Micronutrient Effects on Testosterone Concentrations

Subjects: Nutrition & Dietetics

Contributor: Jay Hoffman

This entry discusses the role of both micro and macronutrients on endogenous testosterone production

Testosterone Concentrations Vitamin D

1. Micronutrient Effects on Testosterone Concentrations

1.1. Vitamin D

Vitamin D is a micronutrient that also acts as a prohormone [1]. Vitamin D has garnered considerable attention in the general and competitive athletic populations, primarily due to its role on various physiological systems in the body, and the effect that vitamin D deficiency has on many diseases [2][3]. Vitamin D has two biological forms, vitamin D3 (cholecalciferol), and vitamin D2 (ergocalciferol). Vitamin D3 is the most bioavailable and most supplemented form of Vitamin D and is synthesized in the skin upon exposure to sunlight. The specific physiological effects of vitamin D and its specific mechanisms are beyond the scope of this paper, but readers are encouraged to explore this elsewhere [4][5]. In brief, vitamin D, whether it is synthesized endogenously or consumed as a food or supplement, undergoes hydroxylation to become active. The first hydroxylation step occurs in the liver where vitamin D is converted to 25-hydroxyvitamin D [25(OH)D]. The second hydroxylation step is performed primarily in the kidney to form 1,25-dihydroxyvitamin D3, also referred to as 1,25-dihydroxycholecalciferol, which is the biologically active form of vitamin D [6][7]. The United States Institute of Medicine has indicated that the range for vitamin D concentrations should be between 25–50 nmol·L^{-1} [8]. Studies on athletes have suggested that the cut-off for vitamin D deficiency should be > 30 nmol·L^{-1} or even higher [1][9][10].

The vitamin D receptor, which plays a central role in the biological action of the vitamin, has been observed in reproductive tissues such as the ovaries, prostate, and testes, as well as in human sperm [11][12][13][14]. Vitamin D receptors are present on the Leydig cells within the testes, where the synthesis of testosterone from cholesterol occurs [15], suggesting an important role of vitamin D on testosterone synthesis. Men with vitamin D deficiency have exhibited significantly lower testosterone concentrations compared to men with normal vitamin D concentrations [16]. Significant associations were also noted between vitamin D concentrations and circulating testosterone and SHBG concentrations, as well as the free androgen index [16]. These findings are consistent with subsequent investigations reporting significant correlations between vitamin D and testosterone concentrations [16][17][18].

Athletes in general are at a higher risk for vitamin D deficiency, especially athletes participating in indoor sports [10][19][20][21]. Vitamin D supplementation is a potential option to maintain normal vitamin D status, but also to potentially increase testosterone concentrations. A double-blind, randomized placebo-control trial of 54 males reported that the group receiving a daily supplementation of 83 µg (3332 IU) of vitamin D for 12 months experienced significant increases in circulating 25-hydroxyvitamin D, TT, and FT concentrations compared to the placebo group [22] (described in **Table 1**). Although it has been suggested that the daily dose of vitamin D supplementation for athletes should be 5000 IU·day^{-1} for improving performance and restoring vitamin D levels [9][23][24], no consensus exists regarding the optimal range for vitamin D levels [8]. Furthermore, the effect of vitamin D supplementation on altering resting testosterone concentrations is still not well understood and requires further research.

1.2. Zinc

Zinc is a mineral that influences and interacts with many biological systems, especially the endocrine system [25]. Zinc has an important role in immune system function and in modulating inflammatory processes [26][27][28][29]. While zinc can be found in many food sources, the more bioavailable form of zinc can be found in animal tissues [30][31][32][33]. The daily recommended intake for zinc is between 14–40 mg·day^{-1} [34]. The physiological role of zinc regarding testosterone biology is related to its requirement in the synthesis and secretion of LH. As previously discussed, LH stimulates testosterone synthesis in the Leydig cells [35][36][37]. Zinc is also important in the conversion of testosterone to DHT [37]. DHT is converted from testosterone by the enzyme 5α—reductase in the cytoplasm of the cell. DHT is primarily found in peripheral tissues such as prostate, skin, hair follicles, and the liver [35][38]. As discussed earlier, DHT is thought to have a stronger androgenic affect than testosterone due to its four-times greater binding affinity for the androgen receptor than testosterone and a three-times slower dissociation rate than testosterone [39][40][41]. DHT has a vital role in the sexual development of males and sexual differentiation of organs and promotes prostate growth; male pattern baldness; and body, facial, and pubic hair growth [35][38][42].

