

Entry Level Clinical Nutrition:
December 2013 Update
Anabolic resistance:
Why it can be more difficult to
increase lean body mass in
aging populations
Part II

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

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Entry Level Clinical Nutrition Update – Part 4 With Dr. Jeff Moss

Summer of Work Exposes Medical Students to System's Ills - NYTimes.com Page 1 of 3

The New York Times

September 9, 2009

Summer of Work Exposes Medical Students to System's Ills

By KEVIN BAKER

SEATTLE — This summer, medical students from the University of Washington took a long look under the hood of the health care system they are about to inherit, and many returned to campus last week with their eyes wide open and their idealism tempered.

Jacob R. Moore, the chief of the Osgood treatment

Summer of work exposes medical students to system's ills, *The New York Times*, September 9, 2009

The students learned not only to deliver babies and suture wounds, but also to order unnecessary tests as protection against lawsuits, to hector specialists into seeing Medicaid patients, to match patients with prescriptions on Wal-Mart's \$4 list. And they saw firsthand what Mr. Osgood called "a tidal wave of chronic disease" — diabetes, hypertension, obesity, depression — that left many questioning how much any one physician could really accomplish.

"I often wondered what we were actually doing to help people," Mr. Osgood said.

Not surprisingly, more than a few students

"...a tidal wave of chronic illness..."

You had to be reimbursed for the treatment they can do early in their careers or waiting until there's a catastrophic surgery, it's a pretty simple.

For 21 years, the University of Washington School of Medicine has dispatched its rising second-year students across the Northwest to provide primary care in rural or underserved areas. The monthlong program is elective, but a record number of students took part this year — 117 from a class of 216.

The school has a cooperative agreement to train medical students from Alaska, Idaho, Montana and Wyoming, none of which has a medical college of its own. The summer program is one of several vehicles, along with loan forgiveness entitlements, designed to lure students back to their home states to practice in areas with a shortage of primary care givers.

This year, the students set out as negotiations were intensifying in Washington over wholesale changes to the health care system they will soon be joining. Whether there will be improvements to the system remains to be seen, but few students returned thinking there was little to fix.

http://www.nytimes.com/2009/09/09/health/policy/09medschool.html?_r=1&th=&mc=th&... 9/9/2009

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**Nestlé Nutrition Workshop Series
Clinical & Performance Program, Vol. 8**

**Nutrition and
Critical Care**

**Luc Cynober
Frederick A. Moore**

**Baracos VE. Overview on
metabolic adaptation to
stress, pp. 1-13.**

**"An understanding of the
nature of stress is
fundamental to the rational
design of nutrient mixtures to
feed patients whose
homeostasis has been altered
by one or more stressors."**

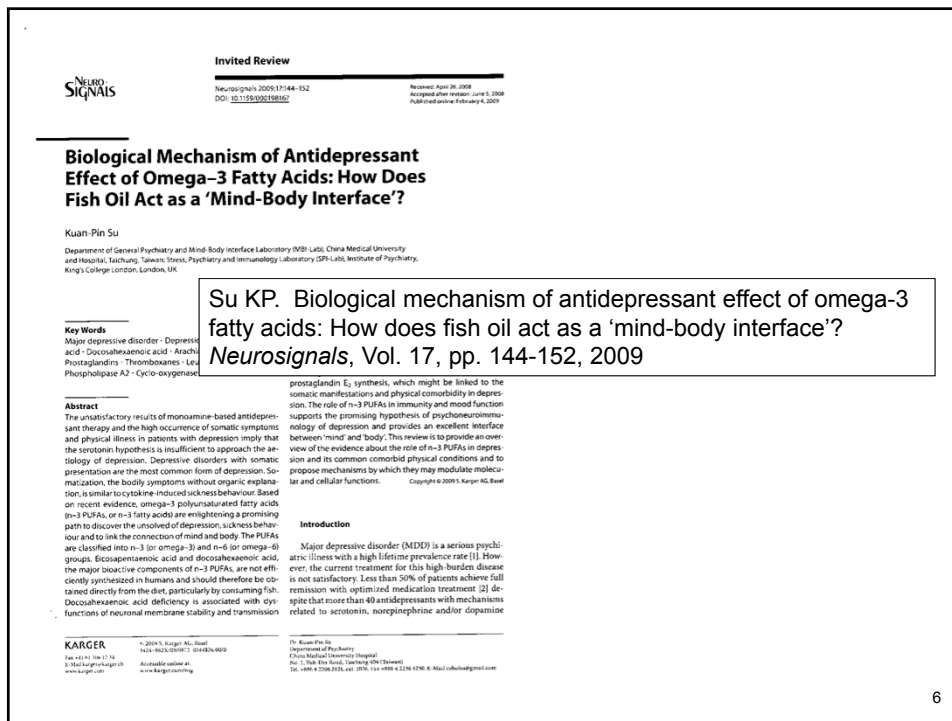
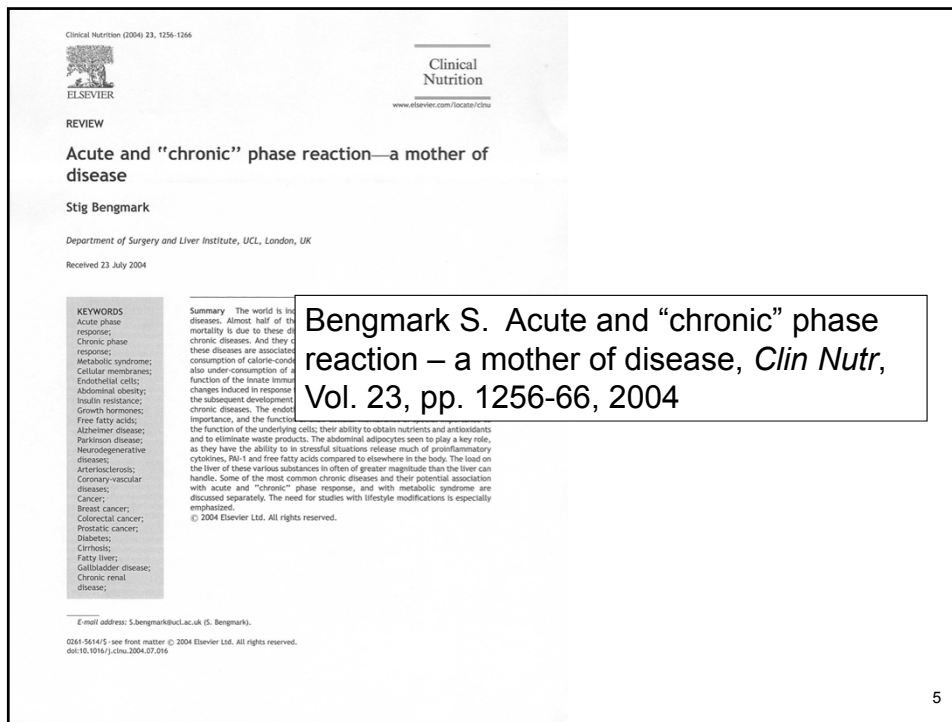
**"All stresses may be
presumed to be associated
with characteristic
modifications in the
metabolism of lipids,
carbohydrates, amino acids,
and micronutrients."**

