Nutritional Support in Intensive Care Unit (ICU) Patients

Topic 18

Module 18.1

Metabolic Response to Stress, Energy Requirements

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Learning Objectives

- Understand the mechanisms of the physiologic response to stress;
- Understand the effects of the critical illness on energy metabolism;
- Understand the effects of the critical illness on the adaptation to starvation;
- Propose rules for energy supply in critically ill patients.

Contents

1. Physiologic response to stress
2. Metabolic response: energy metabolism
3. Energy requirements
4. Adaptation to fasting

Key Messages

- The critical illness induces extensive physiological changes, involving energy metabolism and substrate utilization;
- Resting energy expenditure is increased in patients with severe trauma, sepsis and burns;
- Numerous factors influence resting energy expenditure in critically ill patients: type and severity of illness, organ failure, supportive therapies;
- Precise energy requirements are difficult to determine in critically ill patients. Indirect calorimetry allows more a precise estimate of energy requirements, but simple rules are usually used in clinical practice;
- Prolonged hypocaloric feeding is associated with clinical complications; energy balance should be calculated in the most ill patients;
- Adaptation to fasting is blunted, ketosis is suppressed.

1. Physiologic response to stress

Extensive physiological changes occur in critically ill patients, particularly in those suffering from sepsis, trauma and burns. All body systems are involved, particularly the circulation, the endocrine, metabolic and immune systems.

This response is mainly activated from tissue inflammation and from the central nervous system. It plays a key role for the adaptation of the organism to the various forms of stress, including surgery, trauma and many types of critical illnesses (1), as shown by the inability of patients with cortico-adrenal failure to face minimal stress.

Tissue injury induces an acute local inflammatory response which activates macrophages and endothelial cells which in turn activate cascades of inflammatory mediators, including cytokines, coagulation factors, kinins and others endogenous substances (2).

Both pro-inflammatory cytokines (TNF-α IL-1 and IL-6) and anti-inflammatory cytokines (IL-4 and IL-10) are released to insure an adequate adaptation to the inflammatory stress (Fig. 1, Fig. 3).

The neuro-endocrine response is characterised by the activation of the sympatho-adrenal system, hypothalamo-pituitary axis and other endocrine glands (5). It leads to the release of the stress hormones epinephrine, norepinephrine, cortisol, vasopressin, growth hormone and glucagon (6), (Fig. 2).

There is a synergy between the sympatho-adrenal system and the pituitary-adrenal axis: activation of the sympathetic system leads to a parallel stimulation of the corticotropic axis and vice-versa (5).

The overall response is a dynamic process, allowing a rapid and prolonged adaptation to stress: adrenergic, growth hormone and vasopressin response time are very short (seconds), while the corticotropic response has a delay

