SECTION 14

Metabolism and Nutrition in Critical Illness and Acute Kidney Injury

CHAPTER 72

Energy Requirement and Consumption in the Critically Ill Patient

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OBJECTIVES

This chapter will:

1. Describe the pathogenesis of hypermetabolism in critical illness.
2. Delineate the components of total energy expenditure.
3. Review techniques for the measurement of energy expenditure in critically ill patients.
4. Explain how to estimate energy expenditure in the critically ill.
5. Highlight the distinction between energy requirement and energy consumption in critical illness.

METABOLIC RESPONSE TO CRITICAL ILLNESS

In 1932 Cuthbertson[1] was the first to describe the metabolic response to traumatic injury. Later, he divided the response to such injury into two distinct phases.[2] Characteristics of these phases are listed in Table 72.1. The short-lived "ebb," or hypometabolic, phase immediately after injury is manifested clinically by cold, clammy extremities and a thready pulse. After adequate resuscitation, the patient warms up and cardiac output increases. The flow, or hypermetabolic, phase is characterized by a rise in energy expenditure that peaks at 5% to 60% above normal, depending on the magnitude of the injury. The duration of this phase depends on the severity of injury and the development of complications. Profound metabolic changes occur during this phase, and the increased oxygen consumption supports these interorgan substrate exchanges.

Metabolism in serious sepsis is similar to that of major traumatic injury.[3] A systemic inflammatory response is induced in patients with sepsis as well as in patients with major traumatic injury, and the two groups of patients also experience similar metabolic sequelae. This generalized response is evident in patients with major burn injury,[4] who may exhibit oxygen consumption rates far in excess of those seen in patients with severe sepsis and major trauma.[5] A high percentage of patients with so-called systemic inflammatory response syndrome (SIRS) develop dysfunction of one or more organ systems. A major cause of acute renal failure in critically ill patients is SIRS with associated organ dysfunction. The hypermetabolism associated with sepsis and the inflammatory response is shown in Fig. 72.1 for patients with and without acute renal failure. These data, derived from Uehara et al.,[6] illustrate the similarity in response for both groups of patients, peaking approximately 10 days after admission to an intensive care unit (ICU). The onset of SIRS is the predominant determinant of the degree of hypermetabolism, whereas the development of organ failure portends a prolonged hyperdynamic phase.

Reprioritization of the normal nutritional homeostasis of the body occurs in response to the hypermetabolism and catabolism of the systemic inflammatory response. Marked alterations in carbohydrate, fat, and protein metabolism occur (see Chapters 135, 136, and 138). Hyperglycemia, hypertriglyceridemia, high lactate levels, and high free fatty acid concentrations are characteristic of the critically ill patient and indicate major derangements in intermediary metabolism. Optimal nutritional management of these patients requires an understanding of fuel utilization and the control of energy balance in the flow phase of critical illness.

Physiologic Aspects of Energy Metabolism

The human body can be considered as a continuous energy exchange device in which energy is taken in as food and

TABLE 72.1

Characteristics of the Ebb and Flow Phases of Cuthbertson

EBB PHASE	FLOW PHASE
Hypometabolic	Hypermetabolic
Low core temperature	Raised core temperature
Decreased energy expenditure	Increased energy expenditure
Normal glucose production	Increased glucose production
Mild protein catabolism	Profound protein catabolism
Raised blood glucose	Raised or normal blood glucose
Raised catecholamines	Raised or normal catecholamines
Raised glucocorticoids	Raised or normal glucocorticoids
Low insulin	Raised insulin
Raised glucagon	Raised or normal glucagon
Low cardiac output	Increased cardiac output
Poor tissue perfusion	Normal tissue perfusion
Patient cold and clammy	Patient warm and pink
Preresuscitation phase	Recovery phase

From Cuthbertson DP. Post-shock metabolic response. *Lancet.* 1942;1:433–437.