Zinc also has an indirect role in testosterone synthesis. Zinc is required for normal function of angiotensin-converting enzyme (ACE), a zinc-dependent dicarboxypeptidase, which has a zinc binding site in its cyclitic domain [43][44]. ACE is reported to increase LH production in pituitary, thus impacting androgen production [45]. Zinc deficiency can impair testosterone synthesis and has been demonstrated to correlate with reductions in testosterone concentrations [46][47][48]. Competitive athletes appear to be at a greater risk for zinc deficiency compared to the general population [49][50]. Considering that zinc deficiency appears to be related to hypogonadism, efforts to maintain zinc levels within normal ranges appears important. Several studies have shown that zinc supplementation can restore testosterone concentrations to their normal physiological range [46][47][51]. One study examined the effect of zinc supplementation on both TT and FT concentrations in healthy young adults before and after an exhaustive exercise protocol [52]. Study participants were supplemented with zinc sulfate (3mg·kg·day^{-1}) for four weeks. Investigators reported that zinc supplementation increased both TT and FT concentrations prior to and following the exhaustive exercise protocol compared to pre-supplementation results. In contrast, others reported no difference in either the TT or FT response to exhaustive exercise between male cyclists supplemented with zinc sulfate (30 mg) for four weeks compared to a placebo-controlled group [53].

Although zinc has an important role in the regulation of testosterone production, long-term studies in competitive athletes have not been conducted. Whether zinc supplementation is effective only during periods of zinc deficiency or whether it can augment normal testosterone concentrations regardless of baseline concentrations is not well understood.

2. Magnesium

Magnesium is one of the most abundant minerals in the body. It has an important role in various biological systems including protein synthesis, cellular energy production, cell growth, and reproduction [54]. From an athletic performance perspective, magnesium is involved in skeletal muscle function and energy production, suggesting a possible ergogenic effect [55]. The recommended dietary allowance for magnesium intake for men is between 400 to 420 mg·day^{-1} and 310 to 320 mg·day^{-1} for women [56]. Several studies have reported that athletes do not consume enough magnesium from their diet, resulting in a greater risk for magnesium deficiency [57][58][59][60]. Several investigations have reported a relationship between magnesium and testosterone concentrations [61][62][63]. One study indicated that magnesium supplementation in young healthy men in combination with a four-week endurance training program increased both FT and TT concentrations at rest and following exhaustive exercise [64]. An additional study conducted on nearly 400 older adult men reported a significant correlation between magnesium status and testosterone concentrations ($r = 0.20$, $p < 0.05$) [62]. The mechanism responsible for this relationship has yet to be elucidated. However, it is possible that it may be more indirect than direct. Magnesium is known to have a role in decreasing oxidative stress and inflammation [65][66][67]. Considering that testosterone concentrations can be strongly influenced by oxidative stress [68], it is possible that magnesium's role in decreasing oxidative stress may provide the stimulus to maintain testosterone concentrations during periods of oxidative stress. A strong positive correlation has been reported between total antioxidative capacity and testosterone concentrations ($r = 0.807$) [68]. Magnesium has an important role in maintaining antioxidant capacity and controlling oxidative stress [65][66][67]. Magnesium deficiency has been demonstrated to increase production of oxygen free radicals, increase oxidative tissue damage, decrease antioxidant enzyme activity, decrease cellular antioxidant levels, and increase oxygen peroxide production [69][70][71]. In contrast, normal magnesium levels can prevent oxygen radical formation by removing free radicals and inhibiting xanthine oxidase and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase elevations [72].