Metabolic response to severe sepsis
Plasma IL-6, IL-8, IL-10 and TNFα

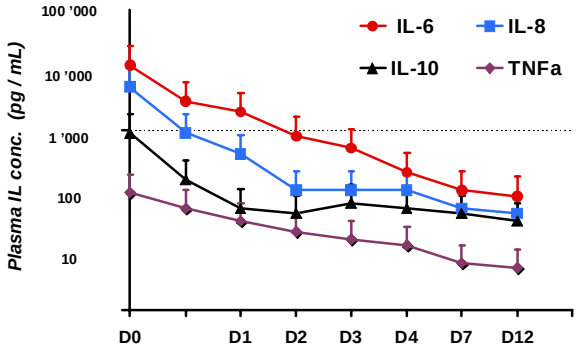


Fig. 1

Plank, LD et al, Ann. Surg. 1998; 228: 146

Plasma hormones in severely burned patients

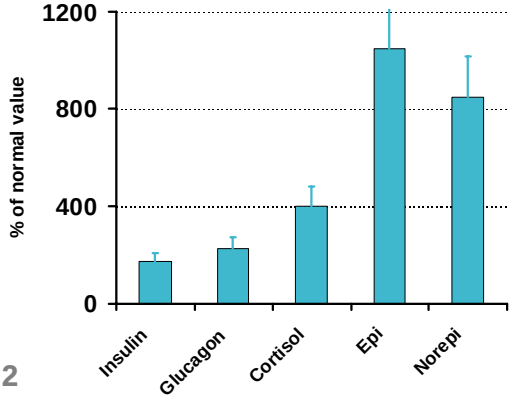
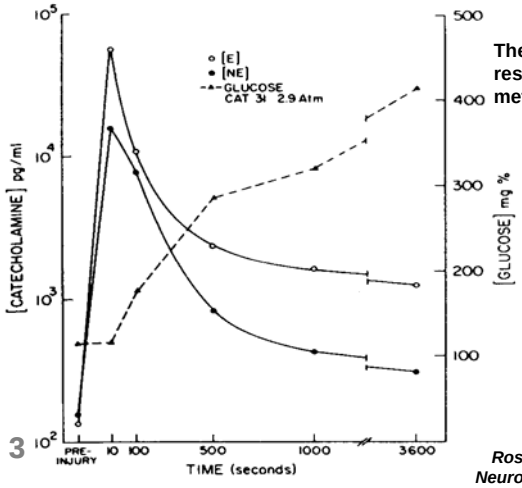


Fig. 2

Wolfe et al, N. Engl. J. Med. 1987; 317: 403

Mechanical brain injury (2.83 atm) in cats: plasma catecholamines and glucose



The endocrine response induces the metabolic response

Fig. 3

Rossner MJ et al, J Neurosurg 1984; 61: 76

of some hours (8).

Factors triggering this response include mental and psychological stress, exercise, pain, hypovolemia, hypothermia, hypoglycemia, and severe metabolic and electrolytes disorders. The magnitude of the neuro-endocrine response is related to the type of injury and severity of stress.
The neuro-endocrine response plays a critical role in maintaining the circulation and perfusion of vital organs, as well as the energy metabolism (Fig. 3). The thyroid axis is down regulated during acute stress, leading to the sick euthyroid syndrome. This may decrease energy metabolism during prolonged stress and critical illness (10).

2. Metabolic response: energy metabolism

The metabolic response to stress is extensive, involving all the major pathways of metabolism. The overall response is characterized by an enhanced metabolic rate associated with increased release of endogenous substrates for energy metabolism and increased inter organ substrate exchanges (11).
Insulin resistance leads to increased plasma glucose concentration and gluconeogenesis and endogenous glucose production. Lipolysis is activated with concomitant release of fatty acids for energy metabolism.

Body composition and metabolism: relationship between body cell mass and resting metabolic rate in healthy subjects

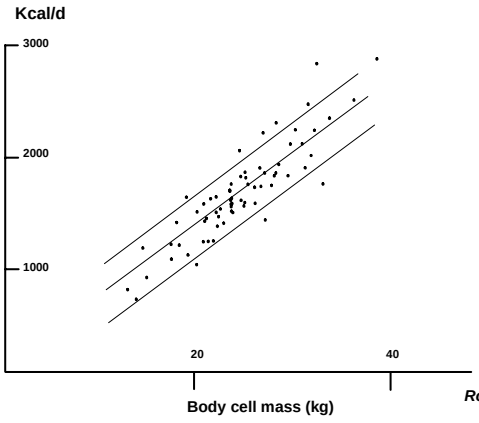


Fig. 4

Roza AM et al, Am J Clin Nutr 1984; 40: 168

In healthy resting subjects, the main determinant of basal energy expenditure is the fat-free mass (FFM) (12) (Fig. 4). FFM includes the tissues with the most active metabolic rate, mainly skeletal muscle and viscera. In subjects with normal FFM, REE amounts to 20 kcal/kg per day, or 1400 kcal for a 70 kg subject.
The specific contribution of the different organs and tissues to REE is highly variable, ranging from 5 kcal/kg per day for fat tissue to 500 kcal/kg for the myocardium (14) (Fig. 5). As a whole the vital organs, that account for only 5% of body weight, consume 60% of REE. Except during the initial phase after injury (the ebb phase), the energy metabolism is stimulated after the initial resuscitation (flow phase). During this flow phase, resting energy expenditure (REE) is increased in critically ill patients, amounting to 120-150% of normal basal values after severe trauma or sepsis (12).
Resting metabolic rate is even higher in patients with major burns, reaching 140-170% (16).