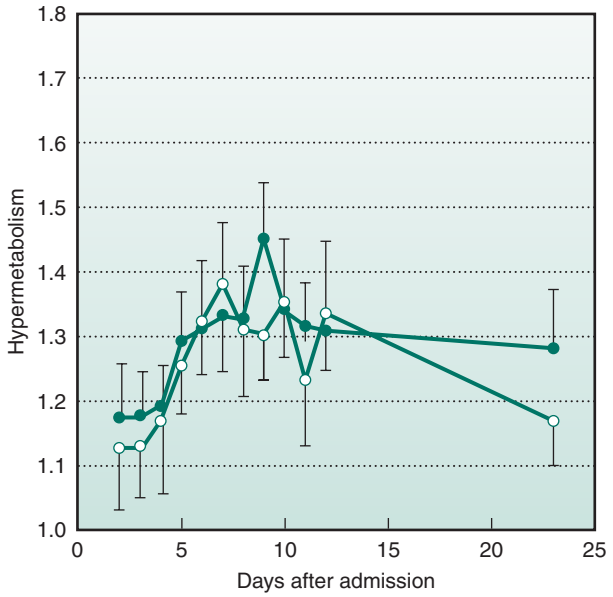

FIGURE 72.1 Hypermetabolism (expressed as the ratio of measured resting energy expenditure [REE] to predicted energy expenditure) for patients with serious sepsis with (n = 5, *closed circles*) or without (n = 7, *open circles*) early acute renal failure from 2 days after admission to the intensive care unit through day 12, with subsequent measurements at day 23.

released as heat (Fig. 72.2). The energy conversion occurs through the oxidation of ingested macronutrients, carbohydrates, fats, and proteins. Oxygen is consumed, carbon dioxide is produced, and heat is generated in proportion to the quantity of substrate oxidized. The heat production, that is, the energy expenditure, of the body can be measured by *direct calorimetry,* in which a sealed, insulated chamber is used to isolate the subject. In steady-state conditions, respiratory gas exchange (measured by *indirect calorimetry*) reflects cellular gas exchange, and under these conditions a close correspondence is found between the direct and indirect calorimetric techniques for determining energy expenditure.[7]

Oxidation of a given substrate is associated with production of a particular quantity of heat for a given quantity of oxygen consumption and a unique ratio of carbon dioxide production (V_{CO_2}) to oxygen consumption (V_{O_2}) (respiratory quotient [RQ]). For instance, the combustion of 1 mole of glucose requires 6 moles of O_2 with release of 6 moles of CO_2 and an RQ of 1.0:

$$C_6H_{12}O_6 + 6\,O_2 \rightarrow 6\,CO_2 + 6\,H_2O$$

whereas combustion of a typical fat (triglyceride of palmitic acid) yields an RQ of 0.703:

$$2\,C_{51}H_{98}O_6 + 145\,O_2 \rightarrow 102\,CO_2 + 98\,H_2O$$

The calculation for protein oxidation must account for the incomplete combustion of protein in the body, where some of the oxygen and carbon remain combined with nitrogen and are excreted as nitrogenous products. Livesey and Elia[8] have published constants for heat release and gas exchange for typical macronutrients.

Components of Energy Expenditure

It is useful to distinguish between the basal metabolic rate, also called the basal metabolic expenditure (BME), and the resting metabolic expenditure (RME). BME refers to the basal requirement occurring in deep sleep and is generally of little clinical relevance. RME applies to the fasted, rested patient in a thermoneutral environment and may be 5% to 10% higher than BME. The thermic effect of food is the energy expended in the assimilation of nutrients, which, in the critical care situation, may be provided enterally or parenterally in a continuous manner. It varies depending on the type of diet consumed and the metabolic state of the patient but approximates 10% of RME. The term *resting energy expenditure* (REE) refers to the energy expenditure of the patient receiving continuous enteral or parenteral nutrition and is the sum of the RME and the thermic effect of food. The remaining component contributing to the total energy expenditure (TEE) is activity energy expenditure. In health, REE typically makes up 60% to 70% of TEE (Fig. 72.3).

