

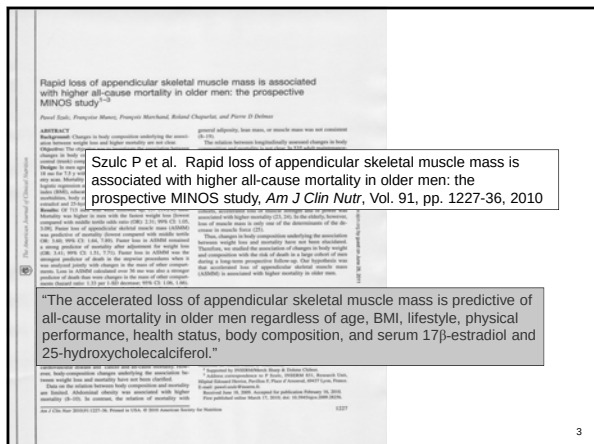
Entry Level Clinical Nutrition – Part 9
Dr. Jeff Moss

Entry Level Clinical Nutrition
Part VII

Protein, amino acid imbalance,
and sarcopenia:
Part III
Diagnostic considerations

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Quality of life issues are the major concerns more than ever now.

4

- What appears to be the most important determinant of quality of life?***

- Optimal lean body mass.***

5

- Why is lean body mass lost?***

- Two reasons.***

- Aging***

- A response to environmental stressors***

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What is the nature of this response?

- *Where does the protein go?*
- *Does it go to production of functional tissue such as muscles, gut lining, ligaments, regulatory factors, detox enzymes? (Anabolic)*
- *Or*
- *Does it go to production of inflammatory mediators such as acute phase proteins and cytokines and production of energy? (Catabolic)*

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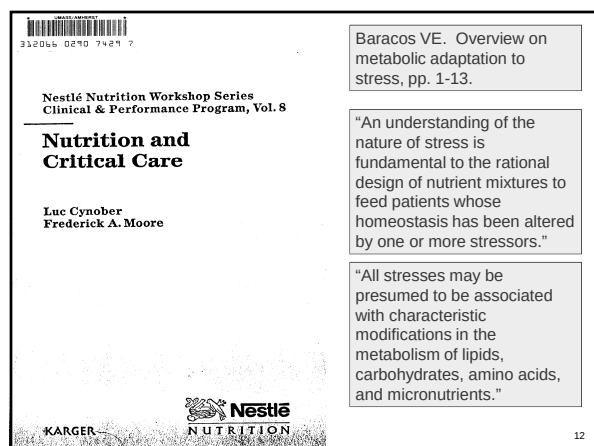
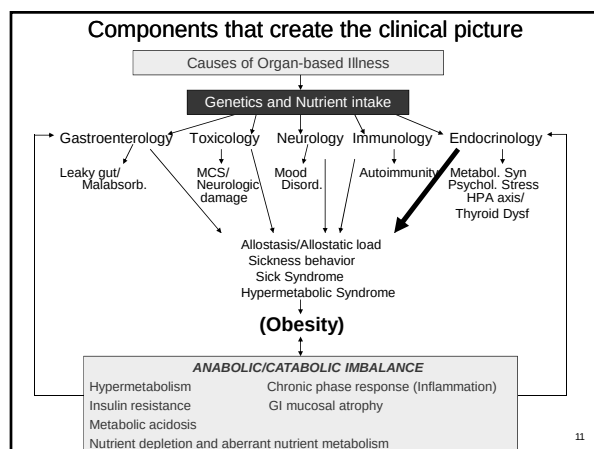
Aging makes it more difficult to respond anabolically.

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Underlying hypotheses of Entry Level Clinical Nutrition:

- Chief complaints in chronically ill patients are not diseases but responses that have gone on too long (Allostatic load).
- The metabolic imbalances that combine to form this response have been well defined by critical care nutritionists.

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[illegible]

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Table 1. Overlapping of symptoms of acute sickness behaviour associated with IFN- α therapy and the somatic symptoms in MDD

Symptoms	Prevalence in IFN- α therapy ^a , %	Prevalence in MDD ^b , %
Fatigue/asthenia	39–90	73
Headache	27–67	33 ^c
Gastrointestinal symptoms	50 ^{c–1}	34–47 ^f
Psychomotor slowing	40 ^c	59–65 ^f
Insomnia	20–39 ^d	63
Irritability	35 ^d	50
Arthralgia	9–36	31 ^e
Musculoskeletal pain	26–32	62–80 ^{e, 2}
Abdominal pain	15–20	21 ^e
Anorexia	13–19	40
Anxiety	13–18 ^g	57
Poor concentration	14 ^d	51

^a [46], unless otherwise specified; ^b [99], unless otherwise specified; ^c [100]; ^d [101]; ^e [102]; ^f [103]; ^g [104].

