

The Role of Nutrition Care in Mitochondrial Health

Presented by Robert Martindale, MD, PhD; Bret Goodpaster, PhD; Eduardo Chini, MD, PhD

References

- Allingstrup MJ, Kondrup J, Wiis J, et al. Early goal-directed nutrition versus standard of care in adult intensive care patients: The single-centre, randomised, outcome assessor-blinded EAT-ICU trial. *Intensive Care Med.* 2017;43(11):1637-1647.
- Aman Y, Qiu Y, Tao J, et al. Therapeutic potential of boosting NAD+ in aging and age-related diseases. *Transl Med Aging.* 2018;2:30-37.
- Amati F, Dubé JJ, Alvarez-Carnero E, et al. Skeletal muscle triglycerides, diacylglycerols, and ceramides in insulin resistance: Another paradox in endurance-trained athletes? *Diabetes.* 2011;60(10):2588-2597.
- Andreux PA, Blanco-Bose W, Ryu D, et al. The mitophagy activator urolithin A is safe and induces a molecular signature of improved mitochondrial and cellular health in humans. *Nat Metab.* 2019;1(6):595-603.
- Arabi YM, Aldawood AS, Haddad SH, et al. Permissive underfeeding or standard enteral feeding in critically ill adults. *N Engl J Med.* 2015;372:2398-2408.
- Ayres JS. A metabolic handbook for the COVID-19 pandemic. *Nat Metab.* 2020 Jul;2(7):572-585.
- Berger F, Ramírez-Hernández MH, Ziegler M. The new life of a centenarian: signalling functions of NAD(P). *Trends Biochem Sci.* 2004;29(3):111-118.
- Bloos F, Trips E, Nierhaus A, et al. Effect of sodium selenite administration and procalcitonin-guided therapy on mortality in patients with severe sepsis or septic shock: A randomized clinical trial. *JAMA Intern Med.* 2016;176(9):1266-1276.
- Bulluck H, Hausenloy DJ. Modulating NAD⁺ metabolism to prevent acute kidney injury. *Nat Med.* 2018;24(9):1306-1307.
- Buso A, Comelli M, Picco R, et al. Mitochondrial adaptations in elderly and young men skeletal muscle following 2 weeks of bed rest and rehabilitation. *Front Physiol.* 2019;10:474.
- Camacho-Pereira J, Tarragó MG, Chini CCS, et al. CD38 dictates age-related NAD decline and mitochondrial dysfunction through an sirt3-dependent mechanism. *Cell Metab.* 2016;23(6):1127-1139.
- Canner PL, Berge KG, Wenger NK, et al. Fifteen year mortality in Coronary Drug Project patients: long-term benefit with niacin. *J Am Coll Cardiol.* 1986;8(6):1245-1255.
- Cesari M, Cherubini A, Guralnik JM, Beresniak A, Rodriguez-Mañas L, Inzitari M, Walston J. Early detection of accelerated aging and cellular decline (AACD): A consensus statement. *Exp Gerontol.* 2021;146:111242.

The Role of Nutrition Care in Mitochondrial Health

Presented by Robert Martindale, MD, PhD; Bret Goodpaster, PhD; Eduardo Chini, MD, PhD

References Continued

Chini EN, Chini CCS, Espindola Netto JM, et al. The Pharmacology of CD38/NADase: An emerging target in cancer and diseases of aging. *Trends Pharmacol Sci.* 2018;39(4):424-436.

Chini EN. Of Mice and Men: NAD⁺ Boosting with niacin provides hope for mitochondrial myopathy patients. *Cell Metab.* 2020;31(6):1041-1043.

Conze D, Brenner C, Kruger CL. Safety and metabolism of long-term administration of niagen (nicotinamide riboside chloride) in a randomized, double-blind, placebo-controlled clinical trial of healthy overweight adults. *Sci Rep.* 2019;9(1):9772.

Dai DF, Chiao YA, Marcinek DJ, et al. Mitochondrial oxidative stress in aging and healthspan. *Longev Healthspan.* 2014;3:6.

de Mello AH, Costa AB, Engel JDG, Rezin GT. Mitochondrial dysfunction in obesity. *Life Sci.* 2018:26-32.
Distefano G, Standley RA, Dubé JJ, et al. Chronological age does not influence ex-vivo mitochondrial respiration and quality control in skeletal muscle. *J Gerontol A Biol Sci Med Sci.* 2017;72(4):535-542.

Else PL, Hulbert AJ. An allometric comparison of the mitochondria of mammalian and reptilian tissues: The implications for the evolution of endothermy. *J Comp Physiol B.* 1985;156(1):3-11.

Filler K, Lyon D, Bennett J, McCain N, et al. Association of mitochondrial dysfunction and fatigue: A review of the literature. *BBA Clin.* 2014;1:12-23.

Fowler AA 3rd, Truwit JD, Hite RD, et al. Effect of Vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: The CITRIS-ALI Randomized Clinical Trial. *JAMA.* 2019;322(13):1261-1270. Erratum in: *JAMA.* 2020;323(4):379. PMID: 31573637; PMCID: PMC6777268.