Magnesium deficiency has also been associated with low-grade systemic inflammation [65][73], and has been shown to increase pro-inflammatory cytokines: tumor necrosis factor-alpha (TNF-α) and interleukin 1 (IL-1) [73][74][75]. Low-grade chronic inflammation has been shown to decrease testosterone concentrations by suppressing testosterone secretion from Leydig cells, resulting in both an inhibitory effect on LH secretion and reduced LH sensitivity at the Leydig cell [76][77]. Increases in TNF-α activates nuclear factor κB (NF-κB), a transcription factor that governs the expression of early-response genes involved in cellular responses to a wide range of signals [78]. NF-κB inhibits the activation of steroidogenic-enzyme genes such as Nur77 and SF-1, which regulate steroidogenesis (biosynthesis of testosterone from cholesterol) in the Leydig cells [77]. Rochelson and colleagues [79] demonstrated, through an in vitro examination, that magnesium sulfate can reduce the nuclear translocation of NF-κB. Others have

demonstrated that magnesium supplementation can reduce inflammatory status and decrease levels of TNF-α and IL-1 [73][80].

Magnesium also appears to reduce the binding of testosterone to SHBG [81]. Most circulating testosterone is bound to SHBG; however, the bioavailability of testosterone is related to the free testosterone concentrations, which is only a fraction of circulating testosterone [82]. Magnesium appears to bind to SHBG resulting in the blocking of testosterone's ability to bind to SHBG, subsequently enhancing testosterone bioavailability. Magnesium deficiency appears to increase testosterone binding to SHBG, potentially decreasing its bioavailability [81]. Whether magnesium supplementation is effective in augmenting testosterone synthesis as an anabolic agent is not well understood.

Table 1. Effect of micronutrient intake on circulating testosterone concentrations.

Source	Participants	Duration	Intervention	Key Findings
[52]	*n* = 10 Healthy college-aged men	4 weeks	• Zinc supplementation group (zinc sulfate 3 mg·kg·day^{-1})	• Significantly elevation of TT and FT before and after an exhaustive exercise protocol compared to pre-supplementation. • ES before the exhaustive exercise protocol TT = 0.59 FT = 1.32 • ES after the exhaustive exercise protocol TT = 0.82, FT = 3.32
[22]	*n* = 54 Healthy overweight men	12 months	• Vitamin D supplementation group (*n* = 31): 83 µg·day^{-1} (3332 IU) • Placebo group (*n* = 23)	• Significant increase in TT and FT in the vitamin D group compared to baseline. • ES for TT in the VD group = 0.63 • ES for FT in the VD group = 0.54
[53]	*n* = 32 Male cyclists	4 weeks	• Zinc supplementation group n = 8 (30 mg·day^{-1}) • Selenium supplementation n = 8	• No significant differences between groups for TT and FT before and after the exhaustive exercise test.

Source	Participants	Duration	Intervention	Key Findings
			(Se, 200 µg sodium selenite) • zinc–selenium *n* = 8 (Zn–Se, 30 mg zinc sulfate–200 µg selenium selenite) • Placebo group *n* = 8 (30 mg·day^{-1})	
[64]	*n* = 30 Healthy college-aged men participating in an aerobic -training program	4 weeks	• Magnesium supplementation + training group *n* = 10 ($MgSO_4$ 10 mg·kg·day^{-1}) • Magnesium supplementation group only *n* = 10 • Training group only *n* = 10	• Significant increase in total and free testosterone concentrations before and after exhaustive exercise in the group who supplemented with magnesium and trained compared the other groups. • ES before TT = 0.37 • ES after TT = 0.46 • ES before FT = 1.11 • ES after FT = 0.45

FT = Free testosterone; TT = total testosterone; ES = effect size. Effect size was estimated as (mean 2 − mean 1)/pooled standard deviation.

