

Entry Level Clinical Nutrition Part VI

Protein, amino acid imbalance,
and sarcopenia:
Part I

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

2

- ***What appears to be the most important determinant of quality of life?***
- ***Optimal lean body mass.***

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Medical News: Walking Speed and Survival Connected - Printable Version Page 1 of 3


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Walking Speed and Survival Connected
By Todd Heale, Staff Writer, MedPage Today
January 04, 2011

MedPage Today Action Points

- Note that this study proposes measurement of gait speed as a standardized, inexpensive, and relatively quick indicator of health and survival in older patients.
- Point out that at present there is no evidence that gait speed improvements are associated with better health-related outcomes, and it would not be reasonable to impose interventions on patients in order to do this.

Review
Walking speed -- an indicator of vitality -- may help clinicians predict how long their older patients will live, a meta-analysis showed.

In a pooled analysis of nine cohort studies, each 1-m/s increase in gait speed was associated with a 12% relative reduction in the risk of death during follow-up (HR 0.88, 95% CI 0.87 to 0.90), according to Stephanie Studenski, MD, MPH, of the University of Pittsburgh, and colleagues.

The risk reduction was consistent across most subgroups -- except for functional status -- with hazard ratios ranging from 0.81 to 0.92 ($P < 0.002$ for all), the researchers reported in the Jan. 5 issue of the *Journal of the American Medical Association*.

If use of gait speed -- a simple indicator of physical function -- as a predictor or survival is implemented in clinical practice, it may help clinicians individualize the treatment of older patients, according to Studenski and her colleagues.

Patients whose gait speed indicates a high probability of living for five to 10 years may be appropriate candidates for preventive interventions that require a long time to work. On the other hand, patients with slow gait speed could be targeted for interventions to ameliorate risks to health and survival.

Additionally, monitoring gait speed over time for deviations may allow for the detection of new health problems that require evaluation.

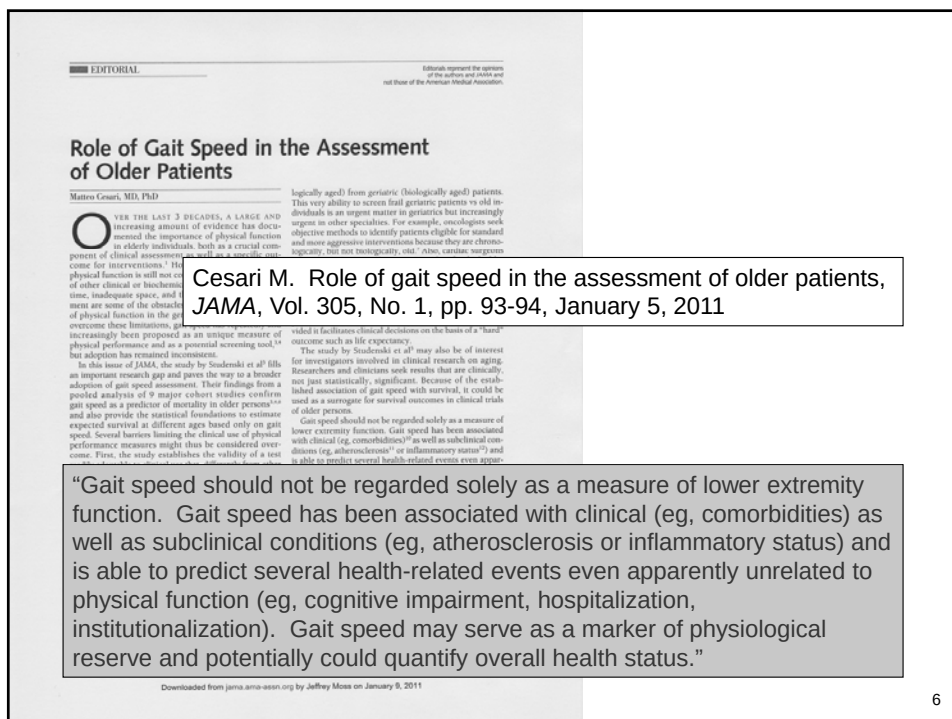
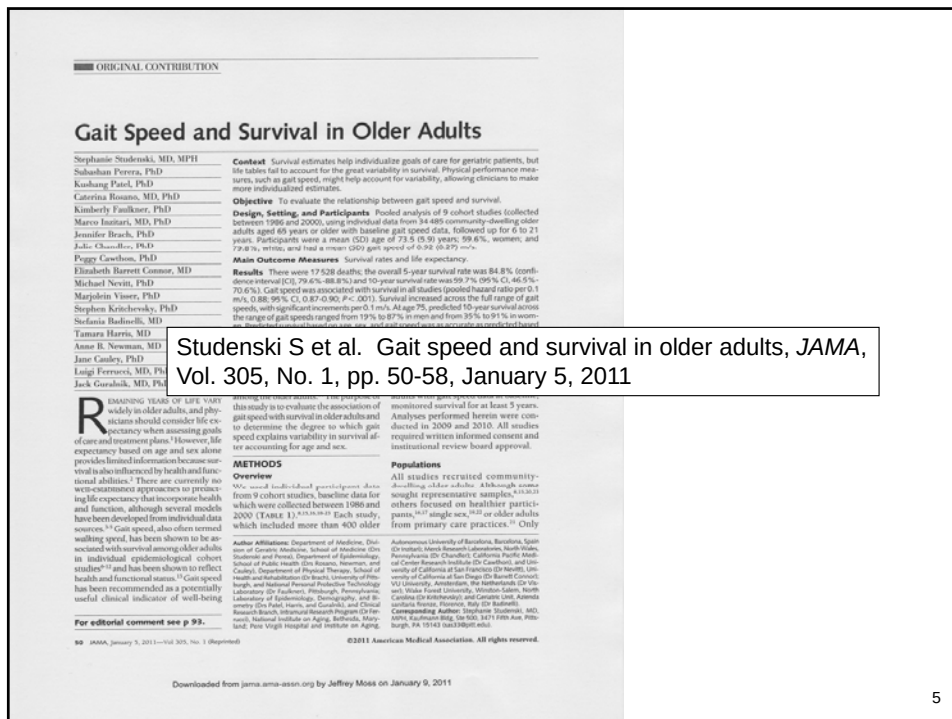
Finally, the authors wrote, gait speed may be useful in the research setting, by allowing for the evaluation of whether interventions to improve walking speed result in

<http://www.medpagetoday.com/tbprint.cfm?tbid=24180> 1/9/2011

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Entry Level Clinical Nutrition – Part 6

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“...gait speed may be considered a new ‘vital sign,’ specifically sensitive for older persons.”

