Nutritional Support in Intensive Care Unit (ICU) Patients

Topic 18

Module 18.2

Use of Macronutrients in ICU

Jean-Charles Preiser
René Chioléro
Pierre Singer

Learning Objectives

- Understand glucose metabolism in critically ill patients;
- Understand fat metabolism in critically ill patients;
- Understand protein metabolism in critically ill patients;
- Understand the concept of glucose: fat ratio;
- Understand the basis of macro nutrient supply.

Contents

1. Insulin resistance
2. Carbohydrate metabolism
3. Fat metabolism
4. Protein metabolism
5. Use of energetic substrates

Key Messages

- Glucose utilization is increased in non-insulin dependent organs and decreased in insulin-dependent organs and tissues;
- Lipolysis is activated by the critical illness, particularly in patients with sepsis and acute inflammatory diseases;
- Fat utilisation is stimulated in fasted and septic patients, reduced in patients with circulatory failure;
- Protein catabolism is increased, and exceeds protein synthesis, promoting an erosion of the fat-free mass. Glucose and insulin decrease protein catabolism;
- Formulas for critically ill patients should include 1.5 – 2.0 g/kg protein per day, carbohydrate and lipids. Lipid supply should be reduced in patients with acute ischemic heart diseases and major burns.

1. Insulin resistance

Insulin resistance is a hallmark of the critical illness (Fig. 1), leading to hyperglycemia and major changes in glucose, fat and protein metabolism (see Module 18.2 for further details).

This has important nutritional consequences, since it may be associated with a decreased efficacy of nutritional support. Insulin resistance influences glucose plasma level, glucose uptake in skeletal muscle and adipose tissue, as well as the endogenous glucose production in the liver and kidney (2).

In healthy subjects, insulin is a major regulator of endogenous glucose production, to achieve a constant level of blood glucose: glucose production is suppressed by carbohydrate-rich meals and stimulated in the post-absorptive state (3) (Fig. 2).

This is not the case in surgical and critically ill patients, in whom the endogenous production of glucose stays high despite carbohydrate administration as a consequence of insulin resistance (Fig. 3) (6).

Prevalence of hyperglycemia in critically ill patients at intensive care unit admission

	Control group	Intensive TT
Patients	783	765
History of diabetes (%)	103 (13)	101 (13)
Admission glycemia		
≤ 6.1 mmol/l	24 %	27%
> 6.1 mmol/l	76 %	73%
> 11.1 mmol/l %	13%	11

Fig. 1

Van den Berghe G et al, N Engl J Med 2001; 345 1359

Effects of intravenous glucose on endogenous glucose production in healthy subjects

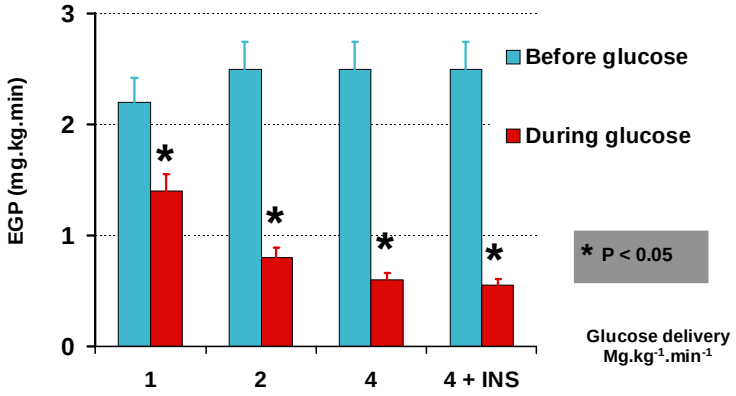
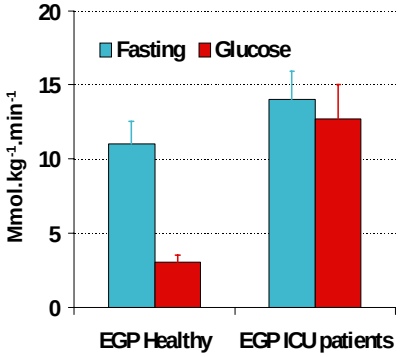


