#### Intravenous Nutrient Therapy: Ingredients and Associated Benefits

## Why IV Therapy?

Nutritional deficiencies caused by medical illnesses with malabsorption or other social factors can disrupt the proper functioning of the human body and manifest in a variety of clinical conditions such as asthma, acute migraine, fatigue, cardiovascular disease, musculoskeletal pain syndromes, and depression. While one of the most common avenues of nutritional supplementation is through oral means, higher serum concentrations of nutrients can be achieved through intravenous (IV) administration as opposed to oral supplementation or even intramuscular (IM) injections<sup>1</sup>. The high serum concentrations of nutrients achievable only through IV therapy have been shown to exhibit direct pharmacological effects and correct intracellular nutrient deficiencies. When used appropriately under physician-guidance, the intravenous administration of nutrients is an effective and better-tolerated means of resolving nutrient imbalance as opposed to many other conventional therapies<sup>2</sup>.

## **IV Ingredients**

#### B Complex: B1, B2, B3, B5, B6

Vitamin B Complex is a mixture of thiamine (vitamin  $B_1$ ), riboflavin (vitamin  $B_2$ ), niacin (vitamin  $B_3$ ), pantothenic acid (vitamin  $B_5$ ), and pyridoxine (vitamin  $B_6$ ). Various B vitamins serve critical functions in key metabolic processes and contribute to the recycling of cellular toxins such as the amino acid, homocysteine<sup>3</sup>. As the most metabolically active organ in the human body, the concentration of certain B vitamins in the brain can be up to fifty times that of plasma, alluding to the importance of these compounds in brain function<sup>4</sup>. Collectively, maintaining a healthy level of vitamin B complex supports energy production and proper brain function, while vitamin B deficiencies may manifest in the form of skin rashes, fatigue, anemia, migraines, or depressive symptoms<sup>5</sup>.

#### Biotin (Vitamin B<sub>7</sub>)

Biotin, also known as vitamin B<sub>7</sub>, is perhaps most well-known in the management and treatment of hair loss. As one of the eight B-vitamins that serve as coenzymes in many metabolic processes, biotin also functions across numerous aspects of brain function, including energy production, nucleic acid synthesis, and neurotransmitter synthesis<sup>6</sup>. High doses of biotin in particular have been shown in studies to have a stabilizing effect on neurodegenerative diseases such as multiple sclerosis or Alzheimer's disease. In addition, biotin's ability to boost the production of cyclic guanosine monophosphate (cGMP), a secondary messenger, indirectly promotes neuronal plasticity and opposes neuron apoptosis<sup>7</sup>. Since brain aging is associated with a decline in cGMP levels, the use of biotin supplements as a preventative agent may have particular merit<sup>8</sup>.

## Cobalamin B12

Vitamin  $B_{12}$ , or cobalamin, is a cofactor associated with two enzymes involved in the conversion of cellular metabolites and the catabolism of fatty acids and amino acids. Some of the downstream metabolites in these pathways include substrates used in DNA, RNA, protein, and lipid production. As such, vitamin  $B_{12}$  plays a critical role in the development, myelination, and function of the central nervous system<sup>9</sup>. Due to its role in metabolism, cobalamin has also been suggested to be an energy enhancer and athletic performance booster<sup>10</sup>. It has been found that vitamin  $B_{12}$  deficiencies are associated with cognitive impairments and affect particularly the elderly and vegetarian or vegan populations who consume limited or no animal products containing natural cobalamin<sup>11</sup>. Other effects of vitamin  $B_{12}$  deficiency include anemia, low blood cell counts, fatigue, and neurological symptoms including numbness and tingling in the extremities; fortunately, vitamin  $B_{12}$  supplements can considerably eliminate risk of cobalamin deficiency<sup>12</sup>.

## Vitamin C

Vitamin C is a powerful antioxidant and is required for the biosynthesis of compounds such as collagen, L-carnitine, and certain neurotransmitters. The antioxidant properties of Vitamin C have been studied in the context of preventing the onset and progression of degenerative diseases that are caused in part by oxidative damage, such as certain cancers and cardiovascular disease. Of its many benefits, the most commonly known functions of vitamin C are associated with its role in immunity. Of note, the antiviral effect of vitamin C has been shown to occur only at high serum concentrations achievable with intravenous administration<sup>13</sup>. There is evidence to suggest that regular prophylactic supplementation of vitamin C shortens the duration and lessens the severity of common colds in the general population, likely due to its antihistamine effects<sup>14</sup>.

