with the reference population from which the standard table is derived. The percentage of fat equals the circumference of the right upper arm and abdomen minus the right forearm (in centimeters) minus 10.2.

Table 9. Circumference Measurements

- Waist to hip circumference ratio
- Mid-upper arm circumference
- Forearm circumference
- Calf circumference

**Bioelectric impedance analysis.**[13,14] Bioelectric impedance analysis (BIA) measures body composition based on the principle that lean mass has a higher electrical conductivity and lower impedance relative to water, based on electrolyte content. BIA is an easy bedside method; electrodes are attached to the extremities and a small electrical current is used to obtain electrical and resistance measurements, which can be converted to lean mass and fat mass measurements. This method is the most common technique used to monitor body composition in compromised patients. However, hydration must be adequate because the measurement of lean body mass is really the measurement of body water, as fat is water-free. Lean body mass is underestimated in a dehydrated patient and, conversely, overestimated in an edematous patient.

**Nitrogen balance.**[11] There are a series of techniques used to determine relative gains or losses in lean body mass based on the balance between nitrogen intake and nitrogen loss (urine). These are most useful in an outpatient setting and include computed tomography (CT), magnetic resonance imaging (MRI), and dual energy x-ray absorptiometry (DXA).[14] These very precise, high-tech scanning procedures use radiographic imaging to determine body composition. Differences in density (CT), color (MRI), or the image of 2 x-ray energies (DXA) define body composition. However, because of cost and the lack of portability, these are not practical screening tools to measure for body composition changes.

Decreased muscle mass and strength is called sarcopenia, which is a Greek term for losing flesh. Sarcopenia is caused by inactivity and poor nutrition. It leads to weakness, disability, skin ulcers, and infections; leads to increased body fat caused by decreased activity and low metabolic rate; and leads to metabolic abnormalities, including diabetes, which leads to decreased quality of life.

Although involuntary weight loss is the initial simple marker of PEM, weight restoration is not a good marker of recovery because fat mass is much easier to gain than lean mass (Figure 3). If lean mass was lost, then lean mass needs to be restored.[22]

**Figure 3.** Weight is regained, but patient is still too weak to walk.
Common Causes of Involuntary Weight Loss and PEM

There are 2 routes to involuntary weight loss. The first is via the acute injury or disease process, where increased nutrient requirements and wasting of body protein are characteristic.\textsuperscript{[5-7,23-26]} The presence of other stressors, such as pain and anxiety, can lead to the same end point. Then, PEM occurs rapidly, due to the lack of any adaptive or protective responses. Often the insult or "stress" resolves, but the weight loss and PEM are never corrected in the recovery phase. With the presence of any catabolic insult, the degree of PEM exceeds the degree of weight loss, as lean mass is not protected. Increased nutrient losses due to gastrointestinal disease can lead to the same end point.

The second route is due to inadequate nutrient intake, in both quality and quantity. This process is very common in the elderly, those with disabilities, those with lack of appetite from chronic illness, those with mental illness, and those with poverty. The onset of severe weight loss precedes the PEM as some adaptation will occur and lean mass is initially spared, but, eventually, PEM will occur.\textsuperscript{[9,26-31]}

Whatever the route, the most common cause of weight loss and PEM is the combination of increased nutrient demands and decreased intake (Table 10).

Table 10. Conditions Associated With Development of PEM

- Catabolic illness, "the stress response" (eg, trauma, surgery, wounds, infection, and corticosteroids)
- Involuntary weight loss exceeding 10% of ideal, for any reason
- Chronic illnesses (eg, diabetes, cancer, mental impairment, arthritis, and renal failure)
- Increased nutritional losses; open wounds, enteral fistulas
- Intestinal tract diseases impairing absorption
Principles of nutrient partitioning (adaptive metabolism). Understanding the metabolic concept of nutrient partitioning into an energy and protein compartment and methods to optimize an efficient nutrient channeling into either energy production or protein synthesis are the first steps to understanding the nutritional support principles. In addition, the role of anabolic agents becomes clearer when considering their role as agents channeling protein substrate into protein synthesis.