¹ Nausea, vomiting, bowel problems.

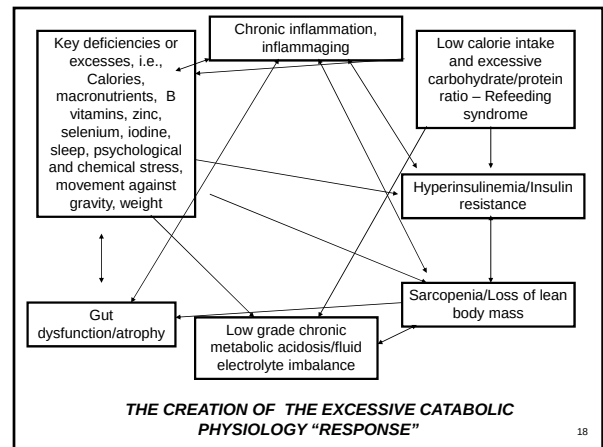
² Result from depressed inpatient population.

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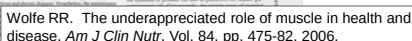
Key metabolic imbalances seen with the acute phase response

- Metabolic acidosis
- Loss of lean body mass (sarcopenia)
- Insulin resistance
- Inflamm-aging (Increased innate immunity and decreased adaptive immunity)
- Suboptimal caloric intake and carbohydrate:protein ratio (Refeeding syndrome)
- Gastrointestinal dysfunction/gut atrophy
- Deficiencies of key micronutrients such as zinc, selenium, and vitamin D

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Sarcopenia: Big picture thoughts on treatment



- **“The importance of muscle mass, strength, and metabolic function in the performance of exercise, as well as the activities of daily living (ADL), has never been questioned. Perhaps less well recognized, muscle plays a central role in whole-body protein metabolism, which is particularly important in the response to stress. Furthermore, abundant evidence points to a key role of altered muscle metabolism in the genesis, and therefore the prevention, of many common pathologic conditions and chronic diseases.”**

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- **“Particular emphasis will be given to the notion that increasing protein or amino acid intakes may optimize muscle strength and metabolism and thereby improve health.”**

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- **“Maintenance of the protein content of certain tissues and organs, such as the skin, brain, heart, and liver, is essential for survival. In the postabsorptive state these essential tissues and organs rely on a steady supply of amino acids via the blood to serve as precursors for the synthesis of new proteins to balance the persistent rate of protein breakdown that occurs in all tissues. It has been recognized since the early 1960s that, in the absence of nutrient intake, muscle protein serves as the principal reservoir to replace blood amino acid taken up by other tissues.”**

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- **“The stressed state, such as that associated with sepsis, advanced cancer, and traumatic injury, imposes greater demands for amino acids from muscle protein breakdown than does fasting. Physiologic responses necessary for recovery may include the accelerated synthesis of acute phase proteins in the liver, synthesis of proteins involved in immune function, and synthesis of proteins involved in wound healing. The demands for precursor amino acids for synthesis of these proteins are significant. For example, quantitative studies of wound healing suggest that a protein intake of >3 g protein·kg⁻¹·d⁻¹ is required to provide the necessary precursors for the synthesis of proteins required for normal healing of a burn injury to 50% of the body.”**

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- “Recent studies in free-living elderly individuals indicate that an increased intake of amino acids improves the physical function and strength of muscle. It is likely that the metabolic function of muscle is also improved by greater than recommended protein intakes, because amino acids not only stimulate the synthesis of myofibrillar proteins but also the synthesis of mitochondrial proteins needed to metabolize substrates. The recent finding that daily supplementation of type 2 diabetic subjects with amino acids improves metabolic control and decreases hemoglobin A1c concentrations is consistent with the expected benefits of stimulating muscle mitochondrial protein synthesis, for the reasons stated above. Also, type 2 diabetic subjects maintained on a high protein intake had improved glycemic control. Insulin sensitivity was also improved by amino acid supplementation above recommended protein intakes in healthy elderly subjects with varying degrees of insulin resistance; both plasma and intrahepatic lipid concentrations were reduced as well.”

