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Symposium on 'Nutrition and the elderly'

Protein–energy malnutrition in older subjects

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The concept of old age is not a new one. Many of the ancient Greek philosophers lived long and full lives, e.g. Isocrates 98 years, Sophocles 91 years, Plato 81 years. The bible refers to the extreme longevity of personages such as Methusaleh. What is new is the greying of populations as opposed to the successful ageing of a few individuals. By the year 2000, approximately two-thirds of the elderly in the world will live in developing countries, e.g. 300 million in China and 170 million in India. By the year 2030, the percentage of older individuals in the population of most developed nations will be approaching 20 %. Individuals over the age of 65 years are faced by a number of challenges that increase the chance of them developing protein–energy malnutrition. These challenges include difficulty in shopping (11 %), in preparing meals (7 %), inability to self-feed (27 %), poverty (15 %), social isolation (30 %), impaired mobility (87 %), visual deficits (8 %), dental problems (16 %), and difficulty in chewing (35 %). As will be further explored later in the present article (pp. 588–589), the development of protein–energy malnutrition is directly responsible for a number of disease processes and functional impairment in old age.

Protein–energy malnutrition is a major problem in older subjects. While estimates of its prevalence vary, it has been reported to be present to some degree in 15 % of community-dwelling older subjects (Morley *et al.* 1989). Severe protein–energy malnutrition occurs in 10–38 % of older outpatients (Miller *et al.* 1990; Wallace *et al.* 1995; Wilson *et al.* 1998), 5–12 % of homebound patients (Morley, 1997), 26–65 % of hospitalized patients (Linn & Jensen, 1984; Morley *et al.* 1989) and 5–85 % of institutionalized older subjects (Sandman *et al.* 1987; Johnson *et al.* 1993; Silver *et al.* 1993; Morley & Silver, 1995). While protein–energy malnutrition is extremely common in older subjects, its presence is rarely recognized by physicians, and even when recognized, it is even more rarely treated (Miller *et al.* 1990; Wilson *et al.* 1998).

The physiological anorexia of ageing

There is now ample evidence that food intake declines over the lifespan (Anonymous, 1994). This occurs in the face of the increased body mass that develops in middle age (Steen *et al.* 1979; Silver *et al.* 1993; Perry *et al.* 1997). The conundrum of why body weight in general, and obesity specifically, increase while food intake declines is resolved by the decline in resting metabolic rate and physical activity with ageing. A shift of body fat from the periphery to visceral fat deposits increases the efficiency of fat accretion together with a decreased ability to oxidize fat (Melanson *et al.* 1997).

Food intake declines with ageing even in very healthy older subjects (Anonymous, 1994). Older subjects appear to be incapable of adjusting their food intake following periods of over- or underfeeding (Roberts *et al.* 1994). Older subjects compensate less precisely for the energy content of oral preloads than do younger subjects (Rolls *et al.* 1995). Many older subjects develop early satiation, making it difficult for them to ingest large amounts of energy at any single meal (Clarkston *et al.* 1997). This early satiation is related to the rate of gastric emptying, and is due to the inability of the fundus to undergo appropriate adaptive relaxation in response to food arriving in the stomach. The inability to elaborate NO, which causes the smooth muscle of the fundus to dilate, appears to be the prime reason for the decline in adaptive relaxation with ageing (Morley & Flood, 1992; Morley *et al.* 1997). The decreased fundal relaxation results in more rapid filling of the antrum. This is associated with increased antral diameter, which has been demonstrated to play a role in signalling satiation (Jones *et al.* 1997). When liquid preloads are administered 1 h before the meal rather than immediately before the meal, the amount of food eaten is increased (Wilson *et al.* 1997). Liquid preloads are predominantly emptied from the stomach in 60 min. This suggests that when older subjects have anorexia, energy supplements should be given at least 60 min before a meal.

Abbreviation: MNA, Mini Nutritional Assessment.

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Unlike the stomach, the duodenum appears to be less important in producing the anorexia of ageing (Cook *et al.* 1997). Cholecystokinin is a gastrointestinal hormone that produces satiation. In anorectic older subjects, cholecystokinin levels are elevated (Bertelemy *et al.* 1992). In animal studies, older animals have been found to be more responsive to the satiating effects of cholecystokinin than are younger animals (Silver *et al.* 1989).