## Magnesium

Magnesium is an abundant mineral in the body that serves as a cofactor in hundreds of enzymatic processes associated with mitochondrial energy production, protein synthesis, muscle and nerve function, blood glucose control, and blood pressure regulation<sup>15</sup>. Studies have shown that serum magnesium has an inverse correlation with high sensitive C-reactive protein, which is a marker of inflammation<sup>16</sup>. While magnesium is present in many foods, data from the 2013-2016 National Health and Nutrition Examination Survey (NHANES) shows that 48% of Americans ingest less magnesium than is estimated to be necessary<sup>17</sup>. In addition, because magnesium promotes the relaxation of vascular and bronchial smooth muscle, intravenous supplementation

of magnesium can serve as effective treatments for angina, asthma, acute migraines, and chronic pain if used under the direct supervision of a healthcare provider<sup>1, 18, 19</sup>.

#### Selenium

The nutrient selenium is incorporated into selenoproteins in the human body that have a wide range of effects from antioxidant and anti-inflammatory effects to thyroid hormone production. Because brain oxidative stress is a cause of cognitive impairment, the antioxidant properties of selenium can protect against decline in brain function. Observational studies in the past conducted by Akbaraly et al. have shown that selenium availability in the plasma decreases with time, and that the extent of plasma selenium depletion is associated with a higher probability of neuropsychological function decline<sup>20</sup>. The antioxidant properties of selenoproteins also contribute to the prevention of inflammation and platelet aggregation, thus limiting the risk and severity of cardiovascular disease. Supplements of selenite may be employed to protect brain health and reduce inflammation in the human body.

#### Zinc

According to the World Health Organization, zinc is classified as an essential element and is the second most abundant transition metal in the human body. It is a critical component of many enzymatic processes that play an important role in immune function, wound healing, cellular metabolism, a proper sense of taste and smell, growth and development<sup>21</sup>. The antioxidant properties of zinc may also offer protection against signs of accelerated aging<sup>22</sup>. It has been suggested that zinc can reduce the severity and duration of cold symptoms by directly inhibiting viral binding to the nasal mucosa and suppressing inflammation<sup>23</sup>. Because the body has no specialized form of zinc storage, regular intake or corrective supplementation of zinc can be important to prevent adverse alterations in immunity; even mild zinc deficiencies can result in suppressed immune function in the form of reduced lymphocyte proliferation<sup>24</sup>.

## Taurine

Taurine is an abundant amino acid that is found in high concentrations in most cells of the human body, with particularly high levels in excitable tissues. The benefits of taurine have been studied in experiments focusing on skeletal muscle, the central nervous system (CNS), and cardiovascular systems. These effects can largely be attributed to the anti-inflammatory properties of taurine that contribute to its ability to diminish muscular damage from intense exercise and prevent diseases of the circulatory system<sup>25</sup>. Taurine has also been shown to play an important role in neuronal development in the cerebral cortex and protects against neurodegenerative abnormalities such as Alzheimer's and Parkinson's disease<sup>26</sup>. Thus, taurine

therapy may be used as a supplement for those hoping to improve athletic capacity, enhance cardiovascular health and protect brain function.

# Glycine

Glycine is known as one of the most simple yet important amino acids in animals, comprising 11.5% of the total amino acid content in the human body<sup>27</sup>. It serves as a precursor for many important metabolites such as creatine, glutathione, purines, and porphyrins. In the central nervous system, glycine serves as an important neurotransmitter and influences peripheral and nervous tissues to control the intake of food, behavior, and body homeostasis<sup>28</sup>. When supplemented at proper dosages, glycine is known to successfully decrease several metabolic disorders in individuals struggling with cardiovascular health, various inflammatory conditions, cancers, diabetes, and obesity. Glycine has also been suggested to enhance quality of sleep and neurological functions due to its role in the central nervous system<sup>27</sup>.