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- ***Why is lean body mass lost?***
- ***Two reasons.***
- ***Aging***
- ***A response to environmental stressors***

8

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)*

9

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

The New York Times

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September 9, 2009

Summer of Work Exposes Medical Students to System's Ills

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.
more at
exclusive
Obgast
treatme

Summer of work exposes medical students to system's ill, *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. Obgast 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. Obgast said.

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

Five to seven, 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 enticements, 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=&enc=th&... 9/9/2009

Entry Level Clinical Nutrition – Part 6

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Plan now so your later years can be comfortably extended

Palliative care, in my view, is the future of care for those of us entering the In-Between Stage. Its aim is to treat symptoms and relieve suffering, and it can be offered when we are first diagnosed with a serious illness.

USA Today, January 11, 2011

New Passages
By Gail Sheehy

Journalist and lecturer Gail Sheehy is the author of 16 books about adult life stages, including *Passages in Caregiving*.

There has been an even more dramatic increase among Medicare beneficiaries, who report three or more chronic conditions, including Passages in Caregiving.

“Sixty-five percent of Americans in mid-life (ages 45-64) live with at least one chronic illness, according to a national 2009 study reported in *Health Affairs*. There has been an even more dramatic increase among Medicare beneficiaries, who report three or more chronic conditions, and that jump occurred equally across, sex, race, ethnicity and income groups.”

what they really want is individualized treatment if desired.

chronic conditions or serious health problems, the need for advance-care planning increases. It should be a routine part of our medical care.

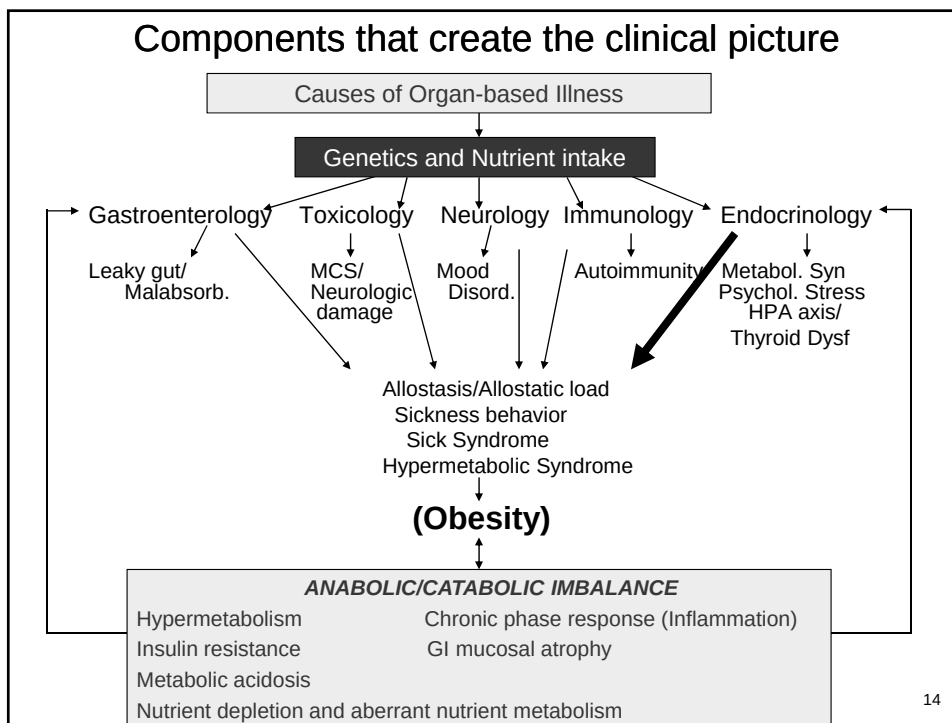
The last thing most of us would want is to be rushed off to the hospital with a stroke or heart attack or emergency surgery and be peppered by harried staff with questions about what extreme measures we want or don't want, when all we can think about is getting out of pain.

Palliative care, in my view, is the future of care for those of us entering the In-Between Stage. Its aim is to treat symptoms and relieve suffering, and it can be offered when we are first diagnosed with a serious illness. It's not the same as hospice, people with a range of cancers, sclerosis, emphysema and shortness of breath,” says Diane Meier, a geriatrician at the Mount Sinai School of Medicine.

Sadly, the more common route is a revolving door from hospital to rehab to rehospitalization, which is especially debilitating for older people. They can't tell day from night. They can't fight antibiotic-resistant infections. They can't talk back to overworked staff. The sense of isolation and total loss of control has an adverse effect on the immune system.

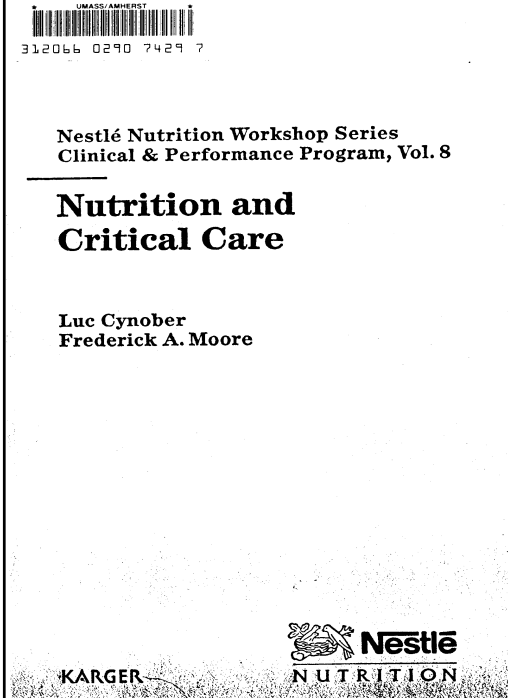
By contrast, groundbreaking research from Harvard and other research centers shows that palliative care may actually prolong life.

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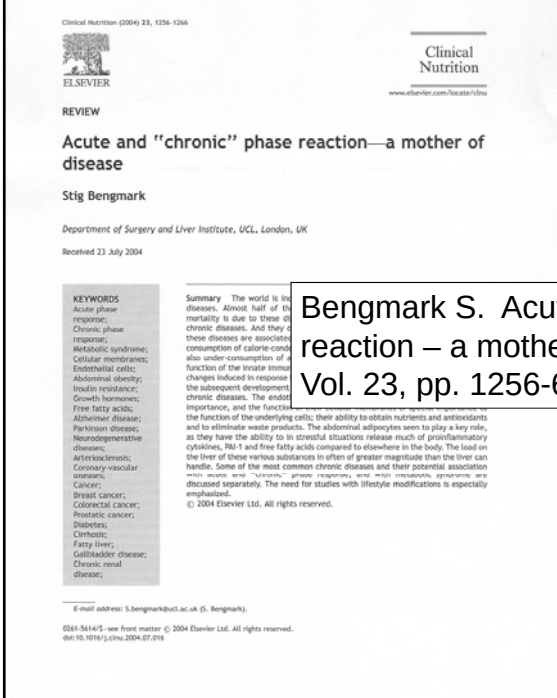


Baracos VE. Overview on metabolic adaptation to stress, pp. 1-13.