In general, normal metabolism is directed by hormones that alter energy production to meet needs and to restore daily losses of protein which occur through the natural tissue synthesis and breakdown pathways.

Principles of nutrient partitioning: energy production and protein synthesis. As previously mentioned, most nutrients that are consumed are converted either to an energy pathway to run the metabolic machinery (with excess stored as fat), or into the protein synthesis pathway to restore and maintain lean body mass (Figure 4).

**Figure 4.** Nutrient partitioning.

**Energy pathway.** Energy is required for all metabolic activities, including protein synthesis, and is rapidly adjusted according to need (Figure 5). Any hypermetabolic state increases demands, and the less efficient use of nutrients for energy results in the nutrient recycling at the level of pyruvate that reverts back to glucose, capturing only a small portion of the potential energy. The byproduct is heat. Therefore, more nutrients are used to meet the demands.

**Figure 5.** Energy pathway of carbohydrates and fat.

**Protein pathway.** Protein is metabolized into amino acids and peptides. With normal anabolic hormone activity, most of the protein byproducts are used for protein synthesis, not for energy. However, energy is required for the synthesis process. Not all amino acids can be used. For instance, the amino acid profile found in vegetables is very different from the human profile and therefore deficient in key amino acids, while the profile of amino acids in egg albumin, milk, and meat protein provides the necessary protein substrate required by humans.

With an inadequate anabolic drive, (i.e., catabolic drive, PEM, aging, or illness), up to 30% of consumed protein ends up being used for energy. Thus, maintaining adequate anabolic activity is critical to maintaining or restoring lean mass.
Nutrient partitioning is also disrupted with the activation of the "stress response" or "flight-fright response." In this case, protein is inappropriately used for fuel and the lean mass loss increases in response to catabolism.

The protein synthesis pathway is driven by endogenous anabolic hormones and growth factors. Adding an anabolic hormone will further increase the ratio of protein synthesis.

**Catabolic illness: "the stress response"**[23-26] Commonly, PEM is due to body injury or insult that produces an abnormal metabolic response; typical characteristics include catabolism and hypermetabolism. Weight loss is inevitable.

The host response to severe illness or infection is an amplification of the flight or fright reaction. The insult (afferent arc) leads to the release of inflammatory mediators, which activates an abnormal hormonal response due to neuroactivation and leads to a marked increase in catecholamines and other hormones (efferent arc), which produces a hypermetabolic-catabolic state (Figure 6). The degree of hypermetabolism and catabolism is largely dependent on the degree of injury or infection. The average percent increase in basal metabolic rate (BMR) with various injury states has been documented (Table 11). The increase in metabolism also corresponds to a change in nutrient use, with 50% coming from fat, 20% (or more) from protein, and 30% from carbohydrates, as opposed to 5% from protein and, with nutrient deficiency, more than 90% of calories coming from fat.[23,30]

**Figure 6. Stress response to injury.**

![Stress Response to Injury Diagram]

**Table 11. Effect of Injury on Metabolic Demands**

<table>
<thead>
<tr>
<th>Insult</th>
<th>Increase in Metabolic Rate Above Basal (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starvation</td>
<td>-10-0</td>
</tr>
<tr>
<td>Elective operation</td>
<td>25-50</td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Long bone fracture</td>
<td></td>
</tr>
<tr>
<td>Multiple blunt trauma</td>
<td>50-70</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
</tr>
<tr>
<td>Head injury</td>
<td></td>
</tr>
<tr>
<td>Thermal injury*</td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>25</td>
</tr>
<tr>
<td>20%</td>
<td>30</td>
</tr>
<tr>
<td>30%</td>
<td>70</td>
</tr>
<tr>
<td>40%</td>
<td>85</td>
</tr>
<tr>
<td>50%</td>
<td>100</td>
</tr>
</tbody>
</table>
Percentages are body surface area affected by thermal injury

There is an entire spectrum of abnormalities that occur after injury, infection, and inflammation due to "stress response." If uncontrolled, the stress response can progress to multiple-organ dysfunction with loss of body protein and direct cell injury by oxidants and other mediators. Critical illness caused by severe trauma, infection, or a wound will activate the stress response, as will an elective surgical procedure (Figure 7). The once protective response then becomes autodestructive, and intense auto cannibalism (catabolism for fuel) occurs with rapid loss of lean body mass (Table 12)\(^{23,24}\)

**Figure 7.** Critical illness caused by severe trauma, infection, or a wound will activate the stress response, as will an elective surgical procedure.

