Changes and Long-Term Effects of the Immune System after COVID-19 Infection

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Abstract: Following the pandemic in 2020, physical health has generally declined. All of this is brought on by modifications to the body's immune system and the consequences of sequelae. The current research gap is caused by the neglect of COVID-19's after effects. In this paper, the relationship between immune system changes, complications and their physical conditions was studied, and preliminary results on the harm and prevention of the sequelae were obtained. The immune system's alterations during the epidemic infection and its consequences are the main topics of this article, including cytokine storms, inflammatory responses, and changes in immune cells. At the same time, the article explores the relationship between complications and underlying health conditions, such as chronic diseases and autoimmune diseases, and the harm they cause. Through observation and analysis in the later stages of the epidemic, the article explores the reasons for the general decline in people's physical fitness and changes in the immune system. In the future, it is hoped that there will be improvements in disease analysis and prevention measures after pandemic diseases.

Keywords: Chronic disease, acute respiratory distress syndrome, long-term covid-19.

1. Introduction

An acute infectious illness is a novel coronavirus infection. It is a series of respiratory tract infection symptoms such as fever, fatigue, dry cough, etc. caused by SARS Co-2 virus invading the respiratory tract. The RNA virus known as SARS-CoV-2 has surface protrusions made of proteins that can attach to the human cell's ACE2 receptor, and then enter the interior of human cells. Once a virus enters human cells, it begins to replicate its own RNA and release proteins, affecting cellular function. Generally speaking, patients infected with COVID-19 can recover after about two weeks, but there are also serious cases of organ failure, complications, frequent chronic diseases and even death. Formally sweeping the globe in 2020, it is known for its fast speed, strong infectivity, and high mortality rate, causing enormous harm to human society. According to relevant reports, there have been approximately 6.65 million confirmed deaths worldwide from 2020 to 2024. Humanity is facing unprecedented challenges that threaten the safety of all human lives. After the human being is injected with the vaccine against COVID-19, it will still cause many complications, such as pulmonary fibrosis, that is, the lung tissue becomes stiff and affects the normal respiratory function; Cardiovascular problems refer to the occurrence of heart disease, arrhythmia, and thrombosis in patients after recovery; Problems with the nervous system, such as headaches, fatigue, lack of concentration, and memory decline; Muscle pain and arthritis [1].

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According to previous reports, patients who received SARS-CoV-2 vaccine developed various newly diagnosed glomerular diseases (GD) in renal histology. IgAN and little change were identified as the most prevalent kidney disorders following an 89-day follow-up [2]. Since the infection of the pandemic in lately two years, the number of deaths caused by the combination of different health conditions of different ages and possible underlying diseases and complications has soared. This phenomenon has become normalized and requires high attention from the whole society as well as prevention and resolution by relevant healthcare institutions.

The alterations and detrimental impacts of the COVID-19 infection on the immune system will be the main topic of this essay, including changes in the human immune system: cytokine storm, inflammatory response, immune cells; The relationship between complications and basic health status: chronic diseases, autoimmune diseases; The harm of complications; Relevant preventive measures and conclusions. This article is dedicated to exploring how to self-strengthen immunity, protect the body from infection, prevent these lesions from leading to cancer, and risk mitigation measures.

2. Changes in the human immune system

2.1. Cytokine Storm

The 2020 novel coronavirus is raging around the world and has attracted the close attention of global health organizations. Many data show that in immunopathology, if some foreign virus activates the immune system to the limit or completely out of control, it will harm the host, the "cytokine storm" is the most lethal onslaught; it involves a sequence of increasing immunological responses, which leads to the immune system fatigue and inefficiency [1]. Respiratory discomfort and organ failure may result from severe cases. An infection with SARS-CoV-2 may lead to the uncontrolled development of cytokine storm syndrome. Along with other cells, mast cells can react to viruses. Autopsy findings from individuals who died from COVID-19 reveal that mast cells build up in the lungs, resulting in pulmonary edema or inflammation and thrombosis [3]. These include lymphocytopenia and an increase in cytokines, which are one of the main causes of rapid expansion and death. By releasing copious amounts of inflammatory substances and active mediators, cytokine storms not only prevent the virus from spreading further throughout the body also cause secondary tissue damage. It has been determined that cytokine storms are the primary cause of COVID-19related deaths; Cytokine can also be said to be a distress signal released by the human body, in order to warn the body's own immune system to fire full fire and then achieve the role of protecting the human body, but damage the virus will also leave a lot of collateral damage. Therefore, in order to prevent the deterioration of the condition of those seriously and critically ill patients, cytokine storm becomes an important treatment

2.2. Inflammatory reaction

In general, infection with the novel coronavirus very acute inflammation (redness, swelling, pain and other major symptoms in the throat), that is, inflammation composed mainly of the reaction of the vascular system. During the outbreak, patients infected with the virus often have dizziness, weakness, runny nose, cough, fever and other symptoms. It will last about two weeks [2].