“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.”

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Bengmark S. Acute and “chronic” phase reaction – a mother of disease, *Clin Nutr*, Vol. 23, pp. 1256-66, 2004

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Considerations for the Catabolic Patient				
Signs & Symptoms	Consider	Treatment Plan	Monitor	Supplementation
Signs & Symptoms: - Feeling "lousy" - Fatigue - Cravings - Depression/anxiety - Poor quality sleep - Poor digestion/absorption/leaky gut - Chronic pain/infection Clinical Findings: - High % body fat - Low bone density - High fasting insulin - Heavy metal burden - Calcium to phosphorus ratio 3:1 - High normal globulin - Cholesterol (220-280) - High LDL, low HDL - High triglycerides - Low normal serum potassium, high normal serum sodium - High normal BUN with normal creatinine - Low urinary sulfate - Genomic variations	Optimize pH	Optimize fluid and electrolyte balance	Morning urinary pH -pH paper	Potassium bicarbonate -K Alkaline (Moss) Magnesium -Magnesium Glycinate (Vital Nutrients)
	Optimize muscle mass (reduce sarcopenia) and amino acid levels	Pay special attention to protein and amino acids	Body composition: -Bioelectric impedance scale Grip strength: -dynamometer	Amino acids -Custom Amino Base (Metabolic Maint.) Protein powders/bars -UltraLean products (Biogenesis) -Paleo products (DFH)
	Reducing inflammation	Reduce inflammation Address food allergies	Inflammatory biomarkers: -HS-CRP -Fibrinogen levels -WBC -Differential	Anti-inflammatory agents -Inflametric (Olympian) -D-Flame (Protocols) -Pain Guard (Perque) Fish Oils -Ultra Pure Fish oil (Vital Nutrients) Food allergy blends -AllerGzymes (DFH)
	Improving insulin sensitivity	Watch carbohydrate/protein ratio	Fasting glucose Fasting insulin Cravings	Metabolic Synergy (DFH)
	Optimize dietary carbohydrate/protein ratios	Replete protein deficiencies and reduce carbohydrate intake along with improvements in dietary quality	Diet diary Optimal protein intake -1.0 – 1.2 g/kg body weight	Protein powders/bars -Paleo products (DFH) -UltraLean (Biogenesis)
	Optimize GI function	Dietary changes, supplementation of digestive aids	Patient signs and symptoms	Betaine HCl (Vital Nutrients) Digestzymes (DFH) Intestinal Repair Complex (Biogenesis)
	Optimize micronutrient deficiencies/imbbalances	Supplementation of multis Possible emphasis on vitamin D, iodine, and zinc	Serum 25 OH vitamin D Fatigue/serum thyroid indicators Zinc taste test	Multi Nutrients (Vital Nutr) Vitamin D (Vital Nutr) Iosol (Moss) Zinc Supreme (DFH)
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Neuro-SIGNALS Invited Review Neurosignals 2009;17:144-152 DOI: 10.1155/2009/144152 Received April 20, 2009 Accepted after revision June 5, 2009 Published online February 5, 2010	
Biological Mechanism of Antidepressant Effect of Omega-3 Fatty Acids: How Does Fish Oil Act as a 'Mind-Body Interface'? Kuan-Pin Su Department of General Psychiatry and Mind-Body Interface Laboratory (MBI-LAB), China Medical University and Hospital, Taichung, Taiwan; Stress, Psychiatry and Immunology Laboratory (SPI-LAB), Institute of Psychiatry, King's College London, London, UK	
Key Words Major depressive disorder - Depressive acid - Docosahexaenoic acid - Arachidonic acid - Prostaglandins - Thromboxanes - Lipid Phospholipase A2 - Cyclo-oxygenase	Abstract The unsatisfactory results of monoamine-based antidepressant therapy and the high occurrence of somatic symptoms and physical illness in patients with depression imply that the serotonin hypothesis is insufficient to approach the aetiology of depression. Depressive disorders with somatic presentation are the most common form of depression. Somatization, the bodily symptoms without organic explanation, is similar to cytokine-induced sickness behaviour. Based on recent evidence, omega-3 polyunsaturated fatty acids (n-3 PUFAs, or n-3 fatty acids) are enlightening a promising path to discover the unsolved of depression, sickness behaviour and to link the connection of mind and body. The PUFAs are classified into n-3 (or omega-3) and n-6 (or omega-6) groups. Docosapentaenoic acid and docosahexaenoic acid, the major bioactive components of n-3 PUFAs, are not efficiently synthesized in humans and should therefore be obtained directly from the diet, particularly by consuming fish. Docosahexaenoic acid deficiency is associated with dysfunctions of neuronal membrane stability and transmission
prostaglandin E₂ synthesis, which might be linked to the somatic manifestations and physical comorbidity in depression. The role of n-3 PUFAs in immunity and mood function supports the promising hypothesis of psychoneuroimmunology of depression and provides an excellent interface between 'mind' and 'body'. This review is to provide an overview of the evidence about the role of n-3 PUFAs in depression and its common comorbid physical conditions and to propose mechanisms by which they may modulate molecular and cellular functions. Introduction Major depressive disorder (MDD) is a serious psychiatric illness with a high lifetime prevalence rate [1]. However, the current treatment for this high burden disease is not satisfactory. Less than 50% of patients achieve full remission with optimized medication treatment [2] despite that more than 40 antidepressants with mechanisms related to serotonin, norepinephrine and/or dopamine	Su KP. Biological mechanism of antidepressant effect of omega-3 fatty acids: How does fish oil act as a 'mind-body interface'? Neurosignals, Vol. 17, pp. 144-152, 2009
KARGER © 2009 S. Karger AG, Basel 1662-4587/09/1702-0144\$30.00 DOI: 10.1155/2009/144152 www.karger.com	Dr. Kuan-Pin Su Department of Psychiatry China Medical University Hospital No. 2, Yuh-Der Road, Taichung 40424 (Taiwan) Tel.: +886 4 2256 2121, ext. 3070; Fax: +886 4 2256 1230; E-Mail: kalsu@cmuh.org.tw