KARGER

**Nestlé
NUTRITION**

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Entry Level Clinical Nutrition Update – Part 4 With Dr. Jeff Moss



Entry Level Clinical Nutrition Update – Part 4

With Dr. Jeff Moss

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 ^e
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 ^{g, 2}
Abdominal pain	15–20	21 ^e
Anorexia	13–19	40
Anxiety	13–18 ^d	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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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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Entry Level Clinical Nutrition:

A new model of functional
medicine that incorporates
allostatic load and the “chronic”
acute phase response

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***This is a relatively easy,
inexpensive way to help
most patients feel better
early on during the course
of therapy no matter what
their “disease” or chief
complaint.***

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A simplified approach to helping patients feel better

- Understanding the true nature of chronic illness: Excessive allostatic load
- Simple, cost effective diagnostic tools
- A simplified, cost effective menu to improve patient quality of life

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Soeters MR & Soeters PB. The evolutionary benefit of insulin resistance, *Clin Nutr*, Vol. 31, pp. 1002-1007, 2012.

"Insulin resistance" is generally regarded as a deleterious condition associated with the metabolic syndrome, type 2 diabetes mellitus and critical illness; disorders that lead to hyperglycemia. In turn, chronically elevated glucose levels are causing many of the ill effects of these conditions. Consequently, much effort has been invested in treating hyperglycemia on its own; glucose targets have only been set for patients with type 2 diabetes mellitus, and not for critically ill patients. In the light of the above, we hypothesize on the evolutionary importance of insulin resistance.

2. Insulin resistance in starvation

A century ago Benedict demonstrated in his classic work "A study on long term fasting" that the human organism could limit its nitrogen losses during long term starvation. Starvation is accompanied by insulin resistance, and this may be targeted inhibition of the effects of insulin in skeletal muscle tolerance tests, and clamp studies.

“The bad image of insulin resistance has obscured its potential benefits as an adaptive mechanism. Insulin resistance (or the ability to selectively modulate the cellular/tissue response to insulin) is evolutionarily well preserved in insects, worms, and vertebrates including humans. Having been under so much evolutionary pressure, its persistence suggests that it benefits survival of the species.”

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Journal homepage: <http://www.elsevier.com/locate/clnu>

Randomized control trials

Impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients: A randomized controlled trial^a

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A B T

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Keywords:
 Malnutrition
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 Lean mass
 Appendicular muscle mass
 Body cell mass

Abstract
 Aim: To evaluate the impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients. Methods: Sixty elderly malnourished or at-risk patients in an intensive rehabilitation unit. All were given a controlled diet for 6 weeks. In a pulse diet (PD) group (n = 30), dietary protein was spread over the first daily meals. In a control diet (CD) group (n = 30), 75% of dietary protein (1.21 g/kg, weighted on average) was consumed in one meal at noon. The patients were evaluated at admission and at 6 weeks for body composition (lean mass (LM), appendicular skeletal muscle mass (ASM), and body cell mass (BCM) indices, measured by X-ray absorptiometry combined with bioelectrical impedance analysis) (primary outcome), hand grip strength, and activities of daily living (ADL), score. Results: Protein pulse feeding was significantly more efficacious than protein spread feeding in improving LM, ASM, BCM, and ADL score. Conclusion: Protein pulse feeding is a simple and effective nutritional intervention to improve lean mass in malnourished and at-risk hospitalized elderly patients.

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“Aging per se is responsible for gradual loss of skeletal muscle mass (40% from 20 to 80 years of age) and muscle function, termed sarcopenia. Sarcopenia is a major cause of the increased prevalence of disability, falls, morbidity and mortality in elderly people.”

“This study demonstrates for the first time that protein pulse feeding has a positive, clinically relevant effect on lean mass in malnourished and at-risk hospitalized elderly patients.”