Numerous mediators that modulate or alter particular aspects of the inflammatory response cause inflammation, which is not caused by a single factor. Additionally, many diseases linked to inflammation exhibit significant changes in immune timing (e.g., cytokine storms associated with COVID-19). In this regard, it is essential that inflammation be studied in humans as a multi-layered phenomenon in the future. Low-grade chronic inflammation, the root cause of many chronic diseases, deserves special attention [4,5]. A previous analysis identified six new cases of recurrence from an earlier autoimmune disease or autoinflammatory condition after vaccination. The study reviewed 464

studies (928 cases) as of August 1, 2022, of which approximately 53.6% were women, and 81.5% (n: 756) of cases developed new symptoms. They all suggest that one of the problems that people may face in the future is low-grade chronic inflammation. There aren't any medications available right now that are intended especially to treat chronic inflammation. Research has assessed the safety and effectiveness of Low Dose Medicine (LDM) and Biological Regulatory Systems Medicine (BrSM), especially in the management of long-term immunological diseases and chronic inflammation. Myocarditis, Guillain-Barre syndrome, and immune thrombocytopenia were the most prevalent illnesses after vaccination. [6] In summary, there might be a connection between the COVID-19 vaccine and inflammatory. SARS-CoV-2 and vaccines may cause autoimmunity via comparable mechanisms. Large-scale, carefully monitored research is required to confirm this association and evaluate additional variables like heredity and other environmental influences.

2.3. Immune cell

Immune cells include lymphocytes, dendritic cells, monocytes, granulocytes, and mast cells. After the pandemic in 2020, authoritative organizations in the medical field updated their integration of immunological knowledge with the latest SARS-CoV-2 research results. The single-cell multi-omics technology, which includes single-cell transcriptomics, flow cytometry, and single-cell T cell receptor 1 1 1 1 2 3 3 3 3 16 16 28 (TCR) and B cell receptor (BCR) analysis, should be the primary focus. Offering the most recent concepts on the molecular mechanisms behind pathogenic immune responses and SARS-CoV-2 is the goal of this technology. According to single-cell multi-omics technology, it is worthwhile to look at the adaptive immune response against SARS-CoV-2, which comprises T cells and B cells. Research has demonstrated that by contrasting the adaptive immune responses brought on by vaccination versus spontaneous infection. It has been studied how important T and B cells are for pathogenesis, defense, and prevention [7]. The interaction between viral particles and antigen-presenting cells or B cell receptors triggers the body's adaptive immune response, which in turn forms immune memory. To protect the host from harm, this memory is valid for up to 17 years. B cells are the main force in protecting the human body from viral infections. Among them, vaccination against COVID-19 has improved the generation and persistence of B cells. The mRNAbased vaccine has been to induce a strong class switching memory B cell response, which will persist over time and be enhanced by further vaccination, indicating that memory B cells are crucial antigens in driving memory response after re-exposure to SARS CoV-2 [7]. Their primary function is to supply memory signals that active B cells emit. The formation of nasal vaccines and the mediation of mucosal immunity (the initial component of defensive mechanisms) have been demonstrated to be significantly influenced by IgA generated by B cells. The progression of the pandemic has led to the emergence of a new variant (Omicron), which may reduce protective T cell immunity and result in more severe disease manifestations [8].

2.4. Viral memory

The World Public Health Organization still has to fight the ongoing wave of COVID-19 because of the appearance of COVID-19 variations (Alpha, Beta, Gamma, Delta, and Omicron). At the same time, more and more rehabilitation patients are reporting symptoms such as decreased resistance, susceptibility to colds and fever, mental fatigue, decreased lung function, decreased taste, fatigue, and joint pain [9]. These symptoms are called long-term COVID-19. Although serum antibodies administered for vaccine production are considered markers of viral immune protection, research has demonstrated that persistent memory immune subsets, which are capable of preventing heterologous infections and rapidly responding to secondary infections, can produce local immunity in the lungs [10]. This requires the assembly of many immune cells to achieve resident memory. Researchers

believe that an ideal vaccine can not only reduce the harm caused by the virus to humans, thereby generating herd immunity. According to research, viruses will continuously optimize to achieve the goal of not being killed by previous antibodies. In response to this phenomenon, increasing memory T cells in the respiratory tract can effectively prevent these viruses from escaping (cells that can respond quickly to respiratory viral infections) Investigations have demonstrated that CD8+T cells found in the respiratory system are crucial for defending the host against viral infections and preventing the virus from spreading throughout the community.