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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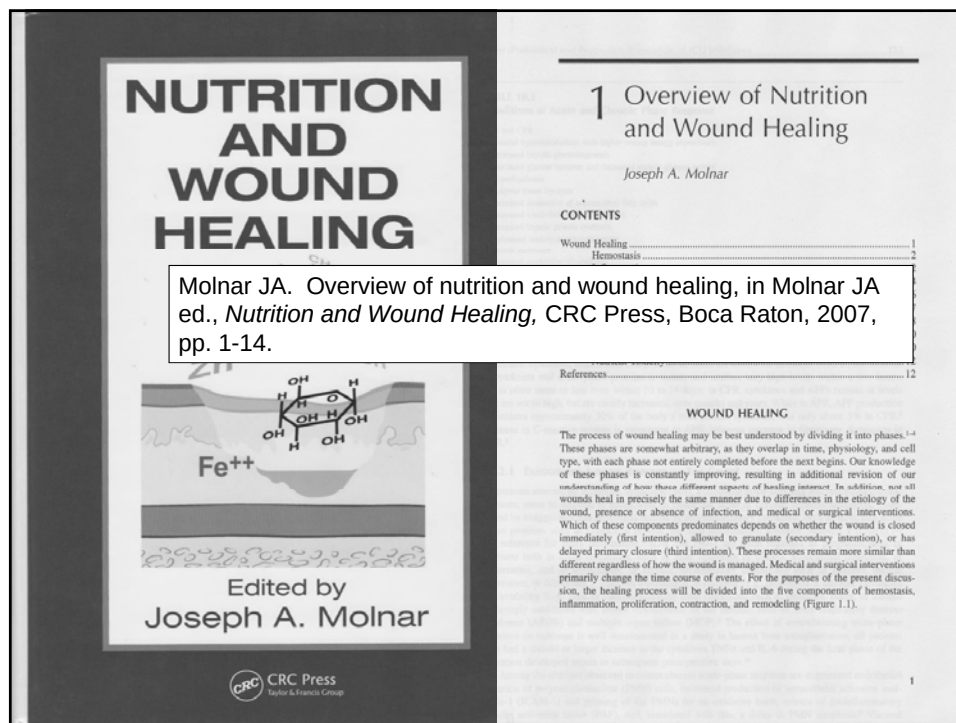
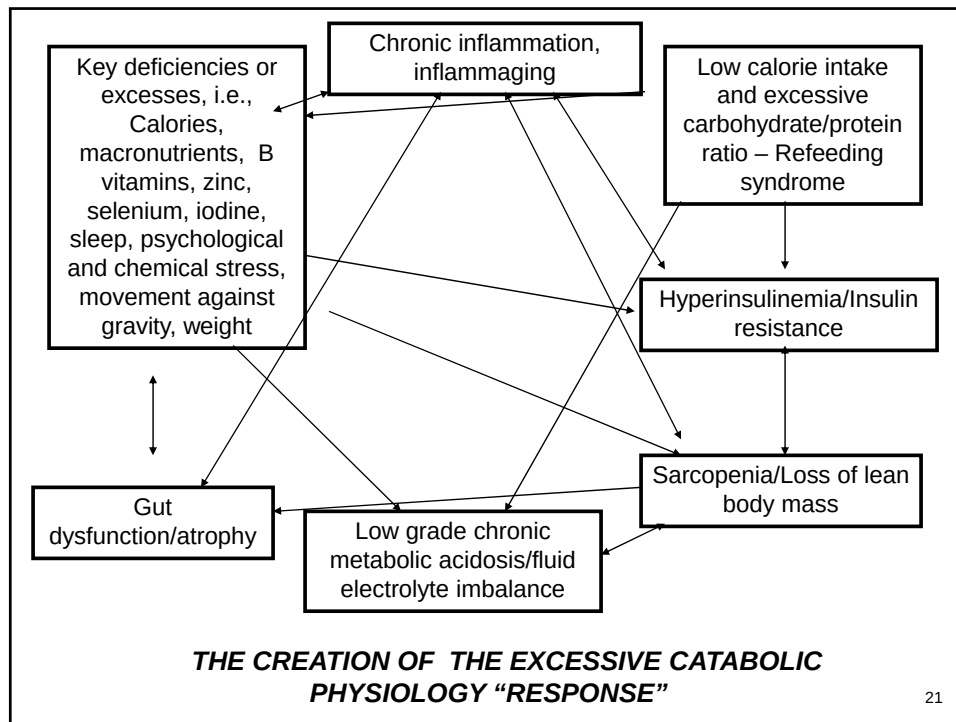
Key metabolic imbalances seen with the acute phase response

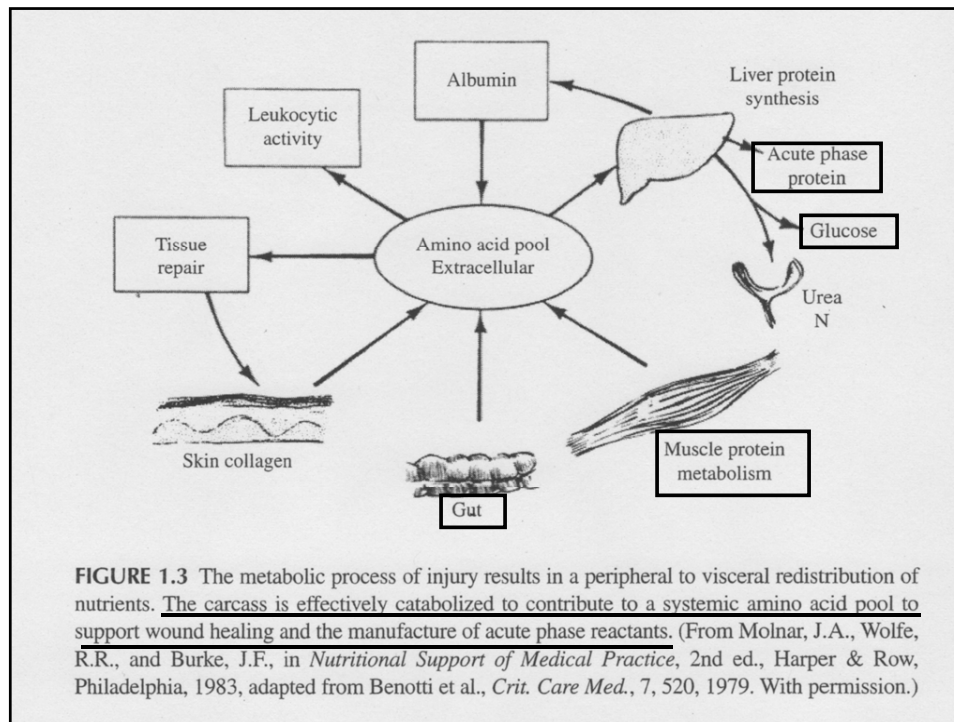
- Metabolic acidosis
- Loss of lean body mass (sarcopenia)
- Insulin resistance
- Inflamm-aging (Increased innate immunity and decreased adaptive immunity)
- Suboptimal caloric intake and carbohydrate:protein ratio (Refeeding syndrome)
- Gastrointestinal dysfunction/gut atrophy
- Deficiencies of key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