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Original article

Sarcopenia: Prevalence and prognostic significance in hospitalized patients

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SUMMARY
Background: Sarcopenia is prevalent in older populations with many causes and varying outcomes however information for use in clinical practice is still lacking.
Aims: The aim of this report is to identify the clinical determinants and prognostic significance of sarcopenia in a cohort of hospitalized acutely ill older patients.
Conclusion: Older people with sarcopenia have poor clinical outcome following acute illness compared with those without sarcopenia.
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1. Introduction

An important challenge of modern medicine is to distinguish physiological changes associated with the process of ageing from

An important example of this challenge is sarcopenia, a condition which is prevalent in older populations with many causes and varying outcomes.¹ It is a syndrome characterized by progressive decline in skeletal mass, decreased strength and functional status

“Older people with sarcopenia have poor clinical outcome following acute illness compared with those without sarcopenia.”

which predict outcomes not many data on hospitalized patients are available. Furthermore a valid and reproducible measurement technique of sarcopenia suitable for clinical practice is still a challenge. The aim of this report is to measure the prevalence and prognostic significance of sarcopenia in a cohort of acutely ill older patients.

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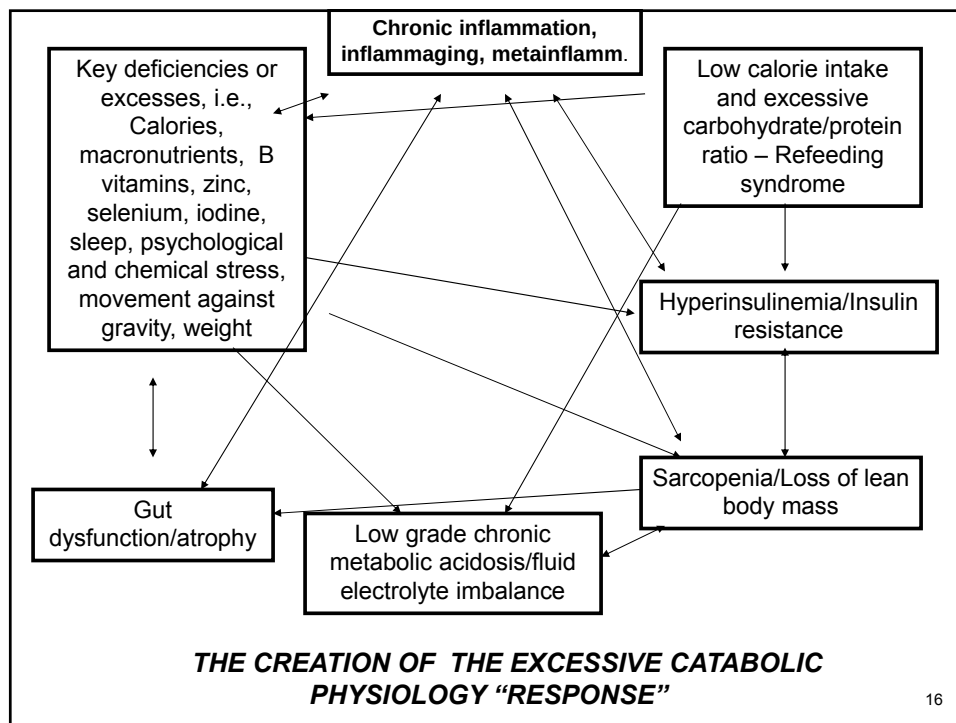
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<http://dx.doi.org/10.1016/j.clnu.2013.01.009>

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Key metabolic imbalances seen with the acute phase response

- Low grade, chronic metabolic acidosis
- Loss of lean body mass (sarcopenia) and its relation to optimal protein intake
- Gastrointestinal dysfunction/gut atrophy
- Inflamm-aging (Increased innate immunity and decreased adaptive immunity)
- Metabolically induced hyperinsulinemia/insulin resistance
- Diet-induced hyperinsulinemia (Refeeding syndrome) and its relation to carbohydrate:protein ratio
- Deficiencies of key micronutrients such as zinc, selenium, and vitamin D

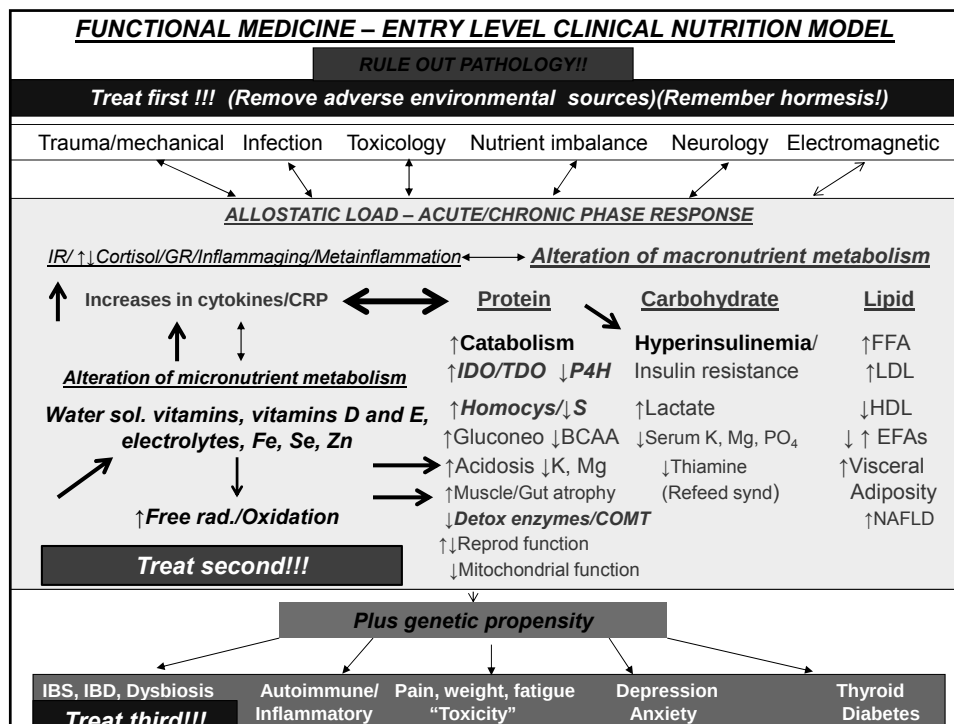
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Entry Level Clinical Nutrition Update – Part 4