Garza-Lombó C, Pappa A, Panayiotidis MI, Franco R. Redox homeostasis, oxidative stress and mitophagy. *Mitochondrion.* 2020;51:105-117.

Goodpaster BH, Park SW, Harris TB, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci.* 2006;61(10):1059-1064.

Gould RL, Pazdro R. Impact of supplementary amino acids, micronutrients, and overall diet on glutathione homeostasis. *Nutrients.* 2019;11(5):1056.

Hogan KA, Chini CCS, Chini EN. The Multi-faceted Ecto-enzyme CD38: roles in immunomodulation, cancer, aging, and metabolic diseases. *Front Immunol.* 2019;10:1187.

The Role of Nutrition Care in Mitochondrial Health

Presented by Robert Martindale, MD, PhD; Bret Goodpaster, PhD; Eduardo Chini, MD, PhD

References Continued

- Jang JY, Blum A, Liu J, Finkel T. The role of mitochondria in aging. *J Clin Invest.* 2018;128(9):3662-3670.
- Jiang Q, Yin J, Chen J, Ma X, et al. Mitochondria-targeted antioxidants: A step towards disease treatment. *Oxid Med Cell Longev.* 2020;2020:8837893.
- Jones DP, Mody VC Jr, Carlson JL, Lynn MJ, Sternberg P Jr. Redox analysis of human plasma allows separation of pro-oxidant events of aging from decline in antioxidant defenses. *Free Radic Biol Med.* 2002;33(9):1290-1300.
- Kalghatgi S, Spina CS, Costello JC, et al. Bactericidal antibiotics induce mitochondrial dysfunction and oxidative damage in Mammalian cells. *Sci Transl Med.* 2013;5(192):192ra85.
- Li Y, Nourbakhsh N, Pham H, Tham R, et al. Evolution of altered tubular metabolism and mitochondrial function in sepsis-associated acute kidney injury. *Am J Physiol Renal Physiol.* 2020;319(2):F229-F244.
- Lou G, Palikaras K, Lautrup S, et al. Mitophagy and neuroprotection. *Trends Mol Med.* 2020;26(1):8-20.
- Marí M, de Gregorio E, de Dios C, et al. A. Mitochondrial glutathione: Recent insights and role in disease. *Antioxidants (Basel).* 2020;9(10):909.
- Massudi H, Grant R, Braidy N, Guest J, Farnsworth B, Guillemin GJ. Age-associated changes in oxidative stress and NAD⁺ metabolism in human tissue. *PLoS One.* 2012;7(7):e42357.
- McCarty MF, O'Keefe JH, DiNicolantonio JJ. Dietary glycine is rate-limiting for glutathione synthesis and may have broad potential for health protection. *Ochsner J.* 2018;18(1):81-87.
- McReynolds MR, Chellappa K, Baur JA. Age-related NAD⁺ decline. *Exp Gerontol.* 2020;134:110888.
- Meng H, Hale L, Friedberg F. Prevalence and predictors of fatigue in middle-aged and older adults: Evidence from the health and retirement study. *J Am Geriatr Soc.* 2010;58(10):2033-2034.
- Migliavacca E, Tay SKH, Patel HP, et al. Mitochondrial oxidative capacity and NAD⁺ biosynthesis are reduced in human sarcopenia across ethnicities. *Nat Commun.* 2019;10(1):5808.
- Moonen H and Van Zanten ARH. Mitochondrial dysfunction in critical illness during acute metabolic stress and convalescence: consequences for nutrition therapy. *Curr Opin Crit Care.* 2020, 26(4):346–354.
- Morales PE, Arias-Durán C, Ávalos-Guajardo Y, et al. Emerging role of mitophagy in cardiovascular physiology and pathology. *Mol Aspects Med.* 2020;71:100822.

The Role of Nutrition Care in Mitochondrial Health

Presented by Robert Martindale, MD, PhD; Bret Goodpaster, PhD; Eduardo Chini, MD, PhD

References Continued

Owen AM, Patel SP, Smith JD, Balasuriya BK, et al. Chronic muscle weakness and mitochondrial dysfunction in the absence of sustained atrophy in a preclinical sepsis model. *Elife*. 2019;8:e49920.

Pereira BI, Akbar AN. Convergence of innate and adaptive immunity during human aging. *Front Immunol*. 2016;7:445.

Pérez LM, Hooshmand B, Mangialasche F, et al. Glutathione serum levels and rate of multimorbidity development in older adults. *J Gerontol A Biol Sci Med Sci*. 2020;75(6):1089-1094.

Picca A, Mankowski RT, Burman JL, et al. Mitochondrial quality control mechanisms as molecular targets in cardiac ageing. *Nat Rev Cardiol*. 2018;15(9):543-554.

Pirinen E, Auranen M, Khan NA, et al. Niacin cures systemic NAD⁺ deficiency and improves muscle performance in adult-onset mitochondrial myopathy. *Cell Metab*. 2020;31(6):1078-1090.e5.

Prasun P. Mitochondrial dysfunction in metabolic syndrome. *Biochim Biophys Acta Mol Basis Dis*. 2020;1866(10):165838.