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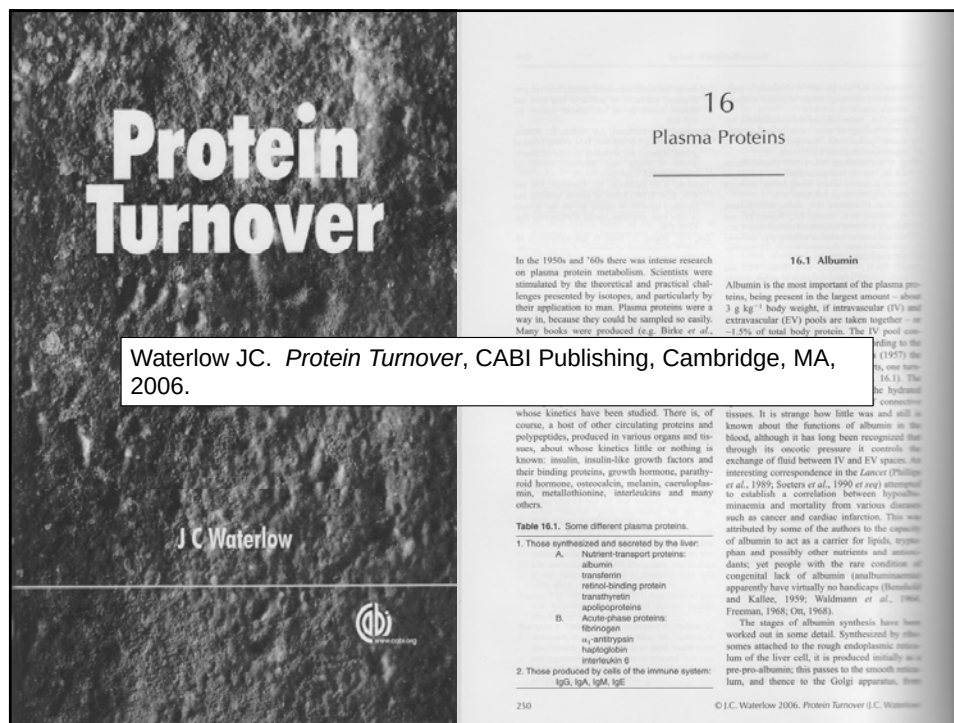




- “During periods of metabolic stress, the body is able to effectively catabolize the carcass (muscle, skin, bone) to support visceral protein synthesis of acute phase proteins, immunoglobulins, inflammatory cells, and collagen, needed to fight infection and heal the wound.”
- “In the case of proteins, intricate shuttling mechanisms have developed to allow redistribution of the substrate from the periphery to the viscera.”

- “This could also apply to micronutrients. Because a large percentage of the body zinc stores are found in the skin, it would not be surprising that if the skin proteins are catabolized, this might allow mobilization of skin zinc to provide cofactors for enzymatic activity in other parts of the body.”

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- “In many patients plasma albumin concentrations are low and it has been suggested that the acute phase proteins compete with albumin for the amino acids required for synthesis.”
- “An interesting hypothesis was proposed by Reeds *et al.* to relate the acute phase protein response to the muscle wasting that occurs in so many clinical conditions.”

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- “At its peak total synthesis of APPs after a stress, from the data of Fleck *et al.*, could amount to as much as 0.85 g of protein per kg per day.”
- “The APPs contain larger amounts of the aromatic amino acids than muscle, and Reeds calculated that it would require the breakdown of 2 g of muscle protein to provide amino acids for the synthesis of 850 mg of APPs.”
- “The other amino acids that are produced in excess from muscle in order to meet the need of aromatics will be oxidized and the nitrogen excreted in the urine.”

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“This would account for a large part of the ‘catabolic’ loss after trauma or in septic states.”

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Proceedings of the Nutrition Society (2005), 64, 285–296
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Physiological functions should be considered as true end points of nutritional intervention studies

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²Department of Clinical Nutrition, University Hospital, Geneva, Switzerland

With the beginning of this volume, the concept of physiological functions as true end points of nutritional intervention studies is presented. The aim of this presentation is to prove that this concept greatly improves the contribution of nutritional intervention studies. The following problems should be considered: many populations undergoing intervention have low mortality, resulting studies with thousands of patients to demonstrate effects of intervention on mortality; nutrition is only a rare cause primary treatment, and in many populations is a prerequisite for survival rather than a therapeutic modality; once the effect of nutritional support is achieved, the extra benefit of modulation of the nutritional support regimen can only be modest; consistently to use a valid end point, because the better it is, the more the score is well done; mortality and morbidity are crude end points for the effect of nutritional intervention, and are influenced by many factors. In fact, it is a year or so later. In the literature the most important contributions include new insights into the pathogenesis of disease, the distinction of disease-related adverse events and functional improvement after therapy. In summary, mortality and morbidity are crude end points that have precluded the development and validation of functional end points, such as muscle, immune and cognitive functions, quality of life, morbidity and mortality are directly related to these functional variables. It is, therefore, of paramount importance to validate functional end points and to consider them as primary rather than surrogate end points.

Clinical end points: Muscle function: Immune function: Cognitive function: Evidence-based medicine

Nutritional depletion, or protein-energy malnutrition, has been associated with a high rate of infection-related mortality and morbidity (Hendrick, 1995). The association is implicit because nutritional depletion has been defined in general as a situation of depleted energy or intake of nutrients leading to disturbed physiological function. In the metabolic and nutritional field (expert) morbidity and mortality are generally considered as the only hard end points. However, a substantial amount of work shows that (1) physiological dysfunction increases the risk of septic complications and mortality (Kusman et al., 2000; Dewey & So, 2001; Calzavara et al., 2002); (2) nutritional markers are highly correlated with alterations of muscular, immune

and cognitive functions (Hogge et al., 1998; Proulx et al., 2001; Genton et al., 2003); (3) nutritional support may improve physiological function (Hendrick et al., 1996; Boudel-Machamen et al., 2001; Magut et al., 2003). These findings raise the question of whether physiological functions can be used as hard end points in nutritional studies. At present, the diagnosis of nutritional depletion and the follow-up of patients with a pre-existing nutritional state rarely include the assessment of physiological function. Although it appears obvious that nutritional state and function are linked, lack of clearly defined and validated functional tests may explain why they are rarely used. Furthermore, the assessment of physiological functions

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- “Nutritional depletion leads to alterations in muscle function and possibly cognitive and immune function.”
- “Nutritional supplementation can reverse some of the physiological dysfunctions occurring with nutritional depletion, but confounding variables are numerous.”
- “Nevertheless, because muscle strength consistently predicts morbidity and mortality, it is suggested that this variable is used as a hard marker of malnutrition-related morbidity and mortality.”