MEASUREMENT METHODS

The measurement of TEE in the critically ill patient raises formidable problems. Continuous whole-body calorimetry[9] is the most accurate means of assessing TEE, but for obvious reasons this technique is not applicable to hospital patients. The doubly labeled water technique for measuring total free-living energy expenditure has been applied widely in healthy individuals.[10] The assumptions underlying this method[11] may be seriously violated in critically ill populations, and the approach relies on measurements over an extended period (typically 10 to 14 days), which renders it of limited value in the intensive care setting. TEE also has been measured over defined periods of time by measuring the changes in body composition that occur so that changes in the energy stores of fat, carbohydrate, and protein can be derived.[12] The total change in energy stores, or energy balance, is the difference between TEE and energy intake. In practice, this method is not applicable to individual patients because of the limited precision with which the energy balance can be measured.

In principle, continuous indirect calorimetry could be used to measure TEE in critically ill patients.[13,14] This technique measures O_2 consumption and CO_2 production

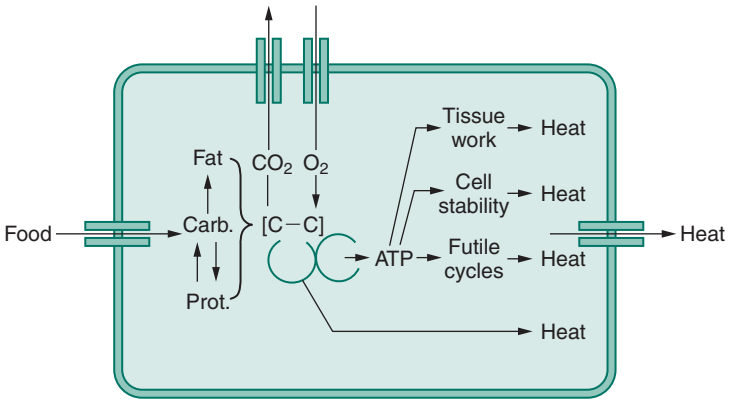

FIGURE 72.2 The human body viewed as an "engine," in which macronutrients are metabolized with associated oxygen consumption and carbon dioxide (CO_2) production and the ultimate generation of heat. (Modified from Kinney JM. Energy metabolism: Heat, fuel and life. In Kinney JM, Jeejeebhoy KN, Hill GL, Owen OE, eds. *Nutrition and Metabolism in Patient Care*. Philadelphia: WB Saunders; 1988:3–34.)

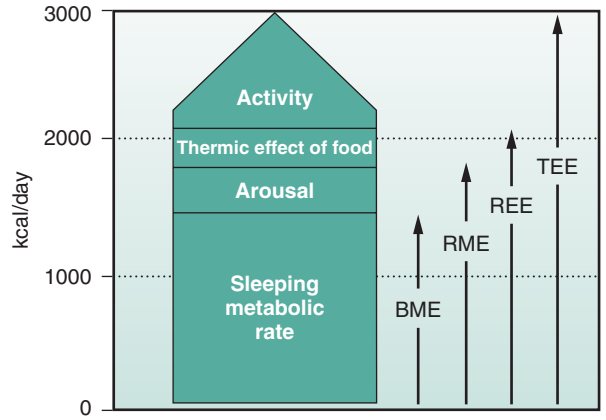

FIGURE 72.3 The components of total energy expenditure (TEE) with typical values for a male with a body weight of 70 kg and 10% body fat. *BME,* Basal metabolic expenditure; *REE,* resting energy expenditure; *RME,* resting metabolic expenditure.

rates, from which energy expenditure can be calculated if the urinary nitrogen excretion rate is known.[8] The classic formula of Weir[15] is generally used:

$$\text{Energy Expenditure (kcal/day)} = 3.94\ V_{O_2}\ \text{(L/day)} + 1.11\ V_{CO_2}\ \text{(L/day)} - 2.17\ U_N\ \text{(g/day)}$$

where U_N is urinary nitrogen excretion, which corrects for the incomplete oxidation of protein in vivo. Ignoring this correction results in less than 2% error on average in energy expenditure even with the higher-than-normal protein oxidation in critically ill patients.[16]

Although it has the advantage of providing estimates of TEE over periods of a day or less, the indirect calorimetry approach is problematic in patients in the early flow phase of their illness. It is suitable for patients on mechanical ventilation, but the errors in oxygen consumption measurement increase markedly with inspired oxygen fraction (F_{IO_2}), particularly above 60%.[17] Recent commercial developments have improved performance in the 60% to 80% range of F_{IO_2}. Conditions such as changing metabolic acid-base status and the use of extracorporeal CO_2 removal or oxygenation devices effectively rule out the indirect calorimetry method.[17,18] These situations commonly apply in the intensive care setting.