# Glutamine

Glutamine is a conditionally essential amino acid widely used in sports nutrition. As the most abundant and versatile amino acid in the body, glutamine serves as an important metabolic fuel and protein synthesis precursor that has been suggested to enhance athletic performance<sup>29, 30</sup>. In addition to its ability to delay fatigue, glutamine has been studied extensively for its role in the immune system. In disease states, the rate of glutamine consumption by immune cells is similar or greater than even that of glucose. Studies have shown that glutamine is an essential nutrient for lymphocyte proliferation and cytokine production, macrophage phagocytic and secretory activities, and pathogen recognition<sup>29</sup>. Because glutamine deprivation can severely impair immune function, glutamine supplementation is suggested as part of protocols to boost immunity.

# MIC (Methionine Inositol Choline)

Methionine, inositol, and choline (MIC) belong to a group of compounds called lipotropics that help lower cholesterol levels and prevent fat build-up in the liver. Methionine is a sulfur-containing amino acid that serves as a precursor for many cellular reactions and plays an important role in lipid metabolism and immune function<sup>31</sup>. Inositol, a carbocyclic sugar, is a vitamin-like substance that lowers blood-glucose levels and contributes to lipid metabolism. When accompanied by a low-calorie diet, inositol supplementation has been shown to effectively accelerate weight loss and increase lean mass in normal human subjects<sup>32</sup>. Lastly, choline is an essential nutrient that breaks down fat as an energy source. In studies performed on athletes, choline was shown to rapidly reduce body mass without any adverse side effects or loss of static strength<sup>33</sup>. In combination with lifestyle changes and a balanced diet, lipotropic supplementation may facilitate the reduction of stored fat and enhance energy levels.

# Glutathione (GSH)

Glutathione is a tripeptide of cysteine, glycine, and glutamine that serves as an important antioxidant and anti-inflammatory compound. It has been shown that antioxidants inhibit the transcription of several inflammatory genes; thus, the antioxidant properties of glutathione can inhibit exaggerated inflammatory responses associated with diseases such as asthma, cystic fibrosis, influenza or acute respiratory distress syndrome. The role of glutathione is also directly indicated for some functions of the immune system including lymphocyte proliferation and neutrophil-mediated phagocytosis<sup>34</sup>. Along with its roles in immunity and inflammation, glutathione has also been suggested to carry anti-aging effects and improve skin properties<sup>35,36</sup>.

# L-Carnitine

L-carnitine is a compound that facilitates the transport of fatty acid-derived acetyl groups from the cytosol to the mitochondria for metabolism and cellular energy production. Studies have shown that carnitine supplementation may improve performance in athletes by speeding up recovery from exercise stress and increasing maximal oxygen consumption<sup>37</sup>. L-carnitine is also thought to have neuroprotective properties. In recent studies, long-term treatment with l-carnitine supplementation resulted in reduced attention deficits in patients with Alzheimer's disease, indicating that l-carnitine may serve as a beneficial therapeutic option for individuals hoping to protect against neurodegeneration<sup>38</sup>.

# Toradol

Toradol is the common name of a non-steroidal anti-inflammatory drug called ketorolac tromethamine that offers powerful pain relief. It is often used in various clinical conditions such as headaches, menstrual disorders, postoperative pain, spinal and soft tissue pain, and arthritis. Toradol functions by blocking cyclooxygenase (COX) enzymes that are needed to produce prostaglandin<sup>39</sup>.

## References

1. Blanchard J, Tozer TN, Rowland M. Pharmacokinetic perspectives on megadoses of ascorbic acid. Am J Clin Nutr 1997;66:1165- 1171.

2. Gaby, Alan R. "Intravenous nutrient therapy: the "Myers' cocktail"." *Alternative medicine review : a journal of clinical therapeutic* vol. 7,5 (2002): 389-403.

3. Kennedy, David O. "B Vitamins and the Brain: Mechanisms, Dose and Efficacy--A Review." *Nutrients* vol. 8,2 68. 27 Jan. 2016, doi:10.3390/nu8020068

4. Uchida Y., Ito K., Ohtsuki S., Kubo Y., Suzuki T., Terasaki T. Major involvement of na+-dependent multivitamin transporter (SLC5A6/SMVT) in uptake of biotin and pantothenic acid by human brain capillary endothelial cells. *J. Neurochem.* 2015;134:97–112. doi: 10.1111/jnc.13092.

