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Adult Starvation and Disease-Related Malnutrition: A Proposal for Etiology-Based Diagnosis in the Clinical Practice Setting From the International Consensus Guideline Committee

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Background & Aims: Multiple definitions for malnutrition syndromes are found in the literature resulting in confusion. Recent evidence suggests that varying degrees of acute or chronic inflammation are key contributing factors in the pathophysiology of malnutrition that is associated with disease or injury. *Methods:* An International Guideline Committee was constituted to develop a consensus approach to defining malnutrition syndromes for adults in the clinical setting. Consensus was achieved through a series of meetings held at the A.S.P.E.N. and ESPEN Congresses. *Results:* It was agreed that an etiology-based approach that incorporates a current understanding of inflammatory response would be most appropriate. The Committee proposes the following nomenclature for nutrition diagnosis in adults in the clinical practice setting. "Starvation-related malnutrition", when there is chronic starvation without inflammation, "chronic disease-related malnutrition", when inflammation is chronic and of mild to moderate degree, and "acute disease or injury-related malnutrition", when inflammation is acute and of severe degree. *Conclusions:* This commentary is intended to present a simple etiology-based construct for the diagnosis of adult malnutrition in the clinical setting. Development of associated laboratory, functional, food intake, and body weight criteria and their application to routine clinical practice will require validation. (*JPEN J Parenter Enteral Nutr.* 2010;34:156-159)

Keywords: malnutrition; starvation; inflammation; chronic disease; obesity

An International Guideline Committee was constituted to develop a consensus approach to defining malnutrition syndromes for adults in the clinical setting. Representatives were enlisted from the international clinical nutrition support community who reported no conflicts of interest and no relevant associations with the nutrition or pharmaceutical industries. Consensus was achieved through a series of meetings held at the ASPEN and ESPEN Congresses with manuscript development by group authorship.

Malnutrition has measurable and important adverse effects on clinical outcomes. Depletion of body cell mass results from reduced intake or assimilation of energy and/or protein. Inflammation also promotes catabolism of skeletal muscle that is at least in part cytokine-mediated.[1-3] In **clinical practice,** nutritional intake in **adults** may be compromised in settings of:

1. Pure chronic starvation without inflammation (e.g. medical conditions like anorexia nervosa).
2. Chronic diseases or conditions that impose sustained inflammation of a mild to moderate degree (e.g. organ failure, pancreatic cancer, rheumatoid arthritis or sarcopenic obesity).
3. Acute disease or injury states with marked inflammatory response (e.g. major infection, burns, trauma or closed head injury).

In the world public health arena, malnutrition is frequently a result of famine secondary to natural disaster or conflict. By contrast, disease-related malnutrition that includes an inflammatory component is commonly observed in diverse clinical practice settings throughout the world. At present, there is no clear consensus on how malnutrition should be defined.[2-4] Multiple definitions for adult malnutrition syndromes are found in the nutrition and medical literature resulting in widespread confusion. Over the past decade, it has become increasingly evident that the pathophysiology of malnutrition associated with disease or injury invariably consists of a combination of varying degrees of under-nutrition or over-nutrition and acute or chronic inflammation, leading to altered body composition and diminished biological function. In this commentary we propose an **updated and simple approach based upon etiology** that incorporates a current understanding of inflammatory response.

Nutrient requirements are altered by the inflammatory milieu. The acute phase inflammatory response impacts nutrition by elevating resting energy expenditure and nitrogen excretion and thereby energy and protein requirements respectively. Nutrition supplementation alone only partly reverses or prevents muscle protein loss in active inflammatory states.[5] However, the anorexia that accompanies inflammation will promote further loss of lean tissue if nutritional intake is inadequate. Therefore adequate feeding may help to limit further lean tissue loss and favorably alter outcomes such as length of hospital stay and mortality.

Critical illness or injury promotes an acute inflammatory response that has a rapid, catabolic effect on lean body mass.[6] This effect may add to the morbidity of these patients in severe cases or may be self-limiting as the critical illness subsides. In contrast, the inflammatory condition in most diseases is chronic in nature with the severity being influenced by the progression and extent of disease. Loss of muscle mass and function may occur insidiously and, in the chronic disease state, occur over months to years.