1. Bendik, I.; Friedel, A.; Roos, F.F.; Weber, P.; Eggersdorfer, M. Vitamin D: A critical and essential micronutrient for human health. Front. Physiol. 2014, 5, 248.
2. Zhang, R.; Naughton, D.P. Vitamin D in health and disease: Current perspectives. Nutr. J. 2010, 9, 65.
3. Holick, M.F.; Binkley, N.C.; Bischoff-Ferrari, H.; Gordon, C.M.; Hanley, D.A.; Heaney, R.P.; Murad, M.H.; Weaver, C.M. Guidelines for Preventing and Treating Vitamin D Deficiency and Insufficiency Revisited. J. Clin. Endocrinol. Metab. 2012, 97, 1153–1158.
4. Bikle, D.D. Vitamin D Metabolism, Mechanism of Action, and Clinical Applications. Chem. Biol. 2014, 21, 319–329.
5. de la Puente Yagüe, M.; Collado Yurrita, L.; Cuadrado Cenzual, M.A. Faculty Opinions recommendation of Role of vitamin D in athletes and their performance: Current concepts and new trends. Fac. Opin. Post-Publ. Peer Rev. Biomed. Lit. 2020, 12, 579.
6. Lips, P. Vitamin D physiology. Prog. Biophys. Mol. Biol. 2006, 92, 4–8.

7. Tripkovic, L.; Lambert, H.; Hart, K.; Smith, C.P.; Bucca, G.; Penson, S.; Chope, G.; Hypponen, E.; Berry, J.; Vieth, R.; et al. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: A systematic review and meta-analysis. Am. J. Clin. Nutr. 2012, 95, 1357–1364.
8. Ross, A.C.; Manson, J.E.; Abrams, S.A.; Aloia, J.F.; Brannon, P.M.; Clinton, S.K.; Durazo-Arvizu, R.A.; Gallagher, J.C.; Gallo, R.L.; Jones, G.; et al. The 2011 Report on Dietary Reference Intakes for Calcium and Vitamin D from the Institute of Medicine: What Clinicians Need to Know. J. Clin. Endocrinol. Metab. 2011, 96, 53–58.
9. Jung, H.C.; Seo, M.W.; Lee, S.; Jung, S.W.; Song, J.K. Correcting Vitamin D Insufficiency Improves Some But Not All Aspects of Physical Performance During Winter Training in Taekwondo Athletes. Int. J. Sport Nutr. Exerc. Metab. 2018, 28, 635–643.
10. Farrokhyar, F.; Tabasinejad, R.; Dao, D.; Peterson, D.; Ayeni, O.R.; Hadioonzadeh, R.; Bhandari, M. Prevalence of Vitamin D Inadequacy in Athletes: A Systematic-Review and Meta-Analysis. Sports Med. 2015, 45, 365–378.
11. Habib, F.; Maddy, S.; Gelly, K. Characterisation of receptors for 1,25-dihydroxyvitamin D3 in the human testis. J. Steroid Biochem. 1990, 35, 195–199.
12. Johnson, J.A.; Grande, J.P.; Roche, P.C.; Kumar, R. Immunohistochemical detection and distribution of the 1,25-dihydroxyvitamin D3 receptor in rat reproductive tissues. Histochem. Cell Biol. 1996, 105, 7–15.
13. Aquila, S.; Guido, C.; Perrotta, I.; Tripepi, S.; Nastro, A.; Andò, S. Human sperm anatomy: Ultrastructural localization of 1α,25-dihydroxyvitamin D3 receptor and its possible role in the human male gamete. J. Anat. 2008, 213, 555–564.
14. Wang, Y.; Zhu, J.; DeLuca, H.F. Where is the vitamin D receptor? Arch. Biochem. Biophys. 2012, 523, 123–133.
15. O’Donnell, L.; Stanton, P.; de Kretser, D.M. Endocrinology of the Male Reproductive System and Spermatogenesis; Feingold, K.R., Anawalt, B., Boyce, A., Chrousos, G., de Herder, W.W., Dhatariya, K., Dungan, K., Grossman, A., Hershman, J.M., Hofland, J., et al., Eds.; Endotext ; MDText.com, Inc.: South Dartmouth, MA, USA, 2000.
16. Wehr, E.; Pilz, S.; Boehm, B.O.; MãRz, W.; Obermayer-Pietsch, B. Association of vitamin D status with serum androgen levels in men. Clin. Endocrinol. 2009, 73, 243–248.
17. Lee, D.M.; Tajar, A.; Pye, S.R.; Boonen, S.; Vanderschueren, D.; Bouillon, R.; O’Neill, T.W.; Bartfai, G.; Casanueva, F.F.; Finn, J.D.; et al. Association of hypogonadism with vitamin D status: The European Male Ageing Study. Eur. J. Endocrinol. 2012, 166, 77–85.
18. Nimptsch, K.; Platz, E.A.; Willett, W.C.; Giovannucci, E. Association between plasma 25-OH vitamin D and testosterone levels in men. Clin. Endocrinol. 2012, 77, 106–112.