Fig. 2

Wolfe RR et al, Metabolism 1979; 28: 210

Glucose endogenous production is not suppressed by glucose infusion in critically ill patients



Variable	Healthy	ICU
1. Fasting		
Glycemia	4.8	7.1*
Insulin	54	115*
2. IV glucose		
Glycemia	5.7#	9.7*#
Insulin	89#	515*#

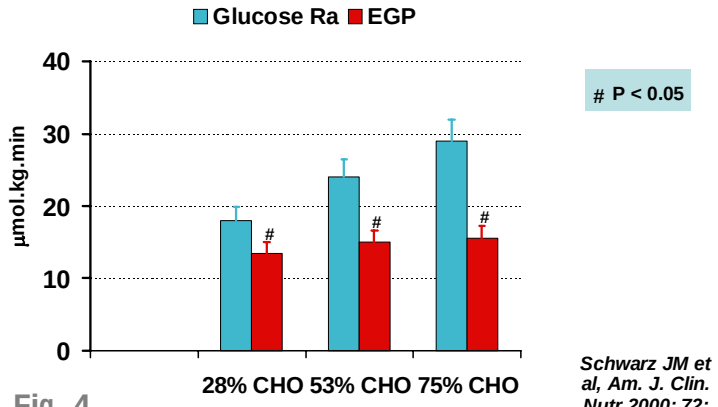
* P < 0.05 vs healthy

# p < 0.05 vs fasting

Fig. 3

Tappy L, Am J Physiol 1995; 268:E630

Effects of enteral carbohydrate on glucose flow (Ra) and endogenous production (EGP) in critically ill patients



Schwarz JM et al, Am. J. Clin. Nutr 2000; 72: 940

Fig. 4

Studies performed in critically ill patients receiving isocaloric nutrition with various proportions of glucose and fat, show that the endogenous production of glucose stays constant for glucose supply ranging from 28 to 75% of total energy (7) (Fig. 4).
Such mechanism allows a large supply of glucose to the glucose-dependent tissues like the immune, inflammatory cells and the wounds.

Insulin-dependent and insulin-independent organs & tissues

Insulin-dependent organs	Insulin-independent-organs
• Liver (Glut-2)	Brain
• Skeletal muscle (Glut-4)	Red blood cells
• Myocardium (Glut-4)	Kidney medulla
• Fat tissue (Glut-4)	Inflammatory & granulation tissues, wounds
	Macrophages

Insulin resistance ➡ preferential glucose supply to insulin-independent tissues

Fig. 5

2. Carbohydrate metabolism

Glucose is efficiently utilized as a substrate in critically ill patients despite insulin resistance.
It should be underlined that insulin resistance is associated with a decreased insulin-mediated glucose uptake, mainly in the skeletal muscle and adipose tissue associated with an increased non insulin-mediated glucose uptake (2) (Fig. 5).
The overall glucose oxidation is normal in most patients (trauma, postoperative, circulatory failure) or increased (major burns or trauma) (Fig. 6) (11).

Glucose oxidation is maintained in burned patients

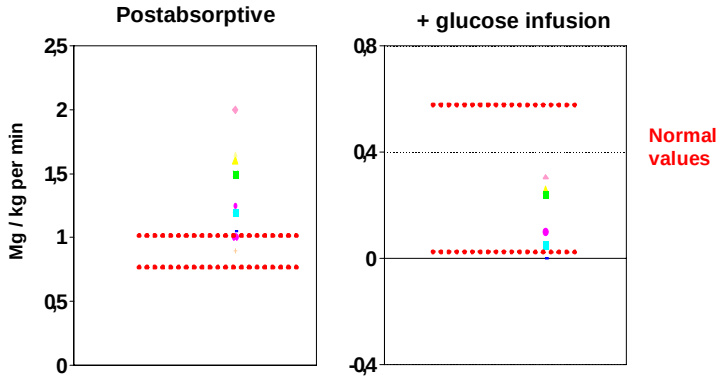


Fig. 6

Wolfe RR et al, Metabolism 1979; 28: 1031

In septic patients, there is a preferential utilization of fat for energy metabolism while glucose oxidation is normal or slightly depressed (Fig. 7) (13).
Fatty acid synthesis from glucose in the liver and other tissues is stimulated in critically ill patients, like in healthy subjects receiving large glucose load. Insulin resistance does not affect this pathway. Stimulation of de novo lipogenesis by glucose-rich formulas is associated with increased thermogenesis (i.e. diet induced increase in metabolic rate) and increased pulmonary CO_2 excretion (7, 14) (Fig. 8).

