Quels apports protéino -énergétiques?

L'agressé

Jean-Charles Preiser

JFN 2010 Lille

8 décembre

Professeur Xavier Leverve
7 octobre 1950 – 7 novembre 2010

TAKE-HOME MESSAGES

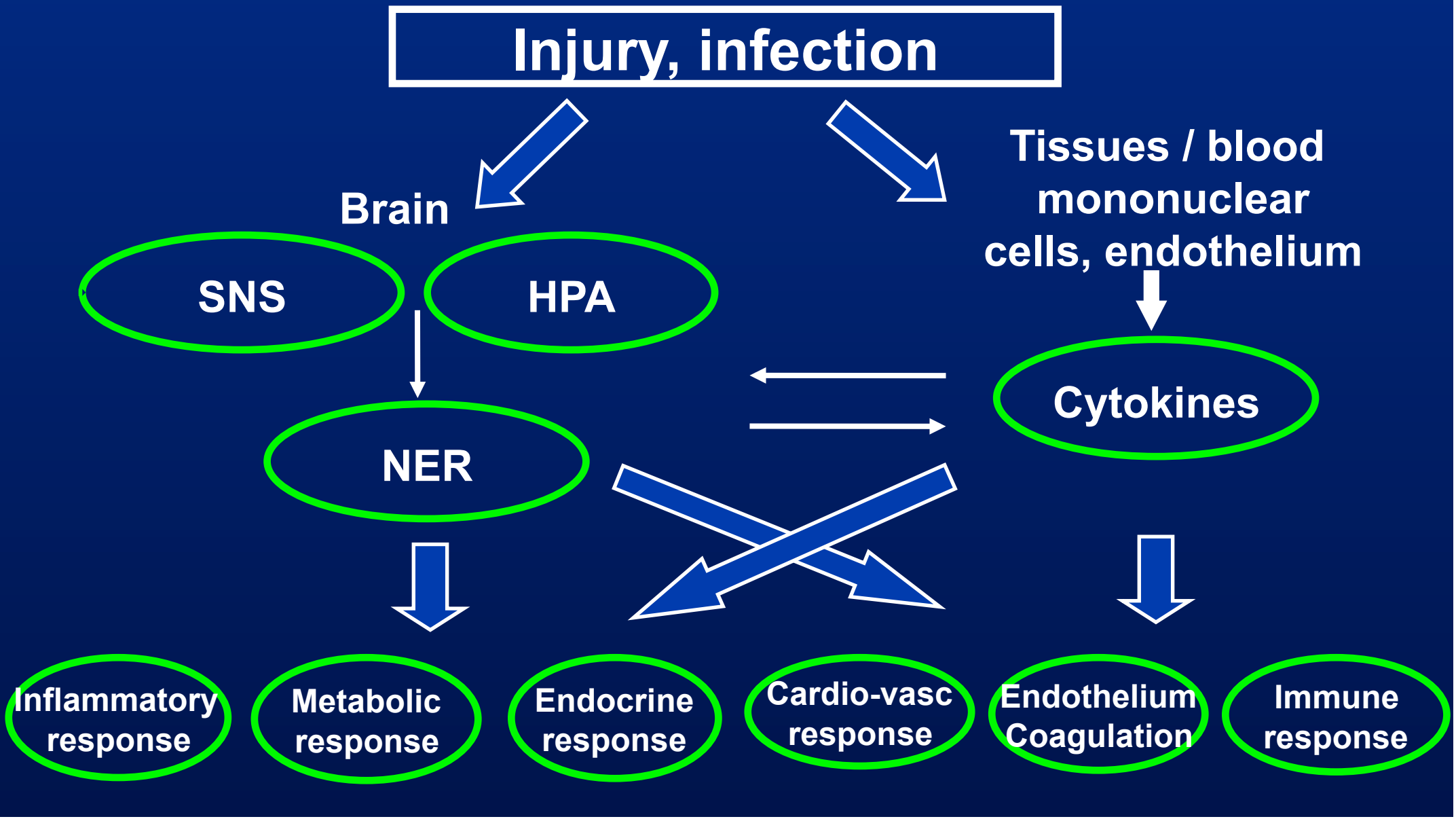
- No hyper alimentation
- In the absence of prior severe malnutrition
  - Target on day 3-5 : 20-25 kcal/kg BW /day
  - Anabolic – recovery phase 25-30 kcal/kg BW /day
- Carbohydrate/lipid ratio 60-70/30-40%
- Protein intake 1.2-1.8 g/kg BW /day

Physiopathologie de l'agression
Une réponse multisystémique intégrée

La réponse à l'agression est:

- Multisystémique,
- Intégrée, avec un pattern reproductible
- Adaptative
- Rôle du système nerveux sympathique, du système endocrinien, des médiateurs inflammatoires

Réponse physiologique au stress, plusieurs voies d'activation



The Ebb Phase

- Hypometabolic
- Hypothermic
- Hypoinsulinemic
- Hypoperfusion
- Hypercortisolism
- Hyperglucagonemia
- Hyperglycemia
- Hypercatecholemia

“The patient warms up,cardiac output increases and the surgical team relaxes…”

The Flow Phase

Cuthbertson. Lancet 1:233, 1942

The Flow Phase

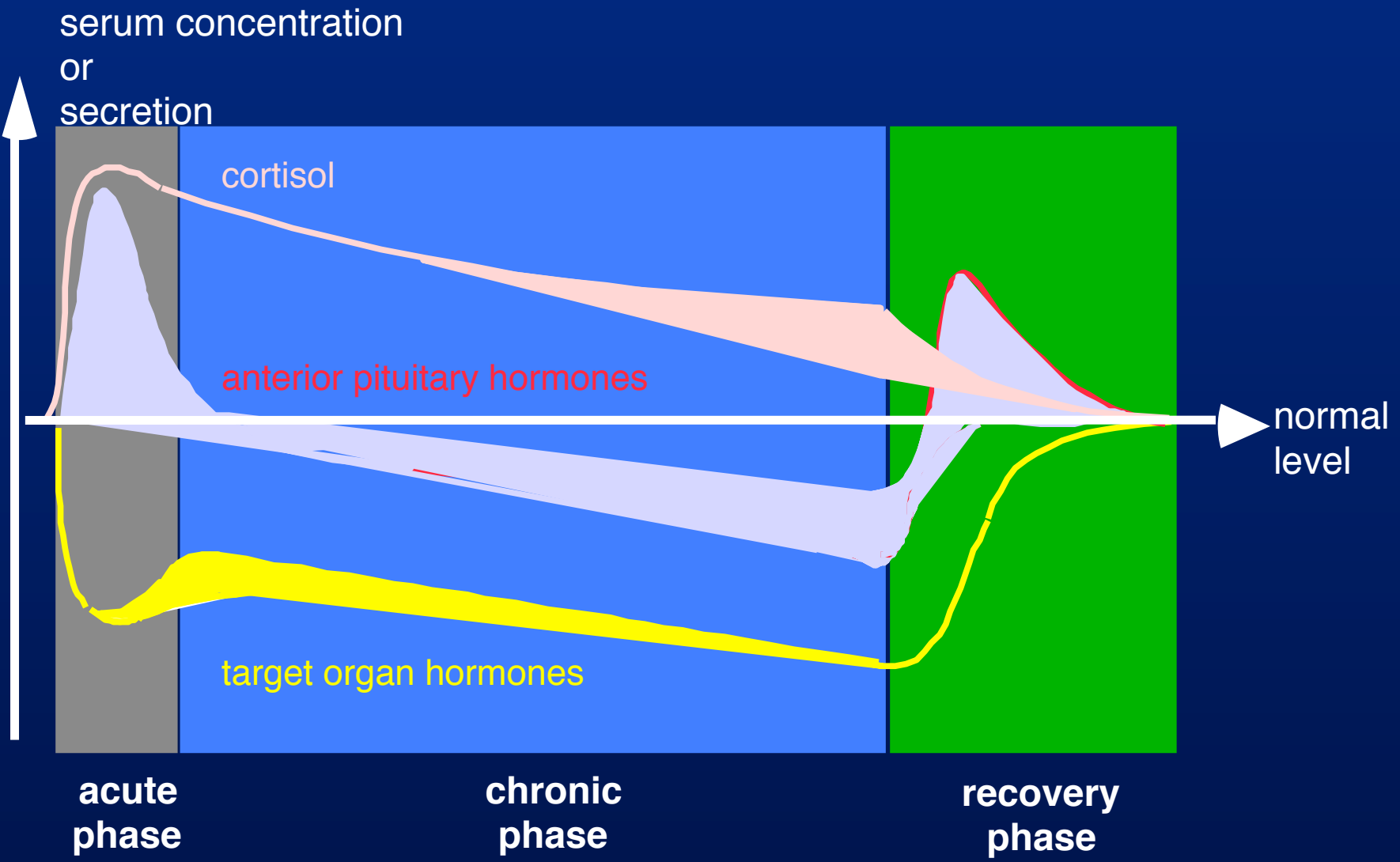
- Hypermetabolic
- Hyperthermic
- Catabolic
- Hyperinsulinism
- Hypercortisolism
- Hyperglucagonemia
- High cardiac output

Response to stress and injury

System	Effectors	Resp. time
→S ymp atho -adrenal	norepinephrine, epinephrine	sec-min
→Vasopressin, endorphins	Vasopressin receptors	min
→ HPA axis	cortisol	hour(s)

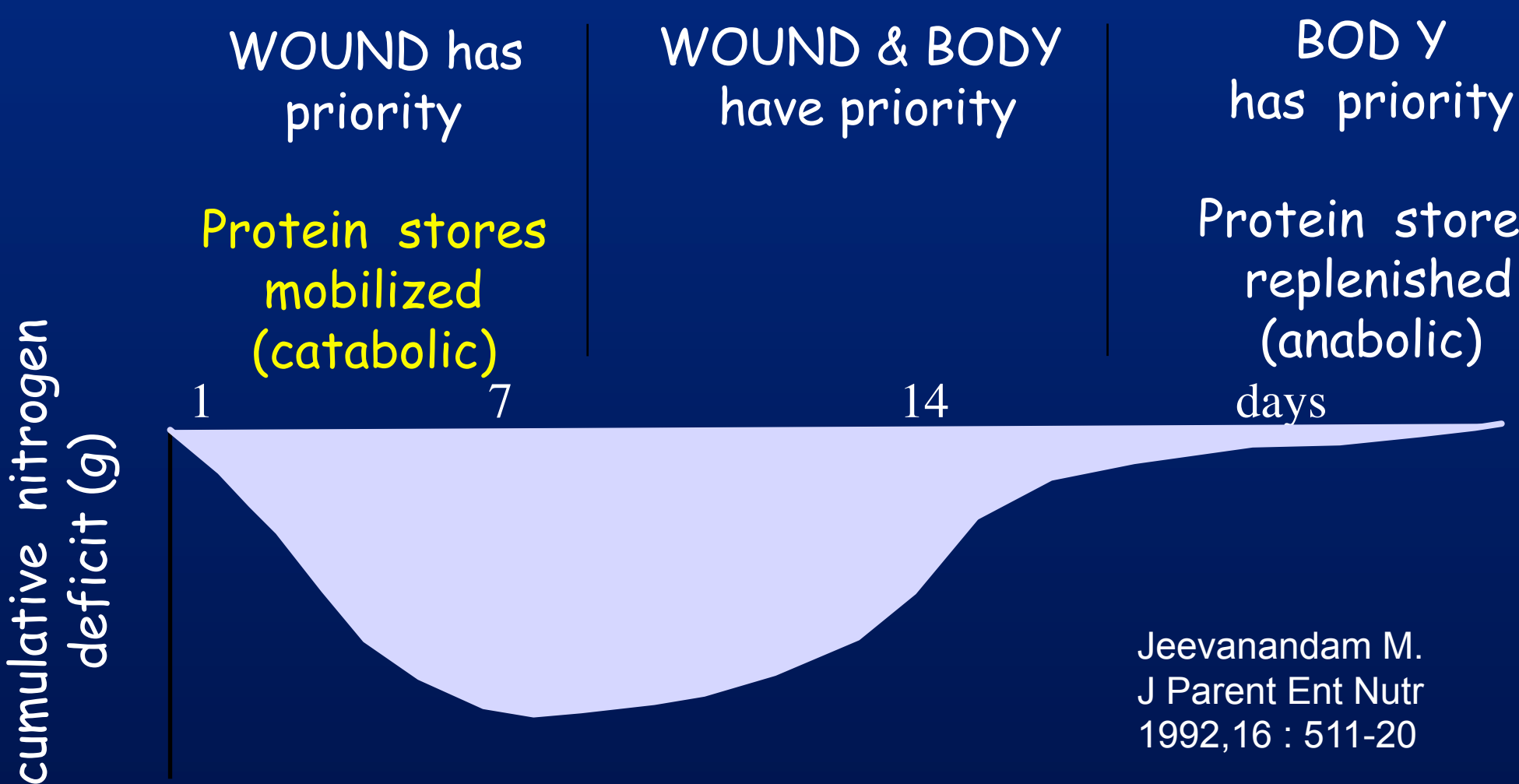
→

ACUTE & PROLONGED CRITICAL ILLNESS : HORMONAL PROFILES



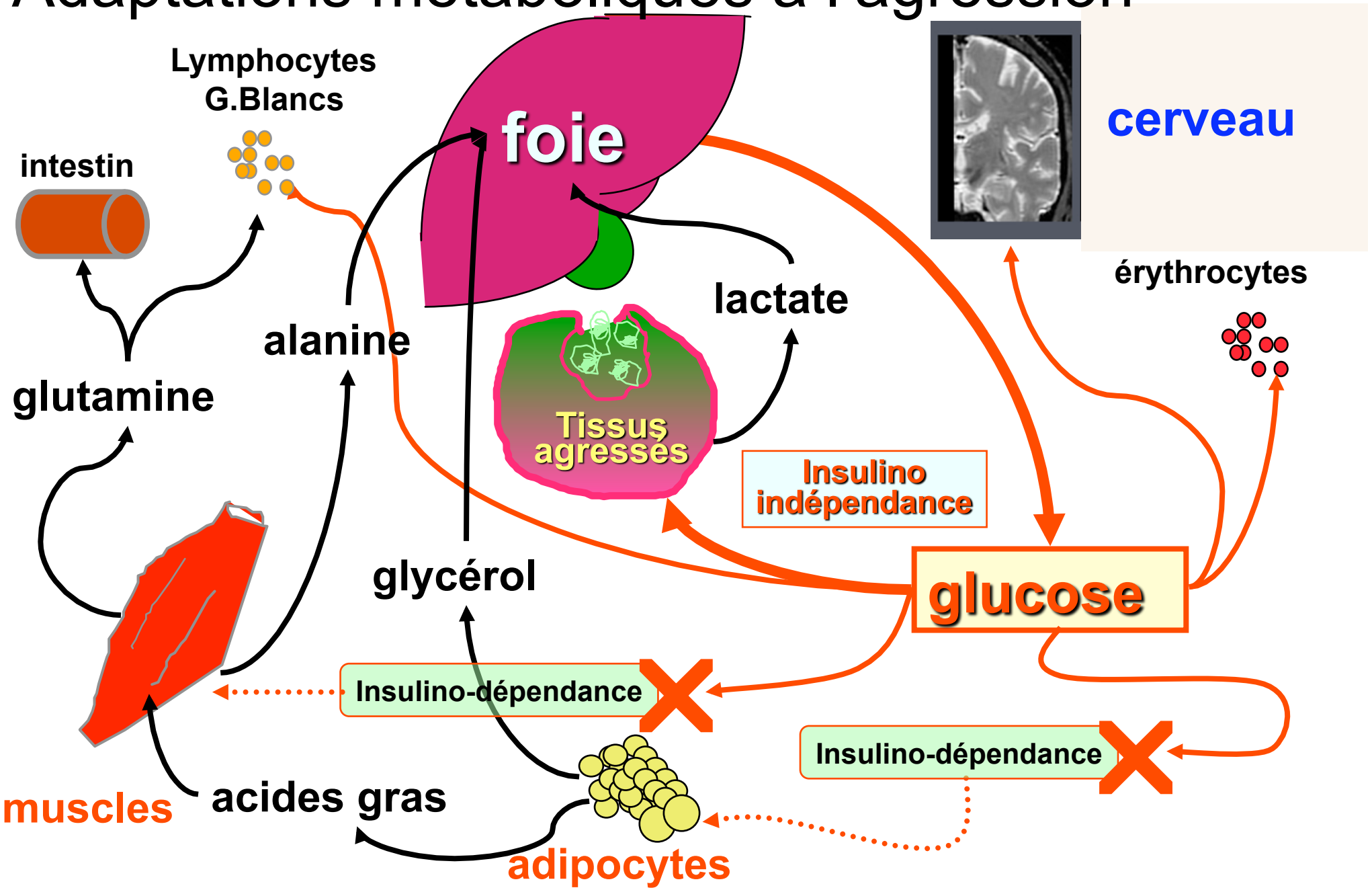
Van den Berghe et al. J Clin Endocrinol Metab. 1998; 83: 1827-1834

