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

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


“Gait speed should not be regarded solely as a measure of lower extremity function. Gait speed has been associated with clinical (eg, comorbidities) as well as subclinical conditions (eg, atherosclerosis or inflammatory status) and is able to predict several health-related events even apparently unrelated to physical function (eg, cognitive impairment, hospitalization, institutionalization). Gait speed may serve as a marker of physiological reserve and potentially could quantify overall health status.”
“...gait speed may be considered a new ‘vital sign,’ specifically sensitive for older persons.”

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

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)
Aging makes it more difficult to respond anabolically.

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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Components that create the clinical picture

- Gastroenterology
- Toxicology
- Neurology
- Immunology
- Endocrinology
- Leaky gut/MCS/Mood
- Autoimmune
- Metabol. Syn
- Thyroid Dysf
- Malabsorb.
- Neur. Disord.
- Psychol. Stress
- Dam. HPA axis/
- Thyroid Dysf

ANABOLIC/CATABOLIC IMBALANCE

- Hypermetabolism
- Chronic phase response (inflammation)
- Insulin resistance
- GI mucosal atrophy
- Metabolic acidosis
- Nutrient depletion and aberrant nutrient metabolism


"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."

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

Table 3. Overlapping of symptoms of acute sickness behavior associated with IFN-γ therapy and the somatic symptoms in MDD

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence in IFN-γ + group (%)</th>
<th>Prevalence in MDD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue/asthenia</td>
<td>29–95</td>
<td>73</td>
</tr>
<tr>
<td>Headache</td>
<td>27–67</td>
<td>33*</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>50–15</td>
<td>34–47</td>
</tr>
<tr>
<td>Psychomotor slowing</td>
<td>49</td>
<td>39–63</td>
</tr>
<tr>
<td>Insomnia</td>
<td>36–10</td>
<td>63</td>
</tr>
<tr>
<td>Fatigue</td>
<td>23</td>
<td>30</td>
</tr>
<tr>
<td>Anorexia</td>
<td>9–16</td>
<td>31*</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>26–32</td>
<td>62–46%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>15–20</td>
<td>21*</td>
</tr>
<tr>
<td>Anemia</td>
<td>13–19</td>
<td>40</td>
</tr>
<tr>
<td>Anorexia</td>
<td>13–19</td>
<td>57</td>
</tr>
<tr>
<td>Poor concentration</td>
<td>14</td>
<td>51</td>
</tr>
</tbody>
</table>

*1=46, unless otherwise specified. *P<0.05, unless otherwise specified. 1: [100, 1: [100], 1: [100, 1: [100], 1: [100], 1: [100].
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

Chronic inflammation, inflammaging

Key deficiencies or excesses, i.e., Calories, macronutrients, B vitamins, zinc, selenium, iodine, sleep, psychological and chemical stress, movement against gravity, weight

Low grade chronic metabolic acidosis/fluid electrolyte imbalance

Sarcopenia, Loss of lean body mass

Hyperinsulinemia/Insulin resistance

Low calorie intake and excessive carbohydrate:protein ratio – Refeeding syndrome

THE CREATION OF THE EXCESSIVE CATABOLIC PHYSIOLOGY “RESPONSE”

• “Cachexia may well represent the devastating flip side of the tremendous achievements of modern medicine, as the incidence of cachexia is also a function of survival of chronic illness.”

• “Many diseases – which rapidly led to death only a few years ago – are now better controlled by new therapies. Even if we cannot cure and eradicate these diseases, their natural history has significantly increased by months and years. Although these new therapeutic strategies represent a remarkable advantage over the previous standards of care, it is impossible to ignore the fact that many more patients are now facing the nutritional and metabolic consequences of prolonged immunological and hormonal challenges due to both the illness process itself and the aggressive therapies.”


Bed rest and muscle disuse, inflammation, infection, endotoxemia, corticosteroids, muscle relaxants, hypoxia, electrolyte imbalances and oxidative stress all have adverse effects on muscle function.
• "Chronic illness, particularly in advanced stages, frequently results in reductions in body weight and alterations in body composition, and this can lead to a syndrome known as cachexia."
• "Currently, it is acknowledged that cachexia is a complex syndrome, frequently present in various chronic diseases."
• "It is estimated that >5 million persons in the United States are affected by this syndrome."
• “There is no single cause of cachexia, and most of the current knowledge is derived from the advanced stages of various chronic illnesses…”
• “Although completely different at first sight, these diseases actually share many pathophysiologic mechanisms, including neuroendocrine abnormalities, inflammatory system activation, increased lipolysis, and muscle wasting.”