Contribution of organs and tissue to resting energy expenditure

Organ	BW %	% total REE	Organ MR Kcal/kg/d
Heart	0.4	10 %	400-600
Kidneys	0.4	8 %	400
Brain	1.9	20 %	240
Liver	2.3	21 %	200
Skeletal muscle	40	22 %	13
Adipose	21	4 %	4.5
Others	33	16	12

Fig. 5

Nelson et al, Am J Clin Nutr 1992; 56: 848

Stress hormones, pro-inflammatory cytokines and other mediators mainly cause such hypermetabolism. Infusion of the stress hormones cortisol, glucagon and epinephrine in healthy subjects induces metabolic changes mimicking important aspects of the metabolic response to injury (Fig. 6, Fig. 7).

The duration of the flow phase varies according to the evolution of the acute illness: it is short lasting after major uncomplicated surgery (days), lasts several weeks after major trauma and sepsis (4, 19) and even months after major burns until the full skin healing.

Variability of REE is extensive, both between different diagnosis categories of patients and over time in a given patient (20) (Fig. 8).

Combined hormone infusion stimulates the metabolic response to injury

74-hr infusion of the stress hormones cortisol, glucagon and epinephrine in nine healthy subjects

Resting metabolic rate measured by indirect calorimetry

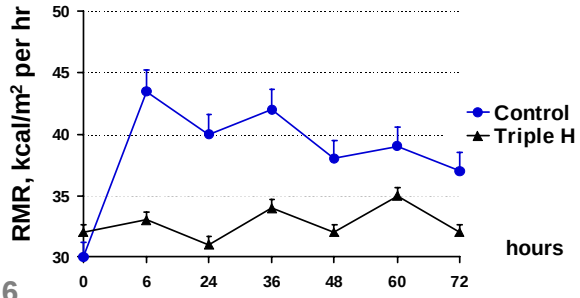


Fig. 6

Bessey P et al, Ann Surg 1983; 200: 264

Energy metabolism in 12 patients with severe abdominal sepsis

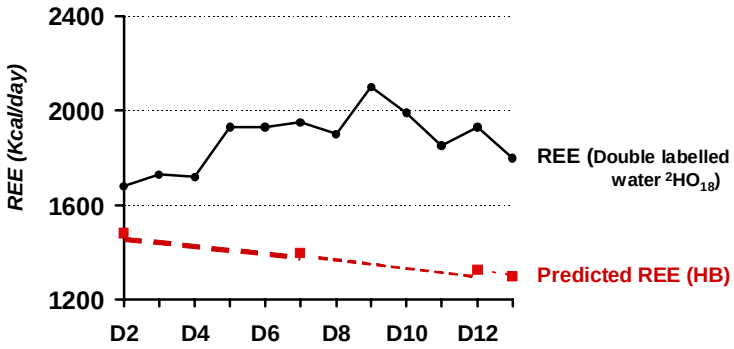


Fig. 7

Plank, LD et al, Ann. Surg. 1998; 228: 146

Metabolic rate in severe brain injury:

data from 7 studies using indirect calorimetry

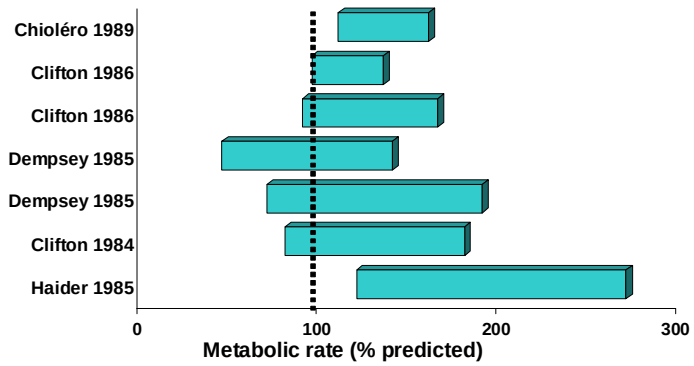


Fig. 8

Chiolero R, 1989

Conditions affecting energy expenditure in healthy subjects

	REE Change
Basal metabolic rate	**-10 %**
Sleeping	**-5 - 10 %**
Nutrition	**+3 - 20 %**
Exercise	**+100 - 1500 %**
Pregnancy	**+10 %**
Growth	**+5 - 15 %**

Fig. 9

Conditions affecting energy expenditure in ICU patient

	REE Change
Fever (per ° C)	+ 10 to 15 %
Sepsis	+ 20 to + 60 %
Trauma	+ 20 to 50%
Burn	+ 40 - 80 %
Treatments	
• Mech. Ventilation (resp. failure)	- 25 - 35 %
• Nutritional support (Burn)	+ 20 %
Agitation	+ 50 – 100%

Fig. 10

Chiolero R, Nutrition 1997;13(9 Suppl):45S-51S.