Metabolic response in ICU patients



Jeevanandam M.
J Parent Ent Nutr
1992,16 : 511-20

Adaptations métaboliques à l'agression



A TYPICAL MULTIPLE TRAUMA PATIENT WITH SEVERE SEPSIS

Risk of death
15-20 %

ARDS,
CRP 280 mg/l

Supportive therapies

Severe metabolic « adaptive » response

Energy balance in ICU patient

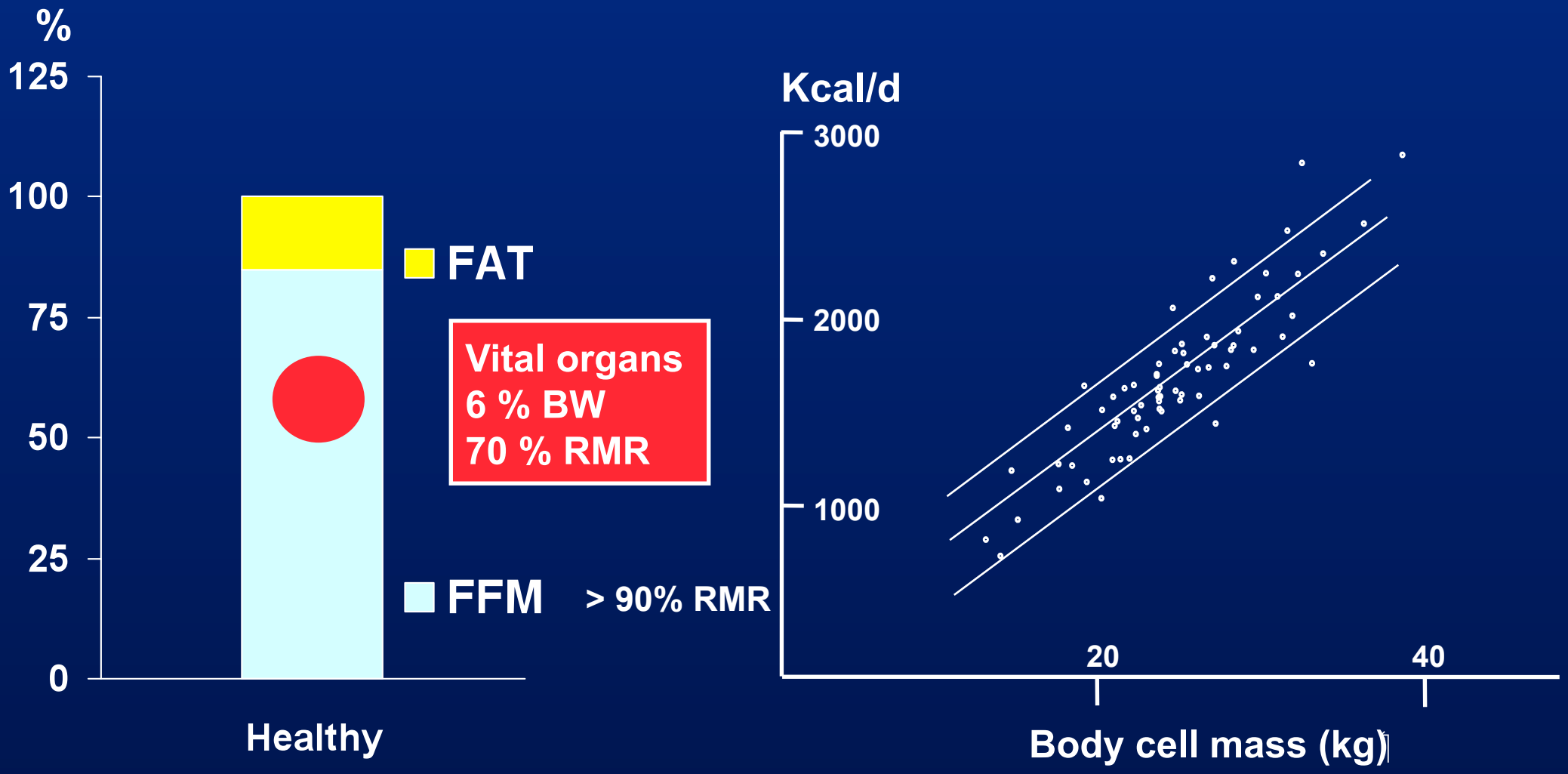
Critical illness

Increased energy expenditure

Components of the energy expenditure

1. **Basal expenditure**
2. **Heat**
   - **Food**
   - **Cold**
3. **Exercise**

Body composition and RMR in healthy subjects
Contribution of fat free mass and vital organs



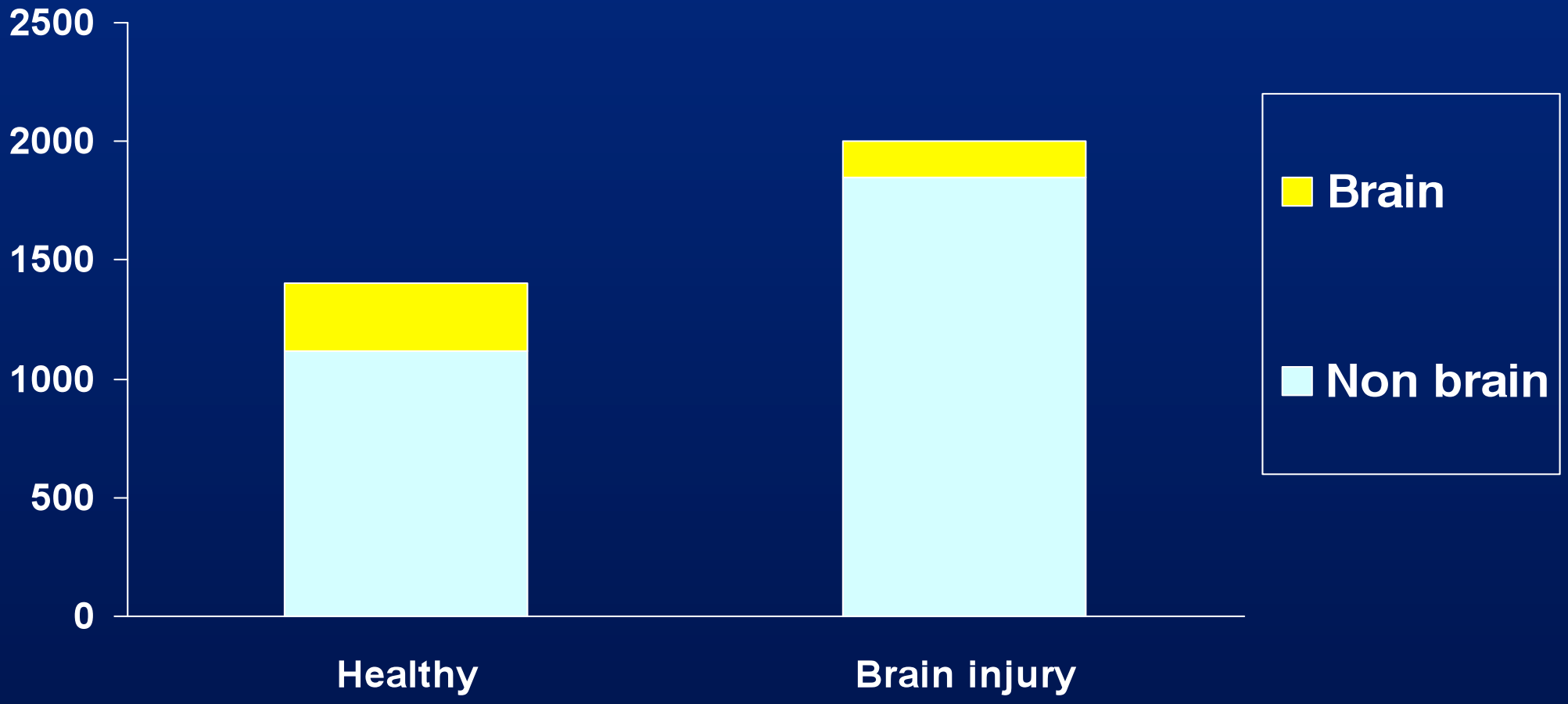
Roza AM et al, Am J Clin Nutr 1984

Components of the energy expenditure of the septic patient

1. **Basal expenditure**
2. **Heat**
   - **Food**
   - **Cold**
3. **Exercise**
4. **Disease process (infection)**
5. **Host response (sepsis)**
6. **Treatments**

Brain VO_2 in comatose oligemic brain injured patients & in healthy sujects

Obrist WD et al, J Neurosurg 1984; 61: 241



Effects of a single injection of endotoxin in healthy volunteers

Michaeli, Clin.Nutrition 2007

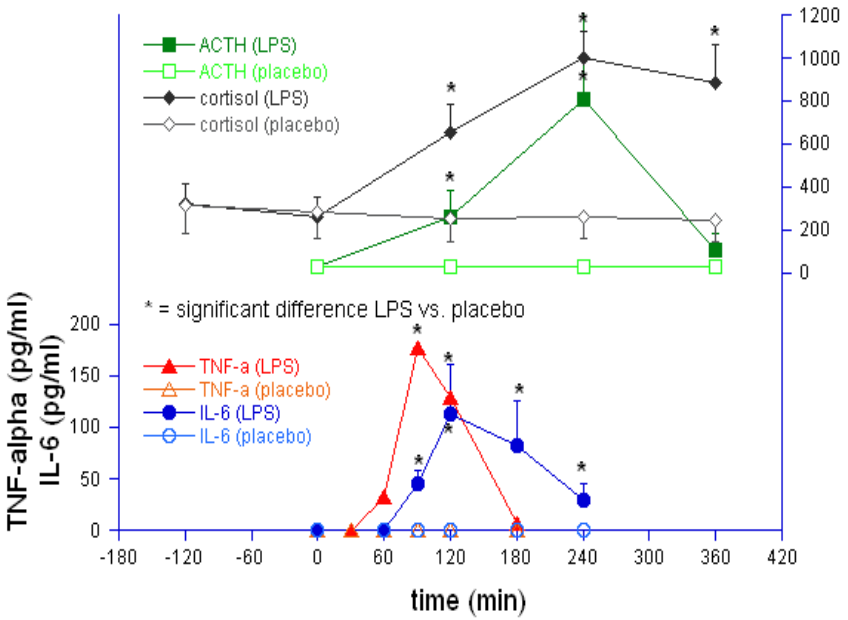
Methods

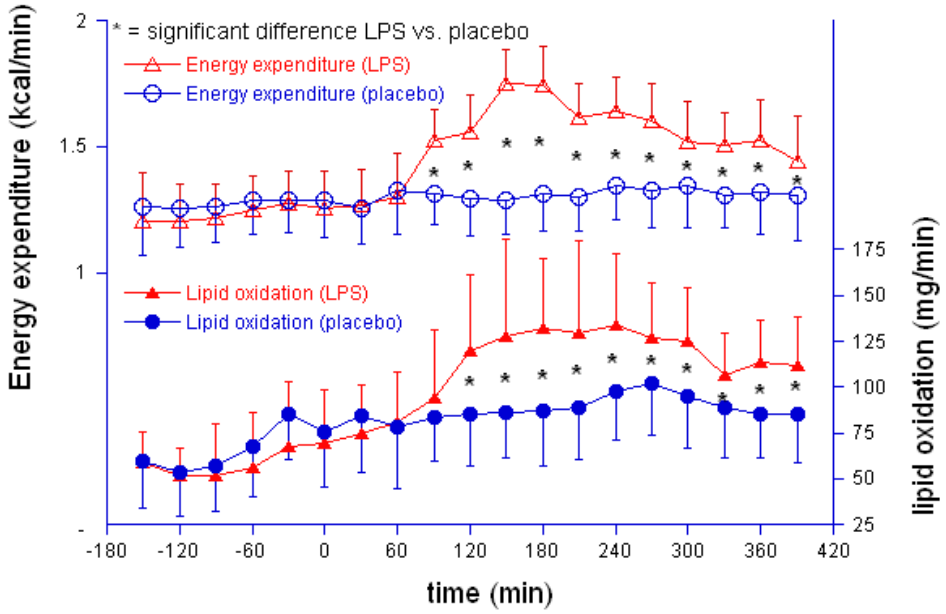
- 8 healthy

m
ale volunteers, 2 independent observations, seperated by 5-10 days

- Intravenous LPS 2 ng/kg bacterial LPS *vs saline*
- Plasma substrate determination
- Indirect calorimetry (energy expenditure, net substrate oxidation)
- ~~Isotope dilution (glucose production, Steele's equation)~~

Effects of endotoxin in healthy volunteers on cytokines and energy expenditure





Michaeli Clin Nutr 2007;26:70

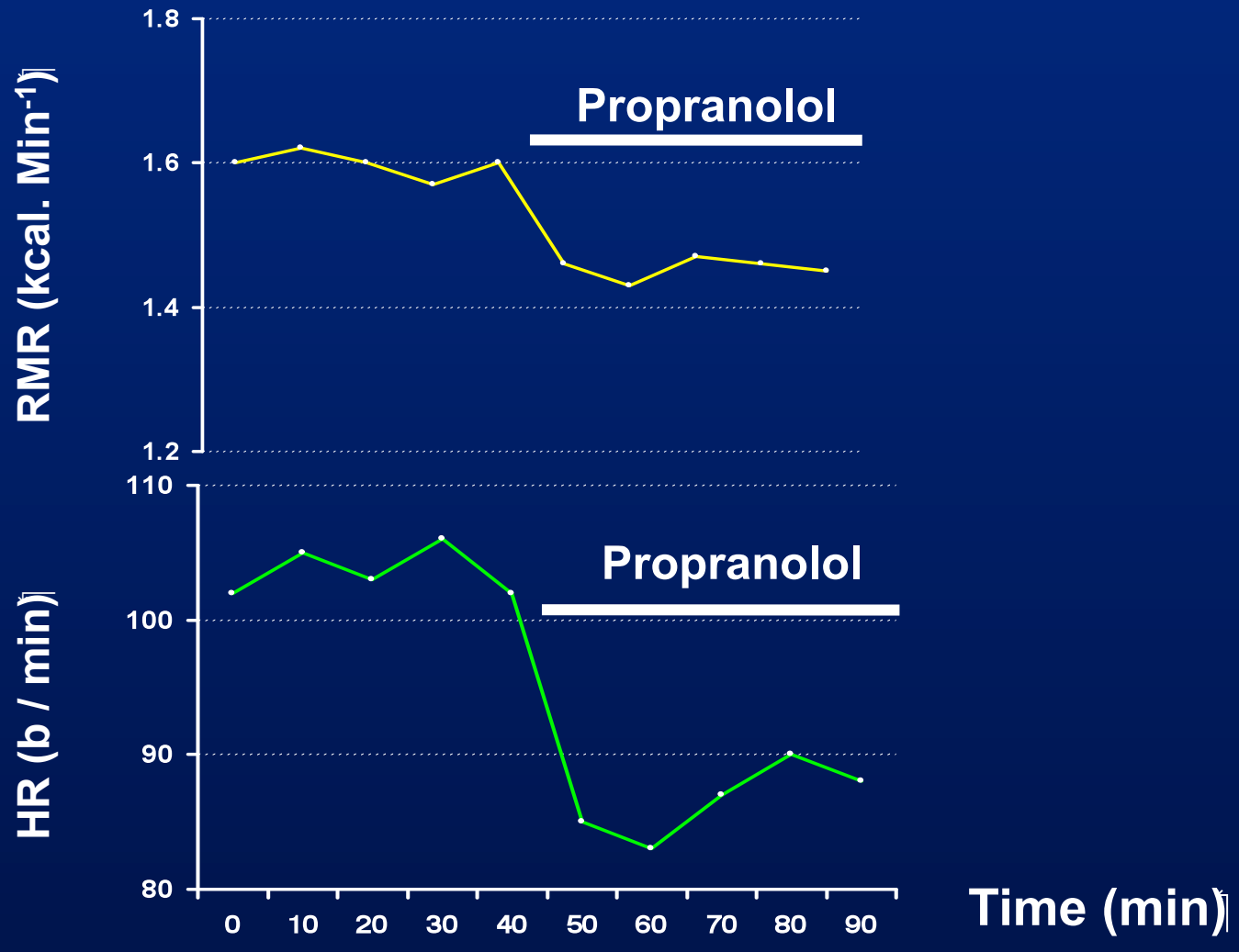
Influencer l'hypermétabolisme

Intervention	Situation	Effet
1. Dirigée sur les systèmes		
• Opiacés	Douleur aigüe	- 9 à – 25%
• Sédation	Agitation	- 20 à –50%
• Ventilation mécanique	Sevrage	- 20 à 30%
• Refroidissement	Fièvre	- 10 à 30%
2. Dirigée sur le métabolisme		
• Bêta-bloqueurs à15%	TCC, brûlure	- 7 -15%

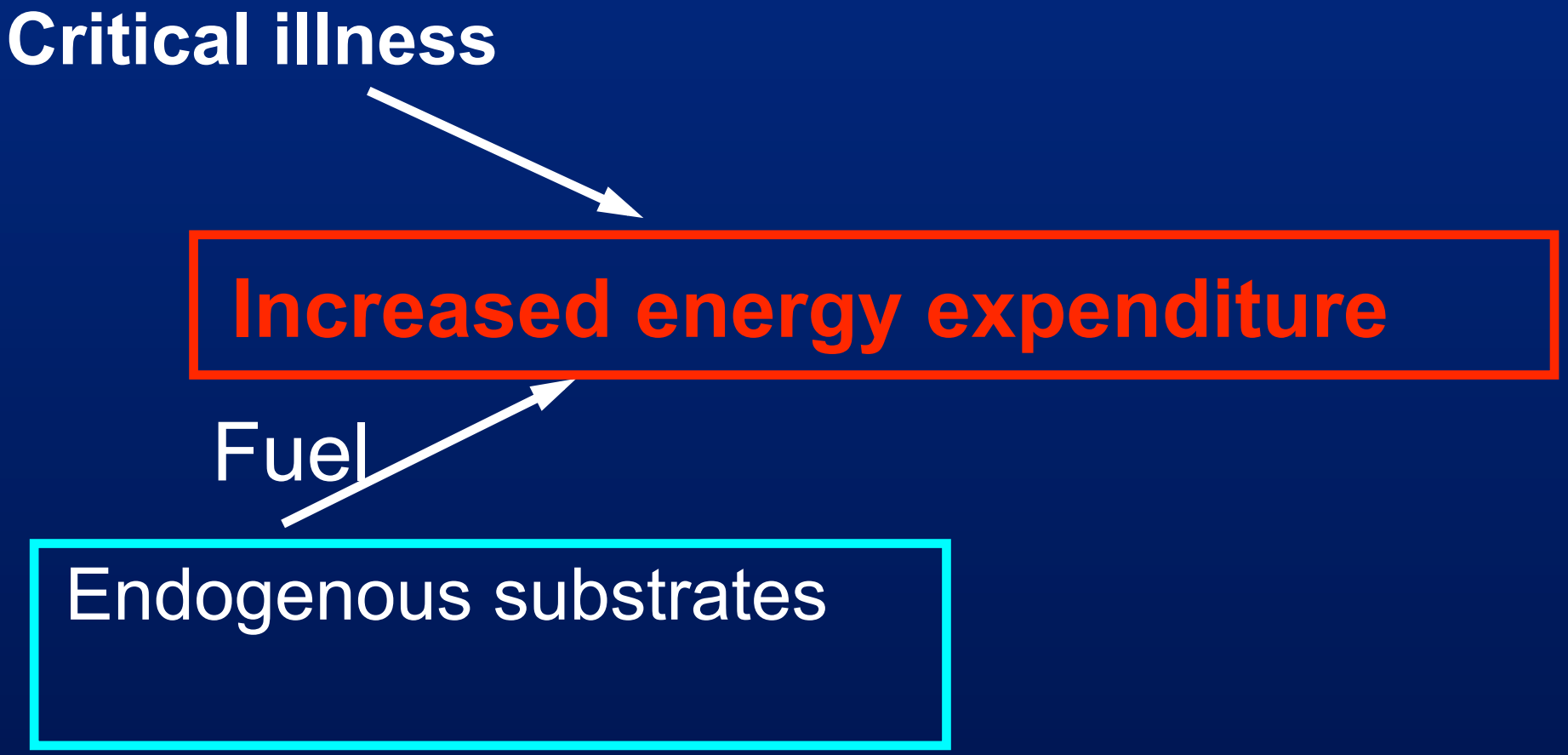
Chioléro R Nutrition 1999

Metabolic and cardiovascular responses to intravenous propranolol in brain injury

