



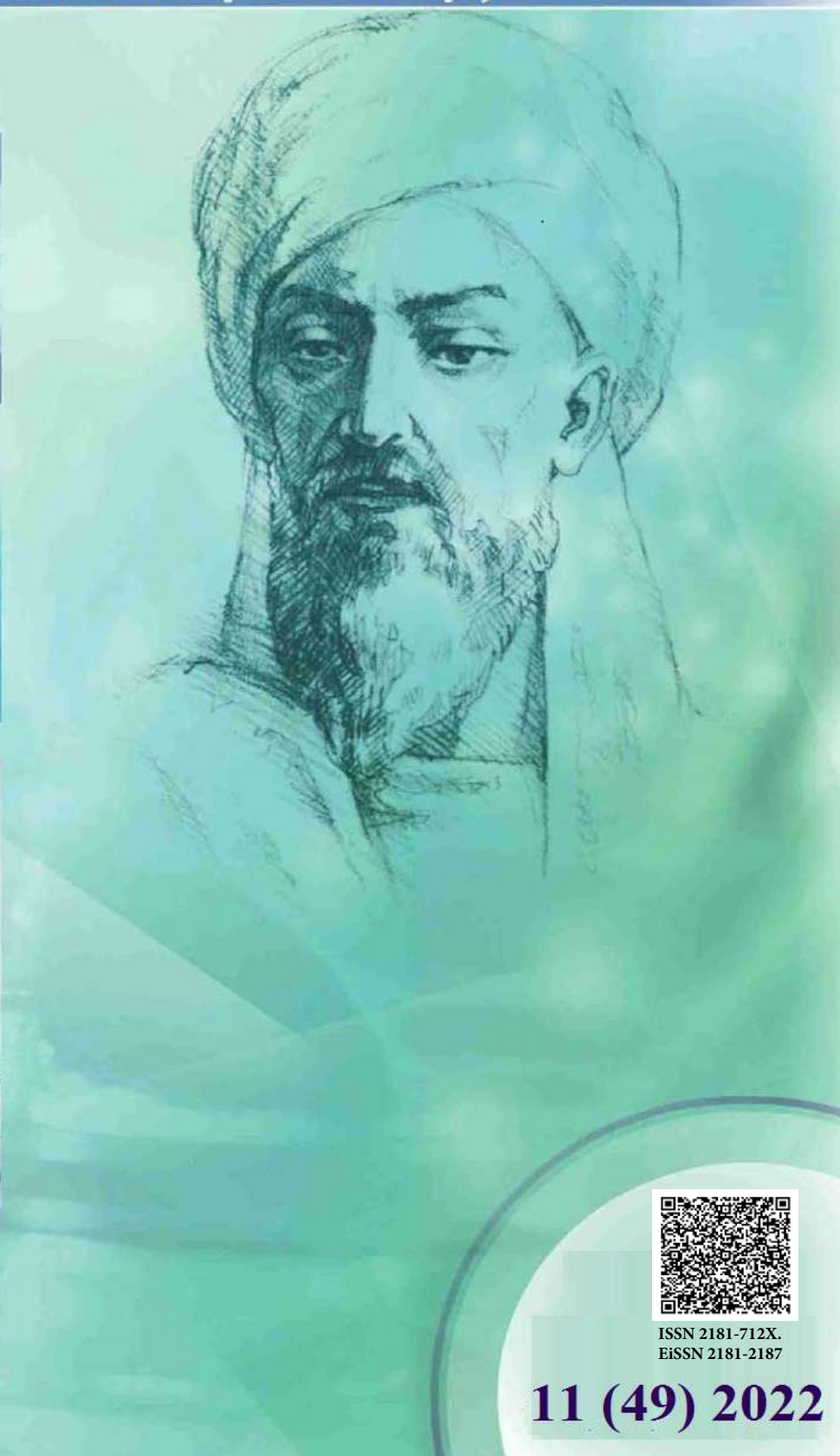
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НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE**