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Treatment: Optimal daily protein intake

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Role of dietary protein in the sarcopenia of aging¹⁻⁴

Stephen Paddon-Jones, Kevin R. Storey, Wayne W. Campbell, Glenn Vague, and Robert R. Wolfe

ABSTRACT
Sarcopenia is a complex, multifactorial process facilitated by a combination of factors including the alteration of anabolic resistance, the loss of muscle mass, and a loss of muscle quality. Sarcopenia is a major cause of disability and mortality in the elderly. The loss of muscle mass is a major cause of disability and mortality in the elderly. The loss of muscle mass is a major cause of disability and mortality in the elderly.

INTRODUCTION
Sarcopenia is a complex, multifactorial process facilitated by a combination of factors including the alteration of anabolic resistance, the loss of muscle mass, and a loss of muscle quality. Sarcopenia is a major cause of disability and mortality in the elderly. The loss of muscle mass is a major cause of disability and mortality in the elderly. The loss of muscle mass is a major cause of disability and mortality in the elderly.

CONCLUSION
Sarcopenia is a complex, multifactorial process facilitated by a combination of factors including the alteration of anabolic resistance, the loss of muscle mass, and a loss of muscle quality. Sarcopenia is a major cause of disability and mortality in the elderly. The loss of muscle mass is a major cause of disability and mortality in the elderly. The loss of muscle mass is a major cause of disability and mortality in the elderly.

REFERENCES
1. Paddon-Jones S, Storey K, Campbell W, Vague G, Wolfe R. Role of dietary protein in the sarcopenia of aging. *Am J Clin Nutr*. 2008;87:1562S-65S.

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- “Although several studies support the 0.8 g·kg⁻¹·d⁻¹ recommendation, others have suggested that a moderately higher protein intake of 1.0-1.3 g·kg⁻¹·d⁻¹ may be required to maintain nitrogen balance and offset a potentially lower energy intake, decreased protein synthetic efficiency, and impaired insulin action in elderly individuals.”

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- “Such recommendations should be weighed against any potential increase in the risk of toxicity or impaired renal function. Very-high-protein diets (>45% energy) have been associated with a host of adverse events, including nausea, diarrhea, increased calcium excretion from diets high in sulfur-containing amino acids, and increased morbidity. However, diets containing a moderate amount of protein (20-35% energy) do not appear to be associated with negative health outcomes.”

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- “There is little evidence to link high protein intakes (up to 2 g·kg⁻¹·d⁻¹) to increased risk for impaired kidney function in healthy, physically active men and women. However, there is evidence that a higher protein intake may facilitate a greater decline in renal function in those with modestly impaired renal function.”

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Morley JE. *J Nutr Health Aging*,
Vol. 12, No. 7, pp. 452-456, 2009

- “The Recommended Daily Allowance of 0.8 g/kg body weight/daily of protein is insufficient to maintain nitrogen balance in older persons. To prevent sarcopenia older persons need between 1.2 to 1.5 g/kg daily. Essential amino acids such as leucine are not only building blocks but increase protein anabolism and decrease protein breakdown.”

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Addressing sarcopenia with
amino acids

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The Journal of Nutrition, Health & Aging
Volume 12, Number 7, July 2008

THE JOURNAL OF NUTRITION, HEALTH & AGING

SARCOPENIA: ITS ASSESSMENT, ETIOLOGY, PATHOGENESIS,
CONSEQUENCES AND FUTURE PERSPECTIVES

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G. OHRN⁸, J. WOOD⁹, R. BAUMEISTER¹⁰, J. PILLARD¹¹, Y. BOHRE¹²,
W. G. CHESMAN¹³, B. VILLAG¹⁴

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Rolland Y et al. Sarcopenia: Its assessment, etiology, pathogenesis, consequences and future perspectives, *J Nutr Health Aging*, Vol. 12, No. 7, pp. 433-450, 2008

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ORIGINAL ARTICLE
EXERCISE ACTION

Amino Acid Supplementation Increases Lean Body Mass, Basal Muscle Protein Synthesis, and Insulin-Like Growth Factor-1 Expression in Older Women

Edgar J. Velozo,¹ Melissa Sheffield-Kramer,¹ Douglas Pedron-Jones,¹ Charles E. DiLillo,¹ Arthur P. Santoso,¹ Steven S. Caporaso,¹ Jon Jung, David L. Chaitin,¹ and Randall J. Vittoria^{1,2}

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Abstract Supplementing dietary protein intake has been implicated in anorexia.

Objective and design: The objective of this study was to determine whether 12-week resistance exercise and BCAA supplementation increased muscle protein synthesis (MPS) in older women. **Setting:** This study was conducted in a laboratory setting. **Subjects:** Twelve healthy, sedentary, and non-supplementing women (mean age 67.1 years) were randomly assigned to either a resistance exercise and BCAA supplementation group, or a resistance exercise and placebo group. **Measurements and main results:** MPS was measured using a stable isotope technique. MPS was significantly higher in the BCAA group compared to the placebo group.