Typically, indirect calorimetry measurements are carried out over short periods of time (less than 1 hour) on patients in a steady-state condition. The latter ensures that the respiratory gas exchange measurements reflect the metabolic gas exchanges. In mechanically ventilated patients, a steady-state measurement of REE closely approximates TEE.[13]

ESTIMATION OF ENERGY EXPENDITURE

In many hospitals, limited access to equipment for measuring energy expenditure necessitates estimation by equations, usually based on prediction of RME that would apply in health, with allowances made for the thermal effect of food, degree of injury or stress, and activity. The principal determinant of RME in health is body size (e.g., weight, fat-free mass, or body surface area). Age and gender are also important factors because of the covariation among RME, age, gender, and fat-free mass. The Harris-Benedict equations,[19] which relate RME measured by indirect calorimetry in healthy adults to weight, age, and gender, were developed in the early 1900s and remain the most widely used equations for estimating energy expenditure. Substantial uncertainty results when applying such equations to individual patients. In particular, use of body weight for patients with fluid retention may be misleading. Use of a pre-illness weight,[20] an adjusted weight,[14] or a "dry" weight (correcting for fluid excess)[21,22] has been advocated. Furthermore, application of a stress factor may not be straightforward given the interindividual variation in the effect of the injury or insult on metabolic expenditure. Coupled with this, the stage of the patient in the typical stress response to illness must be considered. Fig. 72.4 suggests an adjustment to RME between 20% and 50% for a ventilated patient with severe sepsis. When patients are taken off ventilation, their energy consumption may increase significantly. This is illustrated in Table 72.2, where, in sepsis and posttrauma patients, REE approximated TEE during the first week of admission while the patients were ventilated, but over the second week, when many were taken off mechanical ventilation, TEE rose to 170% to 180% of REE.

Equations have been developed from indirect calorimetry measurements in mechanically ventilated critically ill patients in whom less reliance is placed on the use of stress categories. These equations use dynamic physiologic variables, which allow daily recalculation of energy expenditure (Table 72.3). The Swinamer equation[23] was based on REE measurements in 108 (48 trauma, 60 nontrauma) patients on day 1 or day 2 of their ICU admission. The effect of the inflammatory response on metabolic rate is represented by the body temperature, respiration rate, and tidal volume variables, and there is no factor representing type of insult. No nutritional support was provided (except for IV dextrose in some patients). Ireton-Jones et al.[24] developed an equation from 65 (52% burn, 31% trauma) patients requiring nutritional support and subsequently published an amended version based on the same data.[25] Frankenfield et al.[26–28] produced a series of equations, which included an RME prediction in health with a "stress multiplier" in addition

to terms reflecting the inflammatory response. The first of these equations[26] was based on 423 measurements over a maximum of 10 days in 56 multiple-trauma patients (30 of whom developed SIRS). Subsequently, three forms of the "Penn State equations" were constructed from retrospective analysis of 169 measurements in a mix of trauma, surgical, and medical ICU patients (see Table 72.3). All three equations involved similar adjustments to RME as estimated by either the Harris-Benedict equations[19] or the equations developed by Mifflin et al.[29] The Faisy et al.[30] equation, developed from measurement in 70 patients, was shown to better predict energy expenditure in this group than was the use of the Harris-Benedict equations with factors for severity of insult.