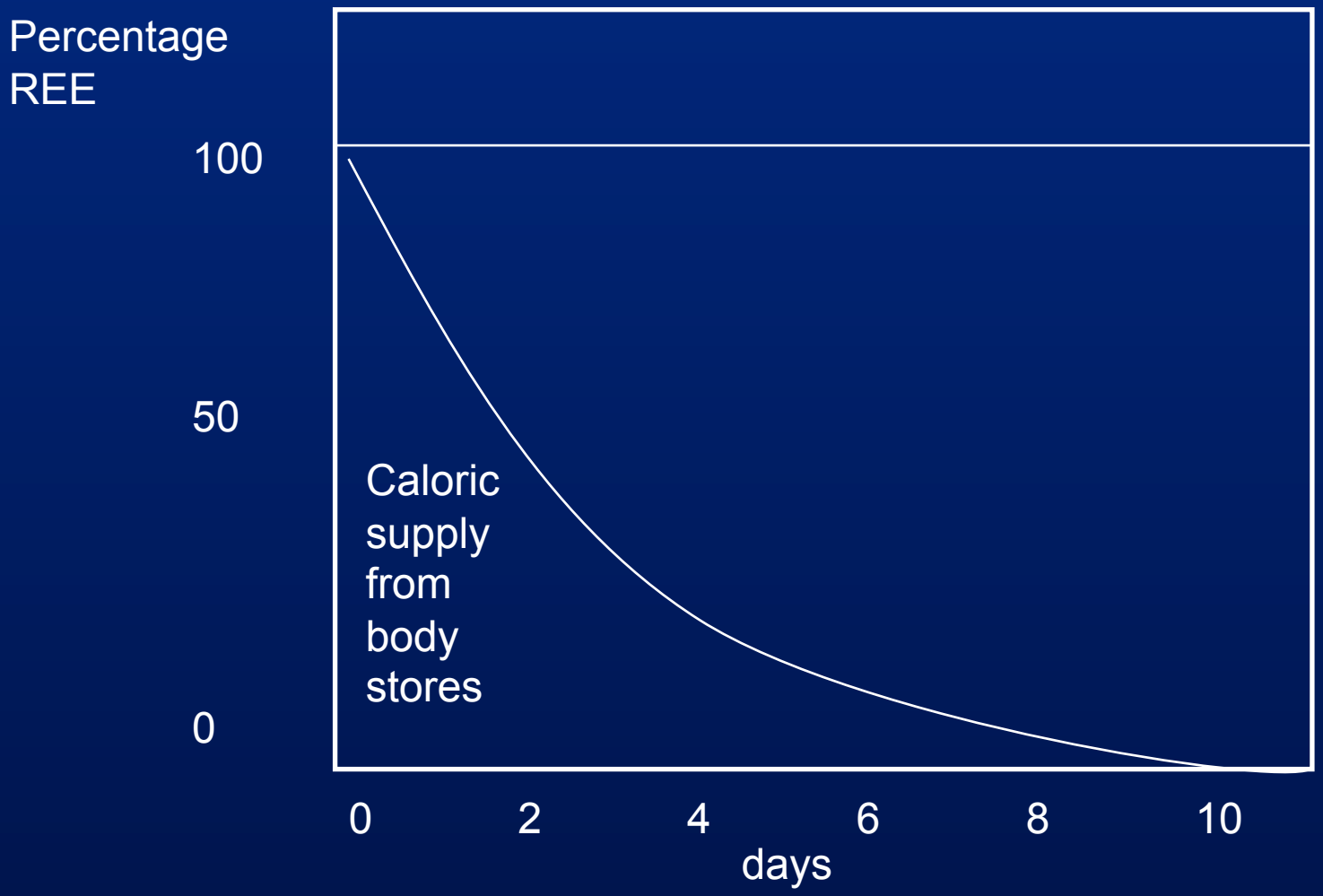
Chiolero RL et al Crit. Care Med. 1989: 17: 328



Energy balance in ICU patient



How does the body match the increased REE?



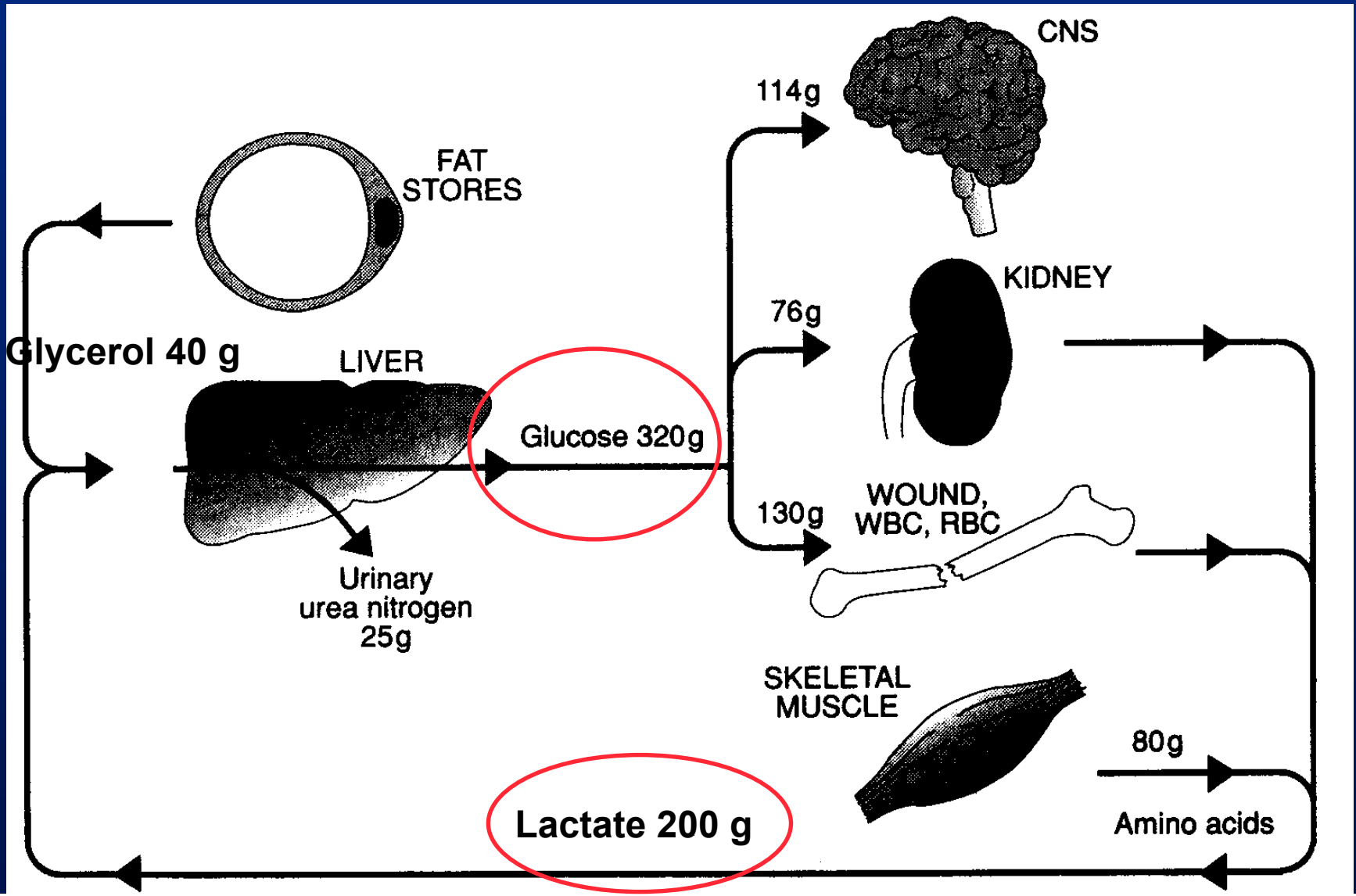
Short starvation in critically ill patients

Tappy L et al Crit Care Med 1998; 26: 860

3 day starvation

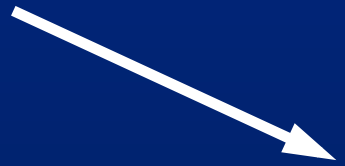
- Resting metabolic rate 1824 kcal/ day
- Glycemia 7.3 mmol/L
- E n d o ge nous glucose production 360 g/ day (1360 kcal/d)
- Net glucose oxidation 28% (512 kcal/ day)

Glucose flow is increased after injury



Energy balance in ICU patient

Critical illness



Increased energy expenditure

Fuel

Endogenous substrates
Nutrition support/therapy

Substrate utilization in energy metabolism

1. Endogenous substrates

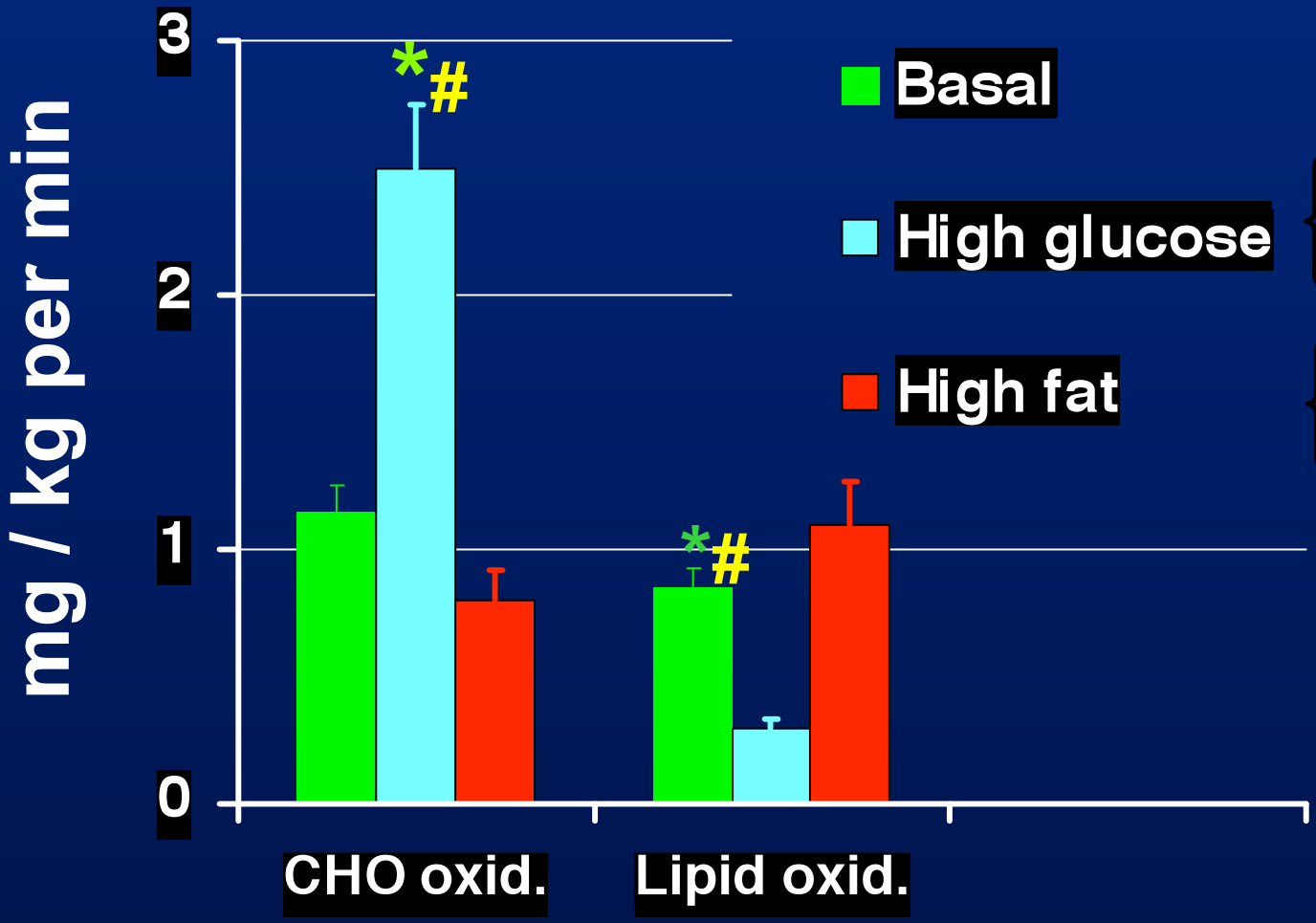
- Substrate mobilisation from body stores
  Proteins, fatty acids
- Interorgan substrate exchanges
  Glucose, lactate, glutamine, glycerol, amino acids