3. Links between complications and underlying health conditions

3.1. Chronic disease

The COVID-19 pandemic has changed daily life, but its impact has been greatest on vulnerable groups - those who themselves have certain chronic conditions. Furthermore, chronic pain is becoming more widely acknowledged as a distinct sign of chronic COVID-19. Common theories for this behavior include "direct neuropathological mechanisms," "systemic inflammatory immune mechanisms," and others [8,9]. Many people who have been cured of COVID-19 are prone to complications, which are more or less related to their own health. As the new coronavirus is an acute respiratory infectious disease, it is easy to accelerate the outbreak of some chronic diseases that people already have in their bodies. Among them, the more common chronic diseases are asthma, pulmonary nodules, diabetes, cardiovascular disease and so on. Previous studies have shown that among 43,465 U.S. children diagnosed with COVID-19 who were in the emergency room or hospitalized, Asthma, neurodevelopmental disorders, anxiety and fear-related disorders, depression, and obesity were the most commonly reported underlying problems. Children who have type 1 diabetes, essential hypertension, or congenital heart and circulation defects are more likely to experience severe sickness both during and after hospitalization [10,11].

3.2. Autoimmune disease

SARS-CoV-2 vaccination has emerged as a major public health concern. However, not everyone is suitable for such vaccines, and the basic health conditions for such vaccines need to be met. In particular, it is necessary to pay attention to the underlying diseases or autoimmune diseases. For example, it mainly targets vulnerable groups. For people with the disease, being reinfected with COVID-19 can be a serious health problem. For this group of people, if the conditions for receiving SARS-CoV-2 vaccine are not met in advance, this will undoubtedly directly lead to an increase in related mortality and disease severity. These demographics may also make treating COVID-19 considerably more challenging. According to current recommendations, in these situations, prompt vaccines and regular booster injections are deemed essential [12]. The aim is to review existing evidence and recommendations related to COVID-19 vaccination for patients with chronic liver disease and provide insights into current issues and future directions [13,14].

The clinical manifestations of COVID-19, the immune response and pathogenesis are similar to those of autoimmune diseases. A strong immune response is involved in the pathogenesis of both diseases.

3.3. Vaccine rejection

There has also been a global pandemic for vaccination against COVID-19. Age groupings and naturally immune people are now included in the undifferentiated COVID-19 immunization coverage who are at least at risk of serious complications from COVID-19. Immunohistopathological evidence suggests that COVID-19 gene vaccines can spread far throughout the body, impacting tissues distant

from the injection site and terminally differentiated. These include the brain and heart and can happen when a severe autoimmune inflammatory response is triggered by the creation of in-situ spike proteins. Since the human body is not a strictly similar system, the immune system will always attack any human cell that produces a non-self antigen. To determine which specific tissues may be impacted, precise pharmacokinetic and pharmacodynamic studies are necessary [15]. Depending on the vaccination platform, immunosuppression in kidney transplant recipients has also been demonstrated to decrease the immunogenicity of SARS-CoV-2 vaccines; the existing evidence indicates that these vaccines are between 50 and 70 percent effective when compared to non-transplant scenarios [16].

4. Risk of complications

4.1. Acute respiratory distress syndrome

The appearance of X-ray opacity in the lateral region of the chest is a characteristic of acute respiratory distress syndrome (ARDS). Usually, the syndrome manifests as hypoxemia, tachypnea, and rapidly increasing dyspnea. A week after a known injury, the start of new or worsening respiratory symptoms is one of the diagnostic criteria, severe hypoxemia, radiographic examination of bilateral lung opacity, and failure to explain respiratory failure with heart failure or excess fluid [17].

According to current theory, ARDS arises when inflammatory mediators are released as a result of lung or extrapulmonary injury. This promotes the development of inflammatory cells in the lung microcirculation and alveoli. Damage to the vascular endothelium and alveolar epithelium by inflammatory cells leads to pulmonary edema, hyaline membrane formation, reduced lung compliance, and impaired gas exchange.

4.2. Septic shock

During the treatment of the pandemic, there have been many previous clinical practices that have shown an association of sepsis in some patients with severe COVID-19.Multiple organ dysfunction syndrome, coagulation malfunction, septic shock, and other symptoms are among the most common signs of this illness.Furthermore, there is scientific evidence that suggests certain biological parallels between sepsis and severe COVID-19, including neutrophil malfunction, cytokine storms, and a hypercoagulable state after blood balance disruption. In addition to a few cases of high-emission low-resistance shock (warm shock), the vast majority of patients will have sympathetic excitation symptoms, patients are conscious, but irritability, anxiety, nervousness, pale face and skin, and cold limbs [18].