Dillon EL et al. Amino acid supplementation increases lean body mass, basal muscle protein synthesis, and insulin-like growth factor-1 expression in older women, *J Clin Endocrinol Metab*, Vol. 94, No. 5, pp. 1630-1637, 2009

Conclusions: BCAA supplementation increased MPS in older individuals. The acute anabolic response to BCAA supplementation is associated with an increase in the rate of protein synthesis.

Key words: Amino acid supplementation, muscle protein synthesis, older women.

Older age is associated with a loss of physical, bone mineral, and nutritional adaptations that facilitate the maintenance of muscle mass and function [1]. The ability to maintain muscle mass and function is critical for the maintenance of physical function, and the ability to maintain muscle mass and function is critical for the maintenance of physical function. The ability to maintain muscle mass and function is critical for the maintenance of physical function. The ability to maintain muscle mass and function is critical for the maintenance of physical function.

A study showing that hormonal deficits associated with aging (i.e., growth hormone, IGF-1) are associated with a loss of muscle mass and function [2]. The ability to maintain muscle mass and function is critical for the maintenance of physical function. The ability to maintain muscle mass and function is critical for the maintenance of physical function. The ability to maintain muscle mass and function is critical for the maintenance of physical function.

Received 15 May 2008; accepted 15 May 2008. Address correspondence and reprint requests to Dr. Edgar J. Velozo at the Department of Anthropology, University of Illinois at Chicago, Chicago, Illinois 60607.

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1630 • Journal of Clinical Endocrinology and Metabolism, May 2009, 93(5):1630-1637

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Two doses per day in seven
women aged 68 ± 2 yr for 3 mo

TABLE 2. Composition of EAA supplements

Amino acid	7.5 g EAA	Total (%)
Histidine	0.82	10.9
Isoleucine	0.78	10.4
Leucine	1.39	18.6
Lysine	1.17	15.5
Methionine	0.23	3.1
Phenylalanine	1.17	15.5
Threonine	1.10	14.7
Valine	0.85	11.5
Total	7.52	100

[illegible]

Amino Acid	Amount (g)	Proportion of total (%)
Histidine	0.488	3.26
Isoleucine	1.286	8.57
Leucine	5.382	35.88
Lysine (HCl)	2.561	17.08
Methionine	0.538	3.59
Phenylalanine	0.698	4.65
Threonine	1.435	9.57
Valine	1.116	7.44
Arginine	1.495	9.97
Total	15.000	100.00

Caloric content = 45 kcal.

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- “It has been suggested that optimal health status, reduced risk of chronic disease and improved outcomes can be realized in the elderly with a protein intake of approximately 1.5 g protein/kg/d. This level of protein intake may be particularly relevant to the elderly during compulsory inactivity. However, the straightforward provision of dietary and protein supplements is often not effective in improving lean mass or muscle function in the elderly.”

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- “The failure of these nutritional supplements is related to a large part to the fact that subjects decrease dietary intake by a caloric amount equivalent to the calories contained in the supplement. The supplements, which are most often liquid meal replacements, induce satiety and affect subsequent intake. This may be one of several reasons why elderly hospitalized patients often eat only one-half of their required dietary intake. On the contrary, constituent amino acid supplementation does not affect satiety, and further, does not alter the metabolic effects of subsequent meals. Increasing protein intake by EAA supplementation may be a promising means of improving protein intake in the elderly.”

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- “The simple addition of bulk protein to the diet is not an optimal solution and entails a large energy component. Increasing protein intake with EAA supplementation is advantageous in terms of efficacy, convenience, flexibility of delivery (capsules, drink) and rapid absorption.”
- “Assuming a complete protein contains about 40-45% essential amino acids, the current provision of 3 x 15 g of EAA would entail a dietary intake of approximately 3 x 35 g of whey protein.”

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Dietary protein recommendations and the prevention of sarcopenia

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Abstract

To show clinicians to select such as the rate of protein and the amount of protein consumed

with each meal to prevent skeletal muscle mass loss

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- “On the basis of recent work, we propose a novel and specific dietary approach to prevent or slow down muscle loss with aging. Rather than recommending a large, global increase in the recommended dietary allowance (RDA) for protein for all elderly individuals, clinicians should stress the importance of ingesting a sufficient amount of protein with each meal. To maximize muscle protein synthesis while being cognizant of total energy intake, we propose a dietary plan that included 25-30 g of high quality protein per meal.”

