

Why 25-dehydroxyvitamin D is a negative acute-phase reactant

To the Editor: In previous publications, we presented evidence that 25-dehydroxyvitamin D (25[OH]D) in serum behaves as a negative acute-phase reactant, ie, that its concentration decreases in the presence of inflammatory states.^{1,2} Low levels may thus reflect low vitamin D stores or inflammation, complicating the clinical interpretation of test results.

We have recently become aware of the mechanism underlying this phenomenon: less than 1% of circulating 25(OH)D exists in unbound form, and the majority is tightly bound to vitamin D binding protein, while 10% to 15% is bound to albumin. Both are negative acute-phase proteins.^{3–5} As the serum concentrations of these proteins decrease, so does that of 25(OH)D. Similarly, the positive acute-phase behavior of copper is explained by the fact that it is bound to ceruloplasmin, a positive acute-phase protein.⁶

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REFERENCES

1. Antonelli M, Kushner I. Low serum levels of 25-hydroxyvitamin D accompany severe COVID-19 because it is a negative acute phase reactant. *Am J Med Sci* 2021; 362(3):333–335. doi:10.1016/j.amjms.2021.06.005
2. Antonelli MJ, Kushner I, Epstein M. The constellation of vitamin D, the acute-phase response, and inflammation. *Cleve Clin J Med* 2023; 90(2):85–89. doi:10.3949/ccjm.90a.22048
3. Yousefzadeh P, Shapses SA, Wang X. Vitamin D binding protein impact on 25-hydroxyvitamin D levels under different physiologic and pathologic conditions. *Int J Endocrinol* 2014; 2014:981581. doi:10.1155/2014/981581
4. Dahl B, Schiødt FV, Gehrchen PM, Ramlau J, Kiaer T, Ott P. Gc-globulin is an acute phase reactant and an indicator of muscle injury after spinal surgery. *Inflamm Res* 2001; 50(1):39–43. doi:10.1007/s000110050722
5. Liberman U, Bikle DD. Disorders in the action of vitamin D. In: Feingold KR, Anawalt B, Blackman MR, et al, eds. *Endotext*. South Dartmouth, MA: MDText.com, Inc.; 2023.
6. Sattar N, Scott HR, McMillan DC, Talwar D, O'Reilly DS, Fell GS. Acute-phase reactants and plasma trace element concentrations in non-small cell lung cancer patients and controls. *Nutr Cancer* 1997; 28(3):308–312. doi:10.1080/01635589709514592
doi:10.3949/ccjm.90c.09001