• “Sarcopenia (aging-associated ‘normal’ muscle wasting)…may not be associated with significant weight change because the loss of muscle mass is counterbalanced by gains in fatty tissue.”
• “It is a characteristic of cachexia that it cannot be cured by nutrition alone.”

• “Currently, no approved therapies for cachexia exist, apart from growth hormone and some appetite stimulants in acquired immunodeficiency syndrome-induced cachexia.”
• “Nonetheless, causative therapy is still not available, although some potential candidates have been tested.”
• “Among them, exogenous oral amino acid (AA) supplementation appears to be very promising. AAs stimulate muscular protein synthesis and mitochondrial biogenesis and improve energy performance in wasting syndromes.”
• “…hypercatabolic syndrome (HS) is a biochemical state characterized by increased circulating catabolic molecules such as hormones (e.g., cortisol, glucagons, catecholamines) and inflammatory cytokines (e.g., tumor necrosis factor [TNF]-α, interleukin [IL]-1β, IL-6), and decreased anabolic insulin effects with subsequent insulin resistance and muscular wasting.”

• “The increase in catabolic hormones and/or molecules (e.g., catecholamines, cortisol, glucagon, TNF-α) and the reduction of anabolic hormone (e.g., insulin) create a hypercatabolic syndrome that has various metabolic consequences, including reduced cytoplasmic and mitochondrial cell protein synthesis and impaired cell functions and energetic metabolism.”
“The availabilility of AAs is a key factor in maintaining both cellular and general metabolism and muscle protein synthesis in mammals.”

“Preliminary data suggest that exogenous oral AA supplements, administered with traditional therapy, counteract muscle wasting and cellular energy reduction, and may improve cardiac function and muscle performance, thereby enhancing the patient’s quality of life.”

“In healthy subjects, AAs in the diet are absorbed after protein digestion. However, the pancreas uses large amounts of AAs to produce digestive enzymes.”

“In HS, the efficiency of the pancreas and mesenteric circulation may be progressively reduced.”

“These conditions lead to impaired AA digestion and absorption and, consequently, to reduced AA plasma patterns that may therefore be insufficient to maintain the protein synthesis and energetic needs of patients with HS.”

“In contrast, individual AAs in nutritional supplements are not digested. They are rapidly absorbed and therefore immediately available in the bloodstream and transported into the cells, where they stimulate cellular protein synthesis and mitochondrial biogenesis…”
“Preliminary data…suggest that oral supplements of a specific mixture of AAs increase muscular number and volume of mitochondria.”

“This point is particularly important for patients with chronic diseases such as diabetes, senescence, and congestive heart failure, where impaired mitochondrial activities and disarrangement of energy metabolism are present in the muscles.”

“…clinical data show that oral AA supplementation reduces blood glucose and improves insulin resistance and cardiac mechanical functions in patients with diabetes.”

“It is important to note that AAs can reactivate glucose cell metabolism in an insulin-independent manner.”

“…these insulin-independent pathways are important for overcoming cellular damage induced by HS that compromises cell metabolism.”
Sarcopenia


“Sarcopenia: a novel epidemic”
• “Advancing age is associated with profound changes in body composition. A change that is increasingly being recognised to have important consequences in old age is the loss of muscle mass and deterioration in muscle quality.”
• “This phenomenon was called sarcopenia by Rosenberg (in 1989), who coined the term from the Greek for ‘poverty of flesh.’”

• “Sarcopenia should be differentiated from cachexia and wasting.”
• “Cachexia refers to a condition of accelerated loss of muscle mass in the context of chronic inflammation, and wasting refers to unintentional weight loss that is largely driven by inadequate dietary intake.”
• “Sarcopenia is probably the result of multiple interacting factors.”
Entry Level Clinical Nutrition – Part 7
Dr. Jeff Moss

• "...clinically significant sarcopenia is a muscle mass of less than two standard deviations below the mean of a young reference group."
• "The prevalence of sarcopenia by this definition increased from 13-24% in persons aged 65-70 years to over 50% of those older than 80 years."
• "The presence of this degree of sarcopenia was associated with a 3- to 4-fold increase in the likelihood of disability in older individuals, independent of age, sex, obesity, ethnicity, socioeconomic status, chronic morbidity and health behaviors."

Physiologic reasons for muscle cachexia and sarcopenia

Signals that could activate muscle protein degradation by this system...include metabolic acidosis, impaired response to insulin and high circulating levels of cytokines. The activation mechanism also involves glucocorticoids.

Thank you!!