The endogenous opioid peptide, dynorphin, plays an important role in modulating the intake of fatty foods. Animal studies have shown a decline in the ability of opioids to drive food intake in older animals, due to a decline in opioid receptor number (Gosnell *et al.* 1983; Kavaliers & Hirst, 1985; Morley *et al.* 1990). Cytokines, such as tumour necrosis factor-α and interleukin-1, appear to play an important role in inhibiting food intake (Roubenoff *et al.* 1994). Older subjects tend to show an increase in cytokines secondary to increased visceral fat (associated with increased tumour necrosis factor-α production), increased bacterial translocation from the gut and increased inflammatory conditions, e.g. osteoarthritis.

Leptin is a protein hormone produced by adipose cells. Leptin levels are closely related to total adipose mass, and more particularly to visceral adiposity (Ostlund *et al.* 1996; Perry *et al.* 1997). Males have lower levels of leptin than females. With ageing leptin levels in females decline in concert with the decline in adiposity with ageing, while leptin levels increase in males despite the decline in adiposity. This increase in leptin levels in older males is due to a decline in the male hormone, testosterone (Morley & Silver, 1995; Sih *et al.* 1997). In our unpublished longitudinal study (R Baumgartner, PJ Garry and JE Morley, unpublished results), the increase in leptin levels was correlated with a decline in 24 h food intake measured by dietary recall. These findings suggest a putative role for leptin in the pathogenesis of anorexia of ageing.

There is a clear decline in smell beginning at the age of about 60 years, and taste acuity declines in most subjects over the age of 70 years (Schiffman, 1993; Morley, 1997). These changes appear to account for the decreased ability of old compared with younger subjects to identify different foods. However, the role of taste and smell in determining food intake, and even food choices, appears to be a small one in elderly individuals.

The previous brief review makes it clear that there is a physiological anorexia of ageing. This places the older subject at major risk of developing severe anorexia when a disease process intervenes. The cause of the physiological anorexia of ageing appears to be multifactorial.

Screening for malnutrition

A number of screening tests for malnutrition risk have been developed. The DETERMINE index of the Nutrition Screening Initiative has been widely used in the USA as an initial screening tool (White *et al.* 1991). This index has very poor sensitivity and specificity. It appears to have some utility as a rapid screen in large epidemiological studies (Posner *et al.* 1993; Rubin *et al.* 1994; Miller *et al.* 1996).

The Mini Nutritional Assessment (MNA) has been developed as a screening test for malnutrition in older subjects. The MNA has been well validated and utilized internationally (Guigoz *et al.* 1994). It is predictive of poor outcomes associated with malnutrition. At present, it appears to be the gold standard by which all other nutritional assessment tests should be judged.

SCALES (Table 1) was developed for physicians and dietitians to use as a screen in the clinic (Morley, 1989). SCALES has been cross-validated with the MNA. It appears to have a superior ability to the MNA to identify subsequent nutritionally-associated problems. SCALES requires obtaining blood tests and perhaps should be used as a second-level screen following an at risk score on the MNA.

Weight loss remains one of the most sensitive indicators of individuals at risk for developing malnutrition. A weight loss of greater than 10 % of the individual's previous weight is highly suggestive of malnutrition, provided the scale is accurate (often a major problem) and the subject does not have a disturbance of water balance. In persons with fluid overload, the measurement of mid-arm circumferences and the calculation of arm muscle circumference appear to be a more accurate indicator of nutritional status. Arm muscle circumference (cm) is calculated as follows:

$$\text{mid-arm circumference (cm)} - \left(\frac{3{\cdot}14 \times \text{triceps skinfold (mm)}}{10} \right).$$

Albumin with its long half-life of approximately 20 d is an excellent indicator of visceral protein stores. Albumin levels below 32 g/l are strongly correlated with mortality in hospitalized patients (Morley, 1997). Albumin levels fall by 5 g/l with recumbency, due to an increase in intravascular fluid volume. Cytokines can produce rapid declines in albumin levels (see p. 589). Transport proteins with shorter half-lives, such as prealbumin (half-life 48 h) and retinol-binding protein (half-life 12 h), are useful indicators of response to therapy, but appear to be no better than albumin as diagnostic tools. In view of the high prevalence of Fe deficiency and chronic disease in older subjects with malnutrition, transferrin levels play little role in the detection of nutritional problems. Total lymphocyte counts also can indicate malnutrition, but tend to be increased in subjects with bacterial infections regardless of their nutritional status. Insulin-like growth factor-1 levels decline with ageing. These levels are under the control of pituitary growth hormone secretion. Insulin-like growth factor-1 levels decline markedly with malnutrition and increase during refeeding, making insulin-like growth factor-1 a sensitive marker of acute dietary changes.