**Table 12. Metabolic Abnormalities Due to the "Stress Response" of Injury**

- Increased catabolic hormones (cortisol and catechols)
- Decreased anabolic hormones (human growth hormone and testosterone)
- Marked increase in metabolic rate
- Sustained increase in body temperature
- Marked increase in glucose demands and liver gluconeogenesis
- Rapid skeletal muscle breakdown with amino acid use as an energy source (counter to normal nutrient channeling)
- Lack of ketosis, indicating that fat is not the major calorie source
Unresponsiveness of catabolism to nutrient intake

Controlling the degree of ongoing injury requires both controlling the host response and, at the same time, supporting the metabolic needs to avoid further deterioration. However, catabolism still outweighs anabolism as the catabolic hormones predominate and the anabolic hormones, growth hormone, and testosterone are decreased (Table 13). Massive protein depletion can occur in days to weeks after a severe injury.

Table 13. Hormonal Response to Injury

<table>
<thead>
<tr>
<th>Hormonal Levels</th>
<th>Glucose Production</th>
<th>Proteolysis</th>
<th>Protein Synthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catecholamine</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
<td>↑↑</td>
</tr>
<tr>
<td>Cortisol</td>
<td>↑↑↑↑</td>
<td>↑↑↑</td>
<td>↑↑</td>
</tr>
<tr>
<td>Glucagon</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
<td>↓</td>
</tr>
<tr>
<td>Insulin</td>
<td>↑↑</td>
<td>↑↑↑</td>
<td>↓</td>
</tr>
<tr>
<td>GH</td>
<td>↓</td>
<td>↓↓↓</td>
<td>↑↑</td>
</tr>
<tr>
<td>Testosterone</td>
<td>↓↓</td>
<td>—</td>
<td>↑</td>
</tr>
</tbody>
</table>

Patients with burns who are unable to meet their nutrient demands will lose over 20% of lean mass within weeks of injury. This loss will reduce healing and increase infection (Figure 8). A recovering burn patient with optimum nutrition will lose at least 10% of lean mass, but nutrition and anabolism are adequate for healing. However, this weight loss needs to be recovered in the rehabilitation period to restore function (Figure 9).

Figure 8. A burn patient with nutrient intake not meeting demands.

Figure 9. A recovering burn patient with optimum nutrition.
Increased glucose production is produced by protein breakdown and converting amino acids, predominantly alanine, into carbon skeletons, which are then transformed in the liver to glucose, resulting in a net protein loss (Figure 10). Nitrogen losses in burns can be converted to 1-2 pounds of muscle per day. Uncomplicated elective surgery will result in 5-10 pounds of lean mass loss during the first 2-3 weeks postoperatively, even with good nutrition (Figure 11).[32-36]

**Figure 10.** Alanine cycle.

**Figure 11.** Nitrogen losses in burns.

Protein partitioning is markedly altered by the increased catabolic and decreased anabolic stimuli, diverting 25% to 30% of the amino acids into the energy partition. Despite adequate macronutrient intake, erosion of the lean mass compartment will occur, and healing will be impaired. The rate of erosion is dependent in part on the degree of insult; major burns are the greatest catabolic stimulus. The addition of protein with high biologic value and hydrolysates, and amino acids with anabolic activity, such as glutamine, will decrease but not eliminate net catabolism. The addition of an anabolic agent will significantly improve the protein partitioning process and accelerate net protein synthesis.