

## Modern Day Human Magnesium Requirements: The RDN's Role

by Andrea Rosanoff, PhD, and Stella Lucia Volpe, PhD, RDN, ACSM-CEP, FACSM

### References

#### Slide 4

1. Storer AC, Cornish-Bowden A. Concentration of MgATP<sup>2-</sup> and other ions in solution. Calculation of the true concentrations of species present in mixtures of associating ions. *Biochem J*. 1976;159(1):1-5.
2. Garfinkel L, Garfinkel D. Magnesium regulation of the glycolytic pathway and the enzymes involved. *Magnesium*. 1985;4(2-3):60-72.
3. Wilson JE, Chin A. Chelation of divalent cations by ATP, studied by titration calorimetry. *Anal Biochem*. 1991;193(1):16-19.
4. Volpe SL. Magnesium in disease prevention and overall health. *Adv Nutr*. 2013;4(3):378S-383S.
5. Abdelgawad IA, El-Mously RH, Saber MM, Mansour OA, Shouman SA. Significance of serum levels of vitamin D and some related minerals in breast cancer patients. *Int J Clin Exp Pathol*. 2015;8(4):4074-4082.
6. Romani AM. Magnesium in health and disease. *Met Ions Life Sci*. 2013;13:49-79.
7. Long S, Romani AM. Role of cellular magnesium in human diseases. *Austin J Nutr Food Sci*. 2014;2(10):1051.
8. Rubin H. Central roles of Mg<sup>2+</sup> and MgATP<sup>2-</sup> in the regulation of protein synthesis and cell proliferation: significance for neoplastic transformation. *Adv Cancer Res*. 2005;93:1-58.
9. George GA, Heaton FW. Effect of magnesium deficiency on energy metabolism and protein synthesis by liver. *Int J Biochem*. 1978;9(6):421-425.
10. Weisinger JR, Bellorin-Font E. Magnesium and phosphorus. *Lancet*. 1998;352(9125):391-396.
11. Dorup I, Skajaa K, Thybo NK. Oral magnesium supplementation restores the concentrations of magnesium, potassium and sodium-potassium pumps in skeletal muscle of patients receiving diuretic treatment. *J Intern Med*. 1993;233(2):117-123.
12. Fischer PW, Giroux A. Effects of dietary magnesium on sodium-potassium pump action in the heart of rats. *J Nutr*. 1987;117(12):2091-2095.

13. Fagher B, Sjögren A, Monti M. A microcalorimetric study of the sodium-potassium-pump and thermogenesis in human skeletal muscle. *Acta Physiol Scand*. 1987;131(3):355-360.
14. Flatman PW, Lew VL. The magnesium dependence of sodium-pump-mediated sodium-potassium and sodium-sodium exchange in intact human red cells. *J Physiol*. 1981;315:421-446.
15. Deng X, Song Y, Manson JE, et al. Magnesium, vitamin D status and mortality: results from US National Health and Nutrition Examination Survey (NHANES) 2001 to 2006 and NHANES III. *BMC Med*. 2013;11:187.
16. Rosanoff A, Dai Q, Shapses SA. Essential nutrient interactions: does low or suboptimal magnesium status interact with vitamin D and/or calcium status? *Adv Nutr*. 2016;7(1):25-43.
17. Rosanoff A, Seelig MS. Comparison of mechanism and functional effects of magnesium and statin pharmaceuticals. *J Am Coll Nutr*. 2004;23(5):501S-505S.
18. Zhang A, Carella A, Altura BT, Altura BM. Interactions of magnesium and chloride ions on tone and contractility of vascular muscle. *Eur J Pharmacol*. 1991;203(2):223-235.
19. Altura BM, Altura BT. Role of magnesium ions in contractility of blood vessels and skeletal muscles. *Magnesium Bull*. 1981;3(1a):102-114.
20. Konishi M. Cytoplasmic free concentrations of Ca<sup>2+</sup> and Mg<sup>2+</sup> in skeletal muscle fibers at rest and during contraction. *Jpn J Physiol*. 1998;48(6):421-438.
21. Yang Z, Wang J, Altura BT, Altura BM. Extracellular magnesium deficiency induces contraction of arterial muscle: role of PI3-kinases and MAPK signaling pathways. *Pflugers Arch*. 2000;439(3):240-247.
22. Yang ZW, Gebrewold A, Nowakowski M, Altura BT, Altura BM. Mg(2+)-induced endothelium-dependent relaxation of blood vessels and blood pressure lowering: role of NO. *Am J Physiol Regul Integr Comp Physiol*. 2000;278(3):R628-R639.
23. Yang ZW, Wang J, Zheng T, Altura BT, Altura BM. Low [Mg(2+)]<sub>o</sub> induces contraction and [Ca(2+)]<sub>i</sub> rises in cerebral arteries: roles of Ca(2+), PKC, and PI3. *Am J Physiol Heart Circ Physiol*. 2000;279(6):H2898-H2907.
24. Turlapaty PD, Altura BM. Magnesium deficiency produces spasms of coronary arteries: relationship to etiology of sudden death ischemic heart disease. *Science*. 1980;208(4440):198-200.
25. Workinger JL, Doyle RP, Bortz J. Challenges in the diagnosis of magnesium status. *Nutrients*. 2018;10(9):1202.

