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The Anorexia-Cachexia Syndrome: Definitions, Evaluation, and Non-Pharmacologic Management

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Introduction: Anorexia-cachexia encompasses a broad, multi-organ syndrome seen in several chronic diseases (1). The purpose of this *Fast Fact* is to review the anorexia-cachexia syndrome (ACS), its clinical evaluation, and its non-pharmacologic management. See other *Fast Facts* for related information: #10 (the role of enteral nutrition in serious illness), #100 (megestrol acetate); #190 (the role of parenteral nutrition for advanced cancer), #279 (cannabinoids), #314 (mirtazapine), and #315 (olanzapine).

Definitions

Sarcopenia: diffuse muscle loss often associated with an increase in fat mass and abdominal circumference (2).

Anorexia: appetite reduction which can be psychogenic (anorexia nervosa) or secondary to an underlying advanced illness (3).

Cachexia: >5% weight loss over 6 months in absence of starvation *or* BMI <20 and weight loss >2%; *or* appendicular skeletal muscle index consistent with sarcopenia and weight loss >2% (4,5).

Pre-cachexia: < 5% weight loss and presence of anorexia (4).

Refractory cachexia: usually described in the published literature in the context of a progressive, incurable non-cancer illness at an advanced stage or an untreatable cancer (4,5).

Pathophysiology and associated disease processes: Typically, ACS involves more than just a loss of appetite and is also associated with nausea, glucose intolerance, meat aversion, early satiety, and/or an unpleasant change in taste and smell (4,5). Increases in cytokine release and other inflammatory mediators (e.g. IL-1, IL-6, IL-10, and TNF-alpha) brought upon by an underlying illness are thought to be the primary culprit across many chronic illnesses including cancer, chronic kidney disease, COPD, AIDS, rheumatoid arthritis, cirrhosis, and congestive heart failure (6-13). These inflammatory mediators along with hormonal mediators like testosterone, insulin-like growth factor, and myostatin cause the ACS via a) intracellular oxidative stress leading to catabolism and the breakdown of proteins (proteolysis); b) resistance of the hypothalamus to respond to orexigenic (appetite-stimulating) neurologic signals; and c) increases in total and resting energy expenditure (3,6-8). The Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire and the North Central Cancer

Treatment Group (NCCTG) Anorexia/Cachexia questionnaire are validated tools to assess ACS (3).

Clinical evaluation: ACS is a clinical diagnosis encountered in a patient with the appropriate degree of weight loss and in the context of an advanced illness. Typically, no additional testing is necessary to confirm the diagnosis, however, clinicians should be aware of potentially reversible ACS etiologies or cofactors and consider targeted testing and/or interventions as appropriate (14,15):

- Uncontrolled disease-related symptoms: e.g. stomatitis, refractory dyspnea, odynophagia, pain.
- Swallowing deficits: e.g. a localized tumor from head and neck.
- GI symptoms: both diarrhea from chemotherapy-induced bowel ischemia and opioid-related constipation are common culprits.
- Endocrine or metabolic disorders: e.g. hyperthyroidism, diabetes mellitus, uremia, hypercalcemia.
- Infections: e.g. HIV, occult abscess, parasitic infections, osteomyelitis.
- Dental issues: e.g. dental caries, thrush, poorly fitting dentures.
- Social issues: food insecurity, poor nutritional literacy, and social isolation, especially in patients with functional impairments who require feeding assistance. Involve social workers as appropriate.
- Mental health disorders: e.g. depression, bulimia, anorexia nervosa, untreated anxiety.
- Medications: numerous drug classes (e.g. chemotherapeutics, antibiotics, anticonvulsants, cardiovascular medications, antidepressants) have been associated with altered taste, early satiety, dry mouth, dysphagia, and nausea. Involving a clinical pharmacist can help identify potential culprits.

Prognostication: ACS is incorporated into numerous prognostication scales and is considered a common manifestation on the terminal illness pathway (16). Refractory cachexia is associated with a prognosis < 3 months (4,5,16). The clinical recognition of ACS can help clinicians assess where a patient may be at on an illness trajectory (see *Fast Fact* #326). Hence, clinicians should utilize the presence of ACS to improve their prognostic disclosure and clinical recommendations regarding the role of pleasure feeding over artificial nutrition especially for refractory cachexia (17) Additionally, the Glasgow Prognostic Index, which involves a simple 0,1,2 scoring system based on the presence of elevated c-reactive protein levels and/or low albumin levels, has been validated to assess the extent of disease-related inflammation and offer reliable prognostic information for cancer and non-cancer illnesses (18-20).

Non-pharmacologic management: ACS can be very distressing given the lack of efficacious therapies. Patient-family strife may result as loved ones may not understand why previously cherished foods lovingly prepared are not being eaten. While a separate *Fast Fact*will review the utility of pharmacotherapies and supplements for ACS, patient counseling is the cornerstone to the clinical management of ACS.

- Education that ACS is not a patient choice, but rather a manifestation of a hormonally-advanced, underlying illness may be the most crucial aspect of ACS care. In fact, experts suggest that the presence of refractory cachexia should prompt a goals of care discussion and nutritional refocusing away from weight gain and caloric intake and more towards alleviating hunger and thirst (5).
- Most experts do not recommend enteral nor parenteral artificial nutrition for refractory cachexia, as neither meaningfully improve quality of life or survival (17).

- Controlled studies in patients undergoing cancer treatment suggest that consultation with a licensed nutritionist may offer quality-of-life benefits in the pre-cachexia phase via improved dietary intake from fortified food, nutritional supplementation, and counseling (21,22). The nutritional counseling often involves liberalizing diet restrictions and encouraging patients to eat frequent, small meals with preferably the bulk of calorie intake occurring the morning. Additionally, some patients may wish to limit exposure to strong aromas and spicy flavors. However, the evidence underlying this nutritional counseling and/or consultation, is not established in patients with more advanced illness (5,23).

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