4.3. Pulmonary fibrosis

The pandemic has spread quickly throughout the world since it was first identified in late 2019. The illness impacts the body's other functional systems, including the kidney, lungs, gastrointestinal tract, and cardiovascular system. Acute respiratory distress caused by the sickness may be asymptomatic or require intensive care unit (ICU) care and mechanical ventilation, which may lead to respiratory failure and death. It quickly became evident that interstitial lung fibrosis symptoms could appear in COVID-19 individuals. Fibroblast proliferation, extensive extracellular matrix deposition, and structural lung tissue deterioration are the hallmarks of pulmonary fibrosis, an interstitial lung disease. The main symptoms are dry cough and progressive dyspnea, especially after strenuous activity. End-stage patients may have dizziness, purple lips and nails, limited movement and other hypoxia.

4.4. White lung and pneumonia

(White lung) is a clinical syndrome in which a large amount of exudate accumulates in the lungs of patients with severe pneumonia, affecting multiple lung lobes and causing a large white area to appear on lung imaging. The majority of the reasons were circulatory and respiratory conditions, including severe heart failure, bacterial pneumonia, and new coronavirus infections. Pneumonia is serious, lung exudate, can form white lung symptoms. The clinical symptoms of white lung may include fever, fatigue, cough, sputum, muscle soreness, etc. In severe cases, chest tightness, shortness of breath and other dyspnea symptoms may occur.

5. Relevant preventive measures

5.1. Healthy diet and moderate exercise

One of the most important daily measures people can take to prevent such a pandemic is to adjust their diet to include high quality protein, vitamins, and fiber. Wash your hands frequently and avoid rubbing your eyes and mouth with your hands directly after going out to prevent the virus from entering the body from the eyes or mouth to cause infection. Frequently open Windows for ventilation, and regularly disinfect walls, floors and desktops are also effective in preventing the new coronavirus. Daily swimming and running can be appropriate, and their resistance and immunity can be enhanced through exercise.

5.2. Psychological health support

Acute neurological symptoms, including neurological, cognitive, and emotional deficits, as well as COVID-19 infections, have been shown to frequently result in neuroinflammation, cognitive decline, loss of smell, and stroke in their victims [19,20]. Lockdowns, social distancing, isolation to contain COVID-19, and stress at work have all had an impact on the mental health of a significant number of people, regardless of age.

6. Conclusion

This article focuses on the changes in the human immune system after infection with the novel coronavirus, the remaining concurrent hazards, and long-term effects. After experiencing the COVID-19 pandemic, many cured patients will have different sequelae, and the immune system in the body will also have changes such as cytokine storms, inflammatory responses, immune cells and so on. Physical health conditions such as chronic disease, self-rejection of vaccines and complications white lung, septic shock risk. There is also a need for increased awareness and daily preventive measures in the wake of this pandemic. Unlike previous scientific studies or reports, this article focuses on observations and analyses of people in the later stages of the pandemic, not in the middle of the COVID-19 pandemic. It should be noted that this paper mainly analyzes the causes of the general decline in people's physical fitness and discusses the changes in the immune system, and does not involve the research of drugs including treatment methods, research vaccines or antiviral sera. It is hoped that in the future scientific research road, there can be more exploration of the causes of disease and a series of chain reactions caused by the recovery of patients or after surgery.

References

- [1] Chen, Y., Xu, Z., Wang, P., Li, X. M., Shuai, Z. W., Ye, D. Q., & Pan, H. F. (2022). New-onset autoimmune phenomena post-COVID-19 vaccination. Immunology, 165(4), 386-401.
- [2] Guo, M., Liu, X., Chen, X., & Li, Q. (2023). Insights into new-onset autoimmune diseases after COVID-19 vaccination. Autoimmunity Reviews, 22(7), 103340.

