

# INFLAMMATION

## Selenium

Subclinical deficiency negatively alters genes that regulate the inflammatory response; Deficiency promotes vascular inflammation.<sup>37,38</sup>

## Manganese

Cofactor to the powerful antioxidant superoxide dismutase that fights inflammation within cells.<sup>1,2</sup>

## Magnesium

Deficiency activates pro-inflammatory chemicals called cytokines; Deficiency will also kick start a damaging immune response by activating cells called leukocytes and macrophages.<sup>3,4,5</sup>

## Glutathione

Repairs damage to cells caused by inflammation; Regulates the production of pro-inflammatory cytokines; Recycles vitamins C and E.<sup>6,7</sup>

## Cysteine

Protects organs such as blood vessels, brain and liver from inflammatory damage; Precursor to glutathione production; Supplementation with N-acetyl cysteine raises glutathione.<sup>8,9</sup>

## Copper

Deficiency lowers enzyme activity (such as superoxide dismutase) that fights inflammation; Lowers damaging isoprostanes, a by-product of inflammation.<sup>34,35,36</sup>

## Vitamin C

Low vitamin C linked to inflammation; Inversely related to C-reactive protein (CRP), a marker for systemic inflammation; Increases glutathione.<sup>10,11,12</sup>

## Zinc

Inflammation raises demand for zinc; Pro-inflammatory chemicals (cytokines) dose dependently decrease in response to zinc repletion.<sup>31,32,33</sup>

## Vitamin D

Potent modulator of inflammation; Helps turn off chronic inflammatory responses; Inhibits pro-inflammatory cytokine production.<sup>13,14</sup>

## Vitamin A

Regulates the cellular immune response to inflammatory signals; Deficiency increases the severity of chronic inflammation; Zinc depletion lowers vitamin A status.<sup>28,29,30</sup>

## Vitamin E

Limits destructive cell behavior caused by inflammatory enzymes gone wild; Reduces damage from tumor necrosis factor alpha (TNF- $\alpha$ ); Deficiency predisposes a person to inflammation-related diseases.<sup>15,16</sup>

## Vitamin B2

Riboflavin (B2) helps minimize pain associated with inflammation; Detoxifies homocysteine, an amino acid that indirectly causes inflammation in various tissues.<sup>26,27</sup>

## Vitamin B6

Low B6 status is linked to high levels of CRP and systemic inflammation.<sup>24,25</sup>

## Coenzyme Q10

Decreases several inflammatory markers (CRP and IL-6) in supplementation trials; Affects genes that control response to inflammatory stress.<sup>21,22,23</sup>

## Glutamine

Decreases cytokine production; Invokes an anti-inflammatory response; Precursor to glutathione.<sup>19,20</sup>

## Lipoic Acid

Neutralizes free radicals caused by uncontrolled inflammation in both water and lipid phases of the cell; Protects endothelial cells from inflammation; Regenerates other antioxidants such as vitamin E, C and glutathione.<sup>17,18</sup>

Copyright 2013 SpectraCell Laboratories, Inc.  
All rights reserved. Doc 395 05.13