The point at which the severity or persistence of inflammation results in a decrease in lean body mass associated with functional impairment would be considered "disease-related malnutrition." This form of malnutrition is at least partially attributable to a decrease in nutrient intake, but is also tightly linked to the effect of the inflammatory state on intermediary metabolism. It is important to recognize the presence or absence of a systemic inflammatory response because the inflammatory component has both diagnostic and therapeutic implications.[3] If inflammation is absent then even advanced malnutrition due to starvation can be readily treated with appropriate nutritional resuscitation. The presence of inflammation often limits the effectiveness of nutritional interventions and the associated malnutrition may compromise the clinical response to medical therapy. If inflammation is present then it is useful to clarify whether it is mild, moderate or severe; and transient or sustained. In acute disease-related malnutrition with a severe degree of inflammation, the priority for nutrition intervention is to provide nutrients to support vital organ system functions and preserve appropriate host responses while acute medical treatment is provided. In chronic disease-related malnutrition with a mild to moderate degree of inflammation, a positive response to nutrition intervention will also require successful medical treatment of the underlying disease or condition. Indeed the prognosis for individuals with advanced malnutrition of this type will be largely determined by the predisposing disease or condition. Nutrition therapy is therefore an important supportive measure to facilitate effective medical treatment of patients with chronic disease and for individuals with selected chronic conditions like diabetes mellitus, metabolic syndrome, and renal failure; medical nutrition therapy is an integral component of treatment.

We propose the use of the following **etiology-based** terminology for nutrition diagnosis in adults in the **clinical practice setting**, as a step toward recognizing the interaction and importance of inflammation on nutritional status:

- When there is chronic starvation without inflammation, we propose the adoption of the term **"starvation-related malnutrition."** Examples of this syndrome include medical conditions like anorexia nervosa.
- When inflammation is chronic and of mild to moderate degree, we propose the term **"chronic disease-related malnutrition."** Examples of this syndrome include organ failure, pancreatic cancer, rheumatoid arthritis or sarcopenic obesity.

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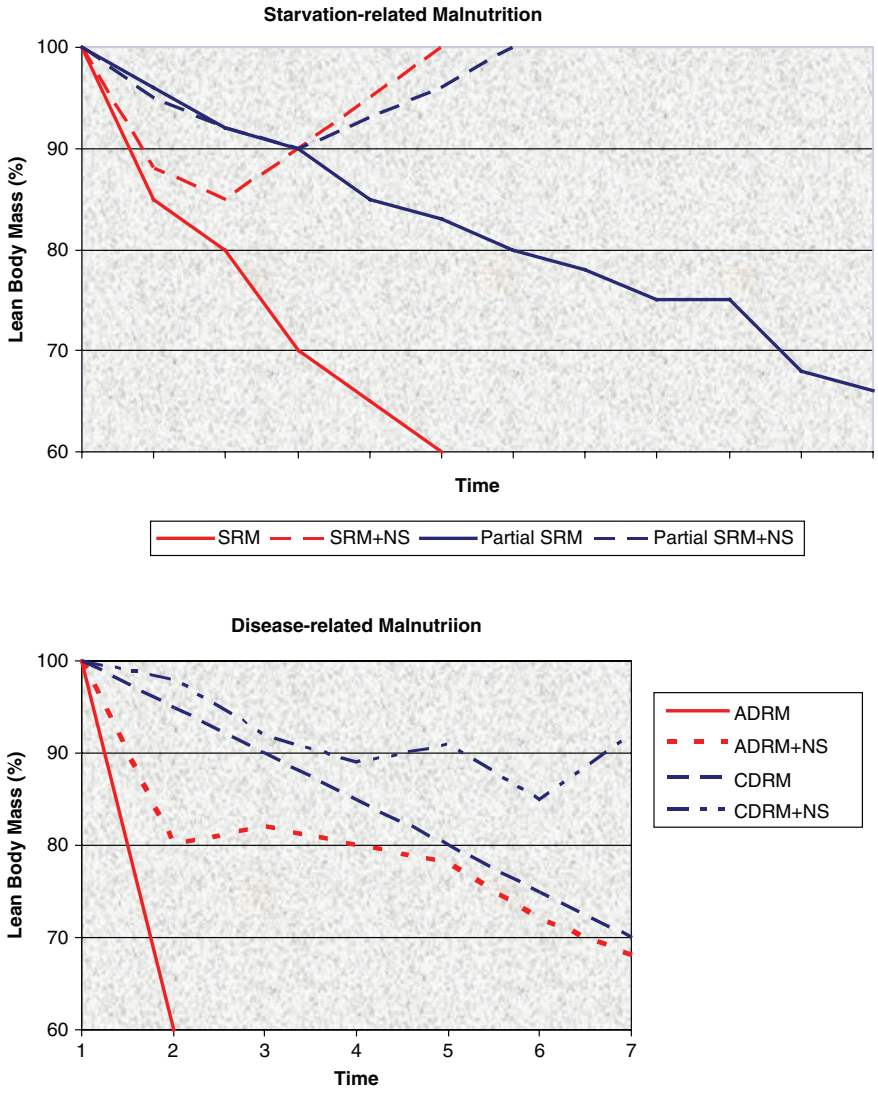

