

Medical hypothesis about the evolving Delta variant and its early treatment

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- The current coronavirus variant has a shorter incubation period and a higher replication rate than previous variants. This necessitates an earlier start of anti-viral treatment despite the efforts of certain forces to hinder access to the necessary medications.
- The current coronavirus variant is capable of cell-cell fusion. This may decrease the effectiveness of antibodies and some drugs. One way to compensate for this is with higher amounts of zinc and its ionophores, especially hydroxychloroquine.

The Delta variant and its sub-variants of SARS-COV-2 are more dangerous than the Alpha variant (B.1.1.7), which peaked in the US in April 2021 ^(Latif and et al., 2021). The sub-variants currently prevalent in the US and the UK ^(Goldstein, 2021), seem to be more dangerous than the original Delta, which was prevalent in June. Unfortunately, scientific papers rarely clarify which sub-variants of Delta were studied, so one must make guesses by dates.

Among the Delta differences ^(Mlcochova et al., 2021) are a much higher reproduction rate ^(Mlcochova et al., 2021) ^(Linsenmeyer et al., 2021), a shorter incubation period ^(Li, Baisheng and et al., 2021), and the ability for cell-cell fusion ^(Mlcochova et al., 2021) ^(Papa et al., 2021). The Delta variant also has mutations in the RBD domain that defeat some antibodies, which makes it especially dangerous for individuals with only vaccine-induced immune response. The cell-cell fusion weakens (but does not eliminate) the activity of antibodies and drugs (including ivermectin).

That might require re-evaluation of dosages of many anti-viral ingredients in the existing COVID-19 treatment and prophylaxis protocols. So far, increasing the dosage of ivermectin appears to work ^(Marik, 2021) ^(FLCCC, 2021). Nevertheless, we need to consider other approaches.

The main anti-viral effect of Zinc in the COVID-19 treatment protocols is disruption of the coronavirus replication within the cells. ^(Read and et al., 2019) and ^(Marreiro et al., 2021) are useful reviews of the antiviral activities of zinc. Thus, Zinc activity is probably not impacted negatively by cell-cell fusion capability of the coronavirus, and increasing the concentration of zinc in the tissues, especially lungs, should be very effective in preventing the replication of the Delta. Higher amounts of Zinc require an ionophore, better than Quercetin. Hydroxychloroquine (HCQ) remains the most suitable ionophore, especially because of its property to

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accumulate in lungs at hundreds time higher concentration than in plasma. Hydroxychloroquine also inhibits SARS-COV-2 directly.

Today, it is obvious that the opposition to hydroxychloroquine was not based on any scientific or medical evidence, just like the current opposition to ivermectin. Thus, one might imagine that even Ivermectin-based protocols might benefit from adding **Hydroxychloroquine + Zinc**.

In the HCQ-containing protocols, HCQ accumulation is usually the slowest step. This problem might be solved by pre-exposure pre-loading with HCQ. Such pre-loading would have some preventative effect of its own (Goenka et al., 2020) (Mathai, 2020). With the elimination half-life estimated between 40 and 120+ days (drugs.com, 2021), one would need to take weekly only about 10% of the loading dose to maintain a constant concentration of HCQ in the lung tissues. Taking a loading dose of 1,200 – 2,000 mg of HCQ (2 x 200 mg daily over 3–5 days) and then 200 mg weekly might be considered the minimal, sub-prophylactic amount. However, it can safely be doubled. Rheumatoid arthritis patients typically take 2,800 mg weekly (i.e., 7x more) for years.

Another option for rapid delivery to the lungs is inhalable HCQ (Klimke et al., 2020) (Tai et al., 2021).

In addition to Zinc pills, Zinc lozenges deserve consideration because of additional benefits they provide in the upper respiratory tract (Hemilä and Chalker, 2021) (Finzi and Harrington, 2021).

Currently, Zinc is usually prescribed in the form of Zinc sulfate. Zinc pyrithione (PubChem, 2021) and Zinc hinokitiol might be of interest as alternatives to Zinc sulfate, because they contain both Zinc and its ionophore. These ionophores also have their own antiviral activity (Qiu et al., 2013) (Krenn et al., 2009). Zinc pyrithione has been shown to block SARS-CoV replication in vitro (Velthuis et al., 2010). Hinokitiol was even proposed as a Zinc ionophore and antiviral for COVID-19 (Hoang and Han, 2020) as an alternative to HCQ.