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MENOPAUZADAN OLDIN VA KEYIN AYOLLAR ORASIDA COVID-19 KASALLIGIDAN SO'NG POSTKOVIDAL SINDIROMINI RIVOJLANISHINI TAHLIL QILISH

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✓ *Rezyume*

Hozirda mavjud ma'lumotlarga ko'ra, SARS-CoV-2 tanadagi har bir a'zoga ta'sir qilishi mumkin. Covid-19 kasalligini davolash fonida menopauza gormoni terapiyasining aspektlari o'rganildi. Ushub maqolada peri va postmenopozal davrning yangi koronavirus infeksiyasi tufayli postkovid sindromi keli chiqishi bo'yicha adabiyotlar tahlili o'tkazildi.

Kalit so'zlari. SARS-CoV-2, COVID-19, asab tizimi, Peri - va postmenopozal davr, postkovid sindrom.

АНАЛИЗ РАЗВИТИЯ ПОСТКОВИДНОГО СИНДРОМА ПОСЛЕ COVID-19 У ЖЕНЩИН В ПРЕ- И ПОСТМЕНОПАУЗЕ

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✓ *Резюме*

Согласно имеющейся на данный момент информации, SARS-CoV-2 может поражать каждый орган в организме. Аспекты менопаузальной гормональной терапии изучались в контексте лечения Covid-19. В данной статье проведен анализ литературы о возникновении постковидного синдрома на фоне новой коронавирусной инфекции пери- и постменопаузального периода.

Ключевые слова. SARS-CoV-2, COVID-19, нервная система пери- и постменопаузальным эффектом, постковидного синдрома.

ANALYSIS OF THE DEVELOPMENT OF POST-COVID SYNDROME AFTER COVID-19 AMONG PRE- AND POST-MENOPAUSAL WOMEN

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✓ *Resume*

According to currently available information, SARS-CoV-2 can affect every organ in the body. Aspects of menopausal hormone therapy were studied in the context of the treatment of Covid-19. In this article, an analysis of the literature on the emergence of post-covid syndrome due to the new coronavirus infection of peri- and postmenopausal period was carried out.

Keywords. SARS-CoV-2, COVID-19, nervous system, peri- and postmenopausal effects, post-covid syndrome.

Relevance

For the past two years, the world has been living in a pandemic caused by a new coronavirus infection COVID-19, and this pandemic has significantly changed the lives of people and the organization of medical care [1]. Much attention is currently paid not only to the acute course of the disease, which

occurs in the form of a respiratory tract infection up to bilateral pneumonia and acute respiratory distress syndrome, but also to long-term consequences [2].

Post-Covid Syndrome (PCS) is a term coined to define the consequences of COVID-19, which are manifested by long-term and persistent symptoms up to 12 weeks. and longer. PCS occurs in 20% of people who have had a coronavirus infection and is protracted in 2.3% of cases. To classify this condition, the code U09.9 was specifically introduced in the ICD-10 [2].

A study by Moreno-Perez et al. [3] showed that more than half of the patients who underwent COVID-19, after 10-14 weeks. after the onset of the disease, residual effects persisted. When analyzing the clinical picture, mild and moderate symptoms mainly prevailed: general weakness, fatigue, shortness of breath, neurological complaints. X-ray and spirometric changes were observed in approximately 25% of the examined [3].

The symptoms of PCS are extremely diverse, since the SARS-CoV-2 virus is tropic to many tissues, however, the consequences of coronavirus infection can be divided into 4 main groups [4, 5]: 1) hypoxic syndrome (respiratory and oxygen deficiency); 2) asthenic syndrome (general weakness, low tolerance to physical activity); 3) syndrome of neuropsychiatric disorders (depressed mood, depression, deterioration in cognitive abilities, anosmia, sleep disturbances); 4) gastrointestinal symptoms (dyspepsia, dysbacteriosis, increased liver enzymes, distortion and decrease in taste sensations).

The subject of increased interest is gender differences in the course of coronavirus infection and in the development of its consequences. While reports of an association between patient gender and clinical outcomes have emerged with the growing number of studies on COVID-19, data on differences in the course of COVID-19 in men and women are conflicting [6-8], highlighting the need for further study of this question.