2. Exogenous substrates

- Carbohydrates, fat, proteins

CHO vs lipids for isocaloric TPN
CHO and lipid net oxidation

Tappy L et al, CCM 1998; 26:860

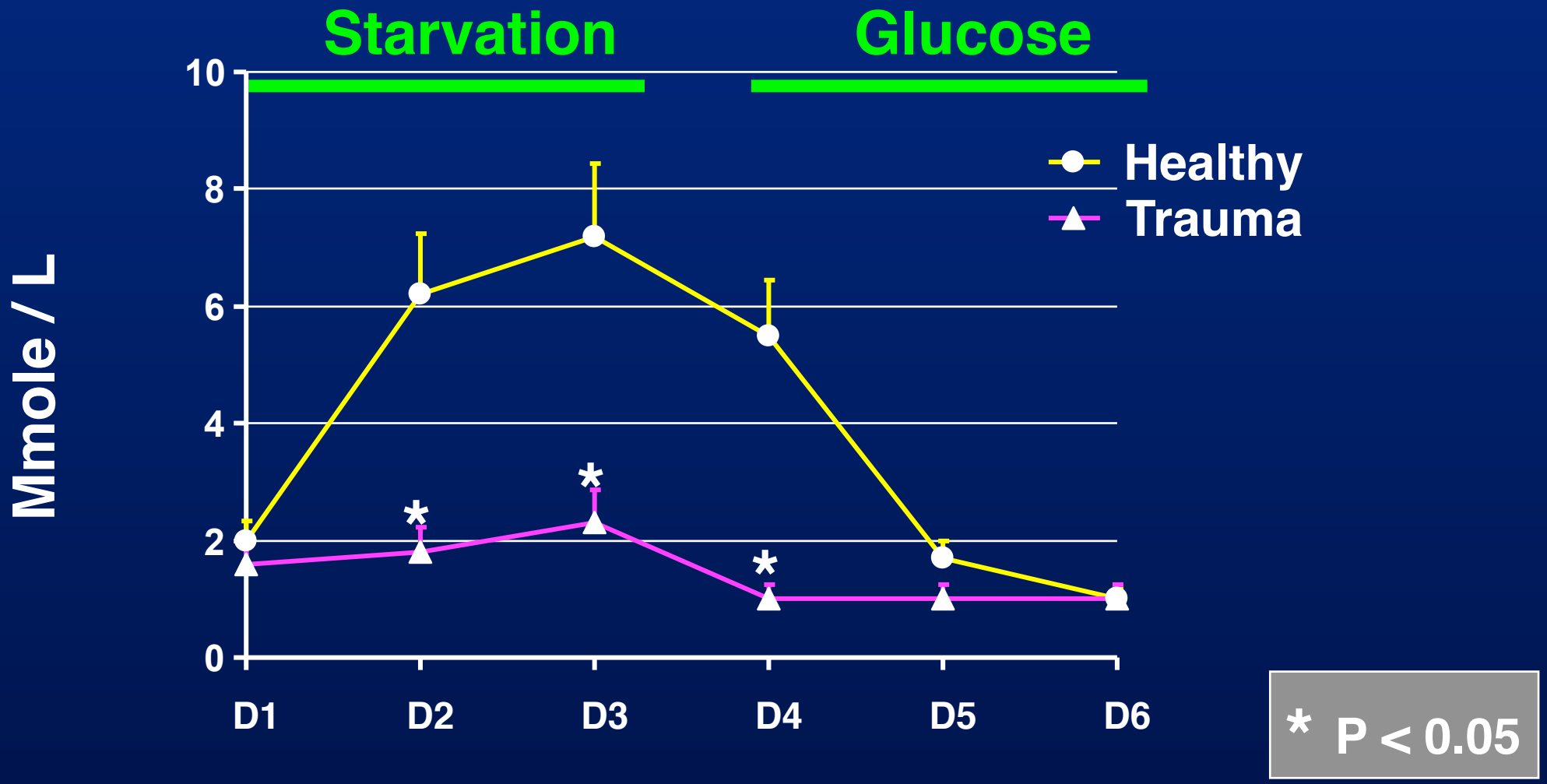


* p <0.05 vs basal

\# p<0.05 vs fat

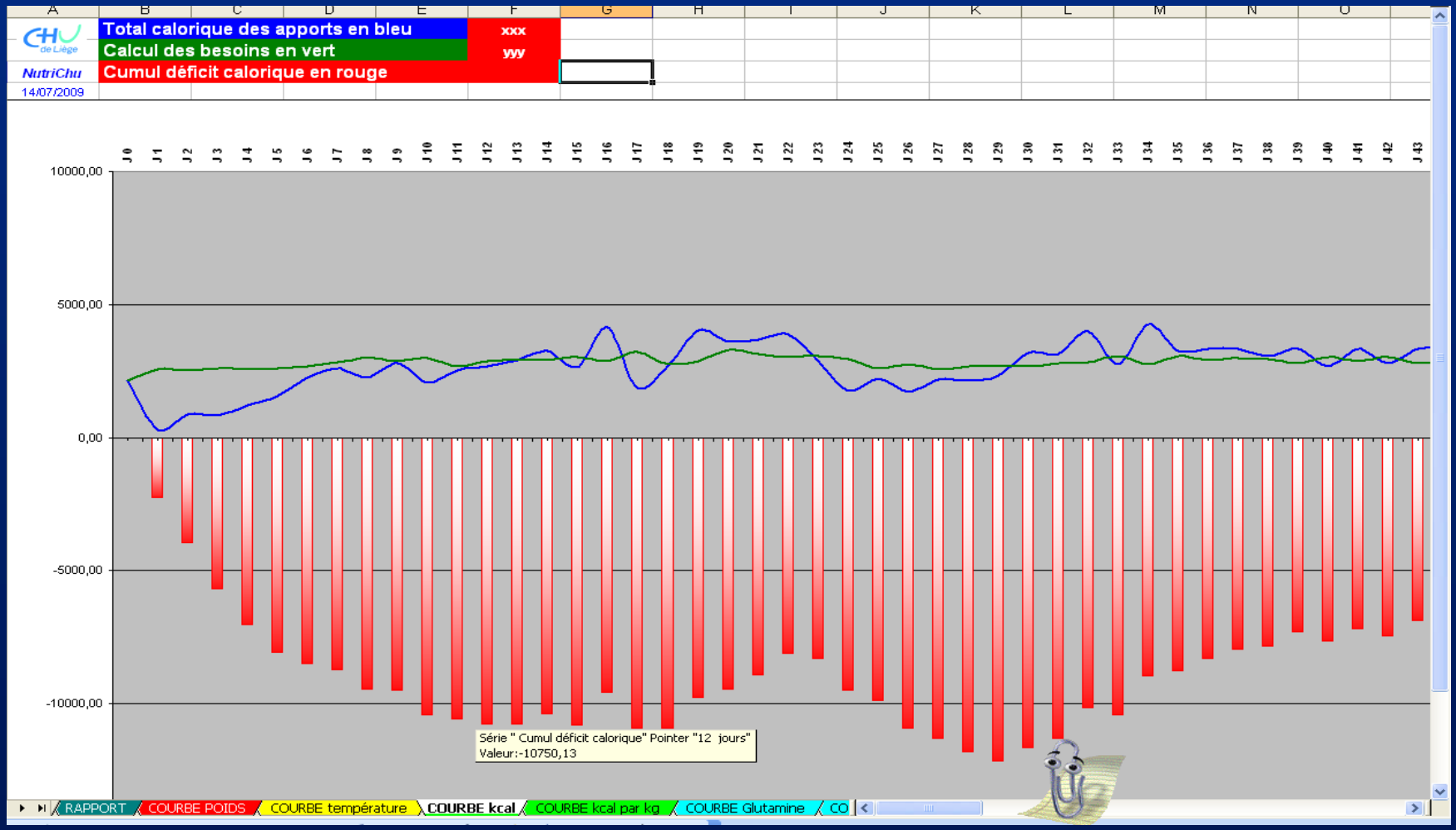
Total plasma ketone bodies in fasting trauma patients

Birkhan RH, J. Trauma 1981; 21: 513



Caloric debt

= energy provided by nutrition / therapy
– resting energy expenditure


Total calorique des apports en bleu
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Calcul des besoins en vert
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Cumul déficit calorique en rouge
NutriChu
14/07/2009
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-5000,00
-10000,00
Série " Cumul déficit calorique" Pointer "12 jours"
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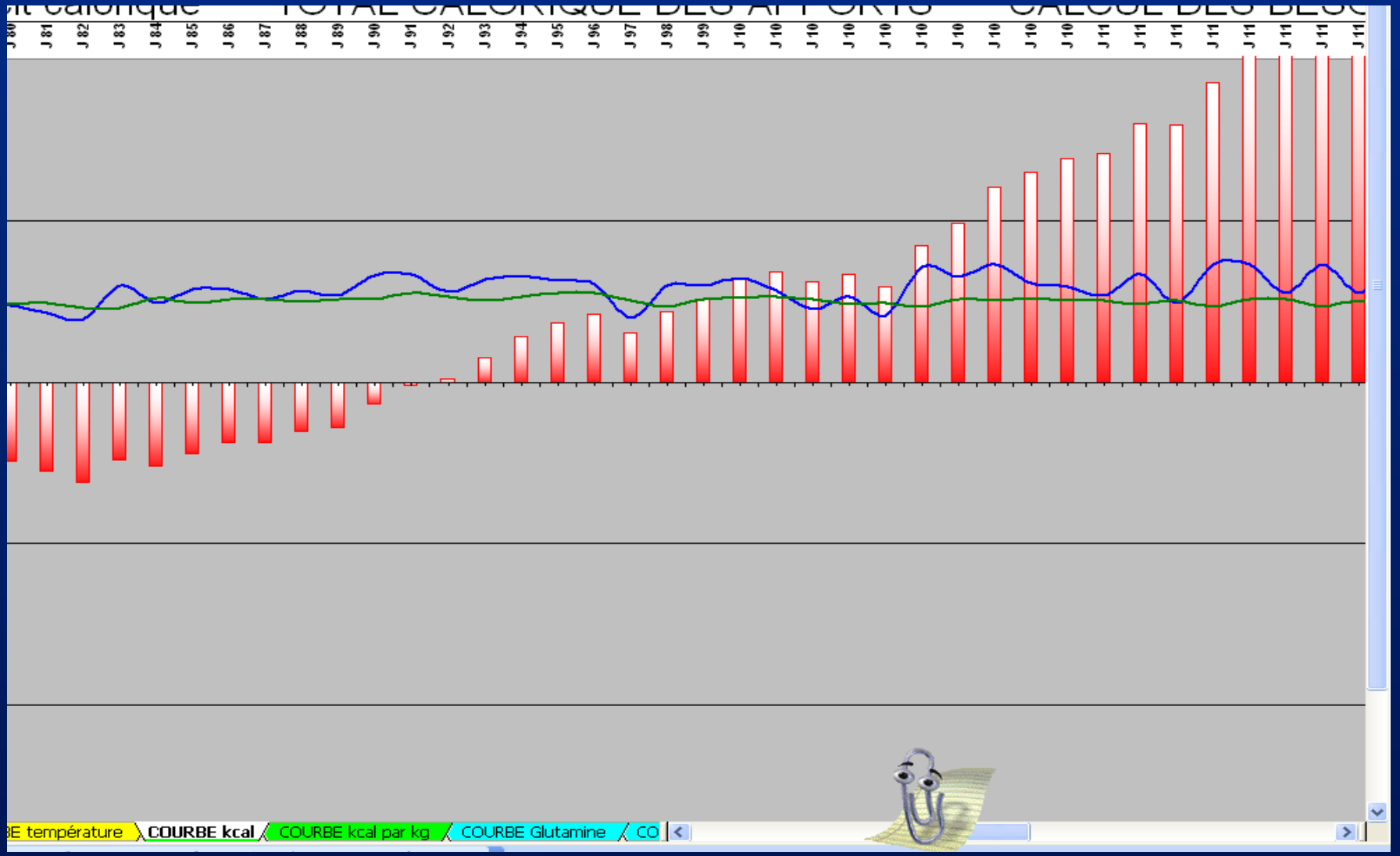
RAPPORT
COURBE POIDS
COURBE température
COURBE kcal
COURBE kcal par kg
COURBE Glutamine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BE température
COURBE kcal
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COURBE Glutamine
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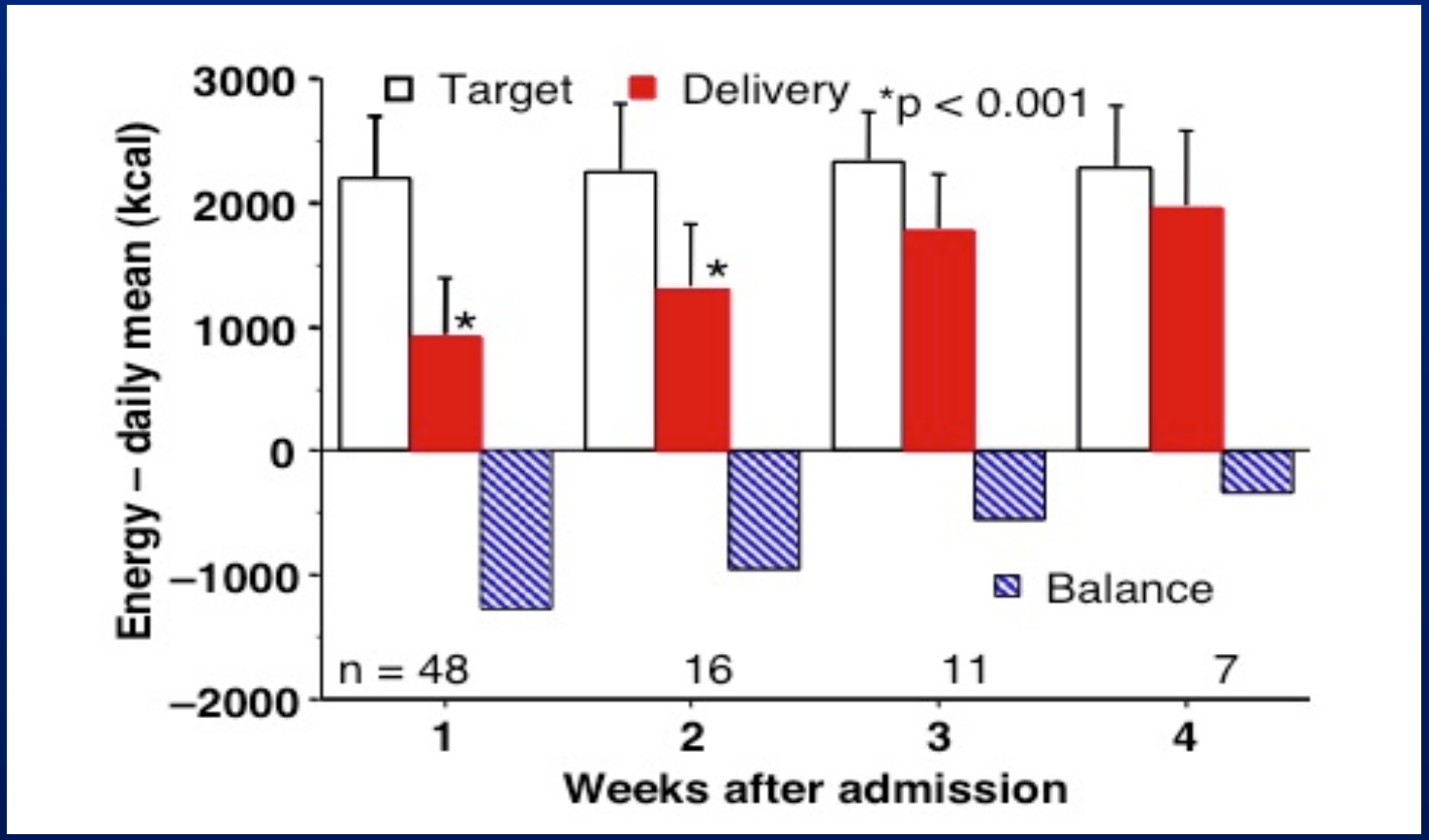
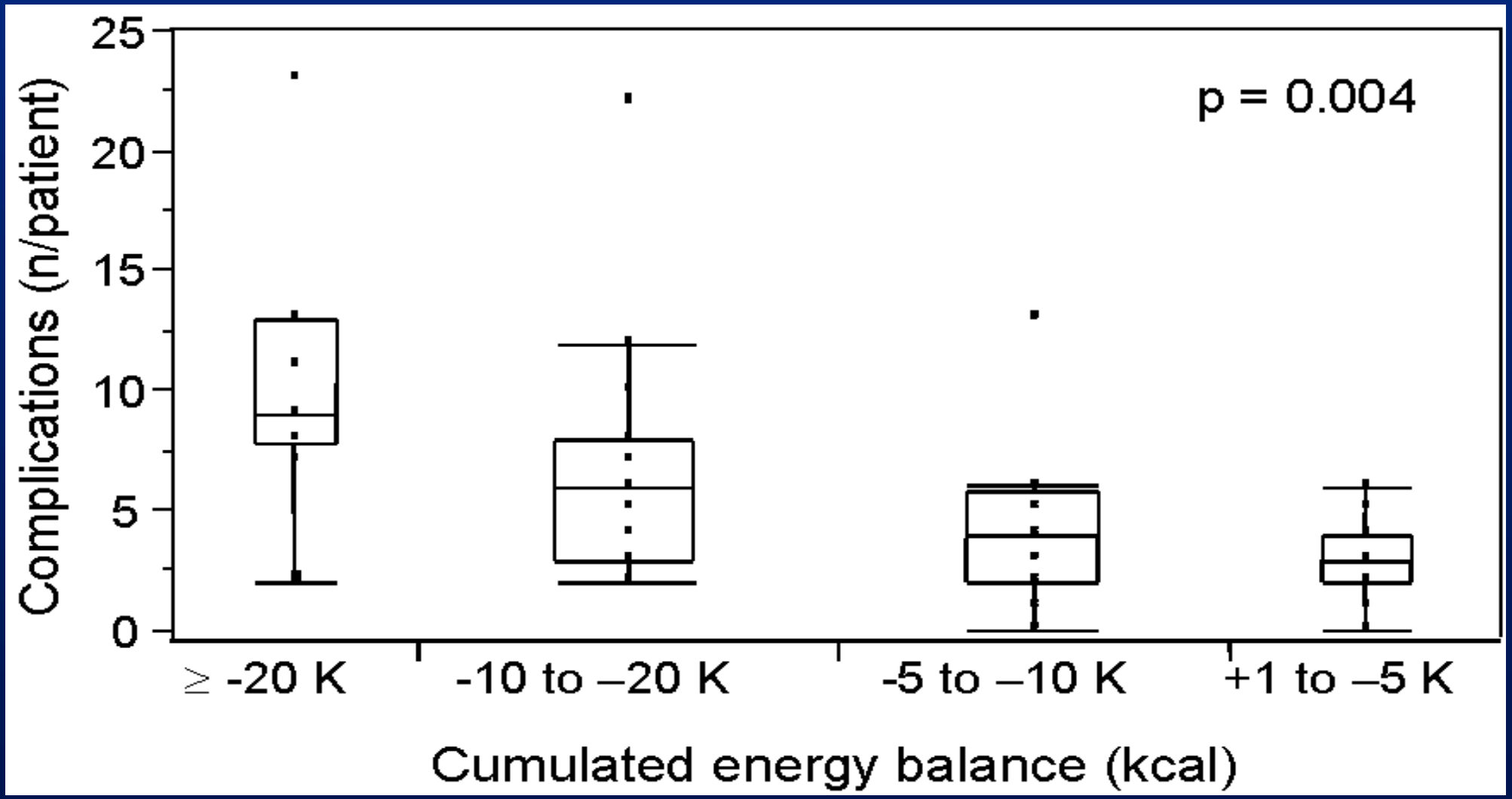
Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients



Clin Nutr 2005;24:502

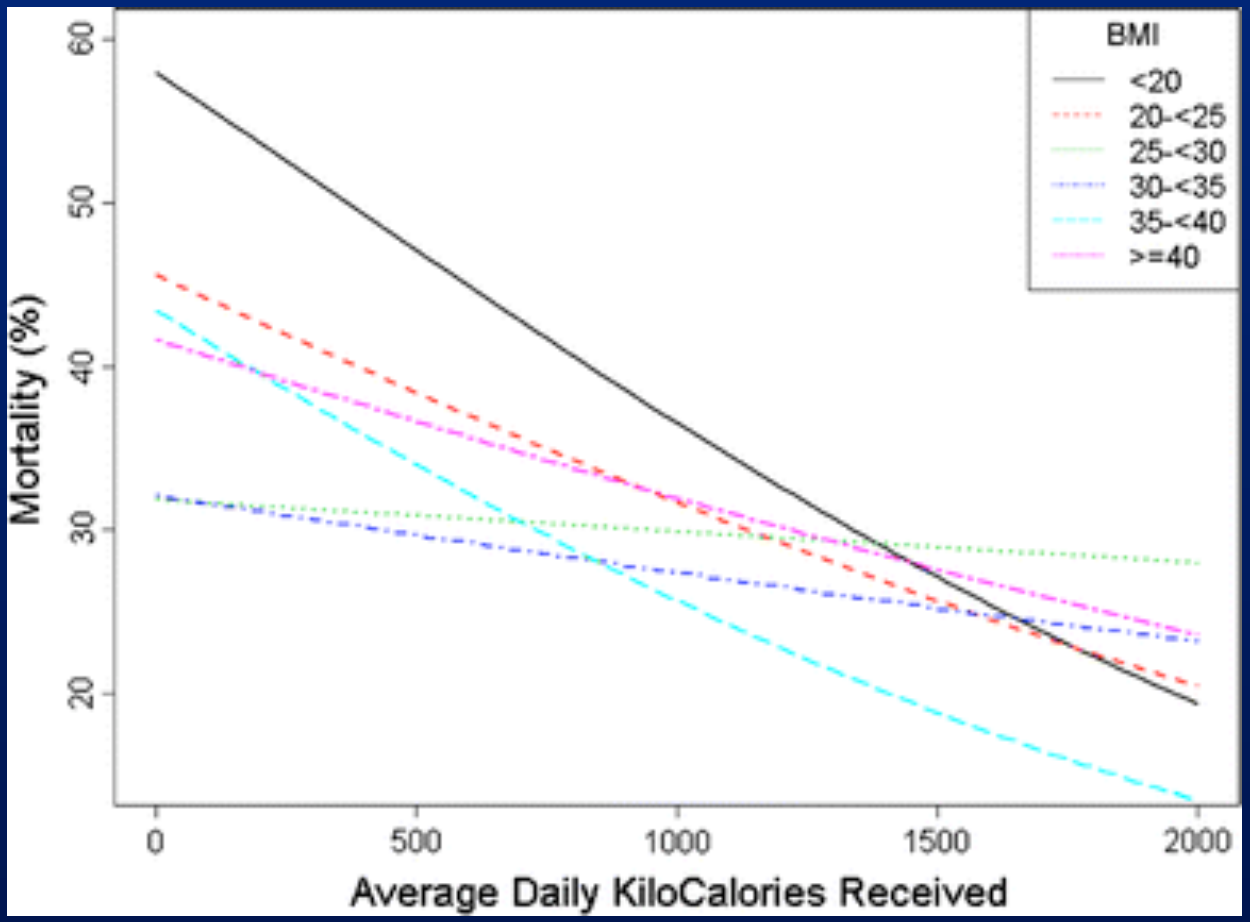
Impact of hypocaloric feeding on ICU outcome