The importance of oral and nasal antiseptics (FLCCC, 2021) (C19 Anonymous, 2021) for prevention and early treatment of COVID-19 has increased. Nasal irrigation or rinsing or (possibly) spray with PVP-I can be recommended for prevention in vulnerable people.

No Competing Interests

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Disclaimers

This is not medical advice.

Securing access to medications necessary or helpful in COVID-19 treatment is a non-pharmacological intervention and is outside of the scope of this article.

References

- C19 Anonymous, A., 2021. *PVP-I for COVID-19: real-time analysis of all 17 studies*. <https://c19pvpi.com>
- drugs.com, 2021. *Plaquenil - FDA prescribing information, side effects and uses*. Drugs.com. <https://www.drugs.com/pro/plaquenil.html>
- Finzi, E., Harrington, A., 2021. *Zinc treatment of outpatient COVID-19: A retrospective review of 28 consecutive patients*. Journal of Medical Virology 93, 2588–2590. <https://doi.org/10.1002/jmv.26812>
- FLCCC, 2021. *I-MASK+ Protocol*. FLCCC | Front Line COVID-19 Critical Care Alliance. <https://covid19criticalcare.com/covid-19-protocols/i-mask-plus-protocol/>
- Goenka, M.K., Afzalpurkar, S., Goenka, U., Das, S.S., Mukherjee, M., Jajodia, S., Shah, B.B., Patil, V.U., Rodge, G., Khan, U., Bandyopadhyay, S., 2020. *Seroprevalence of COVID-19 Amongst Health Care Workers in a Tertiary Care Hospital of a Metropolitan City from India* (SSRN Scholarly Paper No. ID 3689618). Social Science Research Network, Rochester, NY. <https://doi.org/10.2139/ssrn.3689618>
- Goldstein, L., 2021. *Delta Subvariants AY.3, AY.4, and A.25 are Dominant*. The CDC Lies. defyccc.com. <https://defyccc.com/delta-ay-3-ay-4/>
- Hemilä, H., Chalker, E., 2021. *Vitamin C and zinc lozenges for COVID-19?* J Am Pharm Assoc (2003) 61, e39. <https://doi.org/10.1016/j.japh.2021.05.018>
- Hoang, B.X., Han, B., 2020. *A possible application of hinokitiol as a natural zinc ionophore and anti-infective agent for the prevention and treatment of COVID-19 and viral infections*. Medical Hypotheses 145, 110333. <https://doi.org/10.1016/j.mehy.2020.110333>
- Klimke, A., Hefner, G., Will, B., Voss, U., 2020. *Hydroxychloroquine as an aerosol might markedly reduce and even prevent severe clinical symptoms after SARS-CoV-2 infection*. Medical Hypotheses 142, 109783. <https://doi.org/10.1016/j.mehy.2020.109783>
- Krenn, B.M., Gaudernak, E., Holzer, B., Lanke, K., Van Kuppeveld, F.J.M., Seipelt, J., 2009. *Antiviral Activity of the Zinc Ionophores Pyrithione and Hinokitiol against Picornavirus Infections*. Journal of Virology 83, 58–64. <https://doi.org/10.1128/JVI.01543-08>
- Latif, A.A., et al., 2021. <https://outbreak.info/situation-reports/alpha?loc=USA&selected=USA&overlay=false>
- Li, Baisheng, et al., 2021. *Viral infection and transmission in a large well-traced outbreak caused by the Delta SARS-CoV-2 variant - SARS-CoV-2 coronavirus / nCoV-2019* Genomic Epidemiology. Virological. <https://virological.org/t/viral-infection-and-transmission-in-a-large-well-traced-outbreak-caused-by-the-delta-sars-cov-2-variant/724>
- Linsenmeyer, K., Gupta, K., Madjarov, R., Charness, M.E., 2021. *Cryptic Transmission of the Delta Variant AY.3 Sublineage of SARS-CoV-2 among Fully Vaccinated Patients on an Inpatient Ward*. <https://doi.org/10.1101/2021.08.05.21261562>

