

# The VICTAS Trial: *Designed to fail*

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## Complete References

1. Sevransky JE, Rothman RE, Hager DN, et al. (2021) Effect of Vitamin C, Thiamine, and Hydrocortisone on Ventilator-and Vasopressor-Free Days in Patients With Sepsis: The VICTAS Randomized Clinical Trial. JAMA 325:742-751. <https://jamanetwork.com/journals/jama/fullarticle/2776688>
2. Moraes RB, Friedman G, Wawrzyniak IC, et al. (2015) Vitamin D deficiency is independently associated with mortality among critically ill patients. Clinics. 70:326-332. <https://pubmed.ncbi.nlm.nih.gov/26039948>
3. Alker W, Haase H. (2018) Zinc and Sepsis Nutrients 10:976. <https://pubmed.ncbi.nlm.nih.gov/30060473>
4. Noormandi A, Khalili H, Mohammadi M, et al. (2020) Effect of magnesium supplementation on lactate clearance in critically ill patients with severe sepsis: a randomized clinical trial. Eur J Clin Pharmacol 76:175-184. <https://pubmed.ncbi.nlm.nih.gov/31814044>
5. Velissaris D, Karamouzos V, Pierrakos C, et al. (2015) Hypomagnesemia in critically ill sepsis patients. J Clin Med Res 2015;7:911-918. <https://pubmed.ncbi.nlm.nih.gov/26566403>
6. Guerin C, Cousin C, Mignot F, et al. (1996) Serum and erythrocyte magnesium in critically ill patients. Intensive Care Med 22:724-727. <https://pubmed.ncbi.nlm.nih.gov/8880238>
7. Angstwurm MW, Engelmann L, Zimmermann T, et al. (2007) "Selenium in Intensive Care (SIC): results of a prospective randomized, placebo-controlled, multiple-center study in patients with severe systemic inflammatory response syndrome, sepsis, and septic shock." Crit Care Med. 35:118-26. <https://pubmed.ncbi.nlm.nih.gov/17095947>