[illegible]

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- “Amino acid transport into muscle, muscle protein synthesis, and net balance increased similarly in both the young and the elderly suggesting that muscle protein anabolism can be stimulated by oral amino acids in the elderly as well as in young subjects. Similarly, muscle protein synthesis increased to the same extent after an oral intake of either balanced amino acids or essential amino acids in healthy elderly.”

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- “...when glucose was associated with an oral administration of a mixture of amino acids, an increased amino acid delivery and transport into the muscle together with a decreased muscle protein breakdown was achieved...”

47

- “According to the different types of dietary protein, it is possible that their impact on protein metabolism is not the same. The consumption of three different protein sources and its effect on protein metabolism was analyzed in elderly women. A first diet was composed half of animal proteins and half of vegetable proteins, whereas one-third of the proteins consumed in the second diet were from vegetable and two-thirds from animals, and inversely in the third diet. Nitrogen balance was not modified in this study but whole body protein breakdown was not inhibited to the same extent by the meal when the protein source was from vegetables in comparison with meat.”

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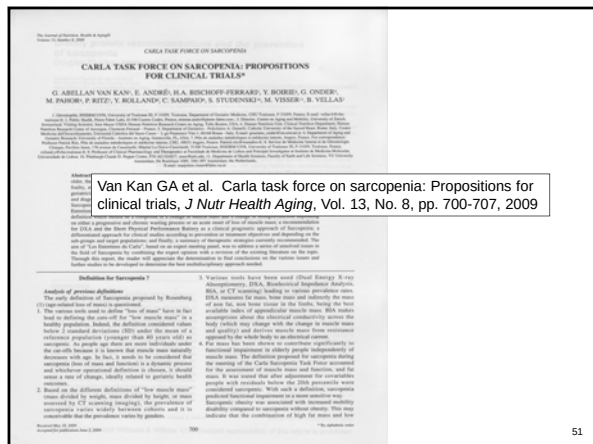
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- “A ‘spread’ diet composed of four meals, spreading daily protein intake over 12 hours was compared to a pulse diet providing 80% of daily protein intake concentrated at midday. The pulse protein pattern was more efficient at improving nitrogen balances and who body protein retention in aged people.”

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- “The response to amino acid intake with concomitant exercise is dependent upon the composition and amount, as well as the pattern and timing of ingestion in relation to performance of exercise. The response of net muscle protein synthesis to consumption of an essential amino acid-carbohydrate supplement solution immediately before resistance exercise is greater than when the solution is consumed after exercise, primarily because of an increase in muscle protein synthesis as a result of increased delivery of amino acids in the leg.”

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Van Kan GA et al. Carla task force on sarcopenia: Propositions for clinical trials, *J Nutr Health Aging*, Vol. 13, No. 8, pp. 700-707, 2009

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- "...the schedule of the protein supplementation was relevant to improve muscle protein synthesis, and a large amount of amino acid supplementation in one meal per day seemed to be more efficient in increasing anabolic effect than intermittent protein intake. Thus, the anabolic effect of protein supplementation may be maximized with a large amount of a highly efficient nutritional supplement (such as essential amino acids and especially leucine) once a day."

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Oral Administration of Amino Acidic Supplements Improves Protein and Energy Profiles in Skeletal Muscle of Aged Rats: Elongation of Functional Performance and Acceleration of Mitochondrial Recovery in Adenosine Triphosphate After Exhaustive Exertion

Carol Chen Scarsbelli, MSc,^{1,2} Roy B. McCauley, PhD,³ Zhaoan Yuan, PhD,⁴
Justin Di Renzo, BCs,⁵ David Patel, BSc,⁶ Jeff Pott, BSc,⁶ Riccardo Raddino, MD,⁷
Zuhair Allebban, PhD,⁸ John Abboud, MD,⁹ Gabriele M. Scarsbelli,¹ Karuna Chihikuri, PhD,
Julius Gardin, MD,¹⁰ Louis Saravottilat, MD,¹¹ Giuseppe Faggiani, MD,¹²
Alessandro Mazzocco, MD,¹³ and Tiziano M. Scarsbelli, MD, PhD^{1,2}*

carabelli CC et al. *Am J Cardiol*, Vol. 101(Suppl), pp. 42E-48E, June 2, 2008

trans-ester transfer were analysed in triplicate. Data were expressed as mean $\pm$ standard error (SEM). Statistical significance was determined by Student's *t*-test. Significant differences between groups were indicated by different letters (*P* < 0.05). The authors thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) for financial support. Received 12 March 2007; accepted 12 June 2007; first published online 12 July 2007

Address correspondence to: Dr. David A. Asch, Department of Psychology, University of Michigan, 735 Tappan St., Ann Arbor, MI 48106-1108. E-mail: asch@umich.edu

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- “The additive beneficial effects of exertion and amino acid (AA) supplementation have...been documented.”
- “AA infusion in healthy untrained subjects at rest was shown to boost protein synthesis by approximately 150%, whereas enhanced availability of free AA to skeletal muscle immediately after performance of physical exercise increased protein synthesis by >200%, suggesting that physical activity and hyperaminoacidemia have additive positive effects on protein synthesis.”

