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Prevalence of anorexia in older persons: a frequently overlooked problem?

“...data confirm that anorexia in older persons is common, associated with poor outcome and often overlooked.”

Aging
HEALTH

Loss of appetite, anorexia, is commonly observed in older persons and associated with adverse outcomes. Anorexia is distinct from hunger, which is the physiological drive to find food. Appetite is associated with seeking food for the enjoyment of food itself, rather than for physiological need, and is conditioned by sensory perception, visual stimuli and both social and cultural factors. Hunger is driven by the need to find food, often resulting in ingestion of nutrients that would otherwise be revolting.

Appetite is carefully regulated by a combination of a central feeding drive and a peripheral satiation system. The interplay of these two systems is modulated by a hormonal feedback system that determines the nutrient status of the organism. The arcuate nucleus releases neuropeptide Y, the most common and potent appetite stimulator, and another hunger mediator, agouti-related peptide. These mediators inhibit the ventromedial hypothalamus, which is a satiety center. Stimulation of the lateral hypothalamic area produces a hunger effect, mediated by α -melanocortin precursors released in the arcuate nucleus. Cocaine-amphetamine-related peptide and melanocortin-stimulating hormone are inhibited by neuropeptide-Y.

Leptin produced by the adipose tissue and insulin from the pancreas inhibit neuropeptide-Y and agouti-related peptide expression and stimulate pro-opiomelanocortin expression, resulting in satiety. Gut hormones produced in response to meals by the upper and lower intestine, including cholecystokinin and peptide YY, produce a short-term signal of satiety by inhibition of neuropeptide-Y and agouti-related peptide. Ghrelin, the only peripheral hormone known to stimulate appetite, is produced by the stomach during fasting and stimulates hunger and eating through neuropeptide-Y expression. Ghrelin may also regulate long-term energy balance, rising in conditions of negative energy balance such as anorexia nervosa, cachexia or starvation. Stretch receptors in the stomach, mediated by nitric acid, travel to the nucleus tractus solitarius

by the vagal nerve, producing the sensation of satiety. Cholecystokinin also produces postprandial satiety through an effect on the nucleus tractus solitarius. Gastrin-releasing peptide, amylin, somatostatin and bombesin also regulate satiety in humans to varying degrees [1].

Systemic inflammation owing to acute or chronic illness directly suppresses appetite. Interleukin-1 β and TNF act on the glucose-sensitive neurons in the ventromedial hypothalamus and the lateral hypothalamus to cause an imbalance between the orexigenic and anorexigenic regulatory pathways [2–4]. In anorexia–cachexia syndrome, the peripheral signals for an energy deficit reaching the hypothalamus fail to produce a response, which propagates development of cachexia [5]. This effect of cytokines directly results in feeding suppression and lower intake of nutrients. In addition, cytokines have a direct catabolic effect on skeletal muscle, leading to wasting and weight loss.

The voluntary suppression of food intake during illness is common to most species [6], although this response seems paradoxical in the face of a need for increased nutrients during healing [7]. Clinicians routinely observe that a return of appetite and the ingestion of food is a sign of patient recovery. Although usual and expected in acute illness, anorexia is frequently associated with chronic diseases and leads to inadequate nutrient intake.

The anorexia that accompanies acute and chronic illness is often related to cachexia. Cachexia is a complex metabolic syndrome associated with underlying illness, and is characterized by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults. Anorexia, inflammation, insulin resistance and increased muscle protein breakdown produce a wasting syndrome. Wasting disease is distinct from starvation, age-related loss of muscle mass, primary depression, malabsorption and hyperthyroidism, and is associated with increased morbidity [8].

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The prevalence of anorexia is thus almost universal in inflammatory disease. The anorexia–cachexia syndrome was first described in cancer patients. Up to 65% of patients with cancer report anorexia with or without weight loss, which is independent of active cancer treatment [9]. Anorexia and protein-energy wasting ranges from 18 to 75% of patients with chronic kidney disease undergoing maintenance dialysis therapy [10]. Cardiac cachexia occurs in 10–15% of patients with New York Heart Association Class II–III heart failure. The 18-month mortality rate in patients with cardiac cachexia approaches 50%, compared with 17% in patients with heart failure without cachexia [11]. Other chronic illnesses have been associated with the anorexia–cachexia syndrome, including chronic pulmonary disease, end-stage dementia, rheumatoid arthritis, liver disease, chronic infections and AIDS [12].

