



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

G6PD deficiency may play a role in COVID-19 severity of illness and death in these groups.

Vascular endothelial dysfunction and coagulopathy have been suggested as complications of COVID-19 based on a report of large vessel ischemic stroke occurring in five US patients under the age 50 years, including two without pre-existing conditions. Similar cases have occurred in China and Singapore.⁹ Coagulopathy has also been observed in people with G6PD deficiency. Albertsen et al¹⁰ reported a fatal hemolytic crisis with disseminated intravascular coagulation and pulmonary microthrombi in a 42-year-old G6PD-deficient African male. Hemolysis results in cell-free hemoglobin, which contributes to activation of the intrinsic coagulation cascade and clot formation. COVID-19 infection could be a trigger for hemolysis and coagulopathy in G6PD-deficient patients, thus explaining the stroke symptoms.

Chloroquine has infrequently been reported to cause hemolysis in G6PD-deficient patients and caution is advised for its use.¹¹ Hydroxychloroquine, its molecular variant, is generally considered safe. Both antimalarial drugs are being trialed as possible treatments for COVID-19. However, a recent report described an acute hemolytic episode occurring in a COVID-19 patient with G6PD deficiency who was treated with hydroxychloroquine.¹² Hydroxychloroquine may increase the oxidative stress in COVID-19 patients with G6PD deficiency, thereby serving as a trigger for hemolytic anemia.

Studies are needed to determine whether a positive correlation exists between G6PD deficiency and COVID-19, with respect to increased susceptibility to infection and severity of illness. This is important for several reasons. First, it will allow for

identification of a subset of COVID-19 patients for whom close monitoring and supportive care may be critical. Second, certain treatments, such as hydroxychloroquine, may be contraindicated in these patients. Third, identification of this relationship may suggest other therapies, such as use of antioxidants, that may prove beneficial for treating COVID-19. Finally, such information will be important for people with known G6PD deficiency to guide their decisions and actions to prevent COVID-19 infection.

Dan J. Vick, MD, DHA, MBA

Health Administration Division
School of Health Sciences
The Herbert H. & Grace A. Dow College of
Health Professions
Central Michigan University
Mount Pleasant, MI

Potential Competing Interests: The author reports no competing interests.

ORCID

Dan J. Vick:  <https://orcid.org/0000-0002-6680-8884>

- Garg S, Kim L, Whitaker M, et al. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 — COVID-NET, 14 States, March 1–30, 2020. *MMWR*. 2020;69(15):458-464.
- Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. *Lancet*. 2008;371(9606):64-74.
- Wu YH, Tseng CP, Cheng ML, Ho HY, Shih SR, Chiu DT. Glucose-6-phosphate dehydrogenase deficiency enhances human coronavirus 229E infection. *J Infect Dis*. 2008;197(6):812-816.
- Johns Hopkins University & Medicine. Coronavirus Resource Center. COVID-19 dashboard. <https://coronavirus.jhu.edu/map.html>. Accessed May 21, 2020.
- Pinna A, Solinas G, Masia C, Zinellu A, Carru C, Carta A. Glucose-6-phosphate dehydrogenase (G6PD) deficiency in nonarteritic anterior ischemic optic neuropathy in a Sardinian population, Italy. *Invest Ophthalmol Vis Sci*. 2008;49(4):1328-1332.
- Cook T, Kursumovic E, Lennane S. Exclusive: deaths of NHS staff from covid-19 analysed. *Hlth Serv J*. April 22, 2020. <https://www.hs-j.co.uk/exclusive-deaths-of-nhs-staff-from-covid-19-analysed/7027471.article>. Accessed April 30, 2020.
- Yancy CW. COVID-19 and African Americans. *JAMA*. 2020. <https://doi.org/10.1001/jama.2020.6548>. <https://jamanetwork.com/journals/jama/fullarticle/2764789>. Accessed April 23, 2020.

- Chinevere TD, Murray CK, Grant E Jr, Johnson GA, Duell F, Hospenthal DR. Prevalence of glucose-6-phosphate dehydrogenase deficiency in U.S. Army personnel. *Mil Med*. 2006;171(9):905-907.
- Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of Covid-19 in the young. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMc2009787>. <https://www.nejm.org/doi/full/10.1056/NEJMc2009787>. Accessed April 29, 2020.
- Albertsen J, Ommen HB, Wandler A, Munk K. Fatal haemolytic crisis with microvascular pulmonary obstruction mimicking a pulmonary embolism in a young African man with glucose-6-phosphate dehydrogenase deficiency. *BMJ Case Rep*. 2014. <https://doi.org/10.1136/bcr-2013-201432>. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3987291/>. Accessed April 14, 2020.
- Sicard D, Kaplan JC, Labie D. Haemoglobinopathies and G-6-P.D. deficiency in Laos. *Lancet*. 1978;2(8089):571-572.
- De Franceschi L, Costa E, Dima F, Morandi M, Olivieri O. Acute hemolysis by hydroxychloroquine was observed in G6PD-deficient patient with severe COVID-19 related lung injury. *Eur J Intern Med*. 2020. <https://doi.org/10.1016/j.ejim.2020.04.020>. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7167571/>. Accessed April 25, 2020.