Marik, P., 2021. *An overview of the MATH+, I-MASK+ and I-RECOVER Protocols. A Guide to the Management of COVID-19.* <https://covid19criticalcare.com/wp-content/uploads/2020/12/FLCCC-Protocols-%E2%80%93-A-Guide-to-the-Management-of-COVID-19.pdf>

Marreiro, D. do N., Cruz, K.J.C., Oliveira, A.R.S. de, Morais, J.B.S., Freitas, B. de J. e S. de A., Melo, S.R. de S., Santos, L.R. dos, Cardoso, B.E.P., Dias, T.M. da S., 2021. *Antiviral and immunological activity of zinc and possible role in COVID-19.* British Journal of Nutrition 1–8. <https://doi.org/10.1017/S0007114521002099>

Mathai, 2020. *Hydroxychloroquine as pre-exposure prophylaxis against COVID-19 in health-care workers: A single-center experience.* <https://www.marinemedicalsociety.in/article.asp?issn=0975-3605;year=2020;volume=22;issue=3;spage=98;epage=104;aulast=Mathai>

Mlcochova, P., Kemp, S., Dhar, M.S., Papa, G., Meng, B., Ferreira, I.A.T.M., Datir, R., Collier, D.A., Albecka, A., Singh, S., Pandey, R., Brown, J., Zhou, J., Goonawardane, N., Mishra, S., Whittaker, C., Mellan, T., Marwal, R., Datta, M., Sengupta, S., Ponnusamy, K., Radhakrishnan, V.S., Abdullahi, A., Charles, O., Chattopadhyay, P., Devi, P., Caputo, D., Peacock, T., Wattal, D.C., Goel, N., Satwik, A., Vaishya, R., Agarwal, M., Mavousian, A., Lee, J.H., Bassi, J., Silacci-Fegni, C., Saliba, C., Pinto, D., Irie, T., Yoshida, I., Hamilton, W.L., Sato, K., Bhatt, S., Flaxman, S., James, L.C., Corti, D., Piccoli, L., Barclay, W.S., Rakshit, P., Agrawal, A., Gupta, R.K., 2021. *SARS-CoV-2 B.1.617.2 Delta variant replication and immune evasion.* Nature 1–8. <https://doi.org/10.1038/s41586-021-03944-y>

Papa, G., Mallery, D.L., Albecka, A., Welch, L.G., Cattin-Ortolá, J., Luptak, J., Paul, D., McMahon, H.T., Goodfellow, I.G., Carter, A., Munro, S., James, L.C., 2021. *Furin cleavage of SARS-CoV-2 Spike promotes but is not essential for infection and cell-cell fusion.* PLOS Pathogens 17, e1009246. <https://doi.org/10.1371/journal.ppat.1009246>

PubChem, 2021. *Pyrrithione zinc* <https://pubchem.ncbi.nlm.nih.gov/compound/3005837>

Qiu, M., Chen, Y., Chu, Y., Song, S., Yang, N., Gao, J., Wu, Z., 2013. *Zinc ionophores pyrrithione inhibits herpes simplex virus replication through interfering with proteasome function and NF-κB activation.* Antiviral Research 100, 44–53. <https://doi.org/10.1016/j.antiviral.2013.07.001>

Read, S., et al., 2019. *Role of Zinc in Antiviral Immunity.* Advances in Nutrition | Oxford Academic. <https://academic.oup.com/advances/article/10/4/696/5476413>

Tai, W., Chow, M.Y.T., Chang, R.Y.K., Tang, P., Gonda, I., MacArthur, R.B., Chan, H.-K., Kwok, P.C.L., 2021. *Nebulised Isotonic Hydroxychloroquine Aerosols for Potential Treatment of COVID-19.* Pharmaceutics 13, 1260. <https://doi.org/10.3390/pharmaceutics13081260>

Velthuis, A.J.W. te, Worm, S.H.E. van den, Sims, A.C., Baric, R.S., Snijder, E.J., Hemert, M.J. van, 2010. *Zn²⁺ Inhibits Coronavirus and Arterivirus RNA Polymerase Activity In Vitro and Zinc Ionophores Block the Replication of These Viruses in Cell Culture.* PLOS Pathogens 6, e1001176. <https://doi.org/10.1371/journal.ppat.1001176>