Drugs affecting EE in the ICU patient

Drug	Condition	Change
• Opiates	Analgesia	- 9%
	Post-op rewarming	- 26 %
	Post-op shivering	- 59 %
• Sedation	Mechanical ventilation	- 20 - 55%
• Barbiturates	Brain injury	- 32 %
• Musc. relaxants	Brain injury	- 42 %
• Catecholamines	Circ failure	+ 32 %
• ß-blockers	Head injury	- 6%
	Burn (adult)	- 7 %

Fig. 11

In healthy subjects, the metabolic rate is increased by feeding, cold exposure, exercise and by growth in children (Fig. 9).
Additional factors influence REE in acutely ill patients (Fig. 10, Fig. 11). The main factors include body temperature, organ failure, pain and supportive and drug therapies (11). Fever increases metabolic rate by 10-15% per degree C, hypothermia does the reverse. Pain, respiratory failure, acute liver failure are all associated with hypermetabolism.
Mechanical ventilation in patients with respiratory failure, sedation, opiates, muscular relaxants, decrease the metabolic rate, while catecholamines increase the metabolism.

Physical activity is usually low in critically ill patients, but may be significant in agitated patients (20) (Fig. 12).
Beta-blockade in burn and trauma patients has been associated with decrease in resting energy expenditure (26) (Fig. 13) and in protein catabolism (28) (Fig. 14, Fig. 15).

Effects of posturing in on the metabolic rate and heart rate in a severely brain injured patient

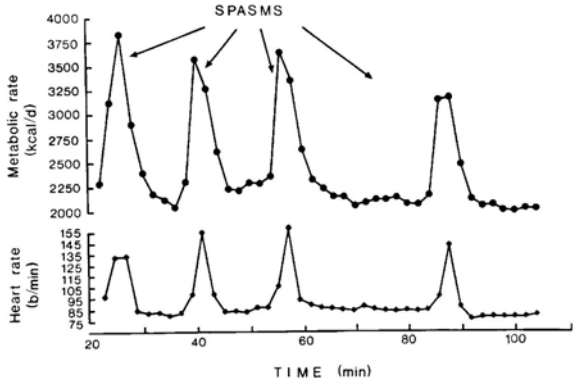


Fig. 12

Chioléro RL 1994

Metabolic and cardiovascular responses to intravenous propranolol in brain injury