19. Close, G.; Russell, J.; Cobley, J.; Owens, D.; Wilson, G.; Gregson, W.; Fraser, W.; Morton, J. Assessment of vitamin D concentration in non-supplemented professional athletes and healthy adults during the winter months in the UK: Implications for skeletal muscle function. J. Sports Sci. 2013, 31, 344–353.
20. Farrokhyar, F.; Sivakumar, G.K.; Savage, K.; Koziarz, A.; Jamshidi, S.; Ayeni, O.R.; Peterson, D.; Bhandari, M. Effects of Vitamin D Supplementation on Serum 25-Hydroxyvitamin D Concentrations and Physical Performance in Athletes: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Sports Med. 2017, 47, 2323–2339.
21. Dubnov-Raz, G.; Livne, N.; Raz, R.; Cohen, A.H.; Constantini, N.W. Vitamin D Supplementation and Physical Performance in Adolescent Swimmers. Int. J. Sport Nutr. Exerc. Metab. 2015, 25, 317–325.
22. Pilz, S.; Frisch, S.; Koertke, H.; Kuhn, J.; Dreier, J.; Obermayer-Pietsch, B.; Wehr, E.; Zittermann, A. Effect of Vitamin D Supplementation on Testosterone Levels in Men. Horm. Metab. Res. 2010, 43, 223–225.
23. Dahlquist, D.T.; Dieter, B.P.; Koehle, M.S. Plausible ergogenic effects of vitamin D on athletic performance and recovery. J. Int. Soc. Sports Nutr. 2015, 12, 1–12.
24. He, C.-S.; Fraser, W.D.; Tang, J.; Brown, K.; Renwick, S.; Rudland-Thomas, J.; Teah, J.; Tanqueray, E.; Gleeson, M. The effect of 14 weeks of vitamin D 3 supplementation on antimicrobial peptides and proteins in athletes. J. Sports Sci. 2015, 34, 1–8.
25. Baltaci, A.K.; Mogulkoc, R.; Baltaci, S.B. Review: The role of zinc in the endocrine system. Pak. J. Pharm. Sci. 2019, 32, 231–239.
26. 135. Micheletti, A.; Rossi, R.; Rufini, S. Zinc status in athletes: Relation to diet and exercise. Sports Med. 2001, 31, 577–582.
27. Miranda, E.R.; Dey, C.S. Effect of Chromium and Zinc on Insulin Signaling in Skeletal Muscle Cells. Biol. Trace Elem. Res. 2004, 101, 19–36.
28. Foster, M.; Samman, S. Zinc and Regulation of Inflammatory Cytokines: Implications for Cardiometabolic Disease. Nutrients 2012, 4, 676–694.
29. König, D.; Weinstock, C.; Keul, J.; Northoff, H.; Berg, A. Zinc, iron, and magnesium status in athletes--influence on the regulation of exercise-induced stress and immune function. Exerc. Immunol. Rev. 1998, 4, 2–21.
30. Freeland-Graves, J.H.; Ebangit, M.L.; Bodzy, P.W. Zinc and copper content of foods used in vegetarian diets. J. Am. Diet. Assoc. 1980, 77, 648–654.
31. Foster, M.; Chu, A.; Petocz, P.; Samman, S. Effect of vegetarian diets on zinc status: A systematic review and meta-analysis of studies in humans. J. Sci. Food Agric. 2013, 93, 2362–2371.

32. Hunt, J.R.; Matthys, L.A.; Johnson, L.K. Zinc absorption, mineral balance, and blood lipids in women consuming controlled lactoovovegetarian and omnivorous diets for 8 wk. Am. J. Clin. Nutr 1998, 67, 421–430.

33. Maret, W.; Sandstead, H.H. Zinc requirements and the risks and benefits of zinc supplementation. J. Trace Elem. Med. Biol. 2006, 20, 3–18.

