Clinical basics

Clinical nutrition: 1. Protein–energy malnutrition in the inpatient

L. John Hoffer

Case

Mr. B is a 60-year-old man with long-standing type 2 diabetes mellitus complicated by retinopathy, moderate renal failure and peripheral vascular disease. He required admission to hospital for a left above-knee amputation. After surgery, the stump healed well, but a deep, infected ulcer developed over his sacrum. The nursing notes indicate that he has eaten less than one-third of the food served him in the 3 weeks since his operation. Before his admission to hospital, he weighed 60 kg, and his height was 1.73 m, giving him a body mass index (BMI), calculated as weight (kg) divided by height squared (m^2), of 20. His weight was not measured on admission, but systematic examination of his muscle bulk and subcutaneous fat suggests a current BMI of about 18.

This patient is suffering from protein–energy malnutrition (PEM), a pathologic depletion of the body's lean tissues caused by starvation, or a combination of starvation and catabolic stress. In this case, the diagnosis is evident from the physical examination, which reveals a combination of generalized fat and muscle loss typical of the disease, and from the history of prolonged grossly inadequate food intake. PEM is easiest to diagnose when fat stores are depleted, but it can occur without apparent fat loss in previously obese patients, in chronic protein deficiency without energy deficiency, and in highly protein-catabolic states. The lean tissues are the fat-free, metabolically active tissues of the body, namely, the skeletal muscles, viscera, and the cells of the blood and immune system. They account for 35%–50% of the total weight of a healthy young adult, with fat (20%–30%), extracellular fluid (20%), and the skeleton and connective tissue (10%–15%) accounting for the rest. Because the lean tissues are the largest body compartment, their rate of loss is the main determinant of total weight loss in most cases of PEM, and it is for this reason that serial body weight measurements are so useful for assessing the tempo and severity of the disease. A weight loss of 40%–50% is usually incompatible with survival, at least in older adults, whereas milder lean tissue depletions induce important biochemical and functional abnormalities. These abnormalities, together with immune system dysfunction, are evident after involuntary weight loss exceeds about 10% and become highly physiologically obtrusive when weight loss exceeds about 15%. PEM is characterized by atrophy and weakness of the skeletal muscles (including the respiratory muscles), reduced heart muscle mass, impaired wound healing, skin thinning with a predisposition to decubitus ulcers, immune deficiency, fatigue, apathy and hypothermia (Fig. 1).[1–9] The extracellular fluid compartment typically expands in PEM, occasionally causing edema. Although lean tissue loss of more than 40% signals imminent death, patients with lesser, but significant, lean tissue loss are at increased risk from their primary disease, its complications and other coincident diseases.

A logical, but inadequate, way to classify the severity of PEM is simply by degree of weight loss.[10] This requires estimation of the patient's "dry" weight (weight corrected for edema or ascites) and a calculation of what percentage this is of normal for that person. For "normal" one can use the weight that would give a BMI of 24. In older adults, the lower end of the normal range for BMI is about 20, so one might consider PEM as *mild or absent* when the BMI is 20 or more (representing a weight deficit of 5%–15%), *moderate* when the BMI is over 16 but less than 20 (weight deficit of 16%–33%) and *severe* when the BMI is 16 or less. In practice, dry

Review

Synthèse

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weight and height are not always easy to determine. A nomogram is available that uses knee height to predict the stature of elderly patients who are bedridden or have spinal deformities.[11]

Classified this way, moderate-to-severe ("advanced") PEM occurs in at least 25% of patients in acute care hospitals, where it is associated with an increased length of stay in hospital, a high rate of medical and surgical complications, and an increased likelihood of dying.[4,8,12–15] However, a classification of PEM based entirely on BMI is inadequate for determining prognosis and treatment imperatives for individual patients. A BMI that is less than 20 is normal for some people, whereas for others it indicates a degree of malnutrition, but one that is not serious enough to require urgent, potentially dangerous nutritional intervention. Nor does a BMI that is greater than 24 rule out severe PEM. In order to classify PEM in a clinically useful way, one must understand its pathophysiology.