Observational study in severely brain injured patients in resting condition

Effect of propranolol		
RMR	- 6%	<0.001
HR	- 12%	<0.001

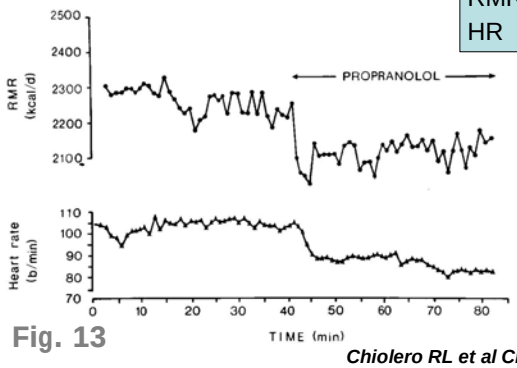


Fig. 13

Chiolero RL et al Crit. Care Med. 1989: 17: 32

Cardiovascular effects of propranolol in severe burned children

HerdonDN et al N. Enl. J. Med. 2001; 345: 1223

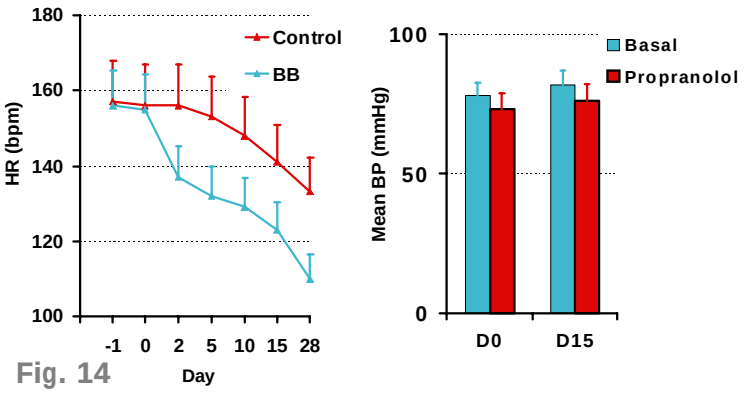


Fig. 14

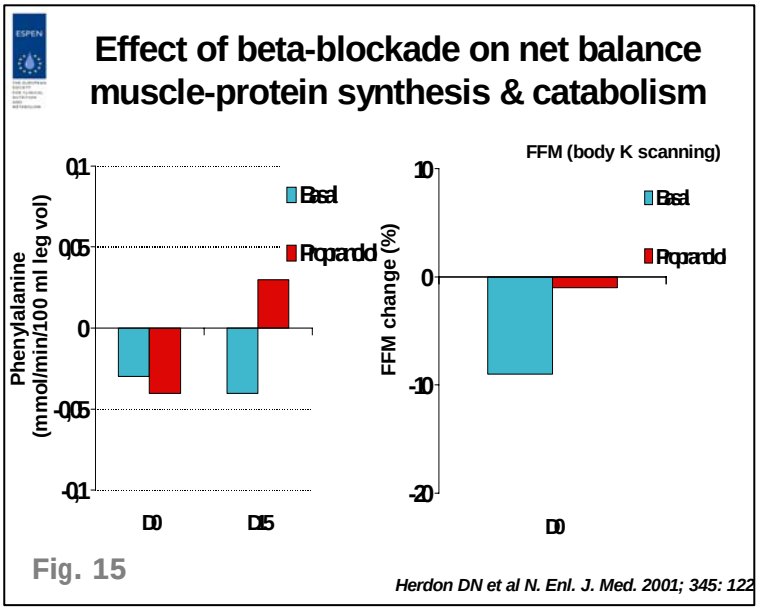


Fig. 15

There is little information on the change of the regional metabolic rate induced by the critical illness. Inflammatory diseases stimulate the regional metabolism, as shown by studies performed in patients with acute pneumonia, which show increased O_2 consumption in the lung (31) (Fig. 16).

Coma is associated with decreased brain O_2 consumption during the initial phase of brain injury (33).

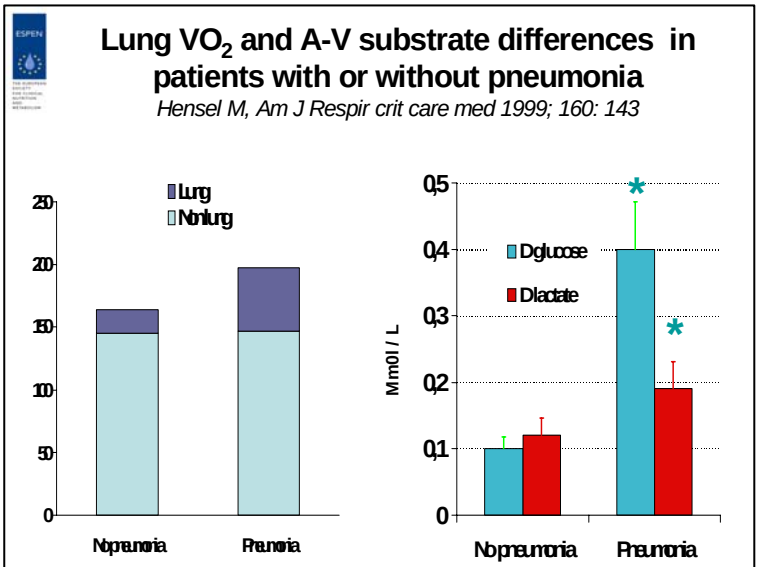


Fig. 16

3. Energy requirements

Clinical assessment of energy expenditure is difficult in critical care and requires the use of sophisticated techniques (see Table 1). Several equations allow the calculation of resting metabolic rate in healthy subjects, based on body weight, height, gender and age (20) (Table 2, Fig. 17).