Villet et al, Clin Nutr 2005, 24: 502



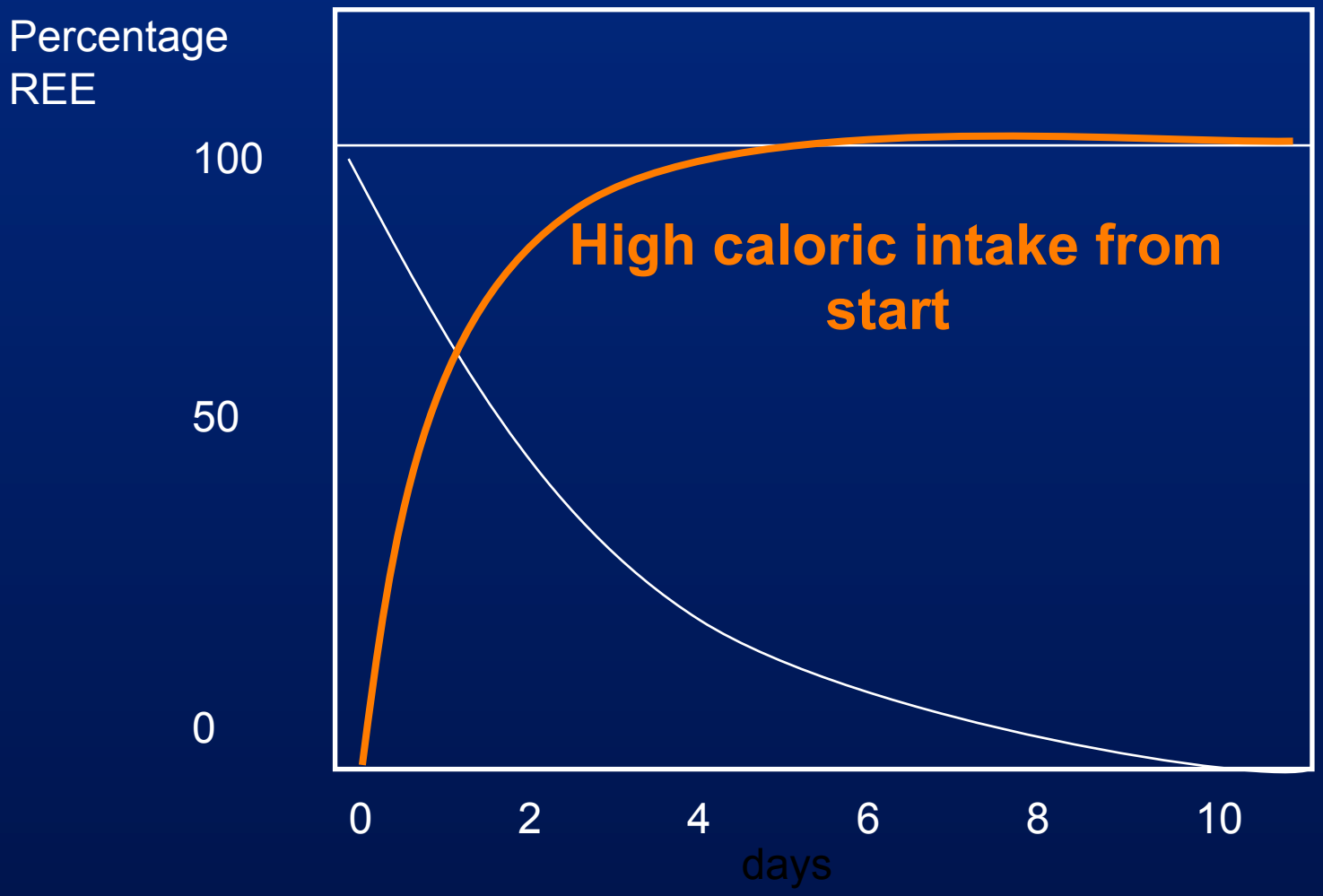
The Relationship Between Nutritional Intake and Clinical Outcomes in Critically Ill Patients: Results of an International Multicenter Observational Study

C. Alberda et al Intensive Care Med. 2009, 35: 1728-37

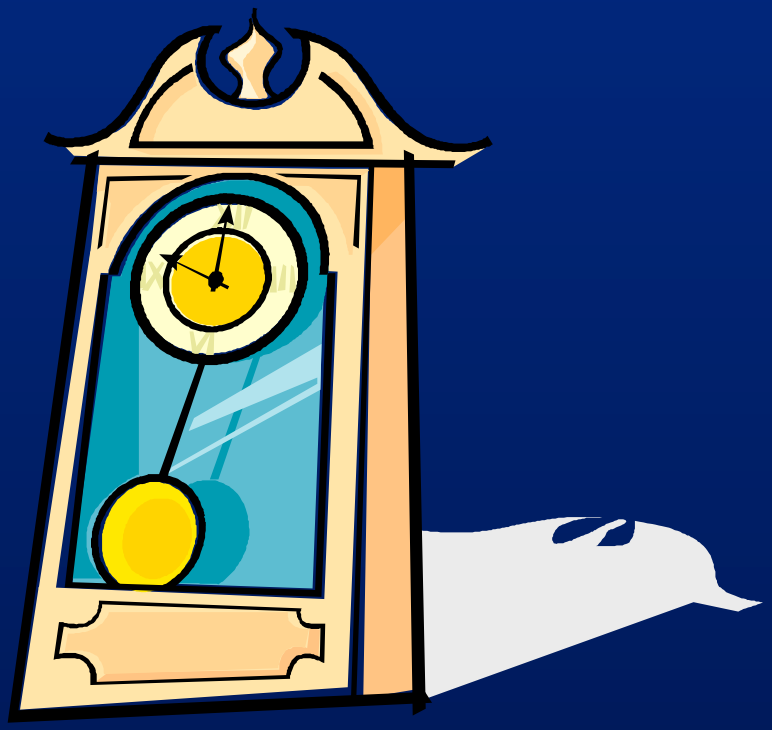


167 ICUs from 37 countries recorded nutrition practice information on a consecutive cohort of 2772 (20 per site) mechanically ventilated adult patients that stayed in the ICU for at least 72 hours.

How many calories should be prescribed?



Le retour de la parentérale?



Volume 325 AUGUST 22, 1991 Number 8

PERIOPERATIVE TOTAL PARENTERAL NUTRITION IN SURGICAL PATIENTS

THE VETERANS AFFAIRS TOTAL PARENTERAL NUTRITION COOPERATIVE STUDY GROUP*

Abstract *Background.* We undertook this study to test the hypothesis that perioperative total parenteral nutrition (TPN) decreases the incidence of serious complications after major abdominal or thoracic surgical procedures in malnourished patients.

Methods. We studied 395 malnourished patients (99 percent of them male) who required laparotomy or noncardiac thoracotomy. They were randomly assigned to receive either TPN for 7 to 15 days before surgery and 3 days afterward (the TPN group) or no perioperative TPN (the control group). The patients were monitored for complications for 90 days after surgery.

Results. The rates of major complications during the first 30 days after surgery in the two groups were similar (TPN group, 25.5 percent; control group, 24.6 percent), as were the overall 90-day mortality rates (13.4 percent and 10.5 percent, respectively). There were more infectious complications in the TPN group than in the controls (14.1 vs. 6.4 percent; P = 0.01; relative risk, 2.20; 95 percent confidence interval, 1.19 to 4.05), but slightly more noninfectious complications in the control group (16.7 vs. 22.2 percent; P = 0.20; relative risk, 0.75; 95 percent confidence interval, 0.50 to 1.13). The increased rate of infections was confined to patients categorized as either borderline or mildly malnourished, according to Subjective Global Assessment or an objective nutritional assessment, and these patients had no demonstrable benefit from TPN. In contrast, severely malnourished patients who received TPN had fewer noninfectious complications than controls (5 vs. 43 percent; P = 0.03; relative risk, 0.12; 95 percent confidence interval, 0.02 to 0.91), with no concomitant increase in infectious complications.

Conclusions. The use of preoperative TPN should be limited to patients who are severely malnourished unless there are other specific indications. (N Engl J Med 1991; 325:525-32.)

Complications Observed within 30 Days of Surgery.*

Table 4. Complications Observed within 30 Days of Surgery.*

Type of Complication	TPN Group (N = 192)	Control Group (N = 203)
	no. of episodes/no. of patients	
Major, infectious		
Pneumonia or empyema	17/16	9/9
Abdominal abscess	2/2	2/2
Extra-abdominal abscess	1/1	0
Fasciitis	3/3	0
Bacteremia or fungemia	8/7	5/5
Other septic complications	0	1/1
Total	31/27	17/13
Patients affected (%)	14.1	6.4
Relative risk (TPN:control) = 2.20		
95% Confidence interval, 1.19–4.05		
Relative risk with control for SGA = 2.23		
Major, noninfectious		
Anastomotic leak	7/6	12/11
Bronchopleurocutaneous fistula	4/3	6/6
Wound dehiscence	1/1	1/1
Decubitus ulcer	1/1	1/1
Chronic respiratory failure (≥4 days)	14/13	12/11
Gastrointestinal complications†	11/10	17/14
Cardiovascular complications‡	15/15	18/15
Pulmonary embolus	0	1/1
Renal failure	0	3/3
Total	53/32	71/45
Patients affected (%)	16.7	22.2
Relative risk (TPN:control) = 0.75		
95% Confidence interval, 0.50–1.13		

The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group* . N Engl J Med 1991;325:525-532.

The NEW ENGLAND JOURNAL of MEDICINE

A snapshot in Germany today

Elke et al *Crit Care Med* 2008;36:1762

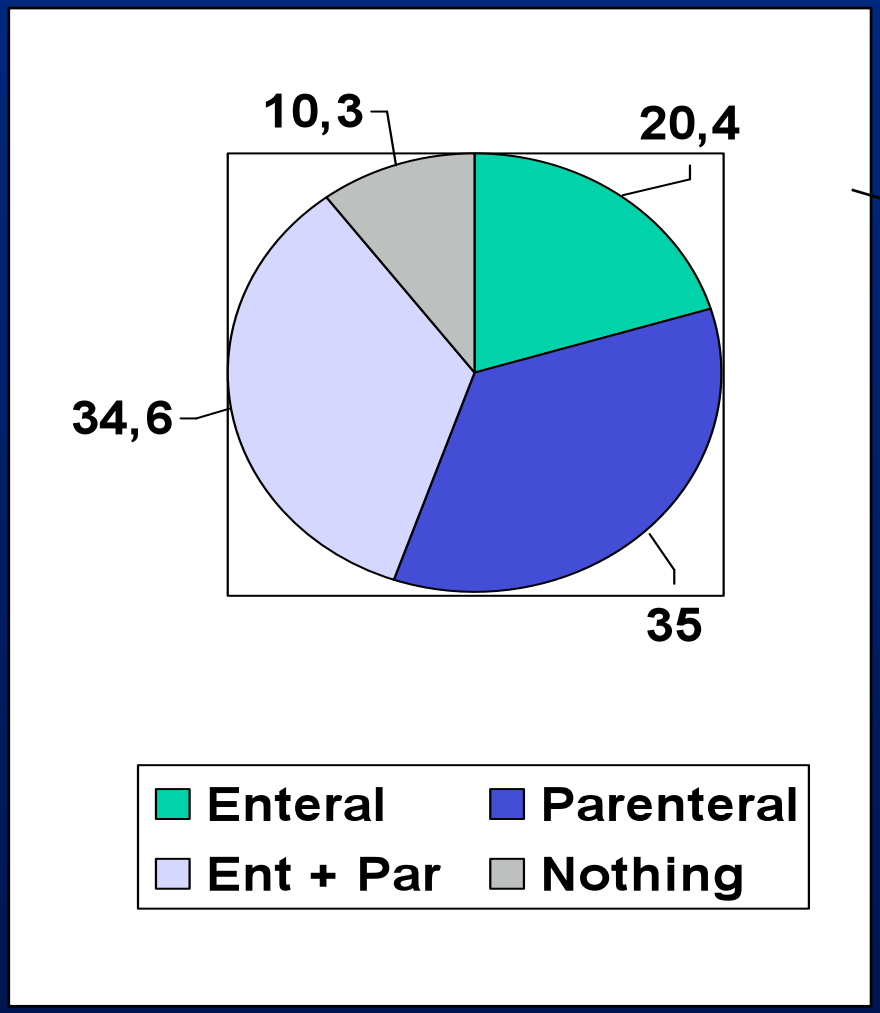
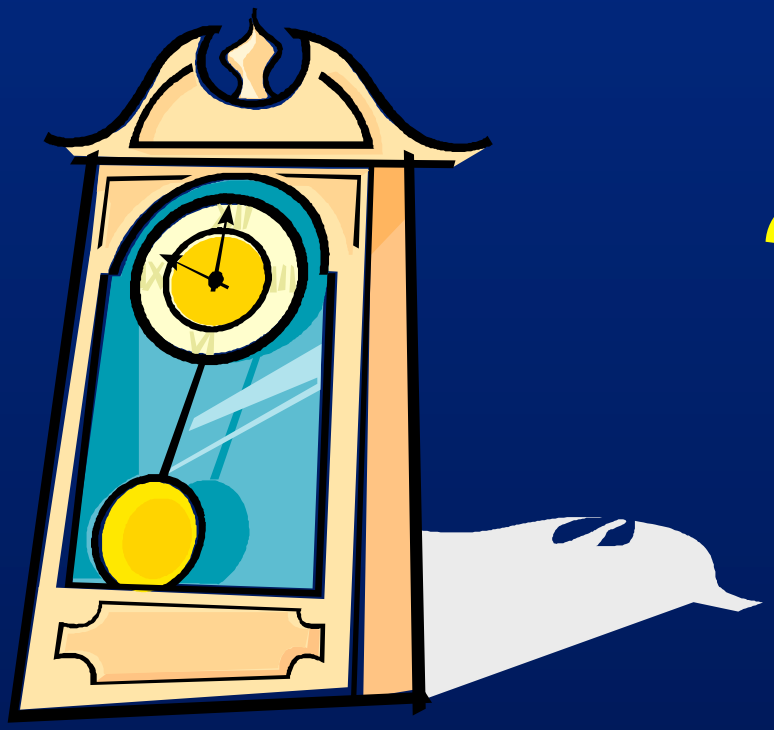


Table 4. Independent predictors for mortality

Variable	Univariate OR	Univariate *p* Value	Multivariate[a] OR	Multivariate[a] 95% CI
Enteral nutrition	0.68	.065	1.13	0.84–1.51
Parenteral nutrition	1.97	.003	2.09	1.29–3.37
APACHE II	1.07	<.0001	1.05	1.02–1.09
Renal dysfunction[b]	2.91	<.0001	2.07	1.30–3.31
Insulin dose (IU/24 hrs)	1.00	.338		
Serum glucose concentration (mg/dL)	1.00	.145		
Age	1.01	.051	1.01	0.99–1.02
Gender	0.90	.609		
Mechanical ventilation	2.88	.083		
Septic shock	1.85	.004	1.54	0.97–2.44

« Hospital mortality was higher in patients receiving exclusively Parenteral (62.3%) or mixed nutrition (57.1%) than enteral (38.9%).
After adjustment (APACHE II, need for mechanical ventilation), the Presence of parenteral was a significant a significant predictor of mortality (OR 2.09 (1.29-3.37)) »

Place de la parentérale chez l'agressé ??



?