With Dr. Jeff Moss



Article in Press

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Review

Malnutrition in the elderly: A narrative review

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ABSTRACT

The focus of nutrition is often on healthy diets and exercise to minimise the risk of developing lifestyle diseases such as cancer, diabetes and cardiovascular disease. However, during the shift into older years often the nutrition priorities change towards meeting increased nutrient needs with less energy requirements, and minimising fear muscle loss. There are several causes of general malnutrition in the elderly that lead to depletion of muscle including starvation (protein-energy malnutrition), sarcopenia and cachexia. The prevalence of protein-energy malnutrition increases with age and the number of comorbidities. A range of clinical and laboratory assessment tools can be used to identify malnutrition in older adults. As 10%

Agarwal E et al. Malnutrition in the elderly: A narrative review, *Maturitas*, Published online ahead of print 2013.

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Contributors	00
Competing interest	00
Funding	00
Provenance and peer review	00
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1. Introduction

The world's population is rapidly aging with estimates that in the first five decades of the 21st century the proportion of the world's population over 60 years will double from 11% to 22%. The expected increase in the absolute number of older adults will triple from 600 million to 2 billion over this period [1]. As the number of older people continues to rise, provision of improved healthcare to the elderly – both in hospital and in the community – is imperative. Often, the focus of nutrition in older adults is a healthy diet and exercise to minimise the risk of developing lifestyle diseases (such as cardiovascular disease, Type 2 diabetes mellitus). However, there is a large body of evidence to indicate that protein-energy malnutrition (PEM) is a common problem in this age group, including in the hospital, nursing home and community setting. Therefore, the purpose of this paper is to summarise the current literature regarding:

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- **“Multicentre studies that have evaluated protein-energy malnutrition (PEM) prevalence in the acute care setting report that 23-60% of elderly patients are malnourished and an estimated 22-28% are at nutritional risk.”**
- **“In comparison to other healthcare settings, there is limited literature on the prevalence of PEM in community-dwelling older adults. However, the reported prevalence indicates a range of 5-30%.”**

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- **In the residential aged care setting, the reported PEM prevalence ranges from 16% to 70% depending on the assessment tool used and the level of care required. In general it is known that the prevalence of PEM increases as the level of care increases.”**

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- **“Dietary management should provide adequate energy and protein intake. However, this alone would be unlikely to address weight loss as sarcopenia is thought to occur regardless of energy balance.”**
- **“Recent evidence indicates that the most effective intervention thus far is a combination of nutrition and resistance training.”**

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Effect of whey protein isolate on strength, body composition and muscle hypertrophy during resistance training
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Current Opinion in Clinical Nutrition and Metabolic Care 2008; 11:40–44

Purpose of review

Sarcopenia (skeletal muscle wasting with aging) is thought to underlie a number of serious age-related health issues. While it may be seen as inevitable, decreasing this gradual loss of muscle is vital for healthy aging. Thus, it is imperative to investigate exercise and nutrition-based strategies designed to build a reservoir of muscle mass as early as possible.

Recent findings

Elderly individuals are still able to respond to both resistance training and the anabolic signals provided by protein ingestion, provided specific amino acids, such as leucine, are present. Whey proteins are a rich source of these essential amino acids and rapidly elevate plasma amino acids, thus providing the foundations for preservation of muscle mass. Several studies involving supplementation with whey protein have been shown to be effective in augmenting the effects of resistance exercise, particularly when supplementation occurs in the hours surrounding the exercise training.

Summary

While further work is required, particularly in elderly people, simple dietary and exercise

Hayes A & Cribb PJ. Effect of whey protein isolate on strength, body composition and muscle hypertrophy during resistance training, *Curr Opin Clin Nutr Metab Care*, Vol. 11, pp. 40-44, 2008.

Introduction

Athletic performance and vanity aside, there are many important reasons for needing to know more about how to build muscle mass (hypertrophy), not the least being the underestimated role of muscle mass in healthy aging. Aside from a negative impact on health, functional ability and lifestyle quality, an age-related decline in muscle mass is thought to underlie conditions that shorten lifespan such as type 2 diabetes and cardiovascular disease [1–3,4**]. It has been long known that resistance exercise is still effective in even very elderly populations [5] and current research shows that some of these undesirable diseases can be partially reversed by resistance training [6,7**]. While some leading researchers in this area believe that sarcopenia may be reversible (at least to a certain extent) [8*], others recommend that tomorrow's older adults should be concerned with building a greater "starting reserve capacity" of muscle mass today to ensure they avoid the unknown threshold that precedes physical frailty and compromised health [9].

In this review we highlight the role that protein supplementation may play in the development of muscle strength and hypertrophy. We also feature the results obtained with whey protein isolate (WPI) – one particular type of protein supplement that appears to have advantages over others in terms of promoting muscle accretion. Finally, we briefly identify and discuss other compounds, i.e. creatine monohydrate and glucose, that have been shown to provide an additional beneficial effect greater than WPI supplementation alone.