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- “In the same study, an inhibitory effect of hyperaminoacidemia on protein breakdown, which is normally increased in the fasted state, was also documented after physical training, hinting that exogenous AA can improve muscle metabolism by contextually increasing muscle protein synthesis and decreasing protein breakdown.”
- “...the combination of physical activity and AA supplementation currently represents the most feasible and safe strategy, providing encouraging data for both prevention and treatment of muscle loss.”

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Nutritional Supplements with Oral Amino Acid Mixtures Increases Whole-Body Lean Mass and Insulin Sensitivity in Elderly Subjects with Sarcopenia

Sebastiano B. Solerte, MD, PhD^{1,2*}, Carmine Guzzano, MD³, Roberto Bonanni, MD⁴, Mariangela Rondelli, MD⁵, Maria Zanone, MD⁶, Cristina Russo, MD, PhD⁷, Eleonora Locatelli, MD⁸, Nicola Schifano, MD⁹, Andrea Giustina, MD, PhD¹⁰ and Marina Forreault, BS¹¹

Solerte SB et al. Nutritional supplements with oral amino acid mixtures increases whole-body lean mass and insulin sensitivity in elderly subjects with sarcopenia, *Am J Cardiol*, Vol. 101(Suppl), pp. 69E-77E, June 2, 2008

Abstract
An 8-week treatment of 100 kcal/day (1.5 kcal/kg of body weight) of essential amino acids (EAA) at 10:00 and 18:00 h. Lean mass was measured with dual-energy x-ray absorptiometry (DEXA) at baseline and 8 weeks. Significant increases in whole-body lean mass were observed in the EAA group compared to the control group. Plasma insulin and glucose levels were also significantly lower in the EAA group compared to the control group. These findings suggest that EAA supplementation may improve muscle mass and insulin sensitivity in elderly subjects with sarcopenia. These preliminary data indicate that nutritional supplements with EAA may represent a safe and effective strategy to improve muscle mass and insulin sensitivity in elderly subjects with sarcopenia. The study is currently ongoing in the form of a randomized controlled trial (NCT00111111). © 2008 Elsevier Inc. All rights reserved. (doi:10.1016/j.amjcard.2008.04.001)

Keywords: Sarcopenia; Amino acids; Insulin sensitivity; Dual-energy x-ray absorptiometry (DEXA); Elderly subjects.

Introduction
Sarcopenia, defined as a reduction in lean mass and muscle strength, is considered a frequent hallmark of the aging process and is present in elderly patients with various clinical syndromes. Sarcopenia is viewed as the consequence of multiple medical, behavioral, and environmental factors that are common in older people.

56

- “Sarcopenia, defined as a reduction in lean mass and muscle strength, is considered a frequent hallmark of the aging process and is present in elderly patients with various clinical syndromes.”
- “Sarcopenia is viewed as the consequence of multiple medical, behavioral, and environmental factors that are common in older people.”

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- “Our data demonstrated that use of AA supplements in elderly subjects with sarcopenia resulted in several important beneficial changes, including an increase in muscle anabolism, as demonstrated by cytokine and growth factor pathways.”
- “In effect, we found a reduction in catabolic cytokines (TNF- α) and increased anabolic growth factors (IGF-1), with consequent increase in the IGF-1/TNF- α) ratio, thus demonstrating a transition from catabolic to anabolic conditions.”

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- *“Therefore, use of nutritional AA supplements in elderly subjects with sarcopenia causes an anabolic shift, suggesting that AA treatment could be extended to most geriatric syndromes in which this disorder is present.”*
- *“These data are confirmed by the evident increase in the whole-body lean mass after 8-18 months of treatment.”*
- *“Furthermore, the increase in lean body mass is presumably the cause of improved insulin sensitivity observed in elderly patients with sarcopenia, as demonstrated by reduced fasting insulin levels...and fasting blood glucose concentrations.”*

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- “The recovery of anabolic conditions that enhance endogenous protein synthesis and ATP production by cells could potentially induce beneficial effects to restore muscle integrity and metabolic functions and, consequently, enhance insulin activity and sensitivity.”
- “This condition could be beneficial in elderly patients with sarcopenia and could be easily achieved with AA supplementation.”