34. 143. Trumbo, P.; Yates, A.A.; Schlicker, S.; Poos, M. Dietary reference intakes: Vitamin A, Vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. J. Am. Diet. Assoc. 2001, 101, 294–301.

35. Hoffman, J.R.; Kraemer, W.J.; Bhasin, S.; Storer, T.; Ratamess, N.A.; Haff, G.G.; Willoughby, D.S.; Rogol, A.D. Position stand on androgen and human growth hormone use. J. Strength Cond. Res. 2009, 23, S1–S59.

36. Wrzosek, M.; Woźniak, J.; Włodarek, D. The causes of adverse changes of testosterone levels in men. Expert Rev. Endocrinol. Metab. 2020, 15, 355–362.

37. Om, A.-S.; Chung, K.-W. Dietary Zinc Deficiency Alters 5α-Reduction and Aromatization of Testosterone and Androgen and Estrogen Receptors in Rat Liver. J. Nutr. 1996, 126, 842–848.

38. Swerdloff, R.S.; Dudley, R.E.; Page, S.T.; Wang, C.; Salameh, W. Dihydrotestosterone: Biochemistry, Physiology, and Clinical Implications of Elevated Blood Levels. Endocr. Rev. 2017, 38, 220–254.

39. Grino, P.B.; Griffin, J.E.; Wilson, J.D. Testosterone at High Concentrations Interacts with the Human Androgen Receptor Similarly to Dihydrotestosterone*. Endocrinol. 1990, 126, 1165–1172.

40. Gao, W.; Bohl, C.E.; Dalton, J.T. Chemistry and Structural Biology of Androgen Receptor. Chem. Rev. 2005, 105, 3352–3370.

41. Wilson, E.M.; French, F.S. Binding properties of androgen receptors. Evidence for identical receptors in rat testis, epididymis, and prostate. J. Biol. Chem. 1976, 251, 5620–5629.

42. Marchetti, P.M.; Barth, J.H. Clinical biochemistry of dihydrotestosterone. Ann. Clin. Biochem. 2013, 50, 95–107.

43. Bernstein, K.E.; Khan, Z.; Giani, J.F.; Cao, D.-Y.; Bernstein, E.A.; Shen, X.Z. Angiotensin-converting enzyme in innate and adaptive immunity. Nat. Rev. Nephrol. 2018, 14, 325–336.

44. Towler, P.; Staker, B.; Prasad, S.G.; Menon, S.; Tang, J.; Parsons, T.; Ryan, D.; Fisher, M.; Williams, D.; Dales, N.A.; et al. ACE2 X-Ray Structures Reveal a Large Hinge-bending Motion Important for Inhibitor Binding and Catalysis. J. Biol. Chem. 2004, 279, 17996–18007.

45. Kwok, T.; Ohlsson, C.; Vandenput, L.; Tang, N.; Zhang, Y.; Tomlinson, B.; Leung, P. ACE inhibitor use was associated with lower serum dehydroepiandrosterone concentrations in older men. Clin. Chim. Acta 2010, 411, 1122–1125.