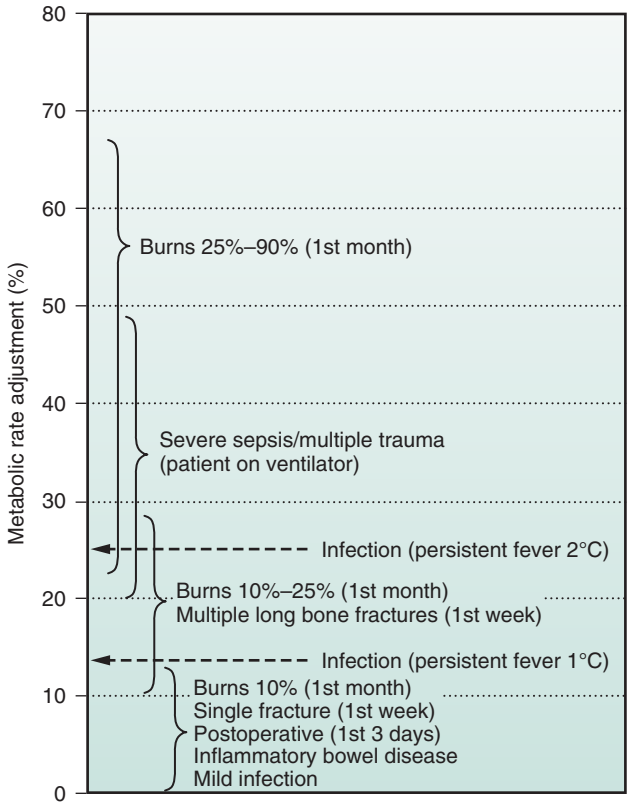

FIGURE 72.4 Approximate adjustments to resting metabolic expenditure (RME) for the effects of disease and injury. (Modified from Elia M. Organ and tissue contribution to metabolic rate. In Kinney JM, Tucker HN, eds. *Energy Metabolism: Tissue Determinants and Cellular Corollaries.* New York: Raven Press; 1992:61–79.)

Validation studies of these equations are limited and have been summarized by Frankenfield.[31] Flancbaum et al.[32] found a poor correlation between energy expenditure predicted by the Ireton-Jones 1992[24] and Frankenfield et al.[26–28] equations and the energy expenditure measured by indirect calorimetry in a group of surgical intensive care patients on mechanical ventilation and nutritional support. MacDonald and Hildebrandt[33] compared 24-hour indirect calorimetry measurements in a heterogeneous group of 76 patients on nutritional support with the predictions from the Harris-Benedict,[19] Ireton-Jones 1992,[24] Swinamer,[23] Frankenfield,[26] and Penn State 1998[27] equations. The Swinamer and Harris-Benedict equations (using a 1.6 stress factor) performed better than the others and predicted energy expenditure within 20% of measured values approximately 88% of the time. The two Ireton-Jones[24,25] and three Penn State equations[27,28] were compared by Frankenfield et al.[28] against resting indirect calorimetry measurements in 47 patients (trauma, surgical, and medical) on mechanical ventilation. The Penn State 2003a equation[28] predicted energy expenditure within 10% of measured values 72% of the time compared with 60% for the Ireton-Jones 1992 equation. The former equation predicted energy expenditure more than 15% above or below measured values 11% of the time versus 32% for the latter. The Ireton-Jones 2002 equation performed less well for this patient group than its predecessor, with predicted energy expenditure within 10% of measured values 36% of the time and outside 15% of measured values 40% of the time.

ENERGY REQUIREMENT VERSUS ENERGY CONSUMPTION

Measurement of energy expenditure in a critically ill patient provides an estimate of energy consumption or energy use

TABLE 72.2

Estimation of Total Energy Expenditure in Patients With Sepsis or Trauma

	TOTAL ENERGY EXPENDITURE		TEE/REE	
	TEE (kcal/day)	TEE/Bwt (kcal/kg/day)	INDIRECT CALORIMETRY[a]	HARRIS–BENEDICT EQUATION[b]
Sepsis				
Week 1	1927 ± 370	25 ± 5	1.0 ± 0.2	1.3 ± 0.2
Week 2	3257 ± 370	47 ± 6	1.7 ± 0.2	2.3 ± 0.3
P[c]	0.046	0.021	0.042	0.027
Trauma				
Week 1	2380 ± 422	31 ± 6	1.1 ± 0.2	1.4 ± 0.3
Week 2	4123 ± 518	59 ± 7	1.8 ± 0.2	2.5 ± 0.3
P[c]	0.049	0.029	0.089	0.039