No evidence-based answer available
Ongoing studies : EPanic

- Impact of Early Parenteral Nutrition Completing Enteral Nutrition in Adult Critically Ill Patients (EPaNIC)
  - EN only: Withholding PN during the first week of ICU stay - exclusively enteral nutrition. If enteral nutrition is insufficient after the seventh day of ICU stay, parenteral nutrition will be started.
  - EN plus early PN: PN will be started the morning of the third ICU hospitalisation day. The amount of PN to be given will be calculated to cover the caloric needs of the patient, based on the enteral energy intake the previous 24 hours

No evidence-based answer available
Ongoing studies : TOP-UP

(Trial Of supplemental Parenteral nutrition in Under- and over weight Patients)

- **The overall objective of this protocol is to present the rationale for and the proposed design for a multicenter, multinational pilot study involving 160 critically-ill** *lean and obese patients to evaluate the safety and feasibility of a study of supplemental parenteral nutrition (PN) plus enteral nutrition (EN) compared to EN with placebo PN*. **If the results of this pilot study are positive, then we will proceed to a large scale trial of 2000 patients to determine the efficacy of this aggressive nutritional strategy.**

No evidence-based answer available
Ongoing studies : SPN

Impact of Supplemental Parenteral Nutrition (SPN)

on clinical outcome measured by the infection rate,

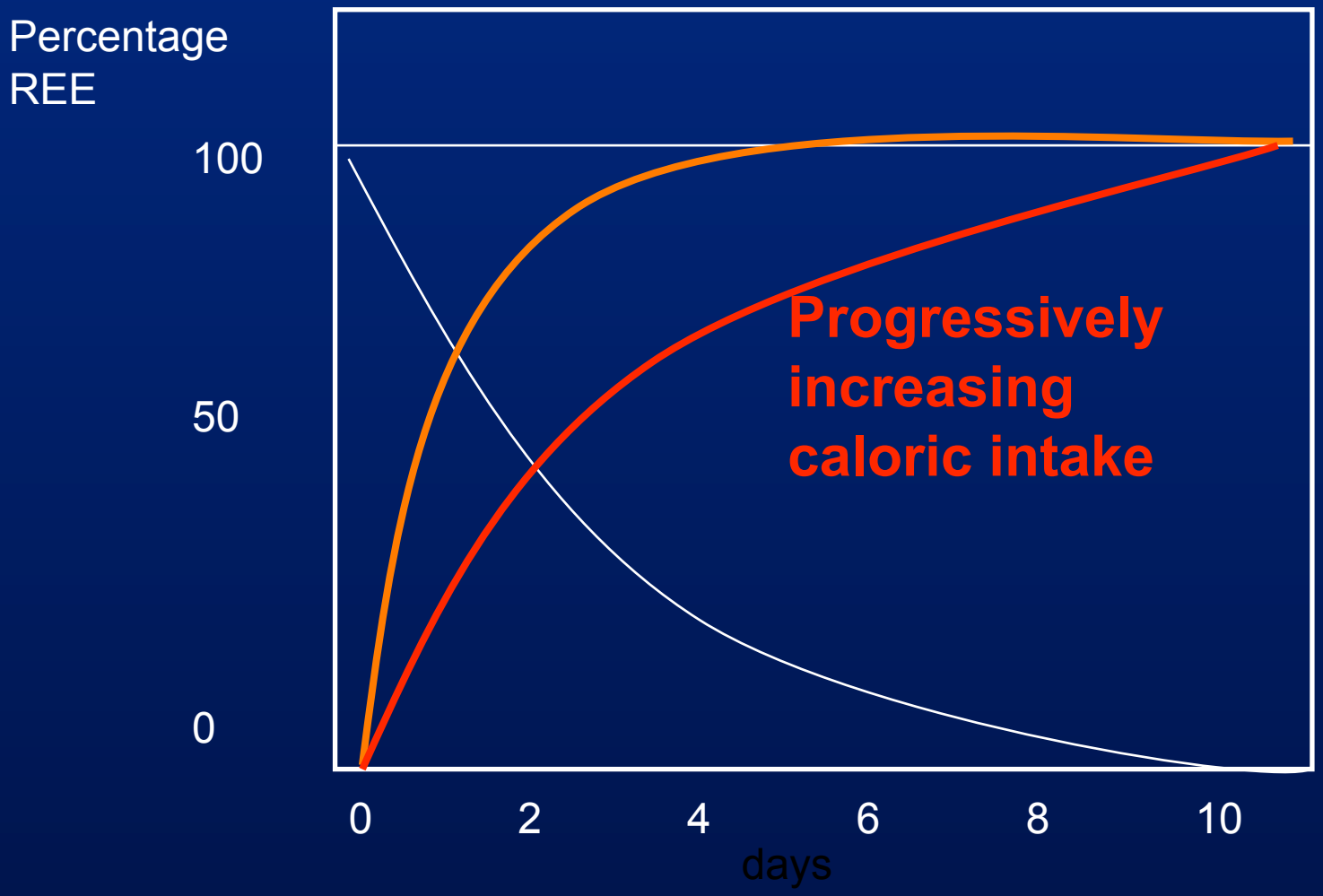
duration of mechanical ventilation and rehabilitation in intensive care unit patients

- At day 3 after admission, if energy input is < 60%; patients are randomized into either the “Control group” (EN alone) or the “SPN group” (EN + PN) to reach 100% of their predicted energy needs.

No evidence-based answer available
Ongoing studies : TiCaCoS

- **The aim of our study is to perform a prospective, randomized, controlled non blinded study in critically patients** *to assess the necessity for measuring daily resting energy expenditure as a guide for nutritional support.* **The primary objective will be to decrease infectious rate of these critically ill patients receiving tight caloric control. The secondary objective will be to evaluate the correlation between energy balance and complication rates in this particular population.**

How many calories should be prescribed?



Refeeding syndrome

JC Melchior QNCARSI 2010

- Le terme de Refeeding Syndrome (équivalent anglo-saxon du RS ou SRI) apparaît dans les années 70 aux débuts de la nutrition parentérale. Mais les risques d'une renutrition mal conduite ou trop rapide sont connus depuis longtemps. La littérature médicale juste décrit après la deuxième guerre mondiale qui rapporte et décrit ce syndrome à la sortie des camps de prisonniers et des camps de concentration

- Le SRI peut être défini comme l'ensemble des conséquences pathologiques de la renutrition, incluant l'hypophosphorémie aiguë, la surcharge hydrosodée, les perturbations hydroélectrolytiques et de l'équilibre acido-basique, les états hyperosmolaires, les carences vitaminiques et les troubles neurologiques périphériques ou centraux. Il comprend également , ainsi que les conséquences cardio-circulatoires et respiratoires secondaires à ces troubles métaboliques

Renutrition du dénutri sévère

JC Melchior QNCARSI 2010

- Le niveau des apports énergétiques doit être modeste et instauré ***de façon progressive***. Un apport énergétique global de 10 à 15 kcal /kg /jour ne dépassant pas 500 kcal /jour, les 3 premiers jours parait raisonnable. Celui-ci pourra atteindre progressivement 30 à 40 kcal /kg /jour, mais pas avant la fin de la première ou de la deuxième semaine si la dénutrition est très sévère.

- En cas de dénutrition sévère ou de jeûne prolongé, l'apport de glucose ne doit pas dépasser 1,5 à 2 mg /kg /jour les trois premiers jours et atteindre un maximum de 4 mg / kg / j à la fin de la première semaine.

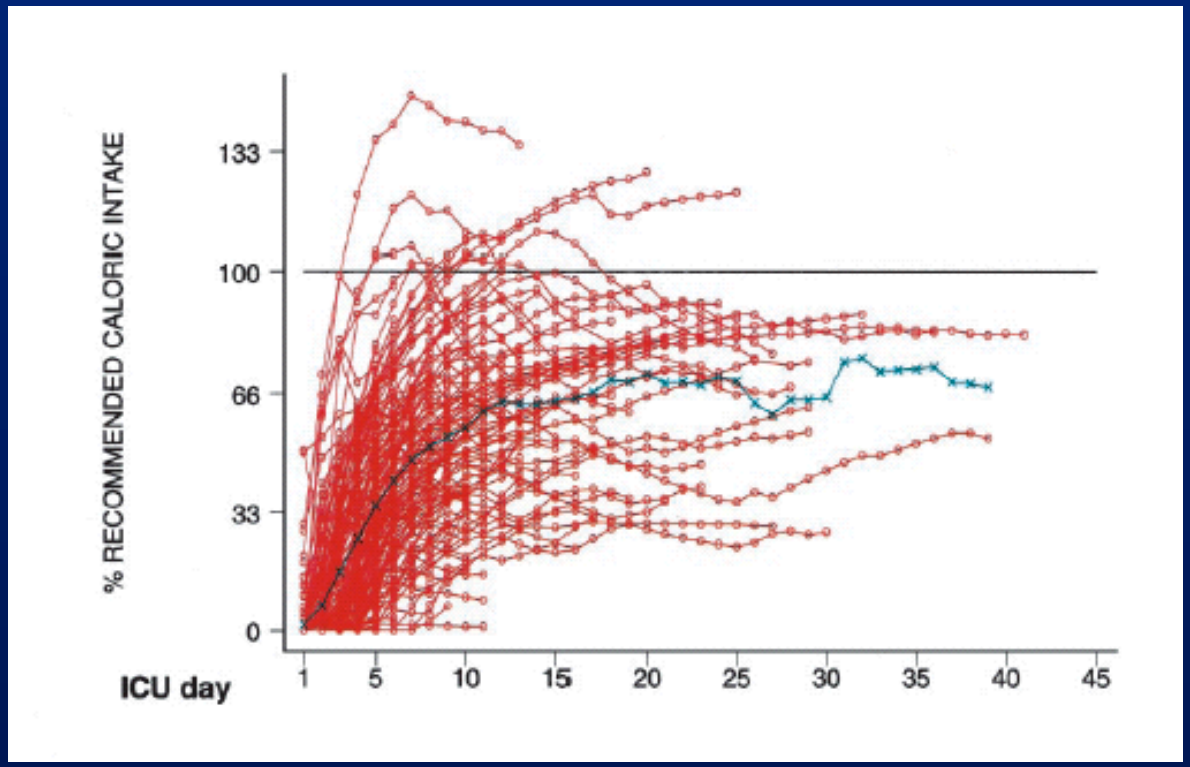
- L'apport protéique doit être ajusté sur la base de 1,2 à 1,5 g / kg / j de poids idéal et peut être atteint en une semaine. Dans tous les cas, les apports protéiques ne doivent pas dépasser 2 à 2,5 g /kg /jour au maximum et tenir compte de la fonction rénale presque toujours altérée dans les dénutritions chronique et chez les malades agressés.

Caloric Intake in Medical ICU Patients*

Consistency of Care With Guidelines and Relationship to Clinical Outcomes

Jerry A. Krishnan, MD; Pat B. Parce, RN; Anthony Martinez, MD; Gregory B. Diette, MD, MHS; and Roy G. Brower, MD

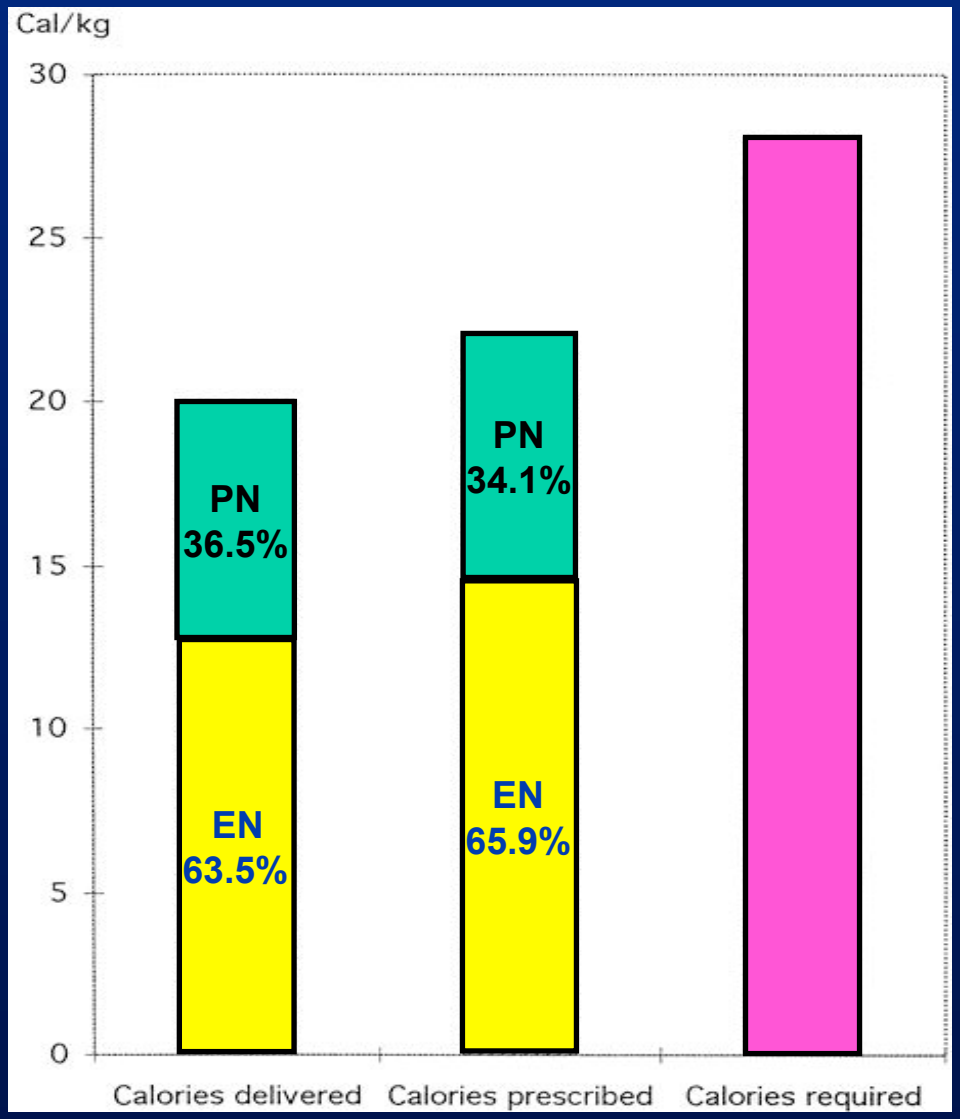
Chest 2003;124:297

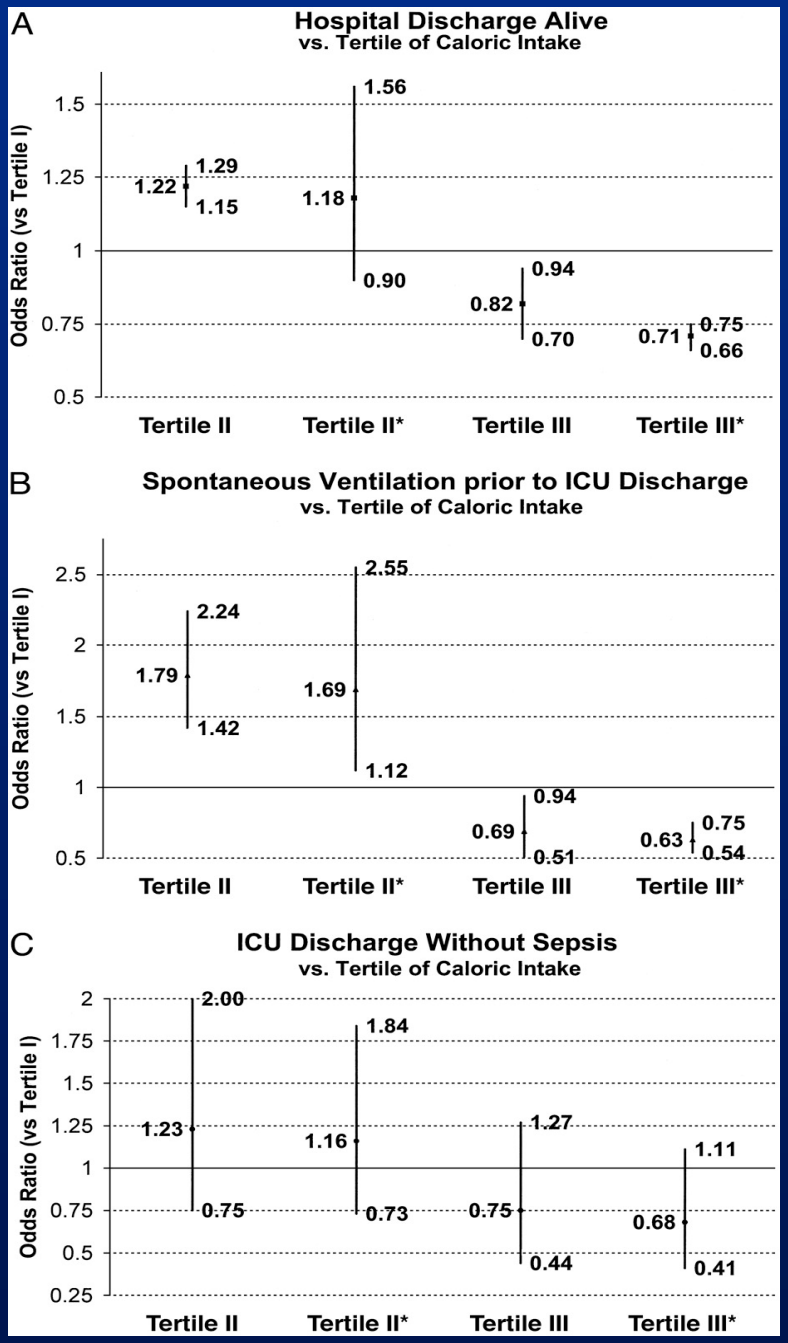


187 patients
ACCP targets
(25 kcal/kg.d or
27.5 kcal/kg.d
During SIRS)

Daily amount of calories delivered

De Jonghe et al Crit Care Med 2001;29:8





Caloric Intake in Medical ICU Patients*

Consistency of Care With Guidelines and Relationship to Clinical Outcomes

Jerry A. Krishnan, MD; Pat B. Parce, RN; Anthony Martinez, MD; Gregory B. Diette, MD, MHS; and Roy G. Brower, MD

ORs and 95% CIs for hospital discharge alive in patients with tertiles II and III of caloric intake

Chest 2003;124:297

Nitrogen balance in ICU patient

Critical illness

Increased nitrogen losses

One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

Margaret S. Herridge, M.D., M.P.H., Angela M. Cheung, M.D., Ph.D., Catherine M. Tansey, M.Sc., Andrea Matte-Martyn, B.Sc., Natalia Diaz-Granados, B.Sc., Fatma Al-Saidi, M.D., Andrew B. Cooper, M.D., Cameron B. Guest, M.D., C. David Mazer, M.D., Sangeeta Mehta, M.D., Thomas E. Stewart, M.D., Aiala Barr, Ph.D., Deborah Cook, M.D., and Arthur S. Slutsky, M.D., for the Canadian Critical Care Trials Group

N Engl J Med 2003;348:683-93.