As can be apprised from the previous discussion, the diagnosis of protein–energy malnutrition is not a simple one and requires an astute eye to make the diagnosis at an early stage.

Table 1. Rapid clinic screen for risk of protein–energy malnutrition: SCALES*

S:	Sadness
C:	Cholesterol < 4·14 mmol/l (1600 mg/l)
A:	Albumin < 40 g/l (40 g/l)
L:	Loss of weight
E:	Eating problems (cognitive or physical)
S:	Shopping problems or inability to prepare a meal

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Conditions associated with protein–energy malnutrition

Malnutrition has been demonstrated to result in a variety of conditions, including anaemia, pressure ulcers, hip fractures, frailty (failure to thrive syndrome), cognitive difficulties, dehydration, orthostatic hypotension and immune dysfunction. Malnutrition produces a major decline in $CD4^+$ T lymphocytes and a decline in the $CD4^+$: $CD8^+$ value (Kaiser & Morley, 1994). These immune alterations are similar to those observed in patients with acquired immune deficiency syndrome. It appears that it is this immune effect that is associated with increased and atypical infections in older subjects with malnutrition (Margolick & Donnenberg, 1997). Table 2 compares the changes in the immune system that occur with ageing to those that are produced by protein–energy malnutrition.

Causes of malnutrition

Malnutrition can occur because of decreased intake, malabsorption, or increased metabolism. Cytokines play a particularly important role in the genesis of malnutrition, as not only do they decrease food intake, but also decrease albumin synthesis and cause a vascular leak, resulting in redistribution of albumin into the extravascular space. The most common cause of malnutrition appears to be depression, with therapeutic diets and cancer being the next most common (Morley 1989; Thompson & Morris, 1991; Katz *et al.* 1994; Morley & Kraenzle, 1994; Wilson *et al.* 1998). The causes of malnutrition are best remembered by the mnemonic, MEALS-ON-WHEELS (Table 3).

A large number of medications are associated with anorexia and malnutrition. These include fluoxetine and other selective serotonin re-uptake inhibitors, digoxin, theophylline and H_2 antagonists. The hypermetabolic causes include hyperthyroidism and pheochromocytoma. When hypertension is not ameliorated in the face of marked weight loss, the diagnosis of pheochromocytoma should be entertained. Other endocrine causes of weight loss are hypercalcaemia and Addison's disease.

Malabsorption in older persons is most commonly associated with gluten enteropathy or pancreatic insufficiency. Hypoalbuminaemia can occur with a protein-losing enteropathy associated with a villous adenoma or the syndrome of cardiac cachexia (Morley, 1997). *Helicobacter pylori* is associated with gastric distress and its eradication may result in weight gain (Portnoi, 1997).

A number of psychological conditions are associated with anorexia and weight loss in older subjects. Older subjects with depression are more likely to lose weight than younger subjects with depression (Blazer *et al.* 1987; Fitten *et al.* 1989). Anorexia and weight loss in subjects with depression are associated with elevated corticotrophin-releasing factor levels in the cerebrospinal fluid (Nemeroff *et al.* 1984). Corticotrophin-releasing factor is a potent anorectic neurotransmitter acting in the hypothalamus (Krahn *et al.* 1988). A number of studies have found that depression is the most common cause of weight loss in patients in the outpatient setting (Westin *et al.* 1988; Thompson & Morris, 1991; Wilson *et al.* 1998) and in nursing homes (Katz *et al.* 1994; Morley & Kraenzle, 1994). Alcoholism in older subjects is associated with severe weight loss.