Data are calculated from 5-day study periods in 12 sepsis and 12 trauma patients. Values are mean ± standard error of mean (SEM).
[a]REE measured by indirect calorimetry.
[b]REE (men) = 66.5 + 13.8 × Bwt + 5.0 × height − 6.8 × age; REE (women) = 655.1 + 9.6 × Bwt + 1.9 × height − 4.7 × age
[c]Comparison of weeks 1 and 2 by paired t-test.
Bwt, Averaged measured body weight over the 5-day study period; *REE,* resting energy expenditure; *TEE,* total energy expenditure.
From Uehara M, Plank LD, Hill GL. Components of energy expenditure in patients with severe sepsis and major trauma: A basis for clinical care. *Crit Care Med.* 1999;27:1295–1302.

TABLE 72.3

Equations for Prediction of Resting Energy Expenditure in Mechanically Ventilated Critically Ill Patients

EQUATION	REFERENCE	PREDICTED ENERGY EXPENDITURE (kcal/day)	R^2
Swinamer	23	RME = 945 (BSA) − 6.4 (A) + 108 (T) + 24.2 (RR) + 817 (V_T) − 4349	0.75
Ireton-Jones 1992[a]	24	REE = 5 (W) − 10 (A) + 281 (sex) + 292 (trauma) + 851 (burns) + 1925	0.34
Ireton-Jones 2002[a]	25	REE = 5 (W) − 11 (A) + 244 (sex) + 239 (trauma) + 804 (burns) + 1784	0.34
Frankenfield[b]	26	REE = 1.5 (RME_{HB}) + 250 (T) + 100 (VE) + 40 (dobut) + 300 (sepsis) − 11000	0.77
Penn State 1998[c]	27	REE = 1.1 (RME_{HB}) + 32 (VE) + 140 (T_{max}) − 5340	0.70
Penn State 2003a[d]	28	REE = 0.85 (RME_{HB}) + 33 (VE) + 175 (T_{max}) − 6433	0.67
Penn State 2003b[e]	28	REE = 0.96 ($RME_{Mifflin}$) + 31(VE) + 167 (T_{max}) − 6212	0.69
Faisy	30	RME = 8 (W) + 14 (H) + $^{32(V}E^{)}$ + 94 (T) − 4834	0.61

[a]For sex, 1 = male, 0 = female; for trauma, 1 = present, 0 = absent; for burns, 1 = present, 0 = absent.
[b]RME_{HB} calculated using actual or adjusted (if greater than 120% of ideal) body weight. For sepsis, 1 = present, 0 = absent based on clinical evidence of presumed infection, systemic inflammation, and organ dysfunction.
[c]RME_{HB} calculated using actual or adjusted (if greater than 120% of ideal) body weight.
[d]RME_{HB} calculated using actual body weight if less than or equal to admission weight, otherwise admission weight. RME_{HB} is calculated using the Harris-Benedict equations (see Table 72.2).
[e]$RME_{Mifflin}$ calculated using actual body weight if less than or equal to admission weight, otherwise admission weight. $RME_{Mifflin}$ is calculated using the Mifflin-St. Jeor equations[29]:

$$RME\,(men) = 10\,(W) + 6.25\,(H) - 5\,(A) - 161$$

$$RME\,(women) = 10\,(W) + 6.25\,(H) - 5\,(A) + 5$$

A, Age; *BSA,* body surface area (m^2); *dobut,* dobutamine dose (μg/kg/min); *H,* height (cm); R^2, coefficient of determination; *REE,* resting energy expenditure; RME_{HB}, resting metabolic expenditure by Harris-Benedict equations[19]; $RME_{Mifflin}$, resting metabolic expenditure by Mifflin-St. Jeor equations[29]; *RR,* respiratory rate (breaths/min); *T,* temperature (°C); T_{max}, maximum temperature (°C); V_E, minute ventilation (L/min); V_T, tidal volume (L); *W,* weight (kg).