GLOBAL ASSESSMENT

At the time of discharge from the ICU, patients who survived the acute respiratory distress syndrome were severely wasted and had lost 18 percent of their base-line body weight (Fig. 2). Seventy-one percent of patients (59 of 83) returned to their base-line weight by one year. All patients reported poor function and attributed this to the loss of muscle bulk, proximal weakness, and fatigue. Most patients had

DISTANCE WALKED IN SIX MINUTES

The distance walked in six minutes improved over the 12 months after discharge from the ICU but still remained lower than the predicted value[38] (Table 3). The patients attributed exercise limitation to global muscle wasting and weakness, foot drop (as a result of nerve-entrapment syndromes that began in the ICU), immobility of large joints (heterotopic ossification[40,41]), and dyspnea. The proportion of

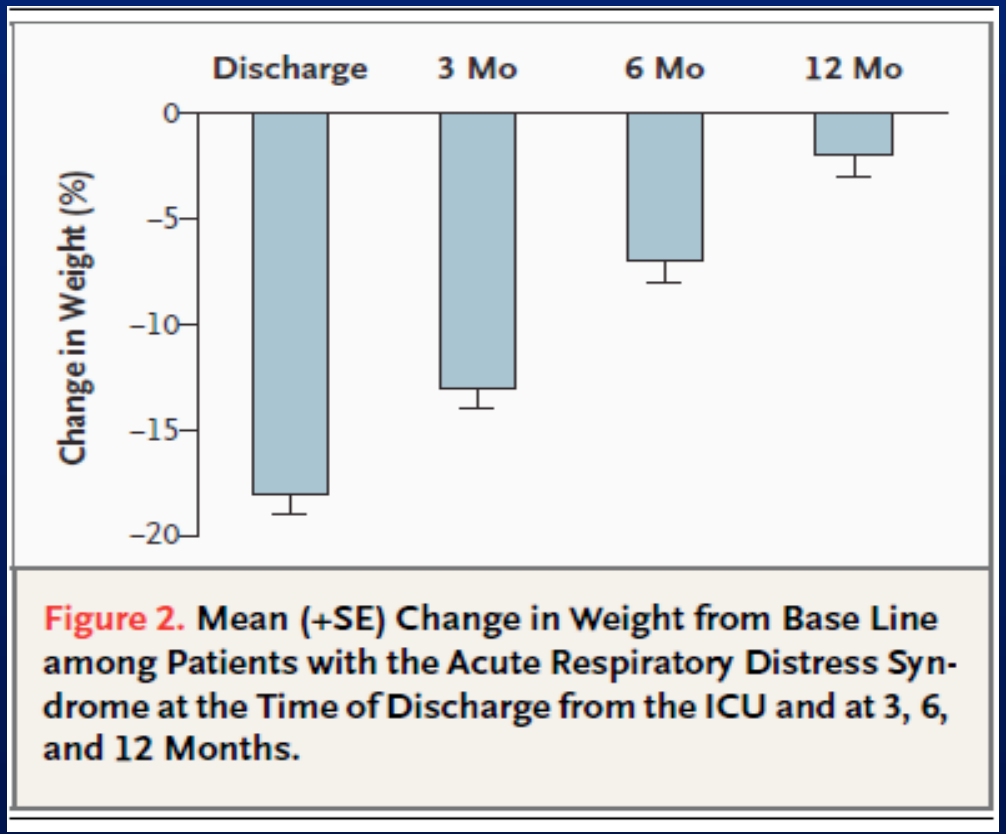
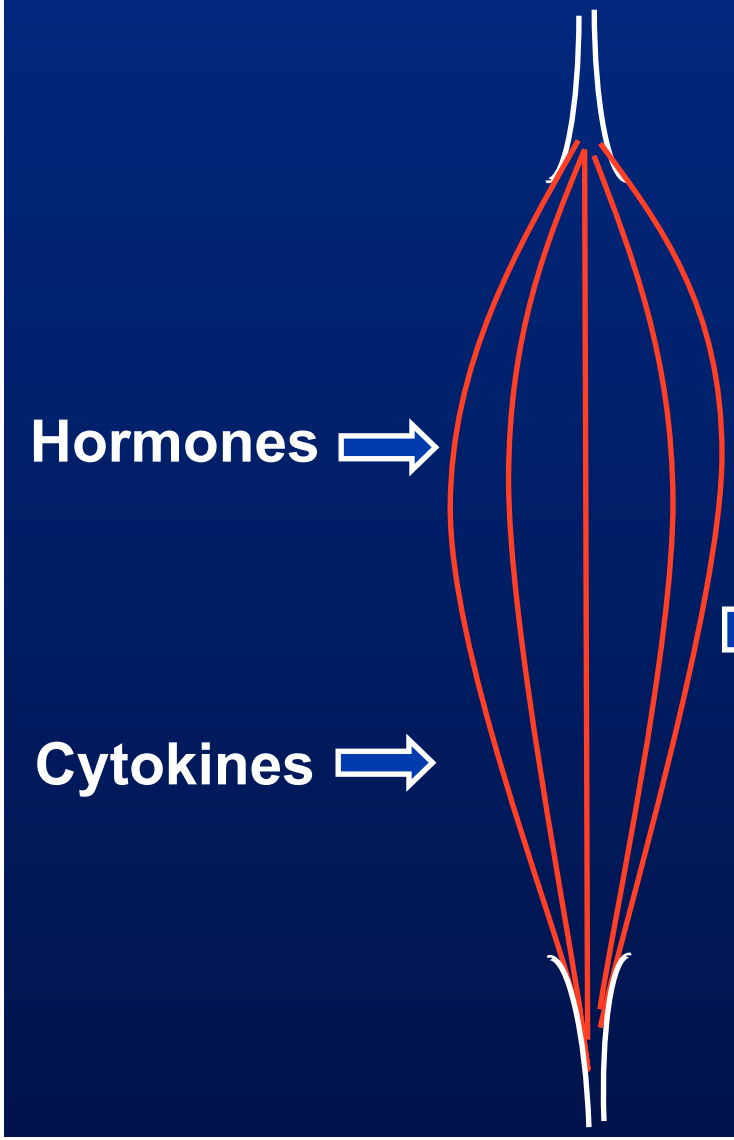


Figure 2. Mean (+SE) Change in Weight from Base Line among Patients with the Acute Respiratory Distress Syndrome at the Time of Discharge from the ICU and at 3, 6, and 12 Months.

Catabolisme protéique: la libération d'AA est un phémomène adaptatif



Hormones

Cytokines

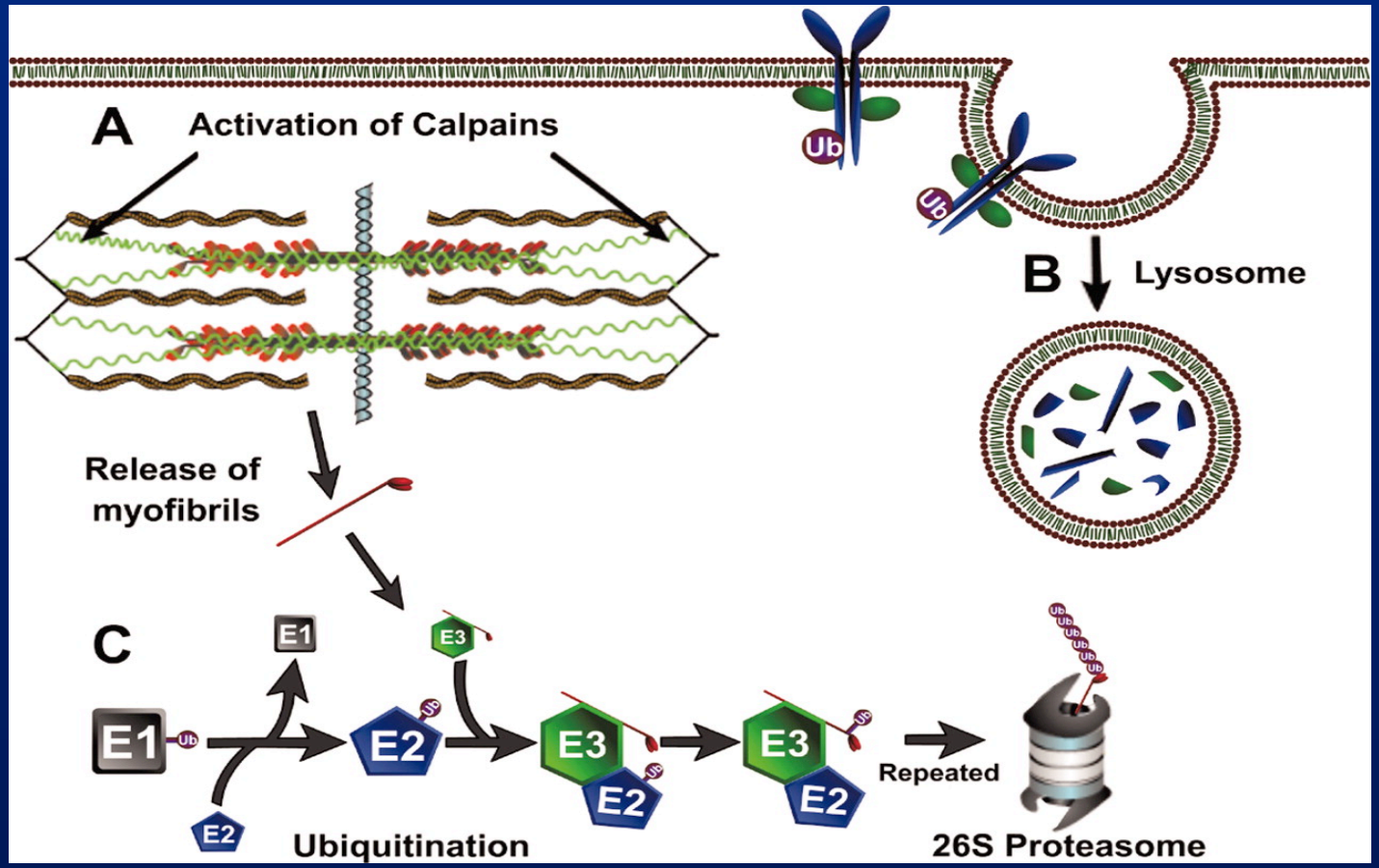
Glutamine

Alanine

Autres AA

AA pour:
cell. immunitaires
inflammation &
cicatrisation
prot. phase aiguë
néoglucogénèse

Stimulation of the major proteolytic systems

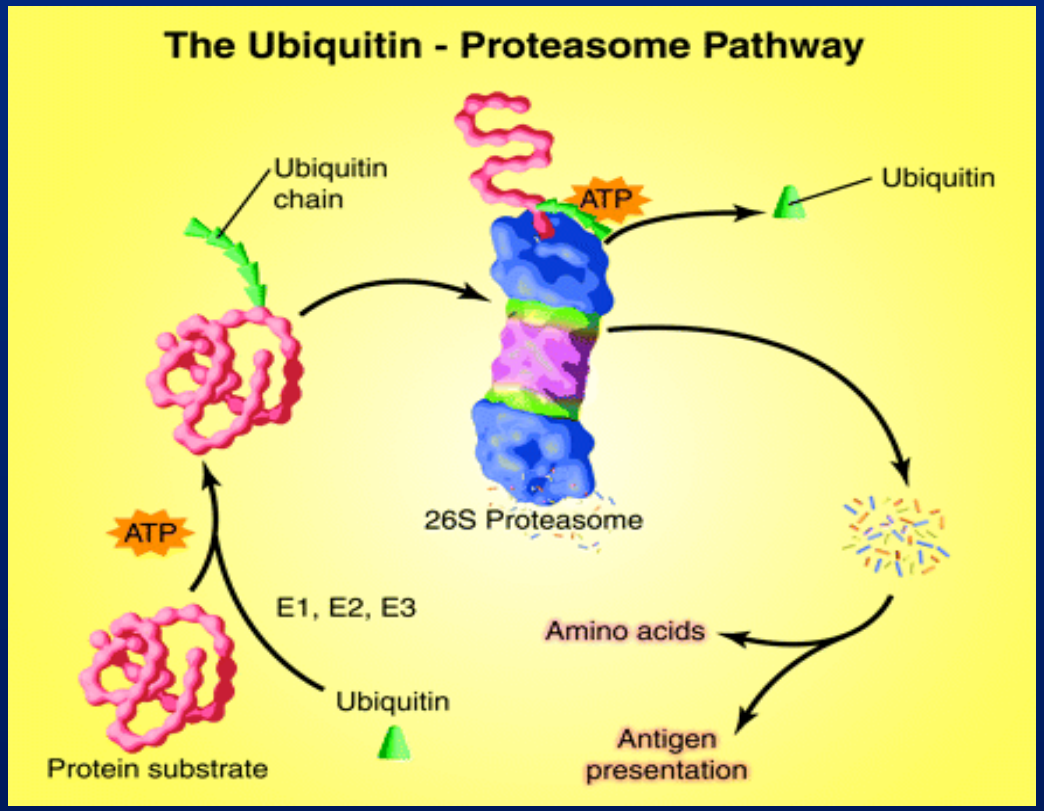


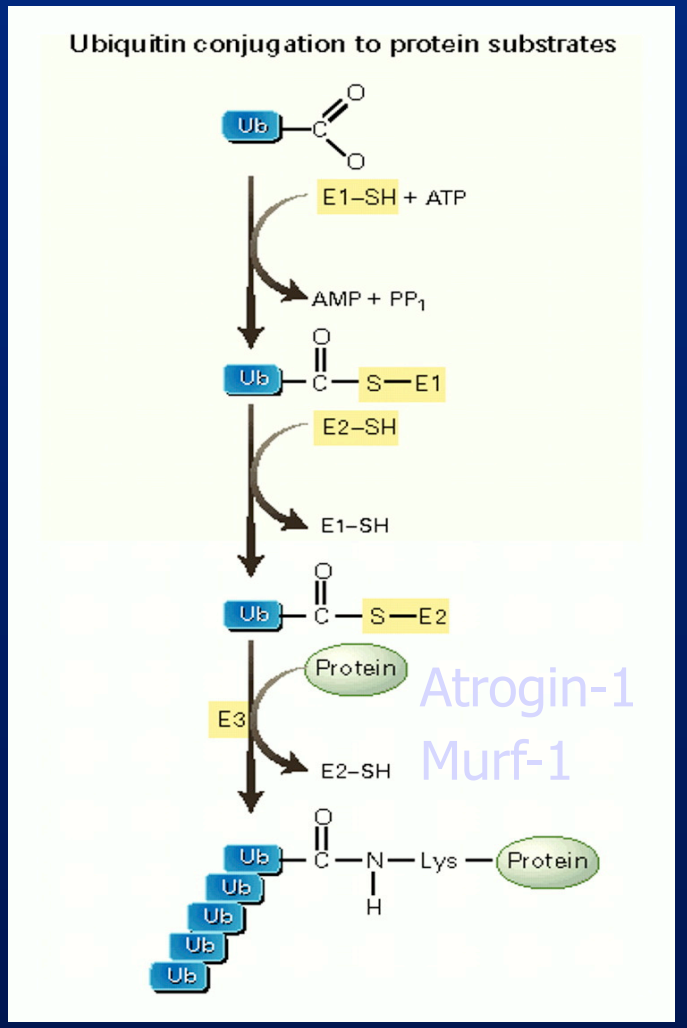
Jackman RW et al., 2004

Based on

Gene expression levels, enzymatic activities, pharmacological inhibitors

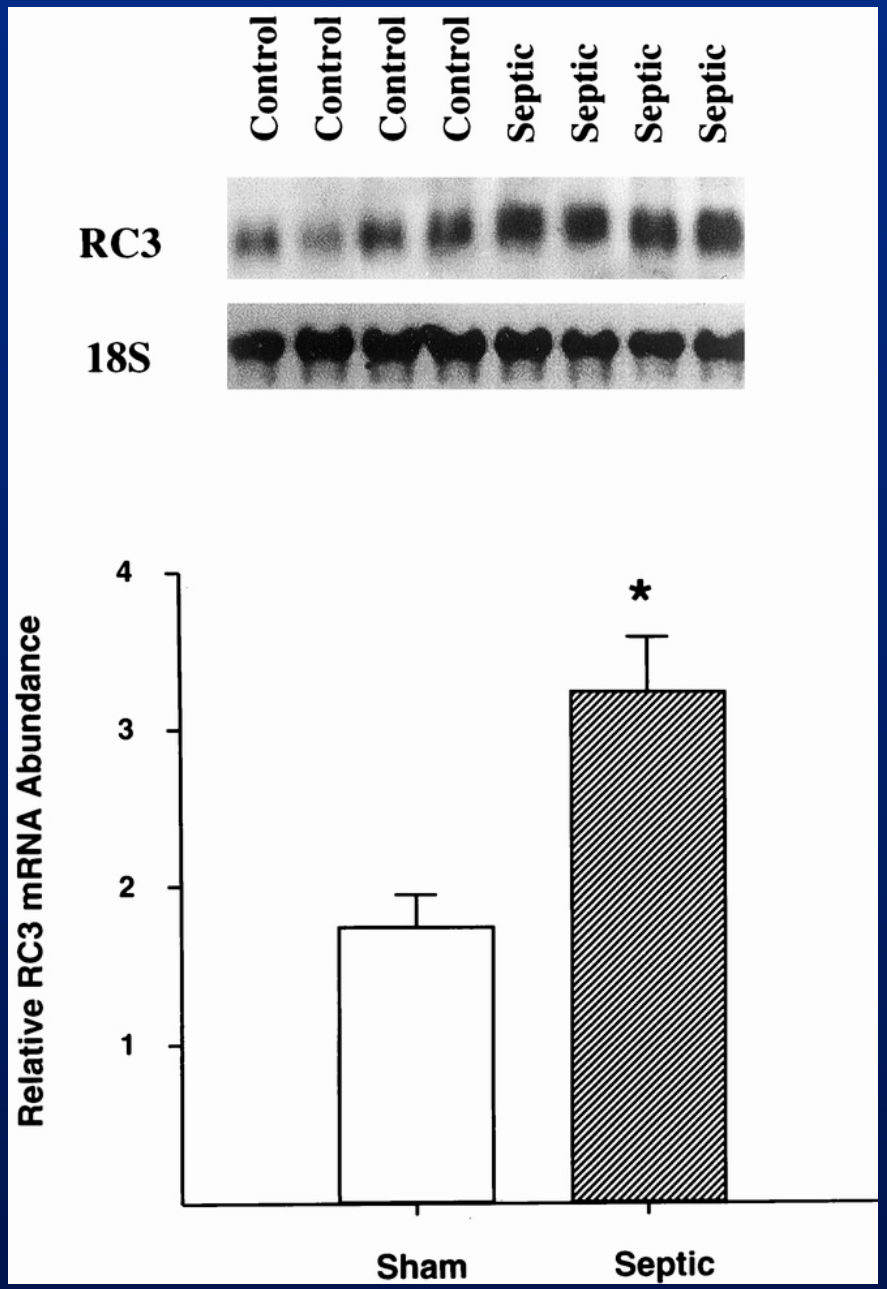
The ubiquitin-proteasome system





Lecker SH et al., 2006

Mitch M et al., 1996



Sepsis → increased gene expression of RC3 in the proteasome subunit ***20S*** in skeletal muscle of rats (Northern blots)

* $P < .05$.