Puthucheary Z, Gunst J. Are periods of feeding and fasting protective during critical illness? *Curr Opin Clin Nutr Metab Care*. 2021;24(2):183-188.

Puthucheary ZA, Astin R, Mcphail MJW, et al. Metabolic phenotype of skeletal muscle in early critical illness. *Thorax*. 2018;73(10):926-935.

Rajman L, Chwalek K, Sinclair DA. Therapeutic potential of NAD-boosting molecules: the in vivo evidence. *Cell Metab*. 2018;27(3):529-547.

Rath E, Moschetta A, Haller D. Mitochondrial function - gatekeeper of intestinal epithelial cell homeostasis. *Nat Rev Gastroenterol Hepatol*. 2018;15(8):497-516.

Rice TW, Wheeler AP, Thompson BT, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: The EDEN randomized trial. *JAMA*. 2012;307(8):795-803.

Roque W, Cuevas-Mora K, Romero F. Mitochondrial quality control in age-related pulmonary fibrosis. *Int J Mol Sci*. 2020;21(2):643.

Ryu D, Mouchiroud L, Andreux PA, Katsyuba E, et al. Urolithin A induces mitophagy and prolongs lifespan in C. elegans and increases muscle function in rodents. *Nat Med*. 2016;22(8):879-888.

The Role of Nutrition Care in Mitochondrial Health

Presented by Robert Martindale, MD, PhD; Bret Goodpaster, PhD; Eduardo Chini, MD, PhD

References Continued

Santanasto AJ, Glynn NW, Jubrias SA, et al. Skeletal muscle mitochondrial function and fatigability in older adults. *J Gerontol A Biol Sci Med Sci.* 2015;70(11):1379-1385.

Sekhar M.D. R.V. (2019) Oxidation Damage Accumulation Aging Theory (The Novel Role of Glutathione). In: Gu D., Dupre M. (eds) *Encyclopedia of Gerontology and Population Aging*. Springer, Cham. https://doi.org/10.1007/978-3-319-69892-2_51-1

Sekhar RV, Patel SG, Guthikonda AP, 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(3):847-853.

Seo AY, Joseph AM, Dutta D, et al. New insights into the role of mitochondria in aging: Mitochondrial dynamics and more. *Journal of Cell Science.* 2010;123:2533-2542.

Standley RA, Distefano G, Trevino MB, et al. Skeletal muscle energetics and mitochondrial function are impaired following 10 days of bed rest in older adults. *J Gerontol A Biol Sci Med Sci.* 2020;75(9):1744-1753.

Supinski GS, Schroder EA, Callahan LA. Mitochondria and critical illness. *Chest.* 2020;157(2):310-322.

Tan C, Gu J, Chen H, et al. Inhibition of aerobic glycolysis promotes neutrophil to influx to the infectious site via CXCR2 in Sepsis. *Shock.* 2020;53(1):114-123.

TARGET Investigators, for the ANZICS Clinical Trials Group, Chapman M, Peake SL, Bellomo R, Davies A, Deane A, Horowitz M, Hurford S, Lange K, Little L, Mackle D, O'Connor S, Presneill J, Ridley E, Williams P, Young P. Energy-dense versus routine enteral nutrition in the critically ill. *N Engl J Med.* 2018;379(19):1823-1834.

Thiessen SE, Van den Berghe G, Vanhorebeek I. Mitochondrial and endoplasmic reticulum dysfunction and related defense mechanisms in critical illness-induced multiple organ failure. *Biochim Biophys Acta Mol Basis Dis.* 2017;1863(10 Pt B):2534-2545.

Tiku V, Tan MW, Dikic I. Mitochondrial functions in infection and immunity. *Trends Cell Biol.* 2020;30(4):263-275.

Tomás-Barberán FA, García-Villalba R, González-Sarriás A, et al. Ellagic acid metabolism by human gut microbiota: consistent observation of three urolithin phenotypes in intervention trials, independent of food source, age, and health status. *J Agric Food Chem.* 2014;62(28):6535-6538.

Wang A, Huen SC, Luan HH, Yu S, et al. Opposing effects of fasting metabolism on tissue tolerance in bacterial and viral inflammation. *Cell.* 2016;166(6):1512-1525.e12.

The Role of Nutrition Care in Mitochondrial Health

Presented by Robert Martindale, MD, PhD; Bret Goodpaster, PhD; Eduardo Chini, MD, PhD

References Continued

Wang X, Ryu D, Houtkooper RH, Auwerx J. Antibiotic use and abuse: a threat to mitochondria and chloroplasts with impact on research, health, and environment. *Bioessays*. 2015;37(10):1045-1053.

Wesselink E, Koekkoek WAC, Grefte S, Witkamp RF, van Zanten ARH. Feeding mitochondria: Potential role of nutritional components to improve critical illness convalescence. *Clin Nutr*. 2019;38(3):982-995.

Zhang M, Jativa DF. Vitamin C supplementation in the critically ill: A systematic review and meta-analysis. *SAGE Open Med*. 2018;6:2050312118807615.

Website:
www.UMDF.org