rather than energy requirement or need. It cannot be assumed that providing energy intake to match energy expenditure is optimal for the management of critically ill patients.[34,35] A typical indirect calorimetric measurement of RME or REE in a sedated, ventilated critically ill patient provides a "snapshot" measure of energy consumption, assumed to approximate TEE, which reflects metabolism of endogenous (and possibly exogenous) nutrient substrates. The effect of brief nursing interventions, such as chest physiotherapy and dressing changes, may increase TEE by little more than 5%.[13] Energy requirement encompasses this objective measure of energy use but also includes other aspects, such as the effect of the route of feeding, problems with nutrient tolerance and assimilation, and whether energy intake should be adjusted to promote tissue gain or loss.

In critically ill patients with multiple injury, Frankenfield et al.[36] found that achievement of energy balance, compared with moderate energy deficit, led to fat deposition but did not improve nitrogen balance. Nitrogen loss did not correlate with energy balance. In these mechanically ventilated patients, energy intake was matched to REE to achieve energy balance. They concluded that high-protein, hypocaloric nutrition support is preferable for these patients. Underfeeding for a period of time may result in improved clinical outcome.[37,38] However, large cumulative energy deficits are associated with adverse outcomes.[39] With enteral feeding, gastrointestinal intolerance is the primary mechanism for protecting the patient from substrate excess. Mechanically ventilated patients receiving narcotic sedation, muscle relaxants, or both, will have reduced splanchnic circulation and, as a consequence, compromised gut motility, which will limit effectiveness of nutrition by this route.

Overfeeding exacerbates the hyperglycemia that accompanies the catabolic stress response, causes excess CO_2 production that potentially prolongs the need for mechanical ventilation, may result in hepatic steatosis and hypertriglyceridemia, and, with excessive protein intake, may produce azotemia and metabolic acidosis.[40] Increased ventilator dependence and length of ICU stay have been associated with high-energy intake.[41] Critically ill patients fed parenterally are vulnerable to overfeeding because of fewer impediments to the delivery of substantial energy loads by this mode of administration compared with enteral delivery. The patient receiving parenteral nutrition has no protective mechanism for dealing with overfeeding and must assimilate substrate. Increased sepsis complication rates in patients with major trauma have been attributed to overfeeding by the parenteral route.[42] Hypocaloric support for critically ill patients who are not malnourished has been suggested as a means to prevent overfeeding-related complications.[43] The question of hypocaloric or hypercaloric nutritional support for critically ill patients continues to receive much attention.

In view of the difficulties associated with estimation of energy requirements in the critically ill, many centers, without access to indirect calorimetry equipment, adopt the simple approach of providing 25 to 30 kcal/kg body weight. The American College of Chest Physicians consensus statement[44] recommends 25 kcal/kg usual body weight for ICU patients, with the additional caveats that caloric requirements may have to be increased 10% to 20% in such patients with SIRS and, for overweight (i.e., body mass index greater than 25) patients, usual body weight should be replaced by ideal body weight. It can be seen from Table 72.2 that over the first week of intensive care for sepsis and posttrauma patients on mechanical ventilation, TEE was 25 to 30 kcal/kg measured body weight, which increased to approximately 50 to 60 kcal/kg in the second week when many of the patients were taken off ventilation. For these patients, it remains to be determined whether provision of more than 25 to 30 kcal/kg is of benefit.[45]

Key Points

1. Hypermetabolism is a characteristic feature of critical illness.
2. Wide variation is seen in the degree and duration of hypermetabolism among individual patients.

3. Predicting energy expenditure for individual patients is difficult.
4. Indirect calorimetry is the preferred approach for assessing energy expenditure in individual patients.
5. Matching energy requirement to energy expenditure may not be optimal for nutritional management.

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