Harris-Benedict equations

These equations are gender specific and are based on body weight (kg), height (cm) and age (yr). They predict the resting energy expenditure (± 10%) in subjects with normal body composition

- Male: REE (kcal/day) = 66.5 + (13.8 x body weight) + (5.0 x body height) – (6.8 x age)
- Female: REE (kcal/day) = 655.1 + (9.6 x body weight) + (1.8 x body height) – (4.7 x age)

Fig. 17

Table 1

Method	Principle	Conditions for use
Calorimetric methods		
Direct calorimetry	Determination of heat produced	Closed environment (entire body in a closed chamber)
Indirect calorimetry	O_2 consumption, CO_2 production, nitrogen excretion	Ventilation, fraction of inspired oxygen (FiO_2) <0.6
Non-calorimetric methods		
Isotopic (doubly-labelled water)	CO_2 production estimated from the difference between labelled hydrogen and labelled oxygen	
Fick method	Cardiac output ´ Difference in oxygen content between arterial and mixed venous blood	Pulmonary artery catheter
Physical activity	Pedometer, accelerometer	Not suitable for ICU patients
Muscular activity	Electromyography	Not assessed in ICU

Table 2

Name	Formula
Harris-Benedict	Males: 66.5 + (13.8x weight) + (5 x height) – (6.8 x age) Females: 655.1 + (9.6 x weight) + (1.9 x height) – (4.7 x age) Correction factors *: • Postoperative: Estimated REE x 1.1 • Multiple fractures: Estimated REE x1.1 to 1.3 • Severe infection: Estimated REE x 1.3 to 1.6 • Burns: Estimated REE x 1.5 tO_2.1 • Fever: Estimated REE x1.1/°C above 37°C
Frankenfield	–1000 + 100 (minute ventilation) + 1.3 (haemoglobin) + 300 (sepsis)
Swinamer	945 (body surface area) – 6.4 (age) + 108 (temperature) + 24.2 (respiratory rate) + 817 (minute ventilation) – 4349
Fusco	–983 – 4(age) + 32 (height in inches)+ 11 (weight)
Ireton-Jones°	1925 – 10 (age) + 5 (weight) + 281 (sex)+ 292 (trauma) + 851 (burn)
Unless otherwise specified, weight is expressed in kilograms, height is expressed in centimetres, body surface area is expressed in square meters and age is expressed in years. * If required, several correction factors can be used simultaneously ° Sex: 0 for females, 1 for males	

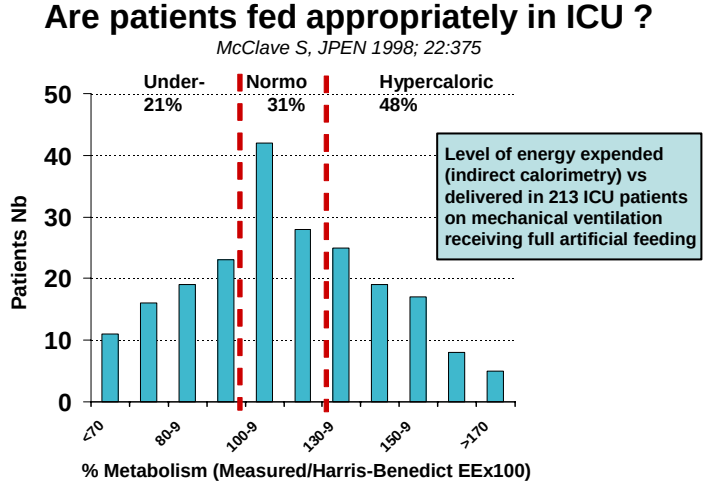


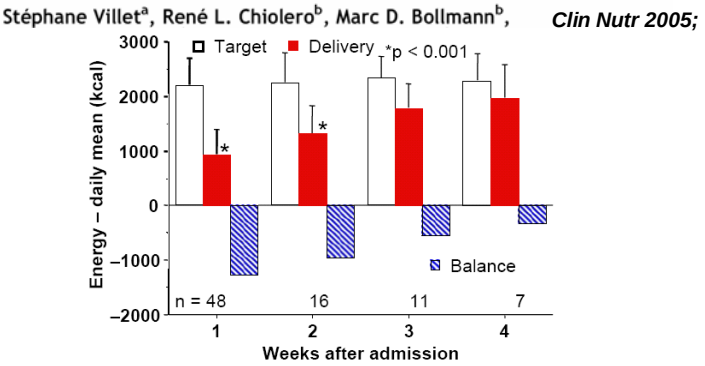
Fig. 18

It underestimates resting energy expenditure in most surgical patients. Correction factors for stress have been proposed, but they have been found to be inappropriate for clinical practice, fostering excessive feeding (35) (Fig. 18).