46. Prasad, A.S.; Mantzoros, C.S.; Beck, F.W.; Hess, J.W.; Brewer, G.J. Zinc status and serum testosterone levels of healthy adults. Nutrition 1996, 12, 344–348.
47. Jalali, G.R.; Roozbeh, J.; Mohammadzadeh, A.; Sharifian, M.; Sagheb, M.M.; Jahromi, A.H.; Shabani, S.; Ghaffarpasand, F.; Afshariani, R. Impact of oral zinc therapy on the level of sex hormones in male patients on hemodialysis. Ren. Fail. 2010, 32, 417–419.
48. Santos, H.O.; Teixeira, F. Use of medicinal doses of zinc as a safe and efficient coadjutant in the treatment of male hypogonadism. Aging Male 2020, 23, 669–678.
49. McClung, J.P. Iron, Zinc, and Physical Performance. Biol. Trace Elem. Res. 2018, 188, 135–139.
50. Chu, A.; Holdaway, C.; Varma, T.; Petocz, P.; Samman, S. Lower Serum Zinc Concentration Despite Higher Dietary Zinc Intake in Athletes: A Systematic Review and Meta-analysis. Sports Med. 2017, 48, 327–336.
51. Koehler, K.; Parr, M.K.; Geyer, H.; Mester, J.; Schänzer, W. Serum testosterone and urinary excretion of steroid hormone metabolites after administration of a high-dose zinc supplement. Eur. J. Clin. Nutr. 2007, 63, 65–70.
52. Kilic, M. Effect of fatiguing bicycle exercise on thyroid hormone and testosterone levels in sedentary males supplemented with oral zinc. Neuro Endocrinol. Lett. 2007, 28, 681–685.
53. Shafiei Neek, L.; Gaeini, A.A.; Choobineh, S. Effect of zinc and selenium supplementation on serum testosterone and plasma lactate in cyclist after an exhaustive exercise bout. Biol. Trace Elem. Res. 2011, 144, 454–462.
54. Volpe, S.L. Magnesium in Disease Prevention and Overall Health. Adv. Nutr. 2013, 4, 378S–383S.
55. Volpe, S.L. Magnesium and the Athlete. Curr. Sports Med. Rep. 2015, 14, 279–283.
56. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. National Academies Press: Washington, DC, USA, 1997.
57. de Sousa, E.F.; Da Costa, T.H.; Nogueira, J.A.; Vivaldi, L.J. Assessment of nutrient and water intake among adolescents from sports federations in the Federal District, Brazil. Br. J. Nutr. 2008, 99, 1275–1283.
58. Juzwiak, C.R.; Amancio, O.M.S.; Vitalle, M.S.S.; Pinheiro, M.M.; Szejnfeld, V.L. Body composition and nutritional profile of male adolescent tennis players. J. Sports Sci. 2008, 26, 1209–1217.
59. Heaney, S.; O'Connor, H.; Gifford, J.; Naughton, G. Comparison of strategies for assessing nutritional adequacy in elite female athletes' dietary intake. Int. J. Sport Nutr. Exerc. Metab. 2010, 20, 245–256.

60. Silva, M.R.; Paiva, T. Low energy availability and low body fat of female gymnasts before an international competition. Eur. J. Sport Sci. 2015, 15, 591–599.
61. Maggio, M.; De Vita, F.; Lauretani, F.; Nouvenne, A.; Meschi, T.; Ticinesi, A.; Dominguez, L.J.; Barbagallo, M.; Dall'Aglio, E.; Ceda, G.P. The Interplay between Magnesium and Testosterone in Modulating Physical Function in Men. Int. J. Endocrinol. 2014, 2014, 1–9.
62. Maggio, M.; Ceda, G.P.; Lauretani, F.; Cattabiani, C.; Avantaggiato, E.; Morganti, S.; Ablondi, F.; Bandinelli, S.; Dominguez, L.J.; Barbagallo, M.; et al. Magnesium and anabolic hormones in older men. Int. J. Androl. 2011, 34, e594–e600.
63. Rotter, I.; Kosik-Bogacka, D.; Dołęgowska, B.; Safranow, K.; Karakiewicz, B.; Laszczyńska, M. Relationship between serum magnesium concentration and metabolic and hormonal disorders in middle-aged and older men. Magnes. Res. 2015, 28, 99–107.
64. Cinar, V.; Polat, Y.; Baltaci, A.K.; Mogulkoc, R. Effects of magnesium supplementation on testosterone levels of athletes and sedentary subjects at rest and after exhaustion. Biol. Trace Elem. Res. 2011, 140, 18–23.
65. Barbagallo, M.; Dominguez, L.J. Magnesium and Aging. Curr. Pharm. Des. 2010, 16, 832–839.
66. Dickens, B.; Weglicki, W.; Li, Y.-S.; Mak, I. Magnesium deficiency in vitro enhances free radical-induced intracellular oxidation and cytotoxicity in endothelial cells. FEBS Lett. 1992, 311, 187–191.
67. Freedman, A.M.; Mak, I.T.; Stafford, R.E.; Dickens, B.F.; Cassidy, M.M.; Muesing, R.A.; Weglicki, W.B. Erythrocytes from magnesium-deficient hamsters display an enhanced susceptibility to oxidative stress. Am. J. Physiol. Physiol. 1992, 262, C1371–C1375.
68. Demirbag, R.; Yilmaz, R.; Erel, O. The association of total antioxidant capacity with sex hormones. Scand. Cardiovasc. J. 2005, 39, 172–176.
69. Blache, D.; Devaux, S.; Joubert, O.; Loreau, N.; Schneider, M.; Durand, P.; Prost, M.; Gaume, V.; Adrian, M.; Laurant, P.; et al. Long-term moderate magnesium-deficient diet shows relationships between blood pressure, inflammation and oxidant stress defense in aging rats. Free. Radic. Biol. Med. 2006, 41, 277–284.
70. Hans, C.P.; Chaudhary, D.P.; Bansal, D.D. Effect of magnesium supplementation on oxidative stress in alloxanic diabetic rats. Magnes. Res. 2003, 16, 13–19.
71. Yang, Y.; Wu, Z.; Chen, Y.; Qiao, J.; Gao, M.; Yuan, J.; Nie, W.; Guo, Y. Magnesium Deficiency Enhances Hydrogen Peroxide Production and Oxidative Damage in Chick Embryo Hepatocyte In Vitro. BioMetals 2006, 19, 71–81.
72. Afanas'Ev, I.B.; Suslova, T.B.; Cheremisina, Z.P.; Abramova, N.E.; Korkina, L.G. Study of antioxidant properties of metal aspartates. Analyst 1995, 120, 859–862.