Figure 1. Hypothetical relationship of Starvation-related Malnutrition (top graph) and Disease-related Malnutrition (bottom graph) assuming the inflammatory condition is relatively constant with changes in lean body mass.
For SRM (Red color solid line), Lean body mass is depleted without nutritional intervention but this can be corrected with nutrition support (NS) (SRM+NS, Red color dotted line). During partial SRM (Blue color solid line), lean body mass depletion is slower but still may be reversed by nutrition support (Partial SRM+NS, Blue color dotted line).
For ADRM (Red color solid line), significant depletion of lean body mass over a short period of time (< 1 month) occurs with no nutritional intervention. With nutritional intervention (Red color dotted line), the loss in lean body mass is abated but loss still occurs if inflammation persists. For CDRM (Blue color dotted line), the loss in lean body mass is gradual and will eventually reach detrimental levels over time (several months). This process could be slowed or potentially reversed with nutritional interventions. In both scenarios, ADRM and CDRM, nutritional intervention may be beneficial but with success dependent on the degree and duration of the inflammatory response.
Key: ADRM, acute disease- or injury-related malnutrition; ADRM+NS, ADRM with nutrition support; CDRM, chronic disease-related malnutrition; CDRM+NS, CDRM with nutrition support; SRM, starvation-related malnutrition; SRM+NS, SRM with nutrition support.SRM- starvation-related malnutrition, SRM+NS- starvation-related malnutrition with nutrition support.

- When inflammation is acute and of severe degree, we propose the term "**acute disease- or injury-related malnutrition.**" Examples of this syndrome include major infection, burns, trauma or closed head injury.

Figure 1 illustrates the theoretical relationship of these malnutrition syndromes with nutritional status (lean body mass).

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Notes

1. This commentary is intended to present a simple etiology-based construct for the diagnosis of adult malnutrition. Discussion of laboratory, functional, food intake or body weight criteria in support of these diagnoses will require further development. Translation of this diagnostic approach to routine clinical practice will require validation.

2. When this diagnostic construct is used, an adult patient may be diagnosed in one or more of these states or may change from one to another. Of particular concern are patients whose acute or chronic disease-related malnutrition progresses with further loss of muscle mass. This concern may be exacerbated by iatrogenic malnutrition whereby patients with acute or chronic disease-related malnutrition receive delayed nutrition intervention and suffer concomitant starvation superimposed on an inflammatory milieu. Since these transitions may be blunted by nutritional intervention, early recognition of the process is imperative. While patients early in the course of a critical illness may not yet be malnourished per the proposed etiology-based construct with clinically evident erosion of lean mass, they will nonetheless warrant early intervention because of the acute metabolic dysregulation and associated catabolism that place them at appreciable nutritional risk. Thus, we propose that patients be evaluated at multiple points over time in clinical settings to ensure that a given patient's nutritional status remains stable or improves. It is noteworthy that the patient with starvation or chronic disease-related malnutrition is prone to deteriorate quickly with any additional acute inflammatory event and warrants particularly close follow up and care should this occur.

3. Individuals who are overweight or obese may be assigned to any of these diagnostic categories as appropriate. Sarcopenic obesity, characterized by muscle loss in the setting of obesity, may represent a chronic low level inflammatory state.[7,8]

4. The focus of malnutrition in this discussion is on lean body mass and effects of energy and protein balance. Micronutrient deficiencies that impact on patient outcomes are also likely, especially if the etiology of lean body mass loss includes inadequate nutrient intake. For example, in the acute inflammatory condition antioxidants are often depleted and replacement may be indicated.

5. Pediatric malnutrition is not addressed in the present commentary because pediatric malnutrition diagnoses have an established history of use and likely distinct pathophysiology.

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