK cell immune response to exercise. *Ann Transplant*. 2005;10(4):43-8. PMID
 53. Zimmer P, Schenk A, Kieven M, Holthaus M, Lehmann J, Lövenich L, et al. Exercise-induced alterations in NK-cell cytotoxicity - methodological issues and future perspectives. *Exerc Immunol Rev*. 2017;23:66-81. PMID
 54. Halpin DMG, Faner R, Sibila O, Badia JR, Agusti A. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? *Lancet Respir Med*. 2020;8(5):436-8. doi
 55. Heffernan KS, Jae SY. Exercise as medicine for COVID-19: an ACE in the hole? *Med Hypotheses*. 2020;142):109835. doi
 56. Mohamed AA, Alawna M. Role of increasing the aerobic capacity on improving the function of immune and respiratory systems in patients with coronavirus (COVID-19): a review. *Diabetes Metab Syndr*. 2020;14(4):489-96. doi
 57. Silva R, Rocco PGL, Stelmach R, Oliveira LMDS, Sato MN, Cukier A, et al. Constant-load exercise versus high-intensity interval training on aerobic fitness in moderate to severe asthma: a RCT. *J Allergy Clin Immunol Pract*. 2022;30:S2213-2198(22)00533-5. doi
 58. Simpson RJ, Campbell JP, Gleeson M, Krüger K, Nieman DC, Pyne DB, et al. Can exercise affect immune function to increase susceptibility to infection? *Exerc Immunol Rev*. 2020;26:8-22. PMID

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