5. Young, Lauren M et al. "A Systematic Review and Meta-Analysis of B Vitamin Supplementation on Depressive Symptoms, Anxiety, and Stress: Effects on Healthy and 'At-Risk' Individuals." *Nutrients* vol. 11,9 2232. 16 Sep. 2019, doi:10.3390/nu11092232

6. Kennedy, David O. "B Vitamins and the Brain: Mechanisms, Dose and Efficacy--A Review." *Nutrients* vol. 8,2 68. 27 Jan. 2016, doi:10.3390/nu8020068

7. McCarty, Mark F, and James J DiNicolantonio. "Neuroprotective potential of high-dose biotin." *Medical hypotheses* vol. 109 (2017): 145-149. doi:10.1016/j.mehy.2017.10.012

8. Domek-Łopacińska, K.U., Strosznajder, J.B. "Cyclic GMP and nitric oxide synthase in aging and Alzheimer's disease." *Mol Neurobiol*, vol. 41 (2–3) Jun. 2010, pp. 129-137. https://doi.org/10.1007/s12035-010-8104-x

9. Allen, Lindsay H. "Vitamin B-12." *Advances in nutrition (Bethesda, Md.)* vol. 3,1 (2012): 54-5. doi:10.3945/an.111.001370

10. AJung, Y Peter et al. "Effects of acute ingestion of a pre-workout dietary supplement with and without *p*-synephrine on resting energy expenditure, cognitive function and exercise performance." *Journal of the International Society of Sports Nutrition* vol. 14 3. 12 Jan. 2017, doi:10.1186/s12970-016-0159-2

11. Bailey, Regan L et al. "High folic acid or folate combined with low vitamin B-12 status: potential but inconsistent association with cognitive function in a nationally representative

cross-sectional sample of US older adults participating in the NHANES." *The American journal of clinical nutrition* vol. 112,6 (2020): 1547-1557. doi:10.1093/ajcn/nqaa239

12. Langan, Robert C, and Andrew J Goodbred. "Vitamin B12 Deficiency: Recognition and Management." *American family physician* vol. 96,6 (2017): 384-389.

13. Harakeh S, Jariwalla RJ, Pauling L. Suppression of human immunodeficiency virus replication by ascorbate in chronically and acutely infected cells. Proc Natl Acad Sci U S A 1990;87:7245-7249.

14. Johnston, C S. "The antihistamine action of ascorbic acid." *Sub-cellular biochemistry* vol. 25 (1996): 189-213. doi:10.1007/978-1-4613-0325-1\_10

15. Rude RK. Magnesium. In: Coates PM, Betz JM, Blackman MR, Cragg GM, Levine M, Moss J, White JD, eds. Encyclopedia of Dietary Supplements. 2nd ed. New York, NY: Informa Healthcare; 2010:527-37.

16. Moslehi, Nazanin et al. "Effects of oral magnesium supplementation on inflammatory markers in middle-aged overweight women." *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences* vol. 17,7 (2012): 607-14.

17. U.S. Department of Agriculture, Agricultural Research Service. Usual Nutrient Intake from Food and Beverages, by Gender and Age, What We Eat in America, NHANES 2013-2016 🗗; 2019.

18. Sun-Edelstein, Christina, and Alexander Mauskop. "Role of magnesium in the pathogenesis and treatment of migraine." *Expert review of neurotherapeutics* vol. 9,3 (2009): 369-79. doi:10.1586/14737175.9.3.369

19. Del Gobbo, Liana C et al. "Circulating and dietary magnesium and risk of cardiovascular disease: a systematic review and meta-analysis of prospective studies." *The American journal of clinical nutrition* vol. 98,1 (2013): 160-73. doi:10.3945/ajcn.112.053132

20. Akbaraly, Tasnime N et al. "Plasma selenium over time and cognitive decline in the elderly." *Epidemiology (Cambridge, Mass.)* vol. 18,1 (2007): 52-8. doi:10.1097/01.ede.0000248202.83695.4e

21. Bhattacharya, Preeti Tomar et al. "Nutritional Aspects of Essential Trace Elements in Oral Health and Disease: An Extensive Review." *Scientifica* vol. 2016 (2016): 5464373. doi:10.1155/2016/5464373