In clinical practice, **simple rules** are used to estimate REE in critically ill patients:
- 20-25 kcal/kg per day in patients with low or moderate stress
- 25-30 kcal/kg per day in patients with marked stress: multiple injury, brain injury, severe sepsis
- 35-40 kcal/kg per day or more in patients with major stress, like extensive burns

In patients with complicated evolution, requiring prolonged nutritional support, it is recommended to perform weekly indirect calorimetry measurements to avoid both gross over- or underfeeding.
It is difficult to match nutrient supply to the needs of acutely ill patients for several reasons:
- The energy requirement is difficult to predict, variability between patients is high, variability in a given patient along the stay is high and the energy expended for activity is difficult to predict (35, 36);
- The route of feeding may alter energy delivery (enteral nutrition).Precise determination of energy requirement is possible at the bedside using indirect calorimetry.

This measurement is usually made over a short period (about 20-30 min) and 24 h energy expenditure is extrapolated. This leads to a significant error, reaching 20-30%.
A precise determination of the 24 hr metabolic rate would require a 24 h measurement, which is not possible in clinical condition.



Progression of energy delivery compared to energy target over 4 weeks: the figure shows that energy delivery increases with time, reducing daily deficit.

Fig. 19

Calculation of the daily energy deficit, defined as the difference between the 24 h energy expenditure and energy delivery, allows to estimate how appropriate is the caloric supply.
Recent studies suggest that prolonged energy deficit is associated with clinical complications, particularly septic complications in critically ill patients (37) (Fig. 19, Fig. 20, Fig. 21).

4. Adaptation to fasting

Healthy subjects have the ability to adapt to starvation, allowing survival in case of prolonged starvation. The mechanisms of adaptation include a progressive decrease in resting metabolism, stimulation of production and utilization of ketone bodies as fuel and a progressive reduction of protein catabolism (40).
Such adaptable mechanisms are blunted by the critical illness (Fig. 22): ketosis is suppressed by stress hormones and cytokines, while protein catabolism stay elevated all over the course of critical illness (42). Thus starvation should be as short as possible in the most severely ill patients, who should receive adequate energy supply as soon as possible after the initial resuscitation.

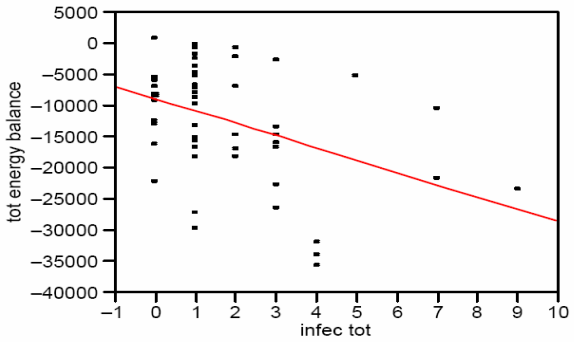
Relationship between complications and cumulated energy deficits by regression analysis

Variables	*F*	*P*
Length of stay	25.18	0.0001
Complications	15.15	0.0003
Infections	9.14	0.0042
Days on antibiotics	17.48	0.0003
Start of nutrition	17.17	0.0002
Days of mechanical ventilation	17.12	0.0002

Fig. 20

Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients

Stéphane Villet[a], René L. Chiolero[b], Marc D. Bollmann[b],



Relation between the progressive negative energy balance and the number of infectious complications.

Fig. 21

Clin Nutr 2005;

Total plasma ketone bodies in fasting trauma patients

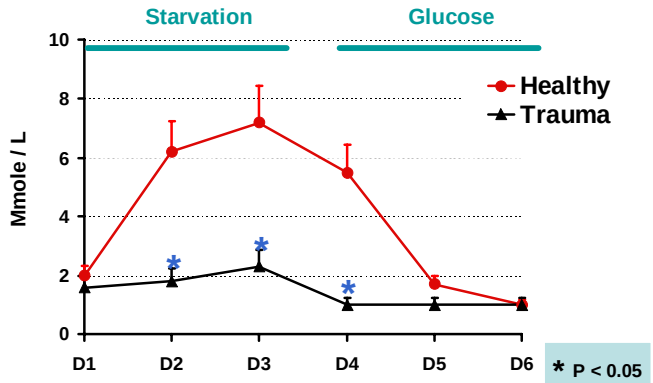


Fig. 22

Birkhan RH, J. Trauma 1981; 21: 513

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