Role of protein supplementation in the development of muscle hypertrophy

Resistance exercise training is considered an integral component of any attempt to build strength and promote muscle hypertrophy, and offset age-related changes in body composition, strength and functional ability [10,11]. Although resistance exercise is fundamentally anabolic, a net gain in muscle mass is only possible via an interaction with protein-containing meals [12]. For this reason, there

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- **“Athletic performance and vanity aside, there are many important reasons for needing to know more about how to build muscle mass (hypertrophy), not the least being the underestimated role of muscle mass in healthy aging.”**
- **“Aside from the negative impact on health, functional ability and lifestyle quality, age-related decline in muscle mass is thought to underlie conditions that shorten lifespan such as type 2 diabetes and cardiovascular disease.”**

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- **“Although resistance exercise is fundamentally anabolic, a net gain in muscle mass is only possible via an interaction with protein-containing meals.”**
- **“Data from both acute response studies and longer-term (6-12 weeks) investigations provide a foundation that suggests the strategic use of protein supplements can play a vital role in the development of muscle hypertrophy during resistance exercise training.”**

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- **“In fact, supplementation may be vital to restoring the diminished acute response to anabolic stimuli (such as resistance exercise or meal consumption) that is characteristic of aging.”**
- **“Additionally, the strategic consumption of a supplement containing whole proteins or essential amino acids close to resistance exercise is consistently shown to dramatically enhance the acute anabolic response to this activity by providing a higher stimulation of protein synthesis and net protein balance compared to placebo treatments.”**

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- **“Recent data also suggest that supplementation between regular meals may provide an additive effect on net protein accretion due to a more frequent stimulation of muscle protein synthesis.”**

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How does protein supplementation increase muscle mass?

- **“...protein supplementation appears to have at least three prominent roles in augmenting muscle protein accretion and promoting hypertrophy.”**

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- **“First, by supplementing close to resistance exercise to ensure a greater stimulation of muscle anabolism in response to this activity.”**
- **“Second, some data suggest that supplementation between meals may promote more frequent stimulation of muscle protein synthesis, thereby promoting a higher net gain in muscle protein on a daily basis.”**
- **“Finally, strategic supplementation with protein that is rich in essential amino acids, particularly leucine, may help restore the acute anabolic response to meals which characteristically diminishes aging.”**

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Types of whey protein

- **“The type of protein consumed may influence results from resistance exercise training due to variable speeds of absorption, differences in amino acid profiles, unique hormonal response or positive effects on antioxidant defense.”**
- **“Whey protein is the collective term for the soluble protein fractions extracted from dairy milk.”**

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- **“Whey protein supplements, i.e. above 80% proteins concentrates (WPC 80) or about 90% protein isolates (WPI 90), have become popular among athletes and others interested in gaining muscle mass.”**

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Beyond its protein content, what are the benefits of whey protein?

- **“Rather than merely increasing the quantity of protein in the diet, these particular proteins may also provide some unique nutritional advantages.”**
- **“Characteristically, these whey protein supplements contain a very high concentration of essential amino acids (45-55 g/100 g of protein) with minimal fat, carbohydrate and lactose.”**

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- **“They are also the richest known source of branched-chain amino acids, particularly leucine (up to 14 g/100 g protein).”**
- **“Whey protein supplements are a rich rare source of cyst(e)ine residues; up to four-fold higher than other high-quality proteins such as casein and soy.”**

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Why is cysteine important?

- **“Briefly, an abundant supply of cyst(e)ine in the blood is necessary for hepatic catabolism of this amino acid into sulfate and protons; a process that downregulates urea production, promotes glutathione synthesis and shifts whole-body nitrogen disposal in favor of preserving the muscle amino acid pool (which is synonymous with muscle anabolism).”**

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- **“Whey protein supplementation (up to 1 g/kg/day) is the only protein source shown to augment this pathway of protein metabolism and it may do so possibly in a dose-dependent manner.”**

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Still more benefits of whey protein

- **“What is more relevant is that when whey protein supplements are consumed as part of a mixed-macronutrient meal, this protein’s rapid absorption kinetics and ability to stimulate a very high rate of muscle protein synthesis is unaltered, but the result is a more prolonged state of anabolism and inhibition of protein degradation as well as a higher net gain in whole body protein.”**

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With the above in mind, what can be concluded?

- **“Due to its amino acid profile and ability to promote higher net protein accretion, the incorporation of whey protein into the diet may enhance the development of muscle hypertrophy and improve body composition during resistance exercise training.”**

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What about timing of supplement ingestion in relation to resistance exercise?

- **“Supplement timing (i.e. the strategic consumption of a protein supplement before and/or after each workout) is thought to be the ideal strategy for promoting muscle hypertrophy from resistance exercise.”**

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- **“Results showed that the group who performed the supplement-timing strategy (PRE-POST) demonstrated a gain in lean body mass (LBM) that was almost double the MOR-EVE group.”**
- **“This group also demonstrated greater improvements in one-repetition maximum strength, which were supported by a greater increase in hypertrophy of the type II fibers and muscle contractile protein content of this group.”**

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Does this research apply to non-athletes?