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The American Journal of Medicine (2007) 120, 337–342



ELSEVIER

CLINICAL RESEARCH STUDY

Grip Strength Predicts Cause-Specific Mortality in Middle-Aged and Elderly Persons

Hideo Sasaki, MD, PhD,^{a,*} Fumiyoshi Kasagi, PhD,^a Michiko Yamada, MD, PhD,^a Shoshiko Fujita, PhD^b

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THE AMERICAN
JOURNAL of
MEDICINE

ABSTRACT

PURPOSE: Handgrip strength is a simple measurement used to estimate overall muscle strength but might also serve as a predictor of health-related prognosis. We investigated grip strength-mortality association in a longitudinal study.

METHODS: A total of 4912 subjects of this study, aged 40–74 years, underwent a baseline examination in 1970 and June 1972. Mortality associated with grip strength were adjusted for potentially confounding factors by Cox proportional hazard analysis.

RESULTS: Multivariate-adjusted HR of all causes of death, except for external causes, for the highest quartile of grip strength in men was 0.52 (95% confidence interval [CI], 0.33–0.80) for the age group 55–64 years, 0.72 (95% CI, 0.53–0.96) for the age 65–74 years, and 0.67 (95% CI, 0.49–0.91) for the age 75+ years. These figures were significantly lower than the HR for the reference group (the third quartile). Significant results were observed in women. Multivariate-adjusted HR of all causes of death except cancer

Sasaki H et al. *Am J Med*, Vol. 120, pp. 337-342, 2007

CONCLUSIONS: Grip strength measurement is useful for assessing approximate overall muscle strength of middle-aged and elderly people, and longitudinal studies revealed that it also predicts health-related prognosis.

“Grip strength is an accurate and consistent predictor of all causes of mortality in middle-aged and elderly persons.”

KEY WORDS: Grip strength; mortality; prognosis; handgrip strength; muscle strength; health-related prognosis.

Further, most of the studies' follow-up periods were less than 10 years after baseline measurement of grip strength.

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0002-9343/\$ - see front matter © 2007 doi:10.1016/j.amjmed.2006.04.018

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Grip and Pinch Strength: Normative Data for Adults
 Virgil Mathiowetz, MS, OTR, Nancy Kashner, OTR, Gloria Volland, OTR, Mary Dowse, OTS, Sandra Rogers, OTS

Occupational Therapy Program, University of Wisconsin-Milwaukee, Milwaukee, WI 53201

ABSTRACT. Mathiowetz V, Kashner N, Volland G, Weber K, Dowse M, Rogers S: Grip and pinch strength: normative data for adults. *Arch Phys Med Rehabil* 66:69-72, 1985.

The primary purpose of this study was to establish clinical norms for adults aged 20 to 75+ years on four tests of hand strength. A dynamometer was used to measure grip strength and a pinch gauge to measure tip, key, and palm pinch. A sample of 310 male and 328 female adults, ages 20 to 74, from the seven-county Milwaukee area were tested using standardized positioning and instructions. Right hand and left hand data were stratified into 12 age groups for both sexes. This stratification provides a means of comparing the score of individual patients to that of normal subjects of the same age and sex. The highest grip strength scores occurred in the 21 to 39 age groups. For tip, key, and palm pinch the average scores were relatively stable from 20 to 59 years, with a gradual decline from 60 to 79 years. A high correlation was seen between grip strength and age, but a low to moderate correlation between pinch strength and age. The newer pinch gauge used in this study appears to read higher than that used in a previous normative study. Comparison of the average hand strength of right-handed and left-handed subjects showed only minimal difference.

KEY WORDS: Exercise test, Erection, Occupational therapy, Physical therapy

Reliable and valid evaluation of hand strength is of paramount importance in determining the effectiveness of various surgical or treatment procedures. In addition, normative data are needed to interpret evaluation data to set realistic treatment goals, and to assess a patient's ability to return to employment.

The most common norms for grip and pinch strength in the literature are those compiled by Kurland¹ in 1954. Kurland sampled 250 individuals in three large age groups (20-29, 30-39, and 40-49) and analyzed was performed to predict the grip (RUL) or left hand (LHL) strength as individual and particular age would demonstrate. Six subjects were tested, their scores were used right-handed subjects. No standardized positioning or instructions were followed. Test-retest and intratester reliability data were not reported. The Ohio pinch meter used in their study is no longer commercially available and there is some question whether data from use of the newer pinch meters can be validly compared to their norms.²

Another study³ established clinical norms for grip strength, employing the Martin Vigorimeter, which has a soft handle and has been used clinically with arthritic patients. However, the Janair dynamometer has been found⁴ to give the most accurate measure of grip strength.

Schmidt and Trews⁵ used the Janair dynamometer to test grip strength in a large sample, 1128 males (53, 10 females (F), of employee applicants at a manufacturing plant. Although the instrument and examination were described in detail, description was not sufficient for replication. Unfortunately, as the handles of the dynamometer were coated with a sand-oil mixture and the data were collected in the competitive situation of a pre-job placement interview, generalization from these results is questionable.

Recently, the American Society of Hand Therapists, suggesting a standardized arm positioning for hand strength tests, concluded that the position of the upper extremity (UE) might influence measurements, and recommended that the patient should be seated with his shoulder abducted and neutrally rotated, elbow flexed at 90° and the forearm and wrist in neutral position.⁶

Table 1: Characteristics of Subjects: Age, Sex, and Hand Dominance

Age	Male				Female			
	N	Age (yr)	R	L	N	Age (yr)	R	L
20-24	22	21.7	22	2	22	21.4	22	0

Age	Male				Female			
	N	Age (yr)	R	L	N	Age (yr)	R	L
25-29	22	26.9	22	0	28	27.3	22	6
30-34	24	31.9	23	1	29	31.8	28	1
35-39	22	36.9	23	0	26	36.8	23	3
40-44	22	41.7	22	0	22	41.7	22	0
45-49	22	46.9	22	0	22	46.9	22	0
50-54	22	51.9	22	0	22	51.9	22	0
55-59	22	56.9	22	0	22	56.9	22	0
60-64	22	61.9	22	0	22	61.9	22	0
65-69	22	66.9	22	0	22	66.9	22	0
70-74	22	71.9	22	0	22	71.9	22	0
75+	22	76.9	22	0	22	76.9	22	0
TOTAL	220		220	3	220		220	7

In testing the variability of wrist position, Pyrie⁷ found no significant difference in grip strength with test positions at 0° and 15° ulnar deviation, 0° and 15° dorsiflexion, or any combination of these. Kraft and Deutsch⁸ found no significant difference with test positions at 0°, 15°, and 30° dorsiflexion (0° ulnar deviation) in measuring grip strength. Both studies^{7,8} found grip strength to be significantly less at 15° of volar flexion.