Pathophysiology

PEM is caused by starvation. It is the disease that develops when protein intake or energy intake, or both, chronically fail to meet the body's requirements for these nutrients.[16] PEM has always been a common disease, and humans have adaptive mechanisms for slowing and, in most cases, arresting its progress. Fat loss is slowed by a reduction in energy expenditure that the body accomplishes both by reducing the metabolic rate per unit of the metabolically active tissues and by jettisoning some of the body's lean tissue (protein) store.[17] Such a protein-depleted body also requires less dietary protein. Muscle protein, which normally accounts for about 80% of the lean tissue mass, bears the brunt of the loss, whereas the "central" lean tissues (liver, gastrointestinal tract, kidneys, blood and immune cells) are relatively spared. As long as the starvation ration of energy and protein is not too low, successful adaptation will reduce energy and protein requirements to match it, restoring homeostasis and maintaining key physiologic functions. The physiologic cost of this adaptation is a lowered metabolic rate and reduced muscle mass (including reduced cardiac and respiratory muscle mass); its clinical consequences include muscular weakness and functional disability, reduced cardiac and respiratory capacity, mild hypothermia and a reduced body protein reserve (Fig. 2).[16]

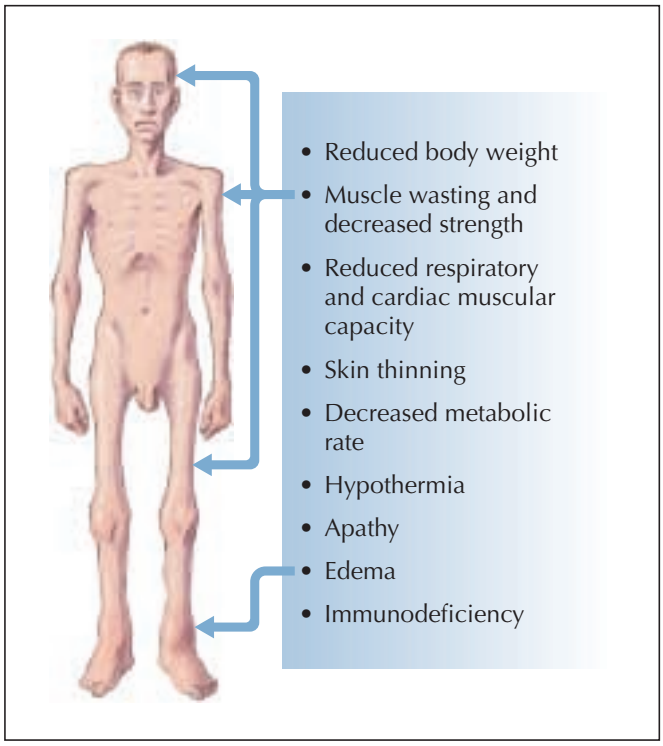

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Fig. 1: Clinical features of PEM. PEM = protein–energy malnutrition.

The contribution of systemic inflammation to PEM

Patients with severe tissue injury commonly develop a hypermetabolic response termed the systemic inflammatory response syndrome (SIRS), which is defined by the presence of 2 or more of the following elements: fever (or profound hypothermia), tachycardia, tachypnea and leukocytosis (or increased numbers of band forms).[18] Other features of the SIRS include changes in acute-phase serum protein concentrations,[19] increased energy expenditure, increased whole-body protein turnover, anorexia and protein wasting.[18] The protein wasting is believed to represent the metabolic cost of rapidly mobilizing amino acids for wound healing and synthesis of immune cells and proteins.[20] Nutritional support is an important part of therapy, but it is provided with the expectation of limiting, rather than reversing, body protein losses.[21]