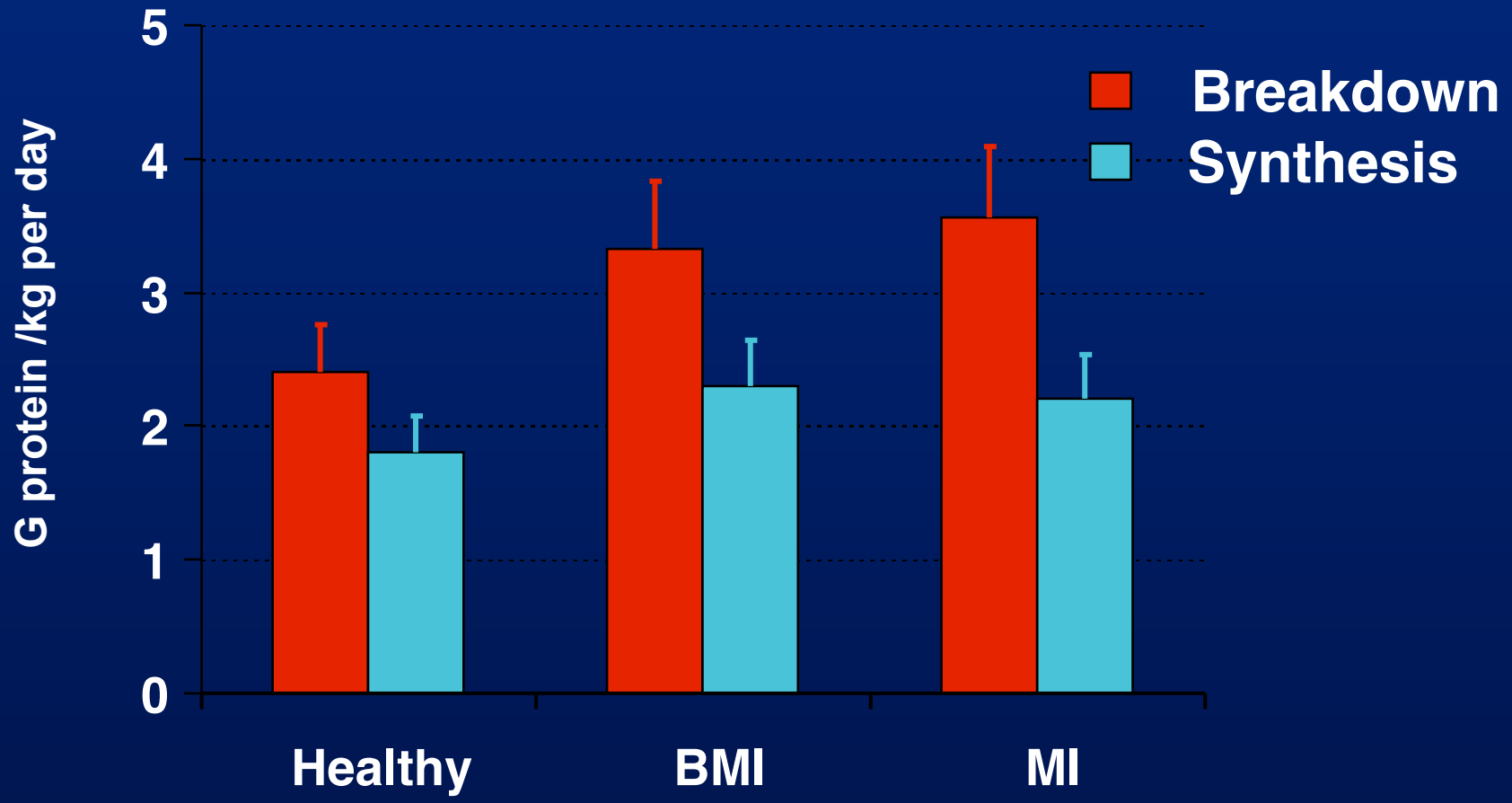
Hobler, Am J Physiol 1999; 277:R434

Weight loss (%)		Protein loss *
5		11.2 - 16.8
10	15.2 - 20.8	
15	19.2 - 24.8	
20	23.0 - 29.0	
25	26.8 - 33.2	

* in vivo neutron analysis. Hill G.L. J Parent Enteral Nutr 16, 197-218, 1992

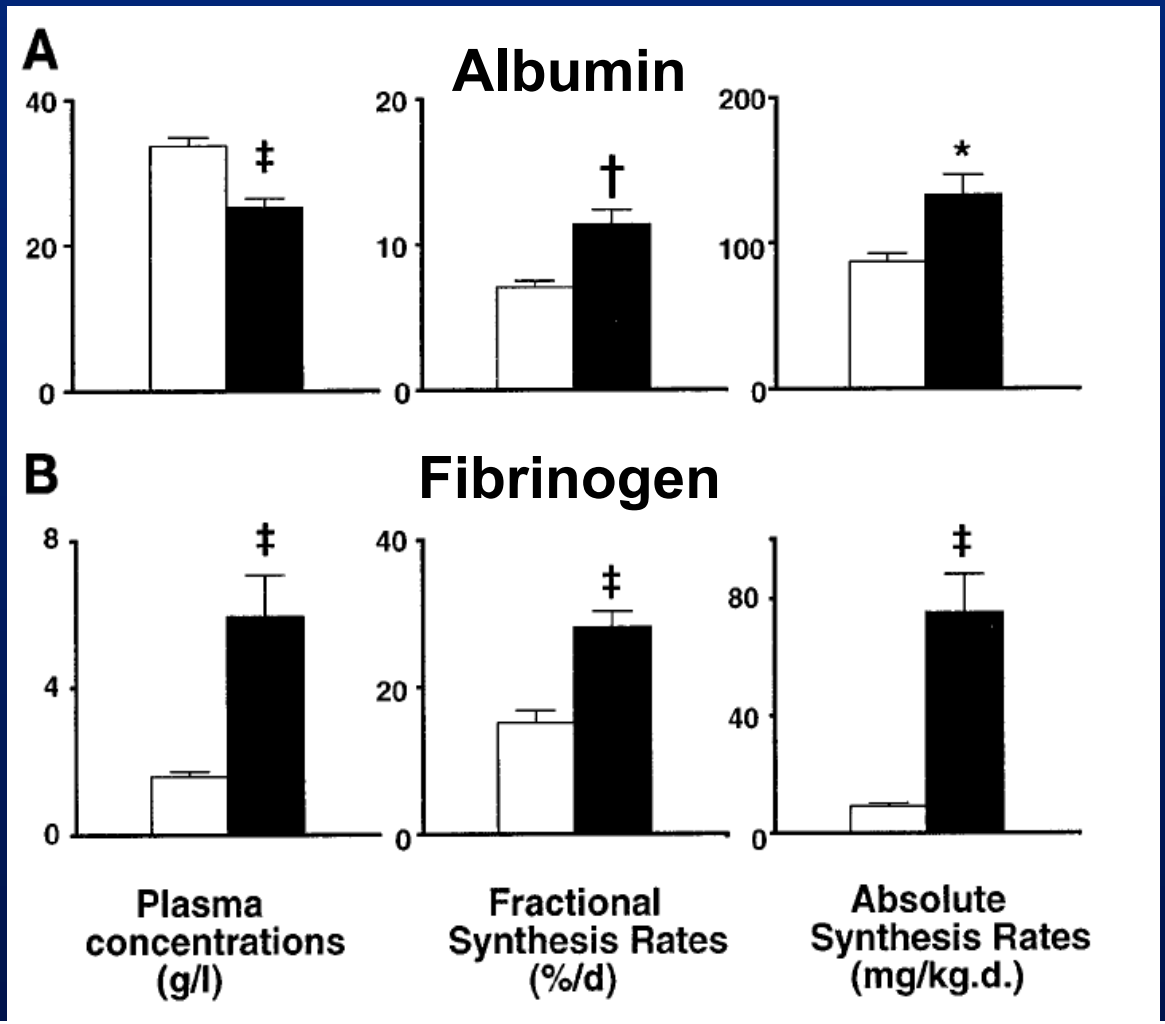
Protein metabolism in trauma patients with or without brain injury

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



Albumin and fibrinogen syntheses increase while muscle protein synthesis decreases in head-injured patients

ODILE MANSOOR,[1,3] MARC CAYOL,[2] PIERRE GACHON,[3] YVES BOIRIE,[3]
PIERRE SCHOEFFLER,[1] CHRISTIANE OBLED,[2] AND BERNARD BEAUFRÈRE[3]

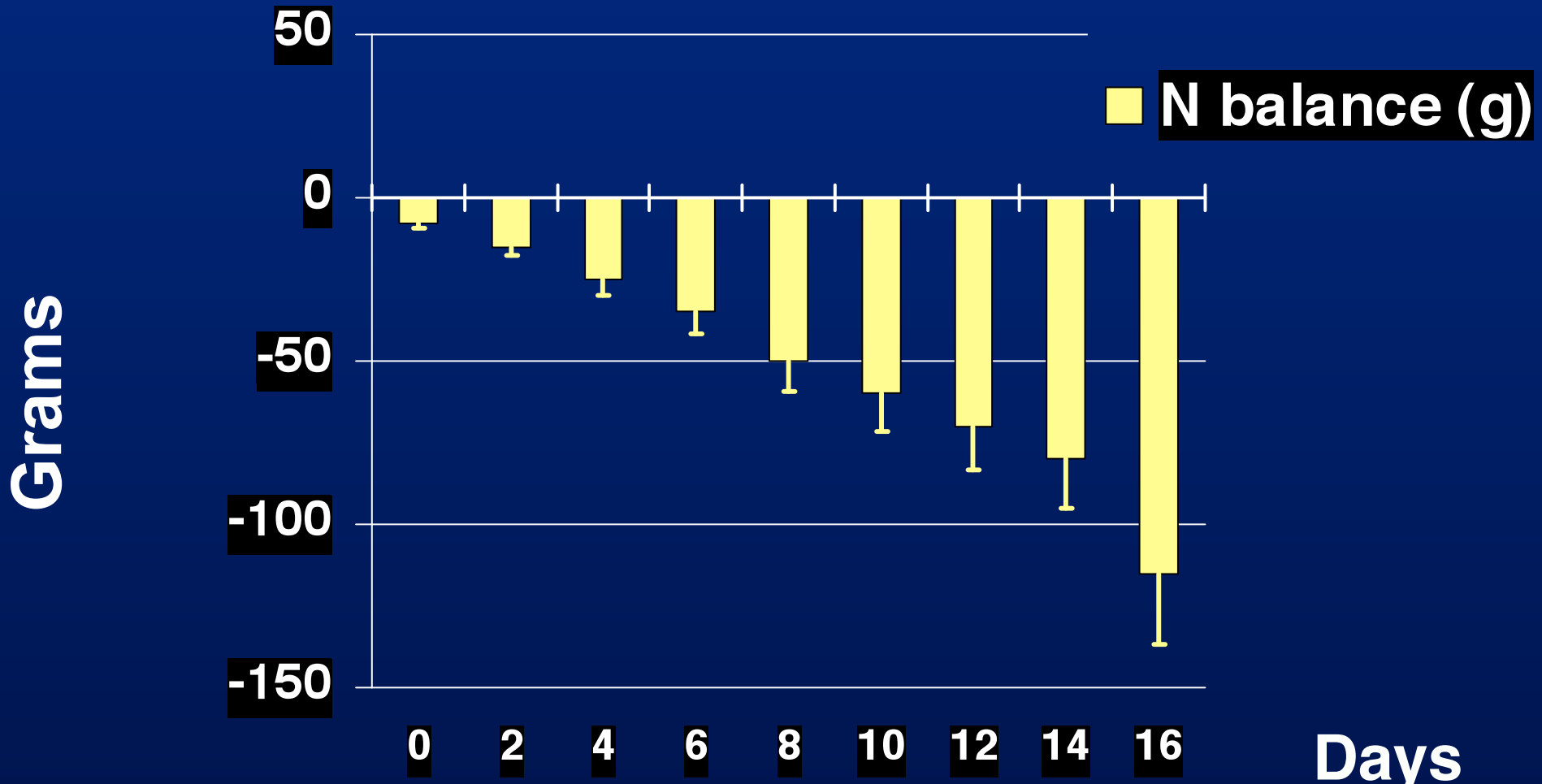


Plasma levels, fractional and absolute synthesis rate of albumin and fibrinogen in brain -injured patients

Am J Physiol 1997; 273: E898

Cumulative N balance in mechanically ventilated patients receiving enteral feeding

Pichard C, Clin Nutr 2000



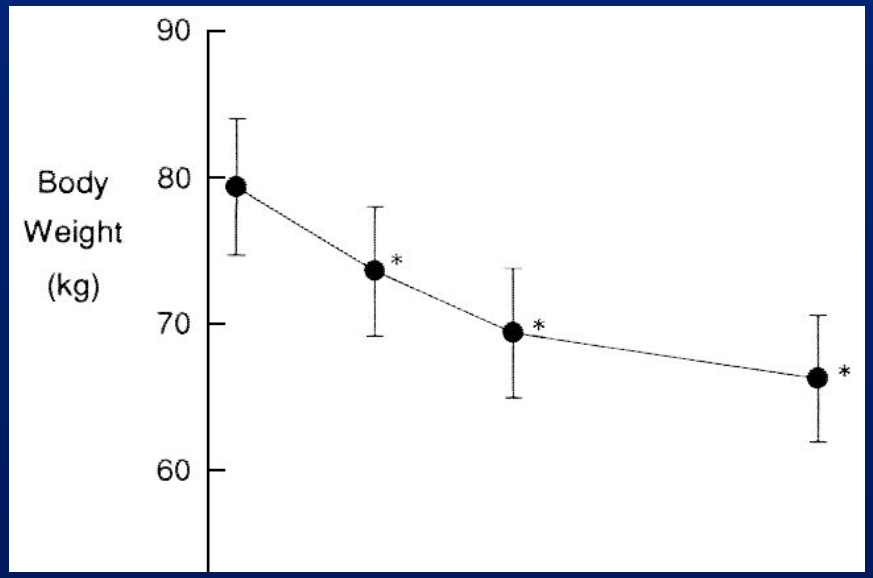
Protein losses during critical illness

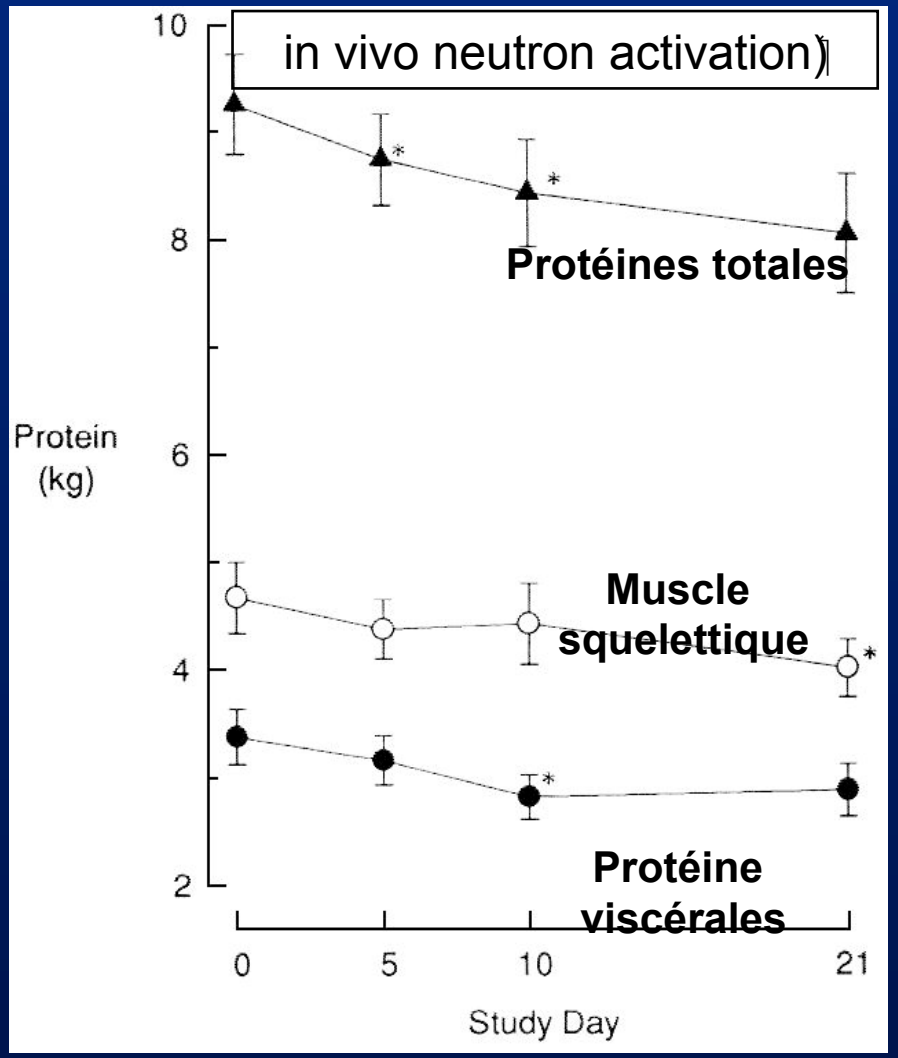
≥ 7 - 14 g nitrogen / d.

≥ 220 - 440 g lean tissue / d

> 80-200 g/d muscular proteins

Composition corporelle chez 12 patients avec péritonite et sepsis sévère recevant une NE hypercalorique