Purpose of the study: Based on the analysis of literature data, to study the influence of the period of peri- and postmenopause on the course of a new coronavirus infection and PCD.

Material and methods

A systematic search, analysis and review of publications regarding the course of COVID-19 in peri- and postmenopausal women, as well as the use of menopausal hormone therapy during the treatment of COVID-19 and PCD, was carried out in the Elibrary, Pubmed, Cochrane and Google academia for the period 2020-2022 Search date: January 2022. The search was conducted using the following keywords: COVID-19, coronavirus infection, menopause, coronavirus infection, menopause.

A number of published reports on the gender characteristics of the course of COVID-19 show that men develop more severe forms of the disease and have a higher mortality rate compared to women [9, 10]. Meta-analyses [11–13] have also demonstrated that men have a higher incidence of COVID-19, a higher risk of developing severe illness, and higher mortality than women. At the same time, it is noted that in young women, PCS developed more often and persisted longer [14].

A recent retrospective study [15] showed that male gender is associated with a higher rate of admission to intensive care units compared to females. In this study, patients had severe COVID-19 and were over 60 years of age, which may have introduced statistical bias.

Jin et al. [16] also reported a high risk of severe outcomes among men with COVID-19 in China. However, this study included only 43 patients. Omar et al. [17] included 88 adult patients in Eastern Sudan and reported no significant difference in mortality between males and females. In addition, women have a higher number of lymphocytes and a faster response of antibodies in the acute phase compared with men [14].

Mechanisms associated with a more favorable course of COVID-19 in women are described in Wray et Arrowsmith [8] and include physiological and immunological pathways, ranging from incomplete inactivation of immune genes by the X chromosome to the decisive role of angiotensin-converting enzyme 2 (ACE2) and regulation of the immune response by sex hormones. Thus, differences in the innate and adaptive immune systems lead to variability in susceptibility to SARS-CoV-2, the frequency and severity of the disease [8].

There is evidence that the likelihood of severe illness and mortality does not differ significantly between men in general and postmenopausal women. In particular, this is demonstrated in the work of Costeira et al. [18], which included data from women from the UK social monitoring application, including 2,637 post-menopausal women, 5,689 women taking combined oral contraceptives (COCs), and 51,193 women taking menopausal hormonal therapy (MGT). Data were adjusted for age, smoking

history, and body mass index values. It was noted that in women aged 18-45 years who took COCs, the symptoms of a new coronavirus infection were the least pronounced, and the lowest percentage of hospitalizations was also observed. The most severe course of COVID-19 was observed in postmenopausal women aged 40-60 years. At the same time, postmenopausal patients using MHT showed better indicators of the course of COVID-19 compared to those who did not use hormonal drugs [18].

A large Chinese study also showed that menstrual status plays a significant role in the severity and prognosis of coronavirus infection.

The spectrum, nature and impact of neurological complications of COVID-19 on the health of an individual and his quality of life are not yet well described and studied due to the relatively short observation period, the complex nature of the pathology and the small number of scientific studies with a high level of evidence on this problem. For the same reasons, measures for the treatment and prevention of delayed and late neurological disorders in people who have had COVID-19 have not been developed. Despite the fact that the mechanisms of the formation of these disorders have not been fully elucidated and the period of follow-up observation is relatively short, at the moment it is obvious that a population of patients who have undergone COVID-19 with persistent neurological disorders is being formed. Symptoms of damage to the central nervous system and peripheral nerves persist for more than 12 weeks after recovery from a viral infection and negatively affect the quality of life and health status. This group of patients requires constant medical support by doctors of various specialties and medical and psychological rehabilitation, the measures of which have not yet been developed.

The use of adult-type stem cells (SCs), including hematopoietic stem cells (HSCs), is a relatively new, promising area of regenerative medicine that allows successful rehabilitation of patients with residual CNS lesions caused by vascular, traumatic, and infectious causes [8-10].