A similar, but far milder, inflammatory condition exists on the general medical and surgical wards. This syndrome, described in recent years as "cachexia" or "cytokine-induced malnutrition,"[22] typically occurs in patients with inflammatory disease or a malignancy associated with continuous involuntary weight loss. Typical features include changes in concentration of acute-phase serum proteins,[19] some of which, such as C-reactive protein, fibrinogen and ferritin, are increased, whereas others, such as transferrin, prealbumin (transthyretin) and albumin, are decreased; the anemia of chronic disease; anorexia; and the partial nullification of a previously successful adaptation to starvation. Because successful adaptation is a key to the prognosis of PEM, it is important to identify factors that reverse it or prevent it from occurring (Table 1). The PEM associated with chronic mild inflammation is not restricted to patients with certain neoplasms or inflammatory diseases. It is increasingly recognized as contributing to the protein wasting associated with organ failure, including chronic renal failure[23] and end-stage heart disease.[24] Protein catabolism

dominates in full SIRS, whereas decreased food intake (plus some degree of failed adaptation) is the major reason for the lean tissue loss in the cachectic syndromes, and positive protein balance can be anticipated if an appropriate nutritional strategy is implemented.[9]

Subjective global assessment

Returning to the problem of classifying the severity of PEM for individual patients, it must be acknowledged that no fully satisfactory classification method currently exists.[25–27] Many experts advocate the technique of subjective global assessment (SGA) developed 20 years ago.[28] SGA involves the assessment of 6 clinical parameters, followed by a personal judgement as to whether the patient has (A) no malnutrition, (B) possible or mild malnutrition, or (C) significant malnutrition (Table 2).[29] The technique is easy to remember and use, if one bears in mind what it aims to find out in light of the pathophysiologic concepts outlined in the previous paragraphs:

- Is there at least a moderate lean tissue depletion?
- Is the lean tissue depletion continuing (failed adaptation)?

The physical examination is crucial in SGA; it may be considered the "thinking person's BMI." With some experience, low-end BMIs can be estimated with reasonable accuracy simply from a careful inspection for loss of subcutaneous fat and decreased mass in the temporal, deltoid, intercostal, upper arm, gluteal, thigh and calf muscles. The question about weight loss in SGA asks about weight loss from *usual* rather than *ideal* body weight. This indicates whether or not adaptation has succeeded. Patients with serious gastrointestinal symptoms or a marked reduction in

Table 1: Factors that prevent adaptation to starvation

• Energy intake or protein intake, or both, too low for adaptation to succeed
• Micronutrient (e.g., potassium, zinc, phosphate) deficiencies
• Systemic glucocorticoid therapy
• Catabolic stress