- [3] Hafezi, B., Chan, L., Knapp, J. P., Karimi, N., Alizadeh, K., Mehrani, Y., Bridle, B. W., & Karimi, K. (2021). Cytokine storm syndrome in SARS-CoV-2 infections: A functional role of mast cells. Cells, 10(7), 1761.
- [4] Tang, L., Yin, Z., Hu, Y., & Mei, H. (2020). Controlling cytokine storm is vital in COVID-19. Frontiers in Immunology, 11, 570993.
- [5] Fioranelli, M., Roccia, M. G., Flavin, D., & Cota, L. (2021). Regulation of inflammatory reaction in health and disease. International Journal of Molecular Sciences, 22(10), 5277.
- [6] Rodríguez, Y., Rojas, M., Beltrán, S., Polo, F., Camacho-Domínguez, L., Morales, S. D., Gershwin, M. E., & Anaya, J. M. (2022). Autoimmune and autoinflammatory conditions after COVID-19 vaccination: New case reports and updated literature review. Journal of Autoimmunity, 132, 102898.
- [7] Primorac, D., Vrdoljak, K., Brlek, P., Pavelić, E., Molnar, V., Matišić, V., Erceg Ivkošić, I., & Parčina, M. (2022). Adaptive immune responses and immunity to SARS-CoV-2. Frontiers in Immunology, 13, 848582.
- [8] Jordan, S. C., Shin, B. H., Rodriguez, E., Vo, A., Ammerman, N., & Zhang, R. (2022). Diminished T-cell immune responses to SARS-CoV-2 omicron variant after BNT162b2 vaccination. Immunology Letters, 248, 123-125.
- [9] Pruner, K. B., & Pepper, M. (2021). Local memory CD4 T cell niches in respiratory viral infection. Journal of Experimental Medicine, 218(8), e20201733.
- [10] Uddbäck, I., Michalets, S. E., Saha, A., Mattingly, C., Kost, K. N., Williams, M. E., Lawrence, L. A., Hicks, S. L., Lowen, A. C., Ahmed, H., Thomsen, A. R., Russell, C. J., Scharer, C. D., Boss, J. M., Koelle, K., Antia, R., Christensen, J. P., & Kohlmeier, J. E. (2024). Prevention of respiratory virus transmission by resident memory CD8+ T cells. Nature, 626(7998), 392-400.
- [11] Kompaniyets, L., Agathis, N. T., Nelson, J. M., Preston, L. E., Ko, J. Y., Belay, B., & Goodman, A. B. (2021). Underlying medical conditions associated with severe COVID-19 illness among children. JAMA Network Open, 4(6), e2111182-e2111182.
- [12] Davis, H. E., McCorkell, L., Vogel, J. M., & Topol, E. J. (2023). Long COVID: Major findings, mechanisms and recommendations. Nature Reviews Microbiology, 21(3), 133-146.
- [13] Shanthanna, H., Nelson, A. M., Kissoon, N., & Narouze, S. (2022). The COVID-19 pandemic and its consequences for chronic pain: A narrative review. Anaesthesia, 77(9), 1039-1050.
- [14] Schinas, G., Polyzou, E., Mitropetrou, F., Pazionis, A., Gogos, C., Triantos, C., & Akinosoglou, K. (2022). COVID-19 vaccination in patients with chronic liver disease. Viruses, 14(12), 2778.
- [15] Polykretis, P., Donzelli, A., Lindsay, J. C., Wiseman, D., Kyriakopoulos, A. M., Mörz, M., Bellavite, P., Fukushima, M., Seneff, S., & McCullough, P. A. (2023). Autoimmune inflammatory reactions triggered by the COVID-19 genetic vaccines in terminally differentiated tissues. Autoimmunity, 56(1), 2259123.
- [16] Vnučák, M., Graňák, K., Beliančinová, M., Jeseňák, M., Macháleková, K. K., Benko, J., Samoš, M., & Dedinská, I. (2022). Acute kidney rejection after anti-SARS-CoV-2 virus-vectored vaccine-case report. NPJ Vaccines, 7(1), 30.
- [17] Saguil, A., & Fargo, M. V. (2020). Acute respiratory distress syndrome: Diagnosis and management. American Family Physician, 101(12), 730-738.
- [18] Lu, L., Liu, L. P., Gui, R., Dong, H., Su, Y. R., Zhou, X. H., & Liu, F. X. (2022). Discovering common pathogenetic processes between COVID-19 and sepsis by bioinformatics and system biology approach. Frontiers in Immunology, 13, 975848.
- [19] Pandey, K., Thurman, M., Johnson, S. D., Acharya, A., Johnston, M., Klug, E. A., Olwenyi, O. A., Rajaiah, R., & Byrareddy, S. N. (2021). Mental health issues during and after COVID-19 vaccine era. Brain Research Bulletin, 176, 161-173.
- [20] Patone, M., Mei, X. W., Handunnetthi, L., Dixon, S., Zaccardi, F., Shankar-Hari, M., Watkinson, P., Khunti, K., Harnden, A., Coupland, C. A. C., Channon, K. M., Mills, N. L., Sheikh, A., & Hippisley-Cox, J. (2022). Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. Nature Medicine, 28(2), 410-422.