В связи с относительно небольшим периодом, прошедшим с начала развития пандемии, в литературе имеется мало работ, оценивающих поздние неврологические нарушения пациентов с long COVID. И еще меньше работ посвящено схемам терапии и реабилитации для данного контингента. Включение в программы реабилитации пациентов с long COVID и неврологическими проявлениями терапии с использованием аутологичных ГСК может потенциально рассматриваться в качестве привлекательной опции и имеет под собой теоретическое и практическое обоснование.

Post covid syndrome and menopause

Despite suggestions that the acute phase of COVID-19 infection is milder in young women, recent reviews have noted that in the group of women under 50, cases of prolonged course of COVID-19 are more common [28], and also highlight the particular severity and polymorphism manifestations of PCS in women. Patients who are in a state of peri- and postmenopause turned out to be a particularly vulnerable group in relation to PCD [8].

The depletion of estrogen-synthetic function of the ovaries affects all organ systems, including the cardiovascular and nervous systems, the intestines, the musculoskeletal system, the genitourinary system, and now, in the era of the COVID-19 pandemic, its vital role in the immune system is quite clear [6].

Newson et al. [3] note that against the backdrop of a pandemic in everyday clinical practice, they observe an aggravation of typical symptoms of the menopausal transition and the postmenopausal period. Moreover, complaints such as fatigue, increased fatigue, reduced stamina, headaches, dizziness, hot flashes and other vasomotor symptoms, poor sleep, decreased concentration and muscle pain, can be a manifestation of not only menopausal syndrome, but and PCS [2]. Such coincidences can create diagnostic difficulties and require additional examinations from clinicians to verify the correct diagnosis [12]. Of course, the presence of menstrual irregularities, an increase in the level of gonadotropic hormones in the blood and the age of the patient will be of key importance here. However, it is known that in some women, menopause can occur quite early, and menopausal symptoms can develop long before the development of clinical amenorrhea. Therefore, physicians should be especially careful regarding the setting of prolonged COVID-19 and PCD, otherwise women with menopausal symptoms will be misdiagnosed. Failure to correctly diagnose such conditions and delay in prescribing MHT can lead to debilitating symptoms that affect physical and mental health, as well as increase the risk of cardiovascular disease, type 2 diabetes, osteoporosis, obesity and dementia [21] associated with a

progressive estrogen deficiency.

Thus, a woman who is in perimenopause and has undergone COVID-19 has a high risk of persistence of pathological symptoms and a significant decrease in the quality of life against this background. Of particular importance to the situation is the fact that many doctors are not wary of either PCS or the timely appointment of MHT [13]. Obviously, in such cases, if there are indications, the initiation of MHT is justified as a sufficiently safe and effective treatment option for women in a similar clinical situation [20].

In general, the results of using HSCs obtained from the bone marrow or peripheral blood did not differ from those when using mesenchymal cells [18]. At the same time, in the chronic phase with vascular injuries (strokes) and traumatic injuries of the brain/spinal cord, the cellular mechanisms involved in secondary damage to neurons, axons, and microglia do not differ, as well as the mechanisms of repair of damaged tissues. CD34+ HSCs derived from peripheral blood or bone marrow have a number of advantages. First, they penetrate the BBB and migrate to the lesions in the brain tissues, which is especially important when they are administered intravenously. Secondly, their ability to neuronal differentiation has been shown. Thirdly, these cells can be obtained relatively easily, in real time and in practically unlimited quantities, from the patient himself, both for administration in a native form and for cultivation. Fourth, a sufficient amount of information has been accumulated on their therapeutic efficacy both in the case of the acute phase of CNS damage and in the treatment of traumatic or ischemic diseases of the brain and/or spinal cord at the late stages [11].

Another important aspect of the COVID-19 pandemic is the high level of stress in society [23]. It is known that stress, depleting the body's reserves, can lead to vegetative psychosomatic reactions, decrease and even impairment of cognitive functions [24]. Obviously, in an environment of increased stress, the menopausal period cannot be considered as the only reason for the increase in complaints of memory loss, low concentration of attention or forgetfulness in a postmenopausal woman. The pandemic has increased the burden women face as they bear most of the housework during lockdown and spend more time with their children or grandchildren. Wenham et al. [25] describe important factors that lead to non-obvious risks to the socioeconomic status and health of women during the COVID-19 pandemic. At the same time, the ability to return to work further complicates the recovery process after COVID-19 and the manifestation of PCS [28]. Thus, in the stressful environment of the current COVID-19 pandemic, MHT for women with menopausal symptoms may have additional benefits.

Menopausal hormone therapy and post-COVID syndrome

Healthcare professionals, physicians and researchers are facing a significant challenge in finding new treatments that can ease the severity of symptoms of both acute and prolonged COVID-19. For PCS, there are still no standards of therapy and there is no coherent understanding of the mechanisms through which it is possible to influence the pathogenesis and severity of this condition [26].

In the absence of clinical recommendations at the moment, one can only rely on expert opinion and extrapolate the experience of foreign colleagues. It has been suggested [27] that perimenopausal women with higher estrogen levels will have a less severe course of COVID-19 compared to women of the same age and with the same body mass index but lower E2 levels. Costeira et al. [18] suggested that the administration of hormonal therapy may provide some protection against COVID-19.

Steward et al. [28] suggest using estrogen-containing drugs in menopausal women with a protracted form of COVID-19 to alleviate vasomotor symptoms, improve cognitive functions, potentiate the immune response, and increase the chances of a favorable outcome of the disease. Considering the possibility of serious negative consequences resulting from estrogen deficiency exacerbated by the COVID-19 pandemic, MHT should be considered not only for women with physiological postmenopause, but also for patients who have undergone hysterectomy and are receiving aromatase inhibitors and estrogen receptor antagonists [28].

Clinical symptoms associated with long COVID can occur even in people who have had mild or asymptomatic SARS-CoV-2. These symptoms are usually polymorphic and associated with CNS damage. At the same time, the authors note their dynamic development over several weeks or months [26]. Survivors of COVID-19 may experience a range of psychiatric symptoms that persist or appear several months after initial infection. In a cohort of 402 people, 4-6 weeks after the onset of COVID-19, 56% of cases had at least one of the psychiatric disorders (post-traumatic stress disorder, depression, anxiety, insomnia, and obsessive-compulsive symptoms) [2]. Anxiety, depression and sleep disorders

were present in about a quarter of patients after 6 months of follow-up in a study published by Chinese scientists [13]. Some of the long-term symptoms reported in the papers were absent in the acute phase of the infection [3]. The most common symptoms are severe fatigue with discomfort after exercise, cognitive impairment (decreased concentration of attention, memory, lack of words), sensory (tinnitus, dizziness), headache, shortness of breath, cough, pain and chest tightness, palpitations, smell and taste disturbance, odynophagia, sweating, muscle-tendon pain, paresthesia (“burning sensation”), digestive disorders (anorexia, abdominal pain, dyspepsia, diarrhea), skin manifestations (itching, urticaria), hair loss, sleep disturbances, irritability, anxiety and depression. Fibromyalgia syndrome is often observed, which is also referred to as long COVID [3].

In a letter to Gersh et al. [20] also outlined three positions regarding MHT in peri- and postmenopausal women suffering from the long-term consequences of COVID-19: 1) the use of monotherapy using transdermal estradiol; 2) the benefits of MHT are more likely to outweigh its risks if treatment is started in perimenopausal women at physiological doses of E2 during the optimal therapeutic window - before the age of 60 years or within 10 years after menopause; 3) combined estrogen-gestagen therapy in a cyclic mode will completely protect the endometrium from the possibility of its malignant transformation. In the case of a combination of transdermal estradiol with progesterone, a reliable, effective and at the same time safe progestogen, such as dydrogesterone (or progesterone), is preferable for postmenopausal women with an intact uterus, since it is these progestogens that are associated with a lower risk of cardiovascular disease. vascular diseases, thrombo-calls and oncorisks (in particular, breast cancer) in comparison with other gestagens. In addition, when prescribing MHT to such patients, one should take into account the severity of the disease, the presence of obesity, a tendency to hypercoagulability, and a history of smoking [20].

In a Brazilian publication, Hipolito Rodrigues et al. [26] also expresses an expert position supporting the prescription of MHT in women with characteristic complaints after suffering COVID-19, and also emphasizes that physicians should instruct their patients taking MHT not to interrupt therapy. The authors suggest that ongoing clinical trials may prove the efficacy of estrogen therapy in alleviating the impact of PKD symptoms in middle-aged and older women [16].

Conclusion

Issues related to the new coronavirus infection are widely discussed today in the medical press, including among obstetricians and gynecologists [30]. Many of them are associated with pregnancy and perinatal outcomes [31, 32]. However, no less significant are the changes that occur in those infected with COVID-19 during pre- and postmenopause. Literature data indicate that the postmenopausal period in women is a risk factor for a more severe course of COVID-19 coronavirus infection in the acute phase. The protracted course of COVID-19, the persistence of symptoms, and the development of severe post-COVID syndrome are associated with the female sex, and peri- and postmenopausal women are most vulnerable. Symptoms of estrogen deficiency and menopause can be similar to those of post-COVID syndrome, and these conditions can coexist and exacerbate each other. Estradiol may be a protective factor for women with COVID-19 by regulating cellular and humoral immunity factors such as cytokines, IL-2, IL-6, IL-8, TNF-a, and C3. According to international experts, the use of MHT will help improve the well-being and quality of life of women, as well as stop the symptoms characteristic of menopause and PCS. When choosing a combined MHT, special attention should be paid to the progestogen in the composition. A reliable, effective and at the same time safe progestogen, such as dydrogesterone (or progesterone), is preferable for postmenopausal women with an intact uterus, since these progestogens are associated with a lower risk of cardiovascular diseases, thrombosis and cancer risks (in particular, breast cancer) in comparison with other gestagens.

LIST OF REFERENCES:

1. Aghagoli G., Gallo Marin B., Katchur N.J., et al. Neurological involvement in COVID-19 and potential mechanisms: A Review. *Neurocrit Care*. 2021 Jun; 34(3): 1062-1071. <https://doi.org/10.1007/s12028-020-01049-4>. PMID: 32661794
2. Bhatia A., Sekhon H.K., Kaur G. Sex hormones and immune dimorphism. // *Scientific World Journal*. 2014:159150. DOI: 10.1155/2014/159150
3. Costeira R., Lee K.A., Murray B., Christiansen C., Castillo-Fernandez J., Lochlainn M.N. et al. Estrogen and COVID-19 symptoms: associations in women from the COVID Symptom Study

- medRxiv 2020.07.30.20164921. DOI: 10.1101/2020.07.30. 20164921
4. De Feo D., Merlini A., Laterza C., Martino G. Neural stem cell transplantation in central nervous system disorders: from cell replacement to neuroprotection. // *Curr Opin Neurol.* 2012 Jun; 25(3): 322-333. <https://doi.org/10.1097/wco.0b013e328352ec45>. PMID: 22547103
 5. Gao L., Xu W., Li T., et al. Stem Cell Therapy: A Promising Therapeutic Method for Intracerebral Hemorrhage. *Cell Transplant.* 2018 Dec; 27(12): 1809-1824. <https://doi.org/10.1177/0963689718773363>. Epub 2018 Jun 5. PMID: 29871521
 6. Garrigues E., Janvier P., Kherabi Y., et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J Infect.* 2020 Dec; 81(6): e4-e6. <https://doi.org/10.1016/j.jinf.2020.08.029>. Epub 2020 Aug 25. PMID: 32853602
 7. Gersh F., Lavie C.J., O'Keefe J.H. Menopause Status and Coronavirus Disease 2019 (COVID-19). *Clin Infect Dis.* 2021 Nov 2;73(9):e2825-e2826. DOI: 10.1093/cid/ ciaa1447
 8. Gersh FL, Lavie CJ. Menopause and hormone replacement therapy in the 21st century. *Heart.* 2020 Apr;106(7):479-481. DOI: 10.1136/heartjnl-2019-315898
 9. Giacomelli A., Pezzati L., Conti F., et al. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: A cross-sectional study. *Clin Infect Dis.* 2020 Jul; 71(15): 889-890. <https://doi.org/10.1093/cid/ciaa330>. PMID: 32215618
 10. Goertz Y.M.J., Van Herck M., Delbressine J.M., et al. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? *ERJ Open Res.* 2020 Oct 26; 6(4): 005422020. <https://doi.org/10.1183/23120541.00542-2020>. PMID: 33257910
 11. Guan W.J., Ni Z.Y., Hu Y., et al. Clinical characteristics of coronavirus disease 2019 in China. // *N Engl J Med.* 2020 Apr; 382(18): 1708-1720. <https://doi.org/10.1056/NEJMoa2002032>. Epub Feb 28. PMID: 32109013
 12. Huang C., Huang L., Wang Y., et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet.* 2021 Jan 16; 397(10270): 220-232. [https://doi.org/10.1016/S0140-6736\(20\)32656-8](https://doi.org/10.1016/S0140-6736(20)32656-8). Epub 2021 Jan 8. PMID: 33428867
 13. Jose R.J., Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. *Lancet Respir Med.* 2020 Jun; 8(6): e46-e47. [https://doi.org/10.1016/S2213-2600\(20\)30216-2](https://doi.org/10.1016/S2213-2600(20)30216-2). Epub 2020 Apr 27. PMID: 32353251
 14. Kremer S., Lersy F, de Seze J., et al. Brain MRI findings in severe COVID-19: A retrospective Observational study. *Radiology.* 2020 Nov; 297(2): E242-E251. <https://doi.org/10.1148/radiol.2020202222>. Epub 2020 Jun 16. PMID: 32544034
 15. Lakhan S.E., Kirchgessner A., Hofer M. Inflammatory mechanisms in ischemic stroke: therapeutic approaches. *J Transl Med.* Nov 17; 7: 97. <https://doi.org/10.1186/1479-5876-7-97>. PMID: 19919699
 16. Lobo R.A., Pickar J.H., Stevenson J.C., Mack W.J., Hodis H.N. Back to the future: Hormone replacement therapy as part of a prevention strategy for women at the onset of menopause. *Atherosclerosis.* 2016 Nov; 254:282-290. DOI: 10.1016/j. atherosclerosis.2016.10.005
 17. Long COVID: let patients help define long-lasting COVID symptoms. *Nature.* 2020 Oct; 586(7828): 170. <https://doi.org/10.1038/ d41586-020-02796-2>. PMID: 33029005
 18. Lu B., Jiang Y.J., Choy P.C. 17-Beta estradiol enhances prostagla in human U937-derived macrophages. *Mol Cell Biochem.* 2004 Jul; 262(1-2):101- 10. DOI: 10.1023/b:mcbi.0000038222.08915.
 19. Mao L., Jin H., Wang M. et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol.* 2020 Jun; 77(6): 683-690. <https://doi.org/10.1001/ jamaneurol.2020.1127>. PMID: 32275288
 20. Miyake S. Mind over cytokines: crosstalk and regulation between the neuroendocrine and immune systems. *Clin Exp Neuroimmunol* 2011;3:1 j.1759-1961.2011.00023.x
 21. Muhamad S.A., Ugusman A., Kumar J., et al. COVID-19 and Hypertension: The what, the why, and the how. *Frontiers in Physiology* 2021; 12: 589. <https://doi.org/10.3389/ fphys.2021.665064>
 22. Muheremu A., Peng J., Ao Q. Stem cell based therapies for spinal cord injury. *Tissue Cell.* 2016 Aug; 48(4): 328-333. <https://doi.org/10.1016/j.tice.2016.05.008>. Epub 2016 Jun 1. PMID: 27318871
 23. Nalbandian A., Sehgal K., Gupta A., et al. Post-acute COVID-19 syndrome. *Nat Med.* 2021 Apr; 27(4): 601-615. <https://doi.org/10.1038/s41591-021-01283-z>. Epub 2021 Mar 22. PMID:

33753937

24. Omar S.M., Musa I.R., Salah S.E., Elnur M.M., Al-Wutayd O., Adam I. High Mortality Rate in Adult COVID-19 Inpatients in Eastern Sudan: A Retrospective Study. // *J Multidiscip Healthc.* 2020 Dec 8;13:1887-1893. DOI: 10.2147/JMDH.S283900
25. Pezzini A., Padovani A. Lifting the mask on neurological manifestations of COVID-19. *Nat Rev Neurol.* 2020 Nov; 16(11): 636-644. <https://doi.org/10.1038/s41582-020-0398-3>.
26. Singal C.M.S., Jaiswal P, Seth P SARS-CoV-2, more than a respiratory virus: its potential role in neuropathogenesis. *ACS Chem Neurosci.* 2020 Jul; 11(13): 1887-1899. <https://doi.org/10.1021/acscemneuro.0c00251>. Epub 2020 Jun 18. PMID: 32491829
27. Stenudd M., Sabelstrom H., Frisen J. Role of endogenous neural stem cells in spinal cord injury and repair. *JAMA Neurol.* 2015 Feb; 72(2): 235-237. <https://doi.org/10.1001/jamaneurol.2014.2927>. PMID: 25531583
28. Stonesifer C., Corey S., Ghanekar S., et al. Stem cell therapy for abrogating stroke-induced neuroinflammation and relevant secondary cell death mechanisms. *Prog Neurobiol.* 2017 Nov; 158: 94-131. <https://doi.org/10.1016/j.pneurobio.2017.07.004>. Epub 2017 Jul 23. PMID: 28743464; PMCID: PMC5671910
29. Sudre C.H., Murray B., Varsavsky T., et al. Attributes and predictors of long COVID. *Nat Med* 2021 Apr; 27(4): 626-631. <https://doi.org/10.1038/s41591-021-01292-y>. Epub 2021 Mar 10. Erratum in: *Nat Med.* 2021 Jun; 27(6): 1116. PMID: 33692530
30. Taquet M., Luciano S., Geddes J.R., Harrison P.J. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. *Lancet Psychiatry.* 2021 Feb; 8(2): 130-140. [https://doi.org/10.1016/S2215-0366\(20\)30462-4](https://doi.org/10.1016/S2215-0366(20)30462-4). Epub 2020 Nov 9. Erratum in: *Lancet Psychiatry.* 2021 Jan; 8(1): e1. PMID: 33181098
31. The Lancet. Facing up to long COVID. *Lancet.* 2020 Dec 12; 396(10266):1861. [https://doi.org/10.1016/S0140-6736\(20\)32662-3](https://doi.org/10.1016/S0140-6736(20)32662-3). PMID: 33308453
32. Tian S., Xiong Y., Liu H., et al. Pathological study of the 2019 novel coronavirus disease (COVID-19) through postmortem core biopsies. *Mod Pathol.* 2020 Jun; 33(6): 1007-1014. <https://doi.org/10.1038/s41379-020-0536-x>. Epub 2020 Apr 14. PMID: 32291399
33. Wang X.W., Hu H., Xu Z.Y., Zhang G.K., Yu Q.H., Yang H.L. et al. Association of menopausal status with COVID-19 outcomes: a propensity score matching analysis. *Biol Sex Differ.* 2021 Jan 29;12(1):16. DOI: 10.1186/s13293-021-00363-6
34. Weissman I.L., Anderson D.J., Gage F. Stem and progenitor cells: origins, phenotypes, lineage commitments, and trans differentiations. *Annu Rev Cell Dev Biol.* 2001; 17: 387-403. <https://doi.org/10.1146/annurev.cellbio.17.1.387>. PMID: 11687494
35. Xu Z., Shi L., Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med.* 2020 Apr; 8(4): 420-422. [https://doi.org/10.1016/S2213-2600\(20\)30085-0](https://doi.org/10.1016/S2213-2600(20)30085-0). Epub 2020 Feb 25. PMID: 32109426
36. Yong S.J., Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. *Infect Dis (Lond).* Oct; 53(10): 737-754. <https://doi.org/10.1080/23744235.2021.1924397>. Epub 2021 May 22. PMID: 34024217; PMCID: PMC8146298

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