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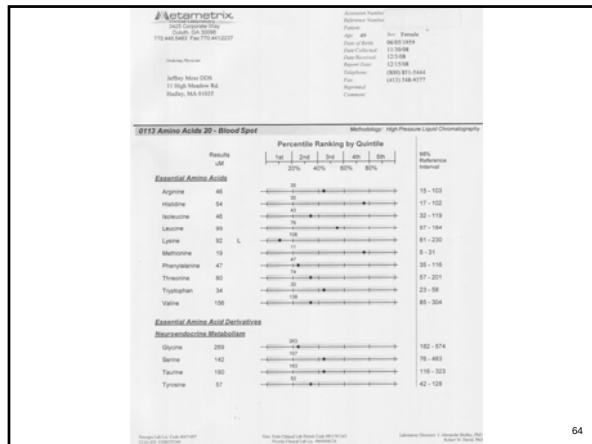
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Treatment:
 Different types of
 whole proteins

Maximizing muscle protein anabolism: the role of protein quality
 Jason E. Tang and Stuart M. Phillips

Purpose of review
 Muscle protein synthesis (MPS) and muscle protein breakdown are simultaneous ongoing processes. Thus, we require evidence for how protein quality can affect anabolic muscle protein synthesis or protein balance. MPS and muscle protein breakdown are regulated by a number of factors, including the availability of amino acids, the rate of protein synthesis, and the rate of protein breakdown. MPS and muscle protein breakdown are regulated by a number of factors, including the availability of amino acids, the rate of protein synthesis, and the rate of protein breakdown.

Recent findings
 Protein supplementation, and the accompanying hyperaminoacidemia, stimulates an increase in MPS and a small suppression of muscle protein breakdown. Beyond the feeding-induced rise in MPS, total incorporation of new muscle protein mass into muscle, forming protein accretion, remains the same. This is because feeding leads to muscle hypertrophy. Amino acid use of the paradigm of nitrogen balance and using to measure the gain in total muscle mass, respectively, however, moderately active skeletal muscle can offset the metabolic associated with the acquisition of high level of MPS. MPS is a key factor in muscle mass and the reduction in metabolic cost that can lead to fat mass accumulation.

Summary
 Muscle size of skeletal muscle is the sum of feeding-induced change in muscle protein mass. Thus, it is likely that increases in MPS are the primary determinants of the acute feeding-induced changes in protein turnover.

Introduction
 In which humans, small increases in skeletal muscle mass (i.e. hypertrophy) can arise when anabolic stimulus is combined with protein energy balance and sufficient dietary protein intake (1-3). To achieve hypertrophy, protein intake must be at least 1.6 g/kg/d (4,5). MPS is a key factor in muscle mass and the reduction in metabolic cost that can lead to fat mass accumulation.

When seeking to maximize protein, it appears milk proteins and their isolated forms, whey and casein, offer an anabolic advantage over soy protein proteins in promoting muscle hypertrophy."

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Dr. Jeff Moss

Treatment:
Reduce inflammation

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Inflammatory burden and amino acid metabolism in cancer cachexia

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Purpose of review
Cancer cachexia is associated with marked alterations in skeletal muscle protein metabolism that lead to muscle wasting and, in some cases, death. The inflammatory response elicited by cancer is a likely, if not primary, mediator of these alterations. This review focuses on the possible relationship between inflammatory signaling and altered

Recent findings

Loss of skeletal muscle in cancer patients can potentially be due to anorexia and early satiety, reduced muscle protein synthesis, and/or increased muscle protein breakdown. Inflammation has been associated with each of these mechanisms. Effects on appetite appear to be mediated by the melanocortin system in the hypothalamus. Studies in animal models of cachexia suggest that modulation of oreogenic and anoregenic pathways in the system may improve nutrient consumption. Inflammatory cytokines such as IL-6 and TNF- α may also contribute to the effects of inflammation on muscle

Durham WJ et al. Inflammatory burden and amino acid metabolism in cancer cachexia, *Curr Opin Clin Nutr Metab Care*, Vol. 12, No. 1, pp. 72-77, January 2009

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(e.g. 70–100% of cancer patients experience fatigue [4]).

“...human studies have found beneficial effects of EPA on body weight, lean body mass, appetite, and quality of life.”

tion of adipose tissue occurs [2]. In cancer cachexia, profound inflammation is both a diagnostic characteristic [3] as well as a possible mechanism for the accompanying anorexia and wasting. In the present review, we focus on the relationship between cancer-induced inflammation and muscle wasting.