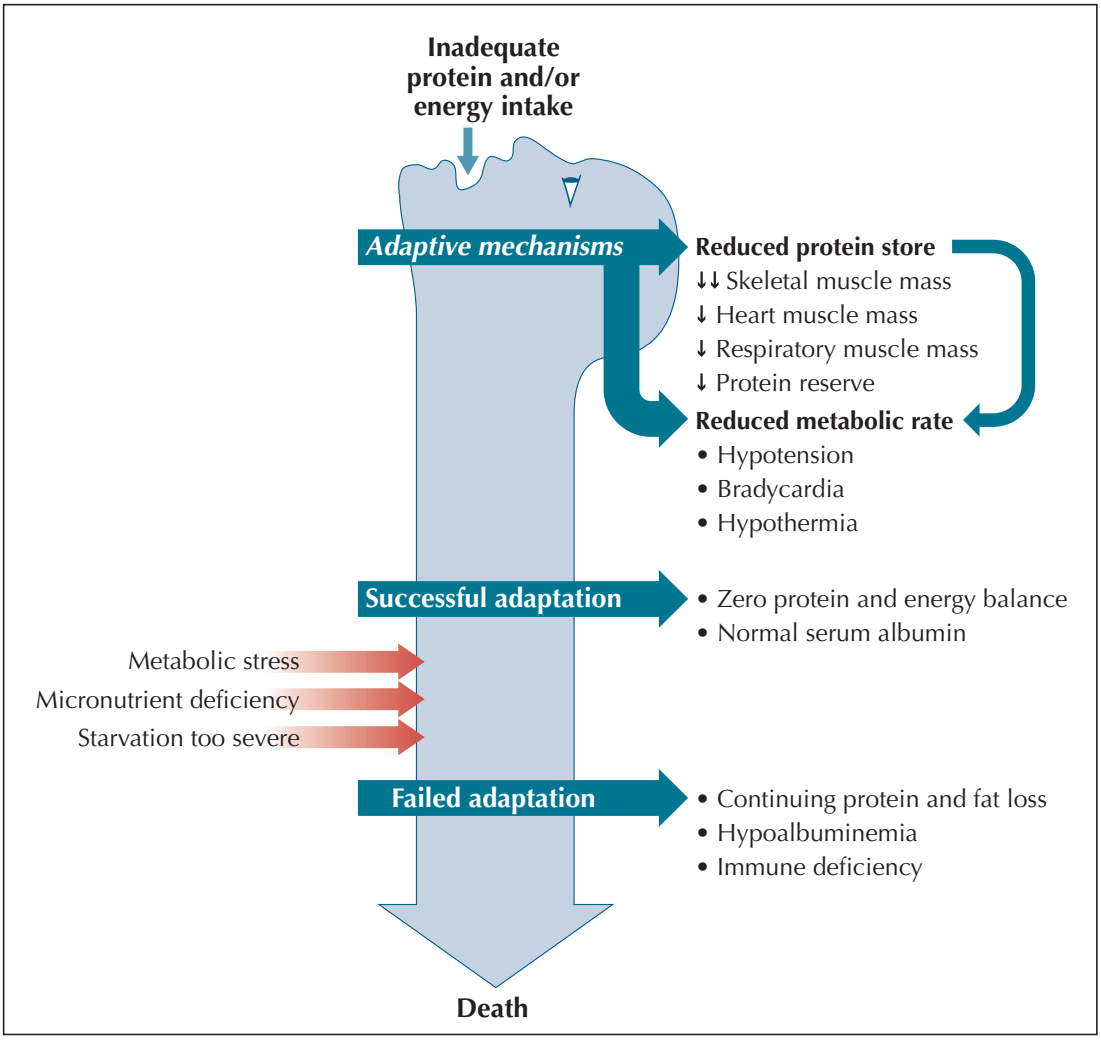

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Fig. 2: Pathophysiology of PEM.

functional ability are unlikely to be eating much food. Using all the items together, the nutritional diagnostician will appreciate that a starving or starving–catabolic patient whose premorbid BMI was 19 is at graver risk than one whose premorbid BMI was 27 and will focus the nutritional intervention proportionately. Nor will he or she overlook the patient whose body weight is constant despite food intake too deficient to be compatible with adaptation. Weight constancy in people losing body substance can only mean they are gaining water. A corollary is that persons developing edema should be *gaining* weight, not maintaining it.

Biochemical response to starvation

Contrary to what is sometimes written, ketosis is neither necessary nor sufficient to diagnose PEM.[16] Mild ketonuria can be normal for lean, healthy adults after the overnight fast, and ketosis is a normal feature of a total fast lasting more than about 24 hours; it is readily prevented or abolished by carbohydrate intakes as low as 50–100 g per day. Because even starving patients usually consume more than this amount of carbohydrate, the vast majority of them are not ketotic. Fasting ketosis is associated with protein catabolism, so it should be prevented by infusing 5% dextrose solution, 2 L per day, to patients who must temporarily be kept fasting.

The relation between hypoalbuminemia and PEM is more complex. The serum albumin concentration is normal in successfully adapted PEM even when advanced, as in some cases of anorexia nervosa, and it falls when adaptation fails. (By contrast, serum levels of the hepatic secretory protein, prealbumin, are reduced in energy deficiency and adapted PEM, and they may be used to screen for patients whose food intake is inadequate and who need closer monitoring.) Because albumin and prealbumin are negative acute-phase proteins, their serum levels fall in response to metabolic stress even in the absence of PEM. The rapid fall in serum albumin that occurs in acute severe inflammation is caused by its redistribution into an expanded extracellular fluid compartment. Hypoalbuminemia also occurs in nephrotic syndrome and in protein-losing enteropathy.