### **Slide 5**

26. Seelig MS, Rosanoff A. *The Magnesium Factor*. 1st ed. New York, NY: Avery Penguin Group; 2003:278-279; 369-370.

### **Slide 7**

27. Smith RM, Smith PA. An assessment of the composition and nutrient content of an Australian Aboriginal hunter-gather diet. *Australian Aboriginal Stud*. 2003;2:39-52.

28. Cullumbine H, Basnayake V, Lemottee J, Wickramanayake TW. Mineral metabolism on rice diets. *Br J Nutr*. 1950;4(2-3):101-111.

29. Kapil U, Verma D, Goel M, et al. Dietary intake of trace elements and minerals among adults in underprivileged communities of rural Rajasthan, India. *Asia Pacific J Clin Nutr*. 1998;7(1):29-32.

30. Abu-Saad K, Shai I, Kaufman-Shriqui V, German L, Vardi H, Fraser D. Bread type intake is associated with lifestyle and diet quality transition among Bedouin Arab adults. *Br J Nutr*. 2009;102(10):1513-1522.

31. Eaton SB, Eaton SB, 3rd. Paleolithic vs. modern diets — selected pathophysiological implications. *Eur J Nutr*. 2000;39(2):67-70.

### **Slide 8**

32. U.S Department of Agriculture ARS. WWIEA NHANES 2005-6 nutrient intakes from food, table 1 by gender and age: mean amounts consumed per individual, one day, NHANES 2005-2006. What We Eat in America.

[https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/0506/table\\_1\\_NIF\\_05.pdf](https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/0506/table_1_NIF_05.pdf). Published 2008.

### **Slide 9**

33. Resnick L. The cellular ionic basis of hypertension and allied clinical conditions. *Prog Cardiovasc Dis*. 1999;42(1):1-22.

34. Resnick LM. Ionic basis of hypertension, insulin resistance, vascular disease, and related disorders. The mechanism of “syndrome X.” *Am J Hypertens*. 1993;6(4):123S-134S.

35. Rosanoff A. Nutritional magnesium is associated with metabolic syndrome, cardiovascular disease and its risk factors, and other NCDs: a bibliography. Magnesium Education website.

<http://www.magnesiumeducation.com/the-mg-hypothesis-of-cardiovascular-disease-a-bibliography>

36. Rosanoff A, Weaver CM, Rude RK. Suboptimal magnesium status in the United States: are the health consequences underestimated? *Nutr Rev*. 2012;70(3):153-164.

37. Rosanoff A. Rising Ca:Mg intake ratio from food in USA Adults: a concern? *Magnesium Res.* 2010;23(4):S181-S193.

**Slide 10**

38. Rosanoff A. Rising Ca:Mg intake ratio from food in USA Adults: a concern? *Magnesium Res.* 2010;23(4):S181-S193.

**Slide 11**

39. Seelig MS, Rosanoff A. *The Magnesium Factor*. 1st ed. New York, NY: Avery Penguin Group; 2003:162, 342-350; see also Further Reading.

**Slide 12**

40. Pharmavite. Common drug classes, drug-nutrient depletions, & drug-nutrient interactions. Pharmavite website.  
[https://www.aafp.org/dam/AAFP/documents/about\\_us/sponsored\\_resources/Nature%20Made%20Handout.pdf](https://www.aafp.org/dam/AAFP/documents/about_us/sponsored_resources/Nature%20Made%20Handout.pdf). Published 2015.

41. Seelig MS, Rosanoff A. *The Magnesium Factor*. 1st ed. New York, NY: Avery Penguin Group; 2003:284-286.

**Slide 13**

42. Rosanoff A, Capron E, Barak P, Mathews B, Nielsen FH. Edible plant tissue and soil calcium:magnesium ratios: data too sparse to assess implications for human health. *Crop Pasture Sci.* 2015;66:1265-1277.

**Slide 15**

43. United States Department of Agriculture. USDA Food Composition Databases.  
<https://ndb.nal.usda.gov/ndb/>. Updated April 2018.

**Slide 19**

44. IOM. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington, D.C.: National Academy Press; 1997.

45. Seelig MS. The requirement of magnesium by the normal adult. *Am J Clin Nutr.* 1964;14:342-390.

46. Nielsen FH. The problematic use of dietary reference intakes to assess magnesium status and clinical importance. *Biol Trace Elem Res.* 2019;188(1):52-59.