Mathiowetz and associates⁹ used standardized procedures (subject position and instructions) to assess the reliability and validity of grip strength and pain evaluations. The highest test-retest reliability for each test was achieved when the mean of three trials was utilized. The Janair dynamometer and the B&L pinch gauge¹⁰ had the highest calibration accuracy of the instruments tested.¹¹ No normative data based on these standardized procedures have previously been reported.

The primary purpose of this study was to establish clinical norms for grip and pinch strength in a large sample of adults aged 20 to 75+ years. The study was funded in part by a grant from the American Occupational Therapy Foundation. Submitted for publication December 15, 1984; accepted March 21, 1985.

Mathiowetz V et al. Grip and pinch strength: Normative data for adults, *Arch Phys Med Rehabil*, Vol. 66, pp. 69-72, 1985

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Table 2: Performance of All Subjects on Grip Strength (pounds)

		Men					Women				
	Hand	Mean	SD	SE	Low	High	Mean	SD	SE	Low	High
20-24	R	121.0	20.6	3.8	91	187	70.4	14.5	2.8	48	95
	L	104.5	21.8	4.0	71	150	61.0	13.1	2.8	33	88
25-29	R	120.8	23.0	4.4	78	158	74.5	13.9	2.7	48	97
	L	110.5	16.2	3.1	77	139	63.5	12.2	2.4	48	97
30-34	R	121.8	22.4	4.3	70	170	78.7	19.2	3.8	46	137
	L	110.4	21.7	4.2	64	145	68.0	17.7	3.5	36	115
35-39	R	119.7	24.0	4.8	76	176	74.1	10.8	2.2	50	99
	L	112.9	21.7	4.4	73	157	66.3	11.7	2.3	48	91
40-44	R	116.8	20.7	4.1	84	165	70.4	13.5	2.4	38	103
	L	112.8	18.7	3.7	73	157	62.3	13.8	2.5	35	94
45-49	R	109.9	23.0	4.3	65	155	62.2	15.1	3.0	39	100
	L	100.8	22.8	4.3	58	160	56.0	12.7	2.5	37	83
50-54	R	113.6	18.1	3.6	79	151	65.8	11.6	2.3	38	87
	L	101.9	17.0	3.4	70	143	57.3	10.7	2.1	35	76
55-59	R	101.1	26.7	5.8	59	154	57.3	12.5	2.5	33	86
	L	83.2	23.4	5.1	43	128	47.3	11.9	2.4	31	76
60-64	R	89.7	20.4	4.2	51	137	55.1	10.1	2.0	37	77
	L	76.8	20.3	4.1	27	116	45.7	10.1	2.0	29	66
65-69	R	91.1	20.6	4.0	56	131	49.6	9.7	1.8	35	74
	L	76.8	19.8	3.8	43	117	41.0	8.2	1.5	29	63
70-74	R	75.3	21.5	4.2	32	108	48.6	11.7	2.2	33	78
	L	64.8	18.1	3.7	32	93	41.5	10.2	1.9	23	67
75+	R	65.7	21.0	4.2	40	135	42.6	11.0	2.2	25	65
	L	55.0	17.0	3.4	31	119	37.6	8.9	1.7	24	61
All	R	104.3	28.3	1.6	32	176	62.8	17.0	0.96	25	137
	L	93.1	27.6	1.6	27	160	53.9	15.7	0.88	23	115
Subjects											

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EDITORIAL

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Sarcopenia and the elusive fountain of youth

Stephen B Hanauer

Nass and colleagues (Nass R et al. [2008] *Ann Intern Med* 149: 601-611) state that "Aging is an inevitable process across all species" and "Frailty is one of the scourges of elderly persons." Sarcopenia, the age-related decrease in skeletal muscle mass and strength, is a major risk factor for frailty, loss of independence, and physical disability in the elderly.

Therapies that prevent or reverse sarcopenia and other hormone-related changes associated with aging have the potential to reduce the morbidity of aging adults and their resultant dependency on families and society.

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therapy including peripheral adenoma, myalgias, arthralgias, and new malignancies were not detected in this study population of otherwise healthy 'seniors'.

As pointed out by the authors and in an editorial published in the same issue (Blackman MR [2008] *Ann Intern Med* 149: 677-

Hanauer SB. Sarcopenia and the elusive fountain of youth, *Nature Clin Pract: Gastroenterology & Hepatology*, Vol. 6, No. 1, p. 1, January 2009.

"Sarcopenia, the age-related decrease in skeletal muscle mass and strength, is a major risk factor for frailty, loss of independence, and physical disability in the elderly. Therapies that prevent or reverse sarcopenia and other hormone-related changes associated with aging have the potential to reduce the morbidity of aging adults and their resultant dependency on families and society."

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Review Article

Emerging Therapies to Treat Frailty Syndrome in the Elderly

E. Paul Cherniack, MD; Hermes J. Florez, MD, PhD; Bruce R. Troen, MD

community-dwelling elderly, the Cardiovascular Health Study, determined that seven percent of those over age 65 and 30 percent of those >80 years demonstrate diagnostic criteria compatible with FS. The presence of FS is a predictor for hospitalization, disability, decreasing

Abstract
Frailty syndrome (FS) has been identified as a major predictor of co-morbidities in the elderly. Interventions with the potential to improve functional status, including nutritional supplementation, exercise, and hormone replacement (beta-methylglutathione and androstenedione). While the potential for these interventions appears to offer significant promise in enhancing the health of the elderly, further research is needed to investigate interventions that directly prevent, delay, and/or ameliorate frailty. Successful therapies may well involve multi-component approaches involving a combination of medication, nutritional supplementation, and exercise. (*Altern Med Rev* 2007;12(3):246-258)

Introduction
Frailty syndrome (FS) has been increasingly recognized as a major predictor of co-morbidities in the elderly. While the definition of this syndrome is not uniform, it is characterized by a reserve and impaired cumulative decline in functional status. The most widely used definition of FS is that of Fried et al, who define FS as including three or more of the following: weakness, slow walking speed, self-reported exhaustion, low physical activity, and unintentional weight loss (Table 1).¹ A large survey of over 5,000

Cherniack EP et al. Emerging therapies to treat frailty syndrome in the elderly, *Alt Med Rev*, Vol. 12, No. 3, pp. 246-258, September 2007

"Sarcopenia and inflammation are believed to be important in the pathophysiology of frailty syndrome."