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## References

8. Belsky JB, Wira CR, Jacob V, et al. (2018) A review of micronutrients in sepsis: the role of thiamine, l-carnitine, vitamin C, selenium and vitamin D. *Nutr Res Rev.* 31:281-290. <https://pubmed.ncbi.nlm.nih.gov/29984680>
9. Klenner FR. (1971) Observations On the Dose and Administration of Ascorbic Acid When Employed Beyond the Range of A Vitamin In Human Pathology. *J Applied Nutrit.* 23:61-87. [https://seanet.com/~alexs/ascorbate/197x/klenner-fr-j\\_appl\\_nutr-1971-v23-n3&4-p61.htm](https://seanet.com/~alexs/ascorbate/197x/klenner-fr-j_appl_nutr-1971-v23-n3&4-p61.htm)
10. Chambers R, Pollock H. (1927) Micrurgical studies in cell physiology: IV. Colorimetric determination of the nuclear and cytoplasmic pH in th e starfish egg. *J Gen. Physiol* 10:739-755. <https://pubmed.ncbi.nlm.nih.gov/19872358/>
11. Clark EJ, Rossiter RJ. (1944) Carbohydrate metabolism after burning. *Q J Exp Physiol Cog Med Sci* 32:279-300. <https://doi.org/10.1113/expphysiol.1944.sp000890>
12. Fowler AA, Truwit JD, Hite RD, et al. (2019) Effect of Vitamin C Infusion on Organ Failure and Biomarkers of Inflammation and Vascular Injury in Patients With Sepsis and Severe Acute Respiratory Failure: The CITRIS-ALI Randomized Clinical Trial. *JAMA* 322:1261-1270. <https://pubmed.ncbi.nlm.nih.gov/31573637>
13. Fowler AA, Syed AA, Knowlson S, et al. (2014) "Phase I Safety trial of intravenous ascorbic acid in patients with severe sepsis." *J Transl Med* 12:32. <https://pubmed.ncbi.nlm.nih.gov/24484547>
14. DesBois M (2021) The Treatment of Infectious Disease Using Vitamin C and other Nutrients. *Orthomolecular Medicine News Service.* <http://orthomolecular.org/resources/omns/v17n04.shtml>
15. Klenner FR (1949) The Treatment of Poliomyelitis and other Virus Diseases with Vitamin C. *South Med Surg.* 111:209-214. <https://pubmed.ncbi.nlm.nih.gov/18147027> <https://vitaminfoundation.org/www.orthomed.com/polio.htm> [https://www.seanet.com/~alexs/ascorbate/194x/klenner-fr-southern\\_med\\_surg-1948-v110-n2-p36.htm](https://www.seanet.com/~alexs/ascorbate/194x/klenner-fr-southern_med_surg-1948-v110-n2-p36.htm)
16. Jungeblut CW (1935) Inactivation of Poliomyelitis virus in vitro by crystalline vitamin C (ascorbic acid) *J Exp Med.* 62:517-521. <https://pubmed.ncbi.nlm.nih.gov/19870431>
17. Cathcart RF (1981) Vitamin C, titrating to bowel tolerance, anascorbemia, and acute induced scurvy. *Med Hypotheses* 7:1359-1376. <https://pubmed.ncbi.nlm.nih.gov/7321921>
18. McCormick WJ (1951) Vitamin C in the Prophylaxis and Therapy of Infectious Diseases. *Arch Pediatr.* 68:1-9. <https://pubmed.ncbi.nlm.nih.gov/14800557> [https://www.seanet.com/~alexs/ascorbate/195x/mccormick-wj-arch\\_pediatrics-1951-v68-n1-p1.htm](https://www.seanet.com/~alexs/ascorbate/195x/mccormick-wj-arch_pediatrics-1951-v68-n1-p1.htm)
19. Hugh D Riordan HD, Hunninghake RB, Riordan NH, et al. (2003) Intravenous ascorbic acid: protocol for its application and use. *P R Health Sci J,* 22:287-90. <https://pubmed.ncbi.nlm.nih.gov/14619456>