Despite its lack of specificity, hypoalbuminemia is an important finding in nutritional assessment. A normal serum albumin concentration in a starving patient is a favourable prognostic finding, for it implies successful adaptation and, in particular, the absence of metabolic stress. Hypoalbuminemia has an adverse prognostic implication, irrespective of whether it is due to metabolic stress or failed adaptation to PEM. Because hypoalbuminemic patients are usually both catabolic *and* starving, the presence of hypoalbuminemia should stimulate a careful nutritional assessment for every patient. A fall in albumin that seems inappropriately steep for the degree of stress indicates either that the severity of the stress or the malnutrition has been misjudged and indicates the need to examine both possibilities carefully (Table 3).

Therapy

The hypothesis that preventing, reversing or limiting advanced PEM will improve a patient's clinical outcome is overwhelmingly biologically plausible, but in each case the anticipated benefit must be balanced against the risks of artificial feeding. In moderate-to-severe PEM, even a relatively short period of adequate protein and energy provision (e.g., 7–14 days) may improve immune function and muscle function enough to improve prognosis.[9,30] In the long term, although body fat can be increased in bedridden patients, they will not regain much in the way of lean tissues until they are mobilized and rebuild their muscles.[31] Mobilization and exercise are essential for nutritional rehabilitation.

The diagnosis even of advanced PEM is frequently missed by physicians and nurses, and when this happens the opportunity is lost to discover whether treating it can im-

Table 3: Characteristics of adapted and maladapted protein–energy malnutrition

Characteristic	Adapted PEM	Failed adaptation
Muscle mass	Reduced	Reduced
Body weight	Reduced but constant	Reduced and falling
Serum albumin	Normal	Reduced
Serum prealbumin	Reduced	Reduced

Table 2: Recognition of advanced protein–energy malnutrition (PEM) by subjective global assessment*

Unremitting, involuntary weight loss that is greater than 10% in the previous 6 months, and especially in the last few weeks (failed adaptation)
Food intake is severely curtailed (objective evidence of starvation)
Muscle wasting and fat loss, with attention to the presence of edema, or ascites present on physical examination (tissue loss is direct proof of serious lean tissue loss, and edema frequently accompanies advanced PEM)
Persistent, essentially daily gastrointestinal symptoms such as anorexia, nausea, vomiting or diarrhea in the previous 2 weeks (strongly predicts inadequate food intake)
Marked reduction in physical capacity (predicts poor intake and is evidence of its consequences)
Presence of metabolic stress due to trauma, inflammation or infection (adaptation impossible)

* Any combination of these conditions (especially the first 3) indicates that the patient has significant PEM.

prove the patient's clinical outcome. Oral nutrition is safest, cheapest and best. When nutritional needs cannot be met by modifications in the diet or its provision, forced feeding must be considered. When the alimentary tract cannot be used, the option of parenteral nutrition is available. In controlled clinical trials that involved this mode of nutrition therapy, clinical outcome was improved in advanced PEM, equivalent to SGA class C, but patients with only mild or questionable PEM fared worse when treated in this aggressive fashion.[32] In critically ill patients who cannot be fed enterally, parenteral nutrition may reduce complications, but it has not yet been shown to reduce mortality.[33] It is possible that variability and a lack of reliable statistics make it difficult to demonstrate even important treatment effects in the intensive care environment. It may also be that our understanding of the best way to administer parenteral nutrition to critically ill patients is inadequate.[33]

Treatment for Mr. B

The hospital's nutritional assessment–feeding assistance team was consulted. The patient was considered to have a good prognosis if his starvation could be reversed. A careful assessment revealed that much of the time his food tray was being delivered to the bedside, where he found it hard to get to because of his amputation, skin ulcer and poor vision. Even when he retrieved the tray, the food on it did not appeal to him. The feeding assistance team (trained community volunteers and family members supervised by the primary nurse and dietitian) made sure that he was properly positioned in front of his food tray for every meal and that the meals served him were small but frequent, with flexible delivery times, so as to cope with his lack of appetite. With the help of family and a discretionary hospital "food fund," his tray often included his favourite foods. A volunteer stayed with him throughout his meals to provide conversation, encouragement and sometimes feeding assistance. His blood glucose was carefully controlled. The ulcer was treated meticulously. His food intake improved. After 4 weeks he was transferred to a rehabilitation hospital in good condition.

Competing interests: None declared.

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