Dementia is commonly associated with weight loss. In general, this appears to be due to a decreased food intake. Subjects with dementia often have pleas for unusual substances. Constant wandering in patients with dementia can be associated with high levels of energy expenditure, resulting in weight loss if energy intake is not appropriately increased. Sophisticated stable-isotope energy studies have failed to demonstrate an increase in basal energy expenditure in subjects with Alzheimer's disease (Niskanen *et al.* 1993; Poehlman, 1993). Subjects with dementia can take up to 60 min to feed at each meal time. Apraxia of swallowing can occur in patients with dementia, requiring the individual feeding the patient to remind the patient to swallow after each mouthful of food.

Other psychological causes of weight loss include a late-life recurrence of anorexia nervosa and late-life paranoia. In addition, certain patients develop anorexia tardive; this is defined as new onset of food refusal related to a desire to maintain a thin body habitus (Miller *et al.* 1991). In some cases, this is associated with a belief that being underweight will prolong lifespan. The genesis of this belief is twofold, i.e. the studies demonstrating that dietary restriction can prolong life in animals, and the incessant messages that low-cholesterol diets will decrease heart disease, the so-called cholesterol phobia.

Table 2. Effects of protein–energy malnutrition on the immune system in older individuals: comparisons with healthy old individuals

	Healthy Old	Old with protein–energy malnutrition
Delayed cutaneous hypersensitivity	Decreased	Markedly decreased
Total lymphocyte count	Normal	Decreased
T-cell proliferation	Decreased	Markedly decreased
$CD3^+$	Decreased	Markedly decreased
$CD4^+$	Normal	Decreased
$CD8^+$	Normal	Mild decrease
$CD4^+$:$CD8^+$	Normal	Decreased
IL-1 release	Decreased	Markedly decreased
IL-2 release	Normal	Decreased
IL-6 release	Increased	Decreased
Antibody production	Increased	Decreased
Gut immune barrier function	Mild decrease	Markedly decreased

IL, interleukin.

Table 3. Meals on wheels mnemonic for the causes of weight loss*

M:	Medications
E:	Emotional (depression)
A:	Alcoholism, anorexia tardive†, or abuse of elders
L:	Late-life paranoia
S:	Swallowing problems (dysphagia)
O:	Oral problems
N:	No money (poverty)
W:	Wandering and other dementia-related problems
H:	Hyperthyroidism, pheochromocytoma
E:	Enteric problems (malabsorption)
E:	Eating problems
L:	Low-salt low-cholesterol diet
S:	Stones

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† New onset of food refusal related to a desire to maintain a thin body habitus (Miller *et al.* 1991).

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A number of studies have shown that special diets in nursing homes are associated with weight loss and the development of malnutrition (Buckler *et al.* 1994; Morley *et al.* 1994). Coulston *et al.* (1990) were unable to demonstrate any positive effects of the American Diabetic Association diet (see Fonesca & Wall, 1995) in nursing home residents with diabetes mellitus. Numerous studies have suggested that the ideal cholesterol levels for survival in older subjects over 70 years of age are substantially higher than the values in younger subjects (for a review, see Sih, 1996). For all these *reasons, the use* of therapeutic diets is not recommended in the majority of older subjects.

Chronic obstructive pulmonary disease causes weight loss through a variety of mechanisms. Perhaps the most dramatic is the hypoxia associated with the increased O_2 utilization associated with the thermic energy of eating. In addition, subjects with chronic obstructive pulmonary disease utilize large amounts of energy by using their accessory muscles to augment their breathing capacity. Medications ingested by subjects with chronic obstructive pulmonary disease may both produce anorexia and increase metabolic rate. To maintain weight in subjects with chronic obstructive pulmonary disease, it is often necessary to provide multiple small meals throughout the day.

Older subjects may develop hypotension following high-carbohydrate meals. This is due to the excessive release of calcitonin gene-related peptide (Edwards *et al.* 1996). Calcitonin gene-related peptide has been demonstrated to produce anorexia in animals (Morley *et al.* 1996). Meal-associated hypotension can result in early satiation.

Dental problems are associated with a decline in daily food intake of approximately 5 % of the total energy ingested by older subjects without dental problems (Sullivan *et al.* 1993). At St Louis University we developed the DENTAL screen for detection of tooth and mouth problems that may interfere with food intake (Bush *et al.* 1996). This screening tool has excellent sensitivity and specificity (Table 4).