- **“This protocol may however, also have important implications for populations that require improvements in strength and body composition, but have a reduced capacity for exercise, such as the frail elderly, cardiac rehabilitation patients or other living with conditions that compromise health, such as HIV, cancer and the various muscular dystrophies.”**

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- **“Importantly, aged individuals showed the same significant elevation in amino acid levels within 2h of ingesting a protein-rich meal as their young counterparts and also displayed the same elevation in acute protein synthesis.”**
- **“Thus, it is likely that supplementing the diet with essential amino acids surrounding a resistance training session would similarly augment the effects of training in elderly individuals, although further work is required in this area.”**

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WHICH IS BEST – WHEY PROTEIN CONCENTRATE OR ISOLATE?

- “The processing of whey concentrate removes the water, lactose, ash, and some minerals.”
- “In addition, compared to whey isolates whey concentrate typically contains more biologically active components and proteins make them a very attractive supplement for the athlete.”

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©Journal of Sports Science and Medicine (2004) 3, 118-130
<http://www.jssm.org>

Review article

*International Society of Sports Nutrition Symposium, June 18-19, 2005, Las Vegas NV;
USA - Symposium - Macronutrient Utilization During Exercise: Implications For
Performance And Supplementation*

PROTEIN – WHICH IS BEST?

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Received: 26 May 2004 / Accepted: 28 June 2004 / Published (online): 01 September 2004

Hoffman JR & Falvo MJ. Protein – which is best? *J Sports Sci Med*, Vol. 3, pp. 118-130, 2004.

Abstract – Summary: Such knowledge can provide an athlete or coach with the greatest benefit and should be consumed. The various techniques utilized to rate protein will be discussed. Traditionally, sources of dietary protein are seen as either being of animal or vegetable origin. Animal sources provide a complete source of protein (i.e. containing all essential amino acids), whereas vegetable sources generally lack one or more of the essential amino acids. Animal sources of dietary protein, despite providing a complete protein and numerous vitamins and minerals, have some health professionals concerned about the amount of saturated fat common in these foods compared to vegetable sources. The advent of processing techniques has shifted some of this attention and ignited the sports supplement marketplace with derivative products such as whey, casein and soy. Individually, these products vary in quality and applicability to certain populations. The benefits that these particular protein sources are discussed. In addition, the impact that elevated protein consumption has on health and safety issues (i.e. bone health, renal function) are also reviewed.

KEY WORDS: Sport supplementation, ergogenic aid, animal protein, vegetable protein.

INTRODUCTION

The protein requirements for athletic populations have been the subject of much scientific debate. Only recently has the notion that both strength/power and endurance athletes require a greater protein consumption than the general population become generally accepted. In addition, high protein diets have also become quite popular in the general population as part of many weight reduction programs. Despite the prevalence of high protein diets in athletic and sedentary populations,

information available concerning the type of protein (e.g. animal or vegetable) to consume is limited. The purpose of this paper is to examine and analyze key factors responsible for making appropriate choices on the type of protein to consume in both athletic and general populations.

Role of Protein

Proteins are nitrogen-containing substances that are formed by amino acids. They serve as the major structural component of muscle and other tissues in

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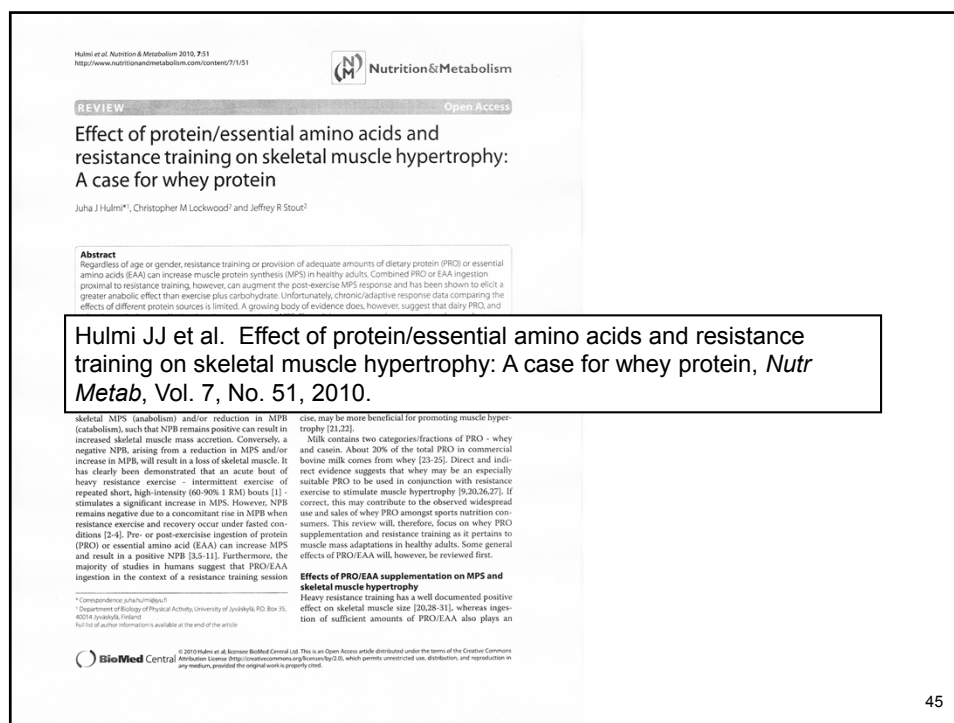
- **“The processing of whey concentrate removes the water, lactose, ash, and some minerals. In addition, compared to whey isolates whey concentrate typically contains more biologically active components and proteins make them a very attractive supplement for the athlete.”**
- **“Although the concentration of protein in this form [isolate] is the highest, it often contains proteins that have become denatured due to the manufacturing process. The denaturation of proteins involves breaking down their structure and losing peptide bonds and reducing the effectiveness of the protein.”**