Characteristics of cancer cachexia

Although descriptions vary, weight loss, anorexia, and inflammation are the cardinal characteristics of cancer cachexia and are correlated with adverse outcomes [2]. Although muscle weakness and fatigue are often present

(blood cells) present in these patients (57).

Although weight loss occurs in roughly half of cancer patients [5], in cachexia, the weight loss represents a marked loss of skeletal muscle and fat. Strictly speaking, cachexia describes the manifestations of a systemic loss

of body weight, lean body mass, and adipose tissue) of a process that was initiated at some point in the past. Accordingly, patients who exhibit characteristics (e.g., systemic inflammation, anorexia) that are associated with the state of cachexia as well as 5% or greater weight loss may be considered 'precachectic' (17). When the loss of body weight reaches 15% or greater the patient is in

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- “Essential amino acids, leucine in particular, are potent stimulators of muscle protein synthesis in healthy individuals.”
- “Until recently, however, it was not known whether this response is also present in cachectic skeletal muscle, in which inflammatory mediators and impaired energetic status may limit the response to amino acids.”
- “Fortunately, recent studies suggest that this response is also present in cachexia.”

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Treatment:

Other benefits of fish oil

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Research Article

Attenuation of Proteasome-Induced Proteolysis in Skeletal Muscle by β -Hydroxy- β -Methylbutyrate in Cancer-Induced Muscle Loss

Smith HJ, Smith TW, Fradette M, et al.

Journal of Clinical Investigation

Abstract

Loss of skeletal muscle is an important determinant of survival in patients with cancer-induced muscle loss. The effect of β -hydroxy- β -methylbutyrate (HMB) on the effect of the ubiquitin-proteasome pathway on skeletal muscle atrophy in the setting of cancer-induced muscle loss was investigated. HMB treatment significantly attenuated the loss of skeletal muscle mass and the ubiquitin-proteasome pathway in skeletal muscle atrophy in the setting of cancer-induced muscle loss.

Smith HJ et al. Attenuation of proteasome-induced proteolysis in skeletal muscle by β -hydroxy- β -methylbutyrate in cancer-induced muscle loss, *Cancer Res*, Vol. 65, No. 1, pp. 277-283, January 1, 2005

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- “Eicosapentaenoic acid (EPA), down-regulates the increased expression of the ubiquitin-proteasome proteolytic pathway in the skeletal muscle of cachectic mice and has been shown to stabilize body weight in cachectic patients with pancreatic cancer.”
- “When patients consumed an energy-dense supplement containing 32 g protein and 2 g EPA, body weight increased, and this was attributed solely to an increase in lean body mass.”

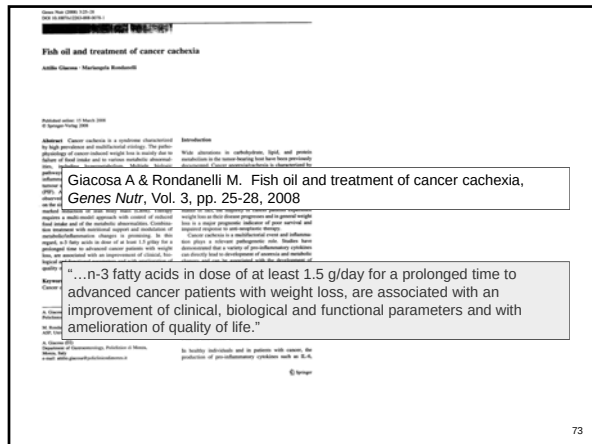
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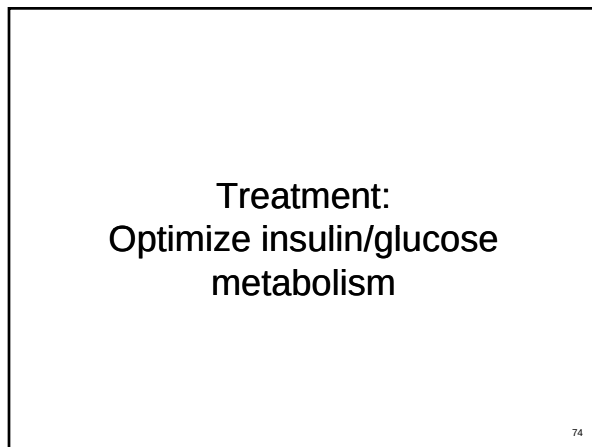
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