The diagnosis of the cause of weight loss in older subjects is one of the most challenging and rewarding of all clinical challenges.

Management of malnutrition

Surprisingly few studies have addressed the efficacy of oral energy supplementation in the management of protein–energy malnutrition. One study in hospitalized elders suggested that a small energy supplement decreased mortality (Larsson *et al.* 1990). Similar findings have been reported in patients with hip fractures (Delmi *et al.* 1990). However, it has been pointed out that in the 'real world' supplements are often given haphazardly (Johnson *et al.* 1993). Using energy supplements as the vehicle for swallowing medications has been advocated, but no evidence supporting this practice has been published.

Table 4. The dental screening initiative to indicate need to see a dentist*†

Dry mouth (2 points)
Eating difficulty (1 point)
No recent dental care, within 2 years (1 point)
Tooth loss (1 point)
Alternative food selection because of masticatory problems (1 point)
Lesions, sores, or lumps in mouth (1 point)

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† Any score ≥ 2 indicates a dental problem that may affect health and nutritional well-being.

Similarly, there is a paucity of information supporting other approaches to supplying energy to malnourished persons. The Veterans Affairs Total Parenteral Nutrition Cooperative Study suggested that total parenteral malnutrition may improve outcomes in severely malnourished patients (Anonymous, 1991). Peripheral parenteral nutrition appears to be less hazardous than total parenteral nutrition, and may be a useful adjunct to oral feeding in older subjects with limited ability to take nutrients orally.

Enteral nutrition has been considered the best form of feeding. In particular, it has been suggested that gut malnutrition leads to increased mucosal barrier permeability to macromolecules, resulting in increased bacterial translocation from the lumen of the gut to the bloodstream (Dietch, 1988). Tube feeding has been reported to decrease mortality and enhance rehabilitation in malnourished older subjects with hip fracture (Bastow *et al.* 1983).

A major component of appropriate management of malnutrition is the identification of the cause and its appropriate management. Treatment of depression reverses weight loss when treatment is successful (Morley & Kraenzle, 1995).

Numerous drugs have been utilized in an attempt to reverse malnutrition in older subjects. Anabolic hormones (testosterone, oxandrolone and growth hormone) have been utilized to reverse catabolic processes in older subjects with severe illnesses (Kaiser *et al.* 1991; Morley, 1997). An orally-active growth hormone secretagogue (MK-677) has been shown to reverse diet-induced catabolism and may be useful for the management of anorexia in older subjects (Murphy *et al.* 1998). Ornithine oxoglutarate has been used to treat anorexia in older subjects in Europe with some success (Brocker *et al.* 1994). It appears to have minimal side-effects at low doses. Duranabinol has been used in Alzheimer's patients and in patients with cancer (Nelson *et al.* 1994). It has the potential to produce delirium. Megestrol, which has been used in middle-aged patients with cancer and acquired immune deficiency syndrome, seems to be poorly orexigenic in older subjects and to produce delirium megacolon, oedema, and congestive heart failure (Aisner *et al.* 1990; Castle *et al.* 1995). The antiserotonergic drug, cyproheptadine acetate, has failed to show dramatic appetite-enhancing effects (Mainguet, 1972). The prokinetic drugs (cisapride and metoclopropramide) have improved food intake in some dyspeptic older subjects. Moclobemide, a monoamine oxidase A (*EC* 1.4.3.4) inhibitor, has been shown to enhance weight gain in non-depressed older subjects.

Conclusion

Protein–energy malnutrition is a major syndrome which occurs commonly in older subjects. Most of the causes of protein–energy malnutrition are treatable. Despite this, physicians rarely diagnose the presence of protein–energy malnutrition, and even more rarely institute appropriate therapy. Early detection is a key to the appropriate management of protein–energy malnutrition. Subjects with depression are particularly prone to develop protein–energy malnutrition.

The management of protein–energy malnutrition requires an aggressive partnership between the physician and the dietitian, with psychiatric consultation being obtained when appropriate. The Malnutrition Cost Survey (Tucker & Miguel, 1996) estimated that early nutritional support in appropriately targetted subjects in a medium-sized institution would result in a cost savings of greater than one million dollars.

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