3. Fat metabolism

In subjects with normal body composition, fat stores amount to 15-30% of body weight and constitute the main energy reserve.
Fat is a preferential substrate for energy metabolism in most critically ill starving patients or with hypocaloric feeding: in fasting condition, fat oxidation fuels 60–70% of the energy expended (13, 16) (Fig. 9).

Energy metabolism in critically ill cardiac and septic patients: RMR & substrate oxidation

- 6 postoperative cardiac surgery patients with acute heart failure (inotropes)
- 6 patients with severe sepsis

	Cardiac	Sepsis	p
Resting MR (kcal/d)	1390	1610	NS
Glucoase net oxidation (μmol/kg/min)	4.3	1.75	< 0.05
Lipid net oxidation (mg/kg/min)	0.60	1.26	< 0.05

Fig. 7

Martinez A et al, Clin Physiol Funct Imaging 2002; 23: 286

Effects of enteral CHO on fractional hepatic DN lipogenesis in healthy ill & critically ill subjects

Minehira K et al, 2001, Clin Nutr 2002; 21: 345

Schwarz JM et al, Am. J. Clin. Nutr 2000; 72: 940

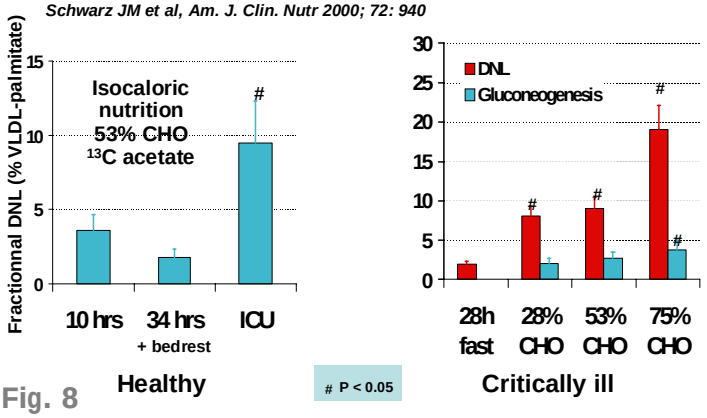


Fig. 8

Substrate oxidation in critically ill patients after 3 day starvation

Resting metabolic rate	1824 kcal/ day
Glycemia	7.3 mmol/L
Endogenous glucose production	360 g/ day (1360 kcal/day)
Net glucose oxidation	28% (512 kcal/ day)
Net fat oxidation	46% (840 kcal /day)
Net protein oxidation	26% (470 kcal/ day
Net protein balance	-117 g/ day

Fig. 9

Metabolic changes in 5 patients with severe sepsis and 5 healthy subjects

Chambrier C, Clinical Science 2000; 99: 321

Basal hormone and metabolite concentrations in control subjects and in patients with sepsis

Values are means ± S.D. Significance of differences compared with control subjects (unpaired Student's tests): *P<0.05; **P<0.01.

Parameter	Control subjects	Septic patients
Plasma glucose (mmol·l^{-1})	3.80 ± 0.23	6.89 ± 2.27**
Plasma lactate (μmol·l^{-1})	372 ± 54	1833 ± 1401*
Plasma NEFA (μmol·l^{-1})	225 ± 51	397 ± 213
Plasma ketone bodies (μmol·l^{-1})	82 ± 47	146 ± 64
Plasma insulin (m-units·l^{-1})	12.0 ± 6.7	14.6 ± 5.0
Plasma glucagon (ng·l^{-1})	374 ± 255	129 ± 24*

Fig. 10

Relationship between free fatty acid (NEFA)