**Slide 21**

47. Zhang X, Li Y, Del Gobbo LC, et al. Effects of magnesium supplementation on blood pressure: a meta-analysis of randomized double-blind placebo-controlled trials. *Hypertension.* 2016;68(2):324-333.

48. Chiu HY, Yeh TH, Huang YC, Chen PY. Effects of intravenous and oral magnesium on reducing migraine: a meta-analysis of randomized controlled trials. *Pain Physician*. 2016;19(1):E97-E112.
49. Bagis S, Karabiber M, As I, Tamer L, Erdogan C, Atalay A. Is magnesium citrate treatment effective on pain, clinical parameters and functional status in patients with fibromyalgia? *Rheumatol Int*. 2013;33(1):167-172.
50. Boyle NB, Lawton C, Dye L. The effects of magnesium supplementation on subjective anxiety and stress — a systematic review. *Nutrients*. 2017;9(5):429.
51. Tarleton EK, Littenberg B, MacLean CD, Kennedy AG, Daley C. Role of magnesium supplementation in the treatment of depression: a randomized clinical trial. *PLoS One*. 2017;12(6):e0180067.
52. Li B, Lv J, Wang W, Zhang D. Dietary magnesium and calcium intake and risk of depression in the general population: a meta-analysis. *Aust N Z J Psychiatry*. 2017;51(3):219-229.
53. Rajizadeh A, Mozaffari-Khosravi H, Yassini-Ardakani M, Dehghani A. Effect of magnesium supplementation on depression status in depressed patients with magnesium deficiency: a randomized, double-blind, placebo-controlled trial. *Nutrition*. 2017;35:56-60.
54. Aydin H, Deyneli O, Yavuz D, et al. Short-term oral magnesium supplementation suppresses bone turnover in postmenopausal osteoporotic women. *Biol Trace Elem Res*. 2010;133(2):136-143.
55. Doyle L, Flynn A, Cashman K. The effect of magnesium supplementation on biochemical markers of bone metabolism or blood pressure in healthy young adult females. *Eur J Clin Nutr*. 1999;53(4):255-261.
56. Cunha AR, D'El-Rei J, Medeiros F, et al. Oral magnesium supplementation improves endothelial function and attenuates subclinical atherosclerosis in thiazide-treated hypertensive women. *J Hypertens*. 2017;35(1):89-97.
57. Verma H, Garg R. Effect of magnesium supplementation on type 2 diabetes associated cardiovascular risk factors: a systematic review and meta-analysis. *J Hum Nutr Diet*. 2017;30(5):621-633.
58. Song Y, He K, Levitan EB, Manson JE, Liu S. Effects of oral magnesium supplementation on glycaemic control in Type 2 diabetes: a meta-analysis of randomized double-blind controlled trials. *Diabetes Med*. 2006;23(10):1050-1056.
59. Daniells S. Magnesium linked to fewer gallstones: increased intake of magnesium from dietary supplemental forms may decrease a man's risk of developing gallstones, suggests a

new study from the US. Decision News Media SAS.

<https://www.nutraingredients.com/Article/2008/02/26/Magnesium-linked-to-fewer-gallstones>.

Updated July 19, 2008.

60. Martynov AI, Stepura OB, Shekhter AB, Mel'nik OO, Pak LS, Ushakova TI. New approaches to the treatment of patients with idiopathic mitral valve prolapse. *Ter Arkh.* 2000;72(9):67-70.

61. Gu WJ, Wu ZJ, Wang PF, Aung LH, Yin RX. Intravenous magnesium prevents atrial fibrillation after coronary artery bypass grafting: a meta-analysis of 7 double-blind, placebo-controlled, randomized clinical trials. *Trials.* 2012;13:41.

62. Kohno H, Koyanagi T, Kasegawa H, Miyazaki M. Three-day magnesium administration prevents atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg.* 2005;79(1):117-126.

63. Miller S, Crystal E, Garfinkle M, Lau C, Lashevsky I, Connolly SJ. Effects of magnesium on atrial fibrillation after cardiac surgery: a meta-analysis. *Heart.* 2005;91(5):618-623.

#### **Slide 22**

64. Yuen AW, Sander JW. Can magnesium supplementation reduce seizures in people with epilepsy? A hypothesis. *Epilepsy Res.* 2012;100(1-2):152-156.

65. Osborn KE, Shytle RD, Frontera AT, Soble JR, Schoenberg MR. Addressing potential role of magnesium dyshomeostasis to improve treatment efficacy for epilepsy: a reexamination of the literature. *J Clin Pharmacol.* 2016;56(3):260-265.