*Additional nutrients affect inflammation. This list is non-exhaustive.*

## REFERENCES

- <sup>1</sup>Li C, Zhou H. The role of manganese superoxide dismutase in inflammation disease. *Enzyme Res* 2011;387:176
- <sup>2</sup>Holley A, Dhar S, Xu Y et al. Manganese superoxide dismutase: beyond life and death. *Amino Acids* 2012;42:139-158.
- <sup>3</sup>Weglicki W. Hypomagnesemia and inflammation: clinical and basic aspects. *Annu Rev Nutr* 2012;32:55-71.
- <sup>4</sup>Sugimoto J, Romani A, Valentin-Torres A et al. Magnesium decreases inflammatory cytokine production: a novel innate immunomodulatory mechanism. *J Immunol* 2012;188:6338-6346.
- <sup>5</sup>Mazur A, Maier J, Rock E et al. Magnesium and the inflammatory response: potential physiopathological implications. *Arch Biochem Biophys*. 2007;458:48-56.
- <sup>6</sup>Lubos E, Kelly N, Oldebeken S et al. Glutathione peroxidase-1 deficiency augments proinflammatory cytokine-induced redox signaling and human endothelial cell activation. *J Biol Chem* 2011;286:35407-35417.
- <sup>7</sup>Ramires R, Ji L. Glutathione supplementation and training increases myocardial resistance to ischemia-reperfusion in vivo. *Am J Physiol Heart Circ Physiol* 2001;281:H679-H688.
- <sup>8</sup>Erickson M, Hansen K, Banks W. Inflammation-induced dysfunction of the low-density lipoprotein receptor-related protein-1 at the blood-brain barrier: protection by the antioxidant N-acetylcysteine. *Brain Behav Immun* 2012;26:1085-1094.
- <sup>9</sup>Sekhar R, Patel S, Guthikonda A et al. Deficient synthesis of glutathione underlies oxidative stress in aging and can be corrected by dietary cysteine and glycine supplementation. *Am J Clin Nutr* 2011;94:847-853.
- <sup>10</sup>Mah E, Matos M, Kawiecki D et al. Vitamin C status is related to proinflammatory responses and impaired vascular endothelial function in healthy, college-aged lean and obese men. *J Am Diet Assoc* 2011;111:737-743.
- <sup>11</sup>Mikirova N, Casciari J, Rogers A et al. Effect of high-dose intravenous vitamin C on inflammation in cancer patients. *J Transl Med* 2012;10:189.
- <sup>12</sup>Lenton K, Sane A, Therriault H et al. Vitamin C augments lymphocyte glutathione in subjects with ascorbate deficiency. *Am J Clin Nutr* 2003;77:189-195.
- <sup>13</sup>Zhang Y, Leung D, Richers B. Vitamin D inhibits monocyte/macrophage proinflammatory cytokine production by targeting MAPK phosphatase-1. *J Immunol* 2012;88:2127-2135.
- <sup>14</sup>Quefeld U. Vitamin D and inflammation. *Pediatr Nephrol* 2013;28:605-10.
- <sup>15</sup>Wells S, Jennings M, Rome C et al. alpha-, gamma- and delta-tocopherols reduce inflammatory angiogenesis in human microvascular endothelial cells. *J Nutr Biochem* 2010;21:589-597.
- <sup>16</sup>Yachi R, Muto C, Ohtaka N et al. Effects of tocotrienol on tumor necrosis factor- $\alpha$ /d-galactosamine-induced steatohepatitis in rats. *J Clin Biochem Nutr* 2013;52:146-153.
- <sup>17</sup>Jones W, Li X, Qu Z et al. Uptake, recycling, and antioxidant actions of alpha-lipoic acid in endothelial cells. *Free Radic Biol Med* 2002;33:83-93.
- <sup>18</sup>Shay K, Moreau R, Smith E et al. Alpha-lipoic acid as a dietary supplement: molecular mechanisms and therapeutic potential. *Biochim Biophys Acta* 2009;1790:1149-1160.
- <sup>19</sup>Kim H. Glutamine an immunonutrient. *Yonsei Med J* 2011;52:892-897.
- <sup>20</sup>Garrett-Cox R, Stefanutti G, Booth C et al. Glutamine decreases inflammation in infant rat endotoxemia. *J Pediatr Surg* 2009;44:523-9.
- <sup>21</sup>Lee B, Huang Y, Chen S et al. Effects of coenzyme Q10 supplementation on inflammatory markers (high-sensitivity C-reactive protein, interleukin-6, and homocysteine) in patients with coronary artery disease. *Nutrition* 2012;28:767-72.
- <sup>22</sup>Schmelzer C, Lindner I, Rimbach G et al. Functions of coenzyme Q10 in inflammation and gene expression. *Biofactors* 2008;32:179-83.
- <sup>23</sup>Sohet F, Neyrinck A, Pachikian B et al. Coenzyme Q10 supplementation lowers hepatic oxidative stress and inflammation associated with diet-induced obesity in mice. *Biochem Pharmacol* 2009;78:1391-400.
- <sup>24</sup>Ulvik A, Midttun O, Ringdal E et al. Association of plasma B-6 vitamers with systemic markers of inflammation before and after pyridoxine treatment in patients with stable angina pectoris. *Am J Clin Nutr* 2012;95:1072-1078.
- <sup>25</sup>Morris M, Sakakeeny L, Jacques P et al. Vitamin B-6 intake is inversely related to, and the requirement is affected by, inflammation status. *J Nutr* 2010;140:103-110.
- <sup>26</sup>Bertollo C, Oliveira A, Rocha L et al. Characterization of the antinociceptive and anti-inflammatory activities of riboflavin in different experimental models. *Eur J Pharmacol* 2006;547:184-191.
- <sup>27</sup>Granados-Soto V, Terán-Rosales F, Rocha-González H et al. Riboflavin reduces hyperalgesia and inflammation but not tactile allodynia in the rat. *Eur J Pharmacol* 2004;492:35-40.
- <sup>28</sup>Garcia O. Effect of vitamin deficiency on the immune response in obesity. *Proc Nutr Soc* 2012;71:290-297.
- <sup>29</sup>Christian P, West K. Interactions between zinc and vitamin A: an update. *Am J Clin Nutr* 1998;68:435S-441S.
- <sup>30</sup>Kim C. Retinoic acid, immunity, and inflammation. *Vitam Horm* 2011;86:83-101.
- <sup>31</sup>Foster M, Samman S. Zinc and regulation of inflammatory cytokines: implications for cardio-metabolic disease. *Nutrients* 2012;4:676-694.
- <sup>32</sup>Wessels I, Haase H, Engelhardt G et al. Zinc deficiency induces production of the proinflammatory cytokines IL-1 $\beta$  and TNF $\alpha$  in promyeloid cells via epigenetic and redox-dependent mechanisms. *J Nutr Biochem* 2013;24:289-297.
- <sup>33</sup>Costarelli L, Muti E, Malavolta M et al. Distinctive modulation of inflammatory and metabolic parameters in relation to zinc nutritional status in adult overweight/obese subjects. *J Nutr Biochem* 2010;21:432-7.
- <sup>34</sup>Bo S, Durazzo M, Gambino R et al. Associations of dietary and serum copper with inflammation, oxidative stress, and metabolic variables in adults. *J Nutr* 2008;138:305-10.
- <sup>35</sup>Schuschke D, Adeagbo A, Patibandla P et al. Cyclooxygenase-2 is upregulated in copper-deficient rats. *Inflammation* 2009;32:333-9.
- <sup>36</sup>DiSilvestro RA, Selsby J, Siefker K. A pilot study of copper supplementation effects on plasma F2alpha isoprostanes and urinary collagen crosslinks in young adult women. *J Trace Elem Med Biol* 2010;24:165-168.
- <sup>37</sup>Kipp A, Banning A, van Schothorst E et al. Marginal selenium deficiency down-regulates inflammation-related genes in splenic leukocytes of the mouse. *J Nutr Biochem* 2012;23:1170-1177.
- <sup>38</sup>Cao Y, Reddy C, Sordillo L. Altered eicosanoid biosynthesis in selenium-deficient endothelial cells. *Free Radic Biol Med* 2000;28:381-389.