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OPINION PAPER

Cachexia: A new definition

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KEYWORDS
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Inflammation;
Involuntary weight loss;
Wasting disease

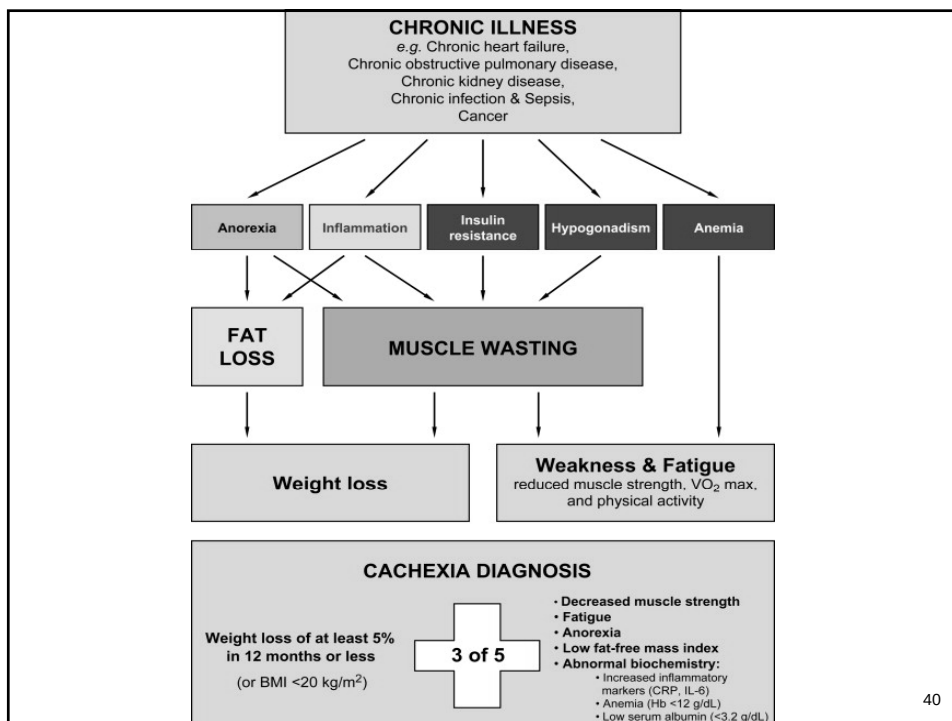
Summary
On December 13th and 14th a group of scientists and clinicians met in Washington, DC, for the cachexia consensus conference. At the present time, there is no widely agreed upon operational definition of cachexia. The lack of a definition accepted by clinicians and researchers has limited identification and treatment of cachectic patient as well as the development and approval of potential therapeutic agents. The definition that emerged is: "cachexia is a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults (corrected for fluid retention) or growth failure in children (excluding endocrine disorders). Anorexia, inflammation, insulin resistance and increased muscle protein breakdown are frequently associated with cachexia. Cachexia is distinct from starvation, age-related loss of muscle mass, primary depression, malabsorption and hyperthyroidism and is associated with increased mortality, while this definition has not been tested in epidemiological or intervention studies, a consensus operational definition provides an opportunity for increased research."
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Definition
Cachexia has long been recognized as a syndrome associated with many illnesses. However, the underlying mechanisms causing cachexia are not well understood and there is no

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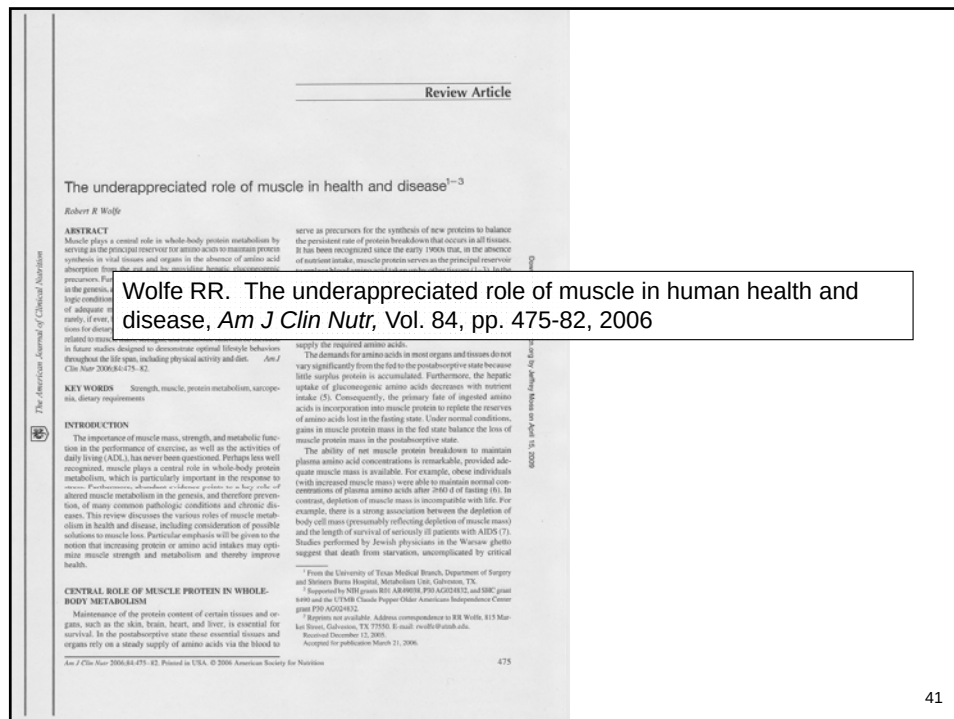
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- “The importance of muscle mass, strength, and metabolic function in the performance of exercise, as well as the activities of daily living (ADL), has never been questioned. Perhaps less well recognized, muscle plays a central role in whole-body protein 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.”

- **“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.”**
- **“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 $>3 \text{ g protein} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ 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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- **“In addition, stimulation of hepatic gluconeogenesis in stressed states further increases the demand for amino acids.”**
- **“Net breakdown of muscle protein is stimulated to provide abundant amino acids to meet these increased demands.”**
- **“...individuals with limited reserves of muscle mass respond poorly to stress.”**

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- **“Whereas muscle mass plays a key role in recovery from critical illness or severe trauma, muscle strength and function is central to the recovery process. The extent and duration of the debilitation resulting from critical illness is dramatic; <50% of individuals employed before entering an intensive care unit return to work in the first year after discharge. Extensive losses of muscle mass, strength, and function during acute hospitalization causing sustained physical impairment were likely contributors to the prolonged recovery. If there is a preexisting deficiency of muscle mass before trauma, the acute loss of muscle mass and function may push an individual over a threshold that makes recovery of normal function unlikely to ever occur. For this reason, >50% of women older than 65 y who break a hip in a fall never walk again.”**

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- **“Sarcopenia, the progressive loss of muscle mass and function that occurs with aging, is a widespread syndrome that has a devastating effect on quality of life and ultimately survival. Progressive sarcopenia is ultimately central to the development of frailty, an increased likelihood of falls, and impairment of the ability to perform activities of daily living. The logical endpoint of severe sarcopenia is loss of quality of life and ultimately institutionalization.”**

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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.”**

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- **“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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Thank you!!

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