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Still more on leucine

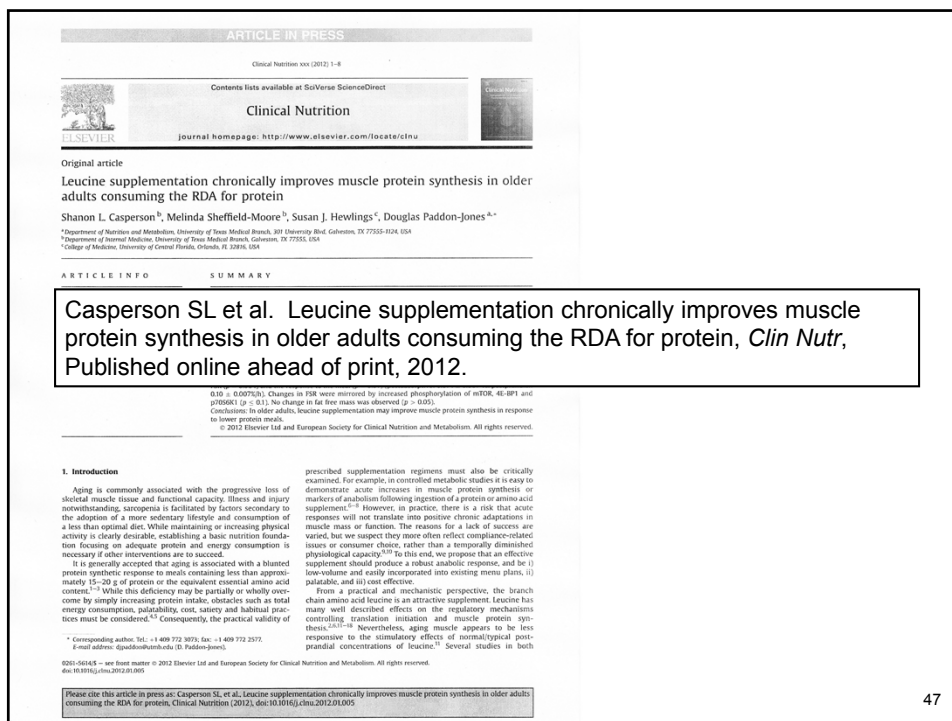
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Entry Level Clinical Nutrition Update – Part 4 With Dr. Jeff Moss



- **“It is probable that the most important component in whey, for increasing protein synthesis and skeletal muscle size is its high concentration of the BCAA, leucine.”**
- **“Leucine, acting as a signaling molecule in the mTOR cascade, has been shown to be a critical amino acid for increasing skeletal muscle synthesis, both *in vitro* and *in vivo* in humans and rats. Leucine may also be involved in suppressing muscle protein degradation, according to investigations *in vitro* and *in vivo* in humans.”**

Entry Level Clinical Nutrition Update – Part 4 With Dr. Jeff Moss



- “It is generally accepted that aging is associated with a blunted protein synthetic response to meals containing less than approximately 15-20 g of protein or the equivalent essential amino acid content.”
- “...in controlled metabolic studies it is easy to demonstrate acute increases in muscle protein synthesis or markers of anabolism following ingestion of a protein or amino acid supplement.

- **“However, in practice, there is a risk that acute responses will not translate into positive chronic adaptations in muscle mass or function.”**
- **“The reasons for a lack of success are varied, but we suspect they more often reflect compliance-related issues or consumer choice, rather than a temporally diminished physiological capacity.”**

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- **“To this end, we propose that an effective supplement should produce a robust anabolic response, and be i) low-volume and easily incorporated into existing menu plans, ii) palatable, and iii) cost effective.”**
- **“While the headline result from the leucine studies mentioned above are encouraging, an important emerging caveat is that leucine supplementation is not unconditionally effective.”**

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“Specifically, ingestion of supplemental leucine appears to be of little benefit to: i) younger adults, and/or, ii) individuals who habitually consume a protein/leucine-sufficient diet.”

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- With the above in mind, Casperson et al conducted a study on eight healthy but sedentary older adults with a daily protein intake of 0.75 – 0.85g protein per kilogram body weight per day, which is near the current RDA.
- Why is this amount significant in relation to this study? As I have pointed out in several newsletters, very often elderly populations will need protein ingestion anywhere from 1.2 – 1.5 g/kg/per day to optimize muscle mass.

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- Therefore, the authors classified the meals ingested by the study subjects as “low protein.” The study was fairly long-term as these studies go (15 days), with the subjects ingesting 4 grams of supplemental leucine with each of three meals per day for days 2-14.

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What were the results of the study?

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- **“Our data suggest that leucine supplementation may be an energetically efficient and practical means of chronically improving muscle protein synthesis in response to a low protein meal in older adults who habitually consume close to the RDA for protein.”**

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- **“...we demonstrated that supplementing regular daily meals with a relatively small amount of leucine improves both mixed-muscle protein synthesis and anabolic signaling in older adults.”**
- **“...while we did not conduct a specific assessment of practical issues such as longer duration compliance, ease of use or palatability, our low-volume approach is intuitively less likely to be burdensome than most traditional higher-volume amino acid supplement regimens.”**

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However, two weeks is not
two months or two years

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http://ajphaphysiol.nutrition.org/content/suppl/2011/02/01/111.13849.
13849.F1.pdf

Prolonged Leucine Supplementation Does Not Augment Muscle Mass or Affect Glycemic Control in Elderly Type 2 Diabetic Men¹⁻³

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Abstract
The loss of muscle mass with aging has been, at least partly, attributed to a blunted muscle protein synthetic response to food intake. Leucine supplementation has been reported to stimulate postprandial insulin release and augment postprandial

Leenders M et al. Prolonged leucine supplementation does not augment muscle mass or affect glycemic control in elderly type 2 diabetic men, *J Nutr*, Vol. 141, pp. 1070-1076, 2011.