22. Evans, J R. "Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration." *The Cochrane database of systematic reviews* ,2 CD000254. 19 Apr. 2006, doi:10.1002/14651858.CD000254.pub2

23. Hulisz, Darrell. "Efficacy of zinc against common cold viruses: an overview." *Journal of the American Pharmacists Association : JAPhA* vol. 44,5 (2004): 594-603. doi:10.1331/1544-3191.44.5.594.hulisz

24. Beck, F W et al. "Changes in cytokine production and T cell subpopulations in experimentally induced zinc-deficient humans." *The American journal of physiology* vol. 272,6 Pt 1 (1997): E1002-7. doi:10.1152/ajpendo.1997.272.6.E1002

25. Schaffer, Stephen, and Ha Won Kim. "Effects and Mechanisms of Taurine as a Therapeutic Agent." *Biomolecules & therapeutics* vol. 26,3 (2018): 225-241. doi:10.4062/biomolther.2017.251

26. Alkholifi, F. K. and Albers, D. S. (2015) Attenuation of rotenone toxicity in SY5Y cells by taurine and N-acetyl cysteine alone or in combination. Brain Res. 1622, 409-413.

27. Razak, Meerza Abdul et al. "Multifarious Beneficial Effect of Nonessential Amino Acid, Glycine: A Review." *Oxidative medicine and cellular longevity* vol. 2017 (2017): 1716701. doi:10.1155/2017/1716701

28. Rajendra S., Lynch J. W., Schofield P. R. The glycine receptor. *Pharmacology and Therapeutics*. 1997;73(2):121–146. doi: 10.1016/S0163-7258(96)00163-5.

29. Cruzat, Vinicius et al. "Glutamine: Metabolism and Immune Function, Supplementation and Clinical Translation." *Nutrients* vol. 10,11 1564. 23 Oct. 2018, doi:10.3390/nu10111564

30. Coqueiro, Audrey Yule et al. "Glutamine as an Anti-Fatigue Amino Acid in Sports Nutrition." *Nutrients* vol. 11,4 863. 17 Apr. 2019, doi:10.3390/nu11040863

31. Martínez, Y. et al. The role of methionine on metabolism, oxidative stress, and diseases. Amino Acids vol. 49 2091–2098 (2017).

32. Tidwell, H. C., Slesinski, F. A. & Treadwell, C. R. Methionine Excretion. Effect of Diet and Methionine Ingestion in Normal Subjects. Exp. Biol. Med. 66, 482–485 (1947).

33. Elsawy, Gehan et al. "Effect of choline supplementation on rapid weight loss and biochemical variables among female taekwondo and judo athletes." Journal of human kinetics vol. 40 77-82. 9 Apr. 2014, doi:10.2478/hukin-2014-0009

34. Ghezzi, Pietro. "Role of glutathione in immunity and inflammation in the lung." *International journal of general medicine* vol. 4 105-13. 25 Jan. 2011, doi:10.2147/IJGM.S15618

35. Julius, M et al. "Glutathione and morbidity in a community-based sample of elderly." *Journal of clinical epidemiology* vol. 47,9 (1994): 1021-6. doi:10.1016/0895-4356(94)90117-1

36. Weschawalit, Sinee et al. "Glutathione and its antiaging and antimelanogenic effects." *Clinical, cosmetic and investigational dermatology* vol. 10 147-153. 27 Apr. 2017, doi:10.2147/CCID.S128339

37. Karlic, Heidrun, and Alfred Lohninger. "Supplementation of L-carnitine in athletes: does it make sense?." Nutrition (Burbank, Los Angeles County, Calif.) vol. 20,7-8 (2004): 709-15. doi:10.1016/j.nut.2004.04.003

38. Bianchetti, A et al. "Effects of acetyl-L-carnitine in Alzheimer's disease patients unresponsive to acetylcholinesterase inhibitors." *Current medical research and opinion* vol. 19,4 (2003): 350-3. doi:10.1185/030079903125001776

39. *Ketorolac for Pain Management: A Review of the Clinical Evidence*. Canadian Agency for Drugs and Technologies in Health, 30 June 2014.