73. Nielsen, F.H.; Johnson, L.K.; Zeng, H. Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. Magnes. Res. 2011, 23, 158–168.
74. Weglicki, W.B.; Dickens, B.F.; Wagner, T.L.; Chmielinska, J.J.; Phillips, T.M. Immunoregulation by neuropeptides in magnesium deficiency: Ex vivo effect of enhanced substance P production on circulating T lymphocytes from magnesium-deficient mice. Magnes. Res. 1996, 9, 3–11.
75. Nielsen, F.H.; Lukaski, H.C. Update on the relationship between magnesium and exercise. Magnes. Res. 2006, 19, 180–189.
76. I Spratt, D.; Orav, J.; Moloney, J.; Bigos, T.; Cox, P. Reproductive axis suppression in acute illness is related to disease severity. J. Clin. Endocrinol. Metab. 1993, 76, 1548–1554.
77. Hong, C.Y.; Park, J.H.; Ahn, R.S.; Im, S.Y.; Choi, H.-S.; Soh, J.; Mellon, S.H.; Lee, K. Molecular Mechanism of Suppression of Testicular Steroidogenesis by Proinflammatory Cytokine Tumor Necrosis Factor Alpha. Mol. Cell. Biol. 2004, 24, 2593–2604.
78. Lawrence, T. The nuclear factor NF-kappaB pathway in inflammation. Cold. Spring Harb. Perspect. Biol. 2009, 1, a001651.
79. Rochelson, B.; Dowling, O.; Schwartz, N.; Metz, C.N. Magnesium sulfate suppresses inflammatory responses by human umbilical vein endothelial cells (HuVECs) through the NFkappaB pathway. J. Reprod. Immunol. 2007, 73, 101–107.
80. Steward, C.J.; Zhou, Y.; Keane, G.; Cook, M.D.; Liu, Y.; Cullen, T. One week of magnesium supplementation lowers IL-6, muscle soreness and increases post-exercise blood glucose in response to downhill running. Graefe’s Arch. Clin. Exp. Ophthalmol. 2019, 119, 2617–2627.
81. Excoffon, L.; Guillaume, Y.; Woronoff-Lemsi, M.; André, C. Magnesium effect on testosterone–SHBG association studied by a novel molecular chromatography approach. J. Pharm. Biomed. Anal. 2009, 49, 175–180.
82. Emadi-Konjin, P.; Bain, J.; Bromberg, I.L. Evaluation of an algorithm for calculation of serum “bioavailable” testosterone (BAT). Clin. Biochem. 2003, 36, 591–596.