Issekutz, Metabolism 1967; 16: 1001

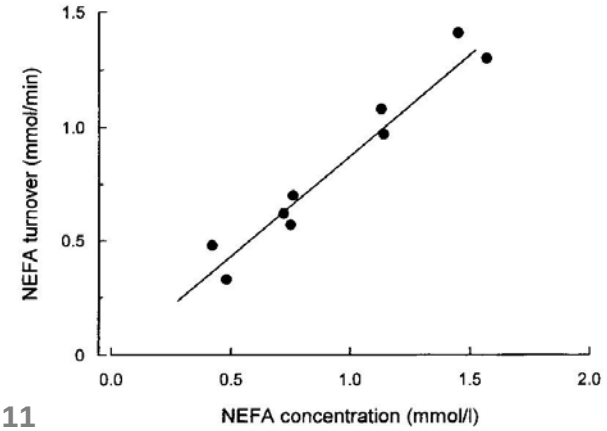


Fig. 11

Fat metabolism: effect of a carbohydrate-rich meal in healthy subjects

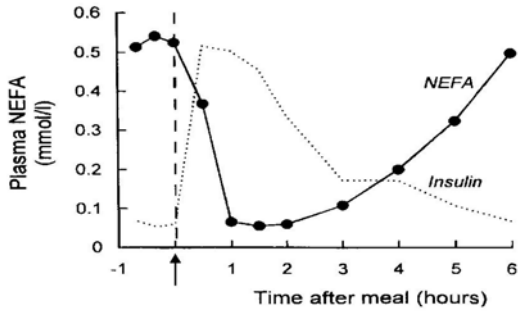


Fig. 12

Frayn KN, Metabolism; 42: 504

Fat metabolism is altered in critically ill patients. Lipolysis is activated in most patients with major stress, consecutive to the release of stress hormones.

Plasma free fatty acid levels are usually normal or elevated (18) (Fig. 10).

As in healthy subjects, fat uptake by the tissue is not directly influenced by insulin in ICU patients. Fat metabolism is influenced by plasma concentration of free fatty acids, and by the relative importance of oxidation and recycling of fatty acids. The rate of utilisation of free fatty acids is directly dependent on their plasma concentration: the higher the level, the higher the utilisation (20) (Fig. 11).

Plasma glucose and insulin levels also influence fat metabolism: when plasma glucose and insulin levels are high, hormone-sensitive lipase and lipolysis are suppressed, while the reverse is true during starvation (22) (Fig. 12). Thus, glucose is a preferential substrate during high supply, while fat is preferentially oxidized during starvation or when glucose supply is low.

4. Protein metabolism

The critical illness induces protein wasting, particularly in patients with septic or traumatic injury: protein catabolism exceeds protein synthesis despite full nutritional support (24, 25) (Fig. 13, Fig. 14). This is an adaptive phenomenon allowing an increased delivery of amino acids to immune and inflammatory cells. Activation is the main mechanism of protein of the ubiquitin proteasome pathway by TNF-α catabolism in acute illness (28) (Fig. 15).

Protein metabolism in trauma patients with or without brain injury

Petersen SR et al, J. Trauma 1993; 34: 653

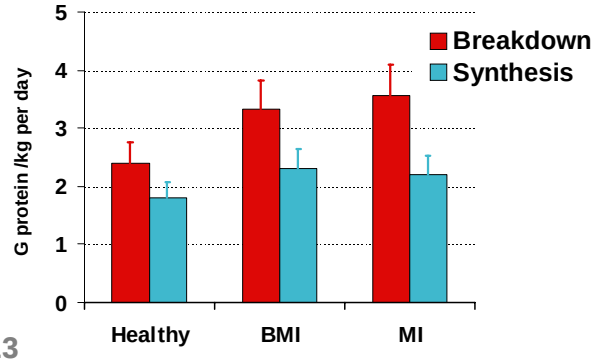


Fig. 13

Cumulative N balance in mechanically ventilated patients receiving full enteral feeding