Introduction
Aging is accompanied by a progressive decline in skeletal muscle mass and strength, termed sarcopenia (1). The progressive loss of skeletal muscle mass and strength results in a decline in functional capacity and predisposes to the development of chronic metabolic diseases, like obesity and type 2 diabetes (2). One of the major causes of sarcopenia seems to be the disruption in the regulation of muscle protein turnover. Recent work indicates that the elderly are less sensitive to the main anabolic stimuli, such as physical activity and/or food intake (3, 4). It has been suggested that increasing the leucine content of a meal can effectively compensate for the blunted muscle protein synthetic response to food intake in the elderly (5, 6). Recently, Katsanos et al. (3) reported that increasing the leucine content of an amino acid mixture (from 24 to 41%) normalizes the muscle protein synthetic response in the elderly when compared with young individuals. These findings were supported by Ricu et al. (6), who observed considerably higher postprandial muscle protein synthetic rates in elderly men after they consumed leucine-enriched meals. As a consequence, it has been suggested that increasing the leucine content of a meal represents an effective dietary strategy to augment the muscle protein synthetic response to food intake in the elderly.

So far only a single placebo-controlled study has been performed to evaluate the proposed clinical relevance of prolonged leucine supplementation in the elderly. We recently reported the impact of 3 mo of leucine supplementation with each main meal on muscle mass and strength in healthy, elderly males (7). No changes in skeletal muscle mass or strength were observed over the 3-mo intervention period. In response, some suggested that the absence of any impact of leucine supplementation on muscle mass and strength could be attributed to the relatively short intervention period and/or to the specific inclusion of healthy, elderly males. As such, we concluded that the impact of prolonged leucine supplementation should be assessed in more compromised elderly subpopulations over a more extensive intervention period (7).

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² This trial was registered at clinicaltrials.gov as NCT00643773.
³ Supplemental Tables 1-3 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at ajphaphysiol.nutrition.org.
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- **“Sixty elderly males with type 2 diabetes (age, 71 ± 1 y; BMI, 27.3 ± 0.4 kg/m²) were administered 2.5 g L-leucine (n = 30) or a placebo (n = 30) with each main meal during 6 mo of nutritional intervention (7.5 g/d leucine or placebo).”**
- **“Body composition, muscle fiber characteristics, muscle strength, glucose homeostasis, and basal plasma amino acid and lipid concentrations were assessed prior to, during, and after intervention.”**

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- **“The present study shows that 6 mo of leucine supplementation (a total of 7.5 g/d) with each main meal does not augment skeletal muscle mass and strength, modulate body composition, or improve glycemic control and blood lipid profile in elderly men with type 2 diabetes who habitually consume sufficient protein.”**

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It should also be noted that, for both the control and experimental groups, dietary protein intake per day was 0.94 ± 0.04 g/kg body weight.

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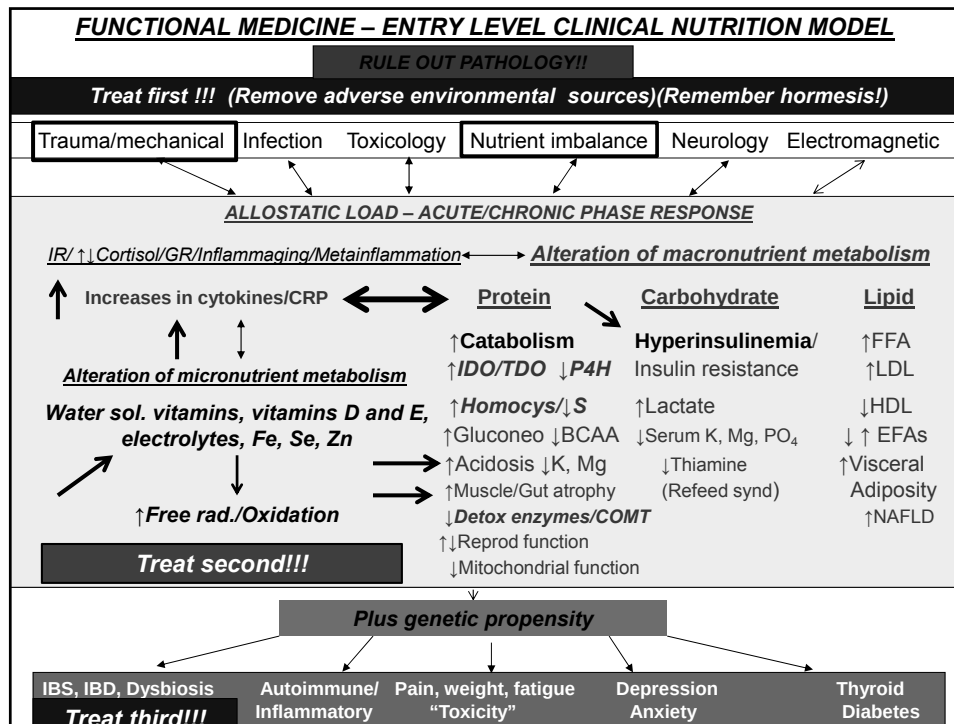
Why did the long term study not demonstrate positive results?

- Suboptimal protein intake (1.2 – 1.5 g/kg/day is ideal)
- The study did not include weight-bearing exercise.

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Thank you!!

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