66. Kirkland AE, Sarlo GL, Holton KF. The role of magnesium in neurological disorders. *Nutrients.* 2018;10(6):730.

67. Vink R. Magnesium in the CNS: recent advances and developments. *Magnesium Res.* 2016;29(3):95-101.

68. Rabadi MH, Blass JP. Randomized clinical stroke trials in 2006. *Curr Vasc Pharmacol.* 2008;6(1):61-66.

#### **Slide 25**

69. Costello R, Nielsen FH, Rosanoff A, Plesset M, Elin R. Monitoring the serum ca/mg ratio in response to magnesium supplementation. Paper presented at: International Magnesium Symposium XV; March 20-22, 2019, Bethesda, MD.

#### **Slide 26**

70. Rosanoff A. Magnesium supplements may enhance the effect of antihypertensive medications in stage 1 hypertensive subjects. *Magnesium Res.* 2010;23(1):27-40.

71. Zhang X, Li Y, Del Gobbo LC, et al. Effects of magnesium supplementation on blood pressure: a meta-analysis of randomized double-blind placebo-controlled trials. *Hypertension*. 2016;68(2):324-333.
72. Barbagallo M, Dominguez LJ, Galioto A, Pineo A, Belvedere M. Oral magnesium supplementation improves vascular function in elderly diabetic patients. *Magnesium Res*. 2010;23(3):131-137.
73. Joris PJ, Plat J, Bakker SJ, Mensink RP. Long-term magnesium supplementation improves arterial stiffness in overweight and obese adults: results of a randomized, double-blind, placebo-controlled intervention trial. *Am J Clin Nutr*. 2016;103(5):1260-1266.
74. Simental-Mendia LE, Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation decreases C-reactive protein levels in subjects with prediabetes and hypomagnesemia: a clinical randomized double-blind placebo-controlled trial. *Arch Med Res*. 2014;45(4):325-330.
75. Guerrero-Romero F, Rodriguez-Moran M. Magnesium improves the beta-cell function to compensate variation of insulin sensitivity: double-blind, randomized clinical trial. *Eur J Clin Invest*. 2011;41(4):405-410.
76. Guerrero-Romero F, Rodriguez-Moran M. The effect of lowering blood pressure by magnesium supplementation in diabetic hypertensive adults with low serum magnesium levels: a randomized, double-blind, placebo-controlled clinical trial. *J Hum Hypertens*. 2009;23(4):245-251.
77. Guerrero-Romero F, Tamez-Perez HE, Gonzalez-Gonzalez G, et al. Oral magnesium supplementation improves insulin sensitivity in non-diabetic subjects with insulin resistance. A double-blind placebo-controlled randomized trial. *Diabetes Metab*. 2004;30(3):253-258.
78. Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves the metabolic profile of metabolically obese, normal-weight individuals: a randomized double-blind placebo-controlled trial. *Arch Med Res*. 2014;45(5):388-393.
79. Lind L, Lithell H, Pollare T, Ljunghall S. Blood pressure response during long-term treatment with magnesium is dependent on magnesium status. A double-blind, placebo-controlled study in essential hypertension and in subjects with high-normal blood pressure. *Am J Hypertens*. 1991;4(8):674-679.
80. Paolisso G, Di Maro G, Cozzolino D, et al. Chronic magnesium administration enhances oxidative glucose metabolism in thiazide treated hypertensive patients. *Am J Hypertens*. 1992;5(10):681-686.

81. Plum-Wirell M, Stegmayr BG, Wester PO. Nutritional magnesium supplementation does not change blood pressure nor serum or muscle potassium and magnesium in untreated hypertension. A double-blind crossover study. **Magnesium Res.** 1994;7(3-4):277-283.

**Slide 27**

82. Baker SM. Magnesium in primary care and preventive medicine: clinical correlation of magnesium loading studies. **Magnesium Trace Elem.** 1991;10(2-4):251-262.

83. Bouida W, Beltaief K, Msolli MA, et al. Low dose magnesium sulfate versus high dose in the early management of rapid atrial fibrillation: randomised controlled double blind study (LOMAGHI Study). **Acad Emerg Med.** 2019;26(2):183-191.

84. Kass L, Rosanoff A, Tanner A, Sullivan K, McAuley W, Plesset M. Effect of transdermal magnesium cream on serum and urinary magnesium levels in humans: a pilot study. **PloS One.** 2017;12(4):e0174817.

**Slide 28**

85. Seelig MS, Rosanoff A. **The Magnesium Factor.** 1st ed. New York, NY: Avery Penguin Group; 2003:277-279; 369-370.

86. Lundberg GD. Magnesium deficiency: the real emperor of all maladies? Medscape website. <https://www.medscape.com/viewarticle/844214>. Published May 11, 2015.