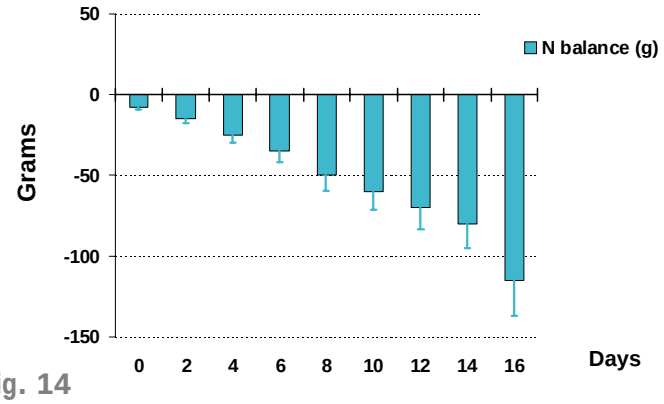


Fig. 14

Model of sepsis-induced muscle cachexia

Hasselgren PO, Ann Surg 2001; 233: 9-17

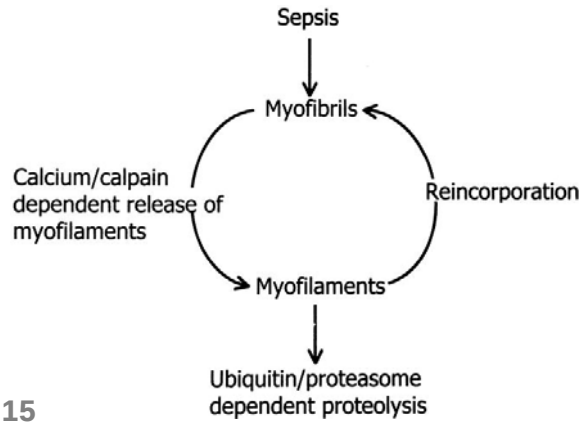


Fig. 15

Body composition (proteins) in patients with abdominal sepsis receiving full enteral support

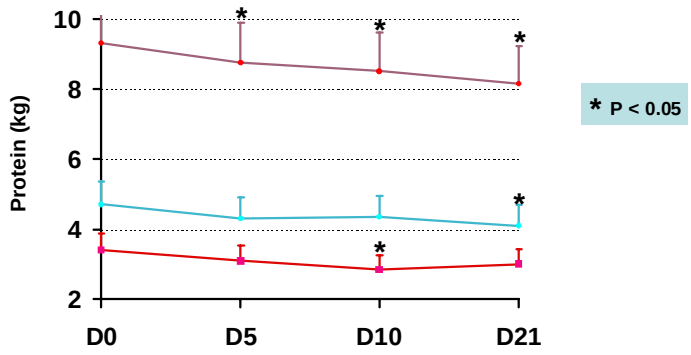


Fig. 16

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

Body composition in septic ICU patients receiving full nutritional support

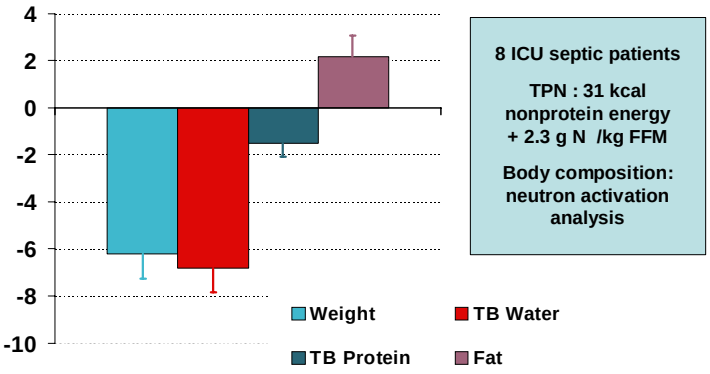


Fig. 17

Streat SJ, J. Trauma 1987;27:262

Protein breakdown & net balance are improved by hypercaloric glucose supply in burns

- 14 severely burned children (> 40% BSA)
- Hypercaloric EN: 1500 kcal/m^2 + 1500/m^2 TBSA/day
- **High CHO diet** (82% CHO, 3% fat, 15% protein) versus **high-fat diet** (42% CHO, 44% fat, 14% protein),
- Reverse crossover design

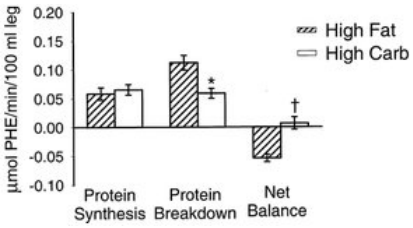


Fig. 18

Prolonged protein catabolism leads to a progressive erosion of fat-free mass, in trauma and septic patients with complicated evolution (30) (Fig. 16).