“In persons admitted to a geriatric acute care or rehabilitation ward, the prevalence of anorexia was 33% in women and 27% in men...”

Anorexia may also be a component of normal aging [1], and is common in community-dwelling adults. A population-based cross-sectional study of subjects over 70 years of age found a 30% prevalence of self-reported anorexia (37% in females and 18% in males). Loss of appetite was related to higher risk of undernutrition (41% in anorexic vs 27% in nonanorexic persons), lower muscular strength and poorer functional capacity [13]. In persons admitted to a geriatric acute care or rehabilitation ward, the prevalence of anorexia was 33% in women and 27% in men [14].

Food intake declines progressively after the third decade of life [15]. This phenomenon is termed ‘physiological anorexia of aging’. A number of physiological factors interact to produce this loss of appetite, including central and peripheral alterations in feeding drive [7,12]. Aging itself has been associated with increased levels of circulating inflammatory components in the blood, including elevated concentrations of TNF- α [16–18], IL-6 [16,19,20], IL-1Ra [21], sTNFR [22], acute-phase proteins such as C-reactive protein and serum amyloid A [23], and high neutrophil counts [24]. Plasma levels of TNF- α have been positively correlated with IL-6, sTNFR-II and C-reactive protein in centenarians, suggesting an activation of the entire inflammatory cascade. However, the increase in circulating inflammatory parameters is very low-grade in healthy elderly humans and

far less than levels seen during acute infection. Serum levels of IL-6 were markedly higher in randomly selected older persons compared with strictly selected healthy older persons, suggesting that inflammatory activity may be a marker of health status [25]. On the other hand, a study of 1727 persons aged 70 years or older found that age was associated with increased circulating plasma levels of IL-6 independent of disease states and disorders of aging [26].

Aging is characterized by progressively increased concentrations of glucocorticoids and catecholamines and decreased production of growth and sex hormones, a pattern reminiscent of that seen in chronic stress. However, the age-associated changes in cytokine production are inconsistent [27]. It is not clear whether changes in cytokine levels are owing to age itself or underlying disease. The increase in plasma levels of IL-6 with age may occur as the result of catecholamine hypersecretion and sex-steroid hyposecretion [28]. Numerous acquired influences (e.g., visceral obesity, smoking and stress among others) also trigger IL-6 release [29]. Subclinical infections such as *Chlamydia pneumoniae* or *Helicobacter pylori*, or dental infections and asymptomatic bacteriuria, may play a mechanistic role [30].

The accumulation of comorbidity in the aging population may be responsible for the anorexia observed in older adults. Proinflammatory cytokines are thought to play a pathogenetic role in age-related diseases such as Alzheimer’s disease [31], Parkinson disease [32], atherosclerosis [33], Type II diabetes [34], sarcopenia [35] and osteoporosis [36]. In general, the data suggest that that low-grade inflammatory activity in older populations is caused by a dysregulated cytokine production, which is further exacerbated by age-associated pathology. This chronic inflammatory state is associated with anorexia and decreased food intake in older populations.

Effective nutritional management mandates early detection of nutritional disorders and early intervention. Several tools have been developed to measure cachexia, but few address appetite or anorexia. The Functional Assessment of Anorexia–cachexia Therapy (FAACT) has been used to measure general aspects of quality of life and specific anorexia–cachexia-related issues in cancer patients [37]. The Simplified Nutritional Appetite Questionnaire (SNAQ) was developed specifically to measure appetite in older institutionalized and community-dwelling persons [38]. The SNAQ has been demonstrated to be an efficient, reliable and valid tool with appraisal parameters that focus on the singular

construct of appetite. This four-question assessment correlates well with the longer appetite, hunger and sensory perception questionnaire [39], and predicts subsequent weight loss in the next 6 months.

Nutritional supplements have produced modest weight gain and reduced mortality in persons who are undernourished, older than 75 years, sick or admitted to a hospital or nursing home. A 26% reduction in mortality was observed in the supplemented compared with control groups [40]. A number of pharmacological agents have been empirically observed to improve anorexia. These medications appear to have a common pathway of modulating cytokine production, suggesting a promising area for future research [41].

The data confirm that anorexia in older persons is common, associated with poor outcome and often overlooked. By contrast to starvation, cachexia is remarkably resistant to hypercaloric feeding. More insight into this common problem is desperately needed.

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