# VICTAS Trial

## References

20. Marik PE, Khangoora V, Rivera R, Hooper MH, Catravas J. (2017) Hydrocortisone, Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Before-After Study. *Chest* 151:1229-1238. <https://pubmed.ncbi.nlm.nih.gov/27940189>
21. Kory P, Meduri GU, Iglesias J, et al. (2021) Clinical and Scientific Rationale for the "MATH+" Hospital Treatment Protocol for COVID-19. *J Intensive Care Med.* 36:135-156. <https://pubmed.ncbi.nlm.nih.gov/33317385>
22. Front Line COVID-19 Critical Care Alliance (2021) EVMS COVID-19 Management Protocol: An overview of the MATH+ and I-MASK+ Protocols. <http://www.flccc.net>
23. Riordan H, Riordan, N, Casciari J (2021) The Riordan intravenous vitamin C (IVC) protocol for adjunctive cancer care: IVC as a chemotherapeutic and biologic response modifying agent. Riordan Clinic. [https://riordanclinic.org/wp-content/uploads/2015/11/RiordanIVCprotocol\\_en.pdf](https://riordanclinic.org/wp-content/uploads/2015/11/RiordanIVCprotocol_en.pdf)
24. Heaney RP. (2014) Guidelines for optimizing design and analysis of clinical studies of nutrient effects. *Nutr Rev* 72:48-54. <https://pubmed.ncbi.nlm.nih.gov/24330136>
25. Montel-Hagen A, Kinet S, Manel N, et al. (2008) Erythrocyte Glut1 triggers dehydroascorbic acid uptake in mammals unable to synthesize vitamin C. *Cell*, 132:1039-1048. <https://pubmed.ncbi.nlm.nih.gov/18358815>
26. Nualart F, Mack L, Garc a A, et al. (2014) Vitamin C Transporters, Recycling and the Bystander Effect in the Nervous System: SVCT2 versus Gluts. *J Stem Cell Res Ther* 4:209. <https://pubmed.ncbi.nlm.nih.gov/25110615>
27. May JM, Harrison FE. (2013) Role of Vitamin C in the Function of the Vascular Endothelium. *Antioxidants & Redox Signaling* 19:2068-2083. <https://pubmed.ncbi.nlm.nih.gov/23581713>
28. Nabzdyk CS, Bittner EA. (2018) Vitamin C in the critically ill - indications and controversies. *World J Crit Care Med* 7:52-61. <https://www.wjgnet.com/2220-3141/full/v7/i5/52.htm>
29. Lee RE. (1961) Ascorbic Acid and the Peripheral Vascular System. *Ann NY Acad Sci.* 92:295-301. <https://doi.org/10.1111/j.1749-6632.1961.tb46129.x>
30. Lee RE, Holze EA. (1951) Nutritional factors in hemodynamics: dissociation of pressor response and hemorrhage resistance in avitaminosis C. *Proc. Soc. Expt. Biol Med.* 76:325-329. <https://pubmed.ncbi.nlm.nih.gov/14827915>
31. Barabutis N, Khangoora V, Marik PE, Catravas JD. (2017) Hydrocortisone and Ascorbic Acid Synergistically Prevent and Repair Lipopolysaccharide-Induced Pulmonary Endothelial Barrier Dysfunction. *Chest* 152:954-962. <https://pubmed.ncbi.nlm.nih.gov/28739448>
32. Parker WH, Rhea EM, Qu ZC. (2016) Intracellular ascorbate tightens the endothelial permeability barrier through Epac1 and the tubulin cytoskeleton. *Am J Physiol Cell Physiol.* 311:C652-C662. <https://pubmed.ncbi.nlm.nih.gov/27605450>

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## References

33. Gu W, Cheng A, Barnes H, et al. (2014) Vitamin C Deficiency Leading to Hemodynamically Significant Bleeding. JSM Clinical Case Reports 2:1046. <https://www.jscimedcentral.com/CaseReports/casereports-2-1046.pdf>
34. Zhao B, Fei J, Chen Y, et al. (2014) Vitamin C treatment attenuates hemorrhagic shock related multi-organ injuries through the induction of heme oxygenase-1. BMC Complementary and Alternative Medicine 14:442-454. <https://pubmed.ncbi.nlm.nih.gov/25387896>
35. Ladumer A, Schmitt CA, Schachner D, et al. (2012) Ascorbate stimulates endothelial nitric oxide synthase enzyme activity by rapid modulation of its phosphorylation status. Free Radic Biol Med. 52:2082-2090. <https://pubmed.ncbi.nlm.nih.gov/22542797>
36. Heller R, Munscher-Paulig F, Grabner R, Till V. (1999) L-Ascorbic Acid Potentiates Nitric Oxide Synthesis in Endothelial Cells. J Biol Chem 274:8254-8260. <https://pubmed.ncbi.nlm.nih.gov/10075731>
37. Dingchao H, Zhduan Q, Xiaodong F. (1994) The Protective Effects of High-Dose Ascorbic Acid on Myocardium against Reperfusion Injury During and After Cardiopulmonary Bypass. Thorac Cardiovasc Surg 42:276-278. <https://pubmed.ncbi.nlm.nih.gov/7863489>
38. Ichim TE, Minev B, Braciak T, et al. (2011) Intravenous ascorbic acid to prevent and treat cancer-associated sepsis? J Transl Med 9:25. <https://pubmed.ncbi.nlm.nih.gov/21375761>
39. Cisternas P, Silva-Alvarez C, Martinez F, et al. (2014) The oxidized form of vitamin C, dehydroascorbic acid, regulates neuronal energy metabolism. J Neurochem 129: 663-671. <https://pubmed.ncbi.nlm.nih.gov/24460956>
40. Wang Y, Lin H, Lin BW, et al. (2019) Effects of different ascorbic acid doses on the mortality of critically ill patients: a meta-analysis. Ann Intensive Care 9:58. <https://pubmed.ncbi.nlm.nih.gov/31111241>
41. Boretti A, Banik BK. (2020) Intravenous vitamin C for reduction of cytokines storm in acute respiratory distress syndrome. PharmaNutrition 12:100190. <https://pubmed.ncbi.nlm.nih.gov/32322486>
42. Iglesias J, Vassallo AV, Patel V et al. (2020) Outcomes of metabolic resuscitation using ascorbic acid, thiamine, and glucocorticoids in the early treatment of sepsis. Chest 158:164-173. <https://pubmed.ncbi.nlm.nih.gov/32194058>
43. de Melo AF, Homem-de-Mello M. (2020) High-dose intravenous vitamin C may help in cytokine storm in severe SARS-CoV-2 infection. Crit Care 24:500. <https://pubmed.ncbi.nlm.nih.gov/32792018>
44. Zhang J, Rao X, Li Y et al. (2021) Pilot trial of high-dose vitamin C in critically ill COVID-19 patients. Ann Intensive Care 11:5. <https://pubmed.ncbi.nlm.nih.gov/33420963>



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## References

45. Lankadeva YR, Peiris RM, Okazaki N, et al. (2021) Reversal of the pathophysiological responses to Gram-negative sepsis by megadose Vitamin C. Crit Care Med 49:e179-e190. <https://pubmed.ncbi.nlm.nih.gov/33239507>
46. Patterson G, Isaacs CM, Fulzele S. (2021) Low level of vitamin C and dysregulation of vitamin C transporter might be involved in the severity of COVID-19 infection. Aging and Disease 12:14-26. <https://pubmed.ncbi.nlm.nih.gov/33532123>
47. Tomassa-Irriguible TM, Lielsa-Berrocal L. (2020) COVID-19: Up to 87% critically ill patients had low vitamin C values. Research Square, preprint. <https://www.researchsquare.com/article/rs-89413/v1>
48. Arvinte C, Singh M, Marik PE. Serum levels of vitamin C and vitamin D in a cohort of critically ill COVID-19 patients of a North American Community Hospital Intensive Care Unit in May 2020. A pilot study. Medicine in Drug Discovery 8:100064. <https://pubmed.ncbi.nlm.nih.gov/32964205>
49. Wagas Khan HM, Parikh N, Megala SM, Predeteanu GS. (2020) Unusual Recovery of a Critical COVID-19 Patient After Administration of Intravenous Vitamin C. Am J Case Rep 21: e925521. <https://pubmed.ncbi.nlm.nih.gov/32709838>
50. Marik PE. (2018) Hydrocortisone, Ascorbic Acid and Thiamine (HAT therapy) for the treatment of sepsis. Focus on ascorbic acid. Nutrients 10:1762. <https://pubmed.ncbi.nlm.nih.gov/30441816>
51. May JM, Qu ZC. (2011) Ascorbic acid prevents oxidant-induced increases in endothelial permeability. Biofactors 37:46-50. <https://pubmed.ncbi.nlm.nih.gov/21328627>
52. Utoguchi N, Ikeda K, Saeki K et al. (1995) Ascorbic acid stimulates barrier function of cultured endothelial cell monolayer. J Cell Physiol 163:393-399. <https://pubmed.ncbi.nlm.nih.gov/7706381>
53. Han M, Pendem S, Teh SL, et al. (2010) Ascorbate protects endothelial barrier function during septic insult: Role of protein phosphatase type 2A. Free Radic Biol Med 48:128-135. <https://pubmed.ncbi.nlm.nih.gov/19840845>