Increasing protein supply is unable to abolish such protein catabolism (32) (Fig. 17).

In patients with burns, protein catabolism has been shown to be improved by intensive glucose and insulin supply although the clinical benefits are yet largely unknown (34) (Fig. 18).

Androgen steroids and exercise also stimulate protein anabolism. Growth hormone therapy has been associated with increased mortality and should be avoided (36).

5. Use of energetic substrates

Both fat and glucose are efficiently utilized in critically ill patients receiving artificial feeding, although the most appropriate proportion remains controversial.
In isocaloric feeding, glucose and fat oxidation is directly related to their proportion in the feeding solution (16) (Fig. 19).
Fat oxidation is decreased during high glucose supply and insulin therapy. Comparison between high glucose-insulin and glucose fat regimens suggests that the former has a better nitrogen sparing effect (34, 38). Glucose is the only substrate oxidized by the ischemic tissues.

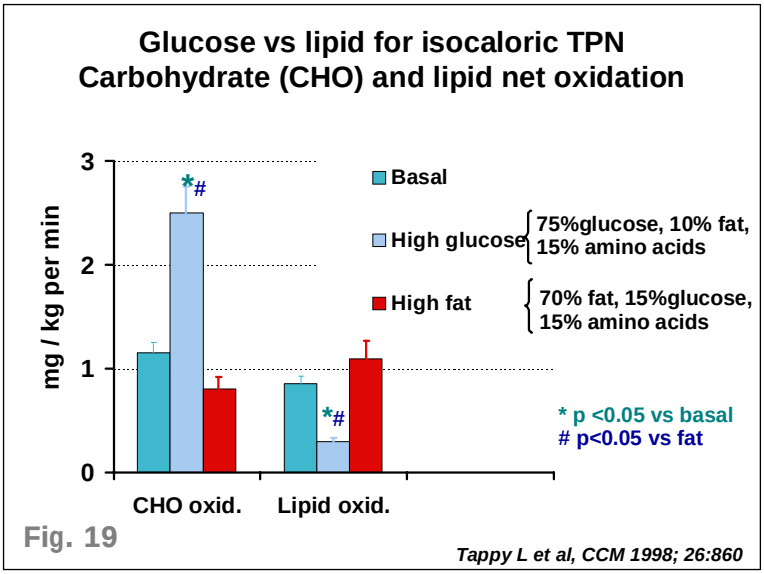
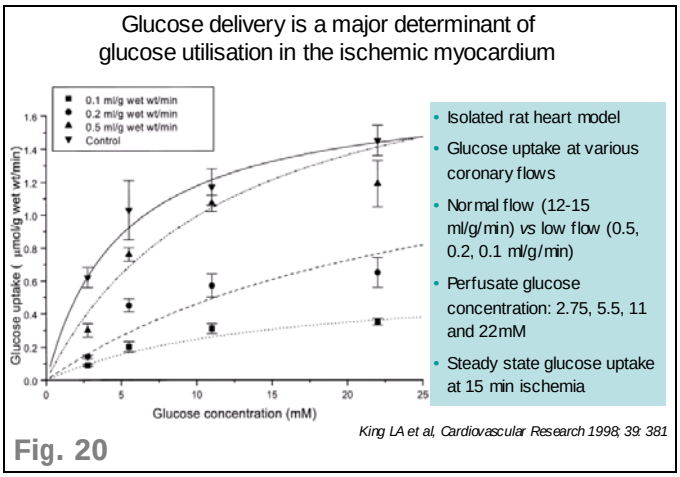


Fig. 19

Tappy L et al, CCM 1998; 26:860

Glucose and insulin have been shown to be an effective metabolic support in patients with severe ischemic cardiac failure (39) (Fig. 20).
In septic and inflammatory diseases, there is a preferential oxidation of fat, while glucose oxidation is slightly reduced or normal (13).
Whatever the composition of the diet, a good control of plasma glucose levels is important, particularly in patients with acute cardiac diseases (41).
In addition as being a substrate for energy metabolism, fatty acids exert important regulatory and signalling actions, which may favourably affect the regulation of metabolism and modulate inflammatory and immune responses.



King LA et al, Cardiovascular Research 1998; 39: 381

Fig. 20

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