<https://doi.org/10.1016/j.mayocp.2020.05.035>

Vitamin D Supplementation During the COVID-19 Pandemic



To the Editor: The coronavirus disease 2019 (COVID-19) pandemic has severe short-term and long-term consequences on individuals, health systems, and economies. Considering the studies on the role of vitamin D in the prevention of acute respiratory infections, supplementation of vitamin D may be reasonable also for the prevention of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and reducing morbidity and mortality in COVID-19 high-risk patients.

Vitamin D deficiency is more common in older age groups, smokers, those who are obese, and in patients with chronic diseases such as diabetes, hypertension, various gastroenterological diseases, and also in African Americans.¹ The

high-risk groups that have more complications and higher mortality in COVID-19 coincide with groups that have a high incidence of vitamin D deficiency. We believe that vitamin D deficiency might be one of the important risk factors for COVID-19 complications and higher mortality.

Studies of vitamin D replacement have shown that vitamin D ameliorates innate immunity (the immediate response of macrophages to invading viruses and bacteria in the mucous membranes),² thereby reducing the incidence and severity of acute respiratory infections.³ This effect requires a sufficient serum level of 25(OH)D3 being crucial for macrophages to activate it into hormone D (calcitriol), which activates genes for the synthesis of antimicrobial factors destroying viruses (such as SARS-CoV-2), fungi, and bacteria.² Also, vitamin D modulates the cellular immune response and, as expected, attenuates the cytokine storm,⁴ the event so fatal in SARS-CoV-2–induced pneumonia. Therefore, we suggest it would be reasonable to supplement vitamin D in subpopulations at risk of vitamin D deficiency and unfavorable COVID-19 outcomes, as well as in individuals already infected with SARS-CoV-2 to achieve optimal 25(OH)D3 concentrations as quickly as possible.

It is challenging to conduct evidence-based medicine in cases such as the COVID-19 pandemic. To the best of our knowledge, there are no data on the effects of vitamin D in SARS-CoV-2 infection; then again, there are reliable data on the beneficial effects of cholecalciferol in attenuating viral respiratory infections in people with low levels of vitamin D. The European Centre for Disease Prevention and Control makes this argument and encourages health care professionals to take actions that are logical in their own

right, based on previously known findings in related fields: “Public health authorities should recognize that extra-scientific factors (e.g. feasibility of implementing scientific advice, time pressure, socio-political factors, institutional factors, economic interests, pressure from neighboring countries etc.) are inherent to the decision-making process. These factors will also influence the implementation of any proposed response measures. Decisions should therefore always be evidence informed, but they will very rarely be purely evidence based.”⁵ In Slovenia, in view of COVID-19 pandemic, medical doctors were urgently advised by leading experts to supplement vitamin D in high-risk and fragile individuals and in COVID-19 patients. With this letter to the editor we address the broader medical community to urgently consider vitamin D supplementation in high-risk patients for adverse COVID-19 outcomes.

Darko Siuka, MD

Division of Internal Medicine
UMC Ljubljana
Ljubljana, Slovenia

Marija Pfeifer, MD, PhD

Faculty of Medicine
University of Ljubljana
Ljubljana, Slovenia

Bojana Pinter, MD, PhD, MS(Econ)

Faculty of Medicine
University of Ljubljana
Ljubljana, Slovenia

Division of Ob/Gyn
UMC Ljubljana
Ljubljana, Slovenia

Potential Competing Interests: The authors report no competing interests.

ORCID

Bojana Pinter:  <https://orcid.org/0000-0001-6521-4593>

1. Kennel KA, Drake MT, Hurley DL. Vitamin D deficiency in adults: when to test and how to treat. *Mayo Clin Proc.* 2010;85(8):752-758.

- Zdrengea MT, Makrinioti H, Bagacean C, Bush A, Johnston SL, Stanciu LA. Vitamin D modulation of innate immune responses to respiratory viral infections. *Rev Med Virol.* 2017;27(1). <https://doi.org/10.1002/rmv.1909>. Epub 2016 Oct 7.
- Martineau AR, Jolliffe DA, Hooper RL, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ.* 2017; 15:356:i6583.
- Khoo AL, Chai LY, Koenen HJ, et al. Regulation of cytokine responses by seasonality of vitamin D status in healthy individuals. *Clin Exp Immunol.* 2011; 164(1):72-79.
- European Centre for Disease Prevention and Control. *Considerations relating to social distancing measures in response to COVID-19 — second update.* Stockholm: ECDC; 2020. <https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-social-distancing-measuresg-guide-second-update.pdf>. Accessed April 17, 2020.

<https://doi.org/10.1016/j.mayocp.2020.05.036>

How Many Lives Will Delay of Colon Cancer Surgery Cost During the COVID-19 Pandemic? An Analysis Based on the US National Cancer Database



To the Editor: By May 13, 2020, 1,342,594 cases of coronavirus disease (COVID-19) had been confirmed in the United States.¹ Of these patients, 80,820 (6%) had died.¹ This rapid viral spread, unencumbered by an effective treatment or vaccine, required wise health care resource utilization decisions. Consequently, many centers throughout the world have decided to delay elective surgical procedures including those for cancer to avoid health care system exhaustion.²

Surgical management of colon cancers is considered the cornerstone of treatment, especially in early-stage disease.^{3,4} Our team at Mayo Clinic derived results based on the American College of Surgeons National Cancer Database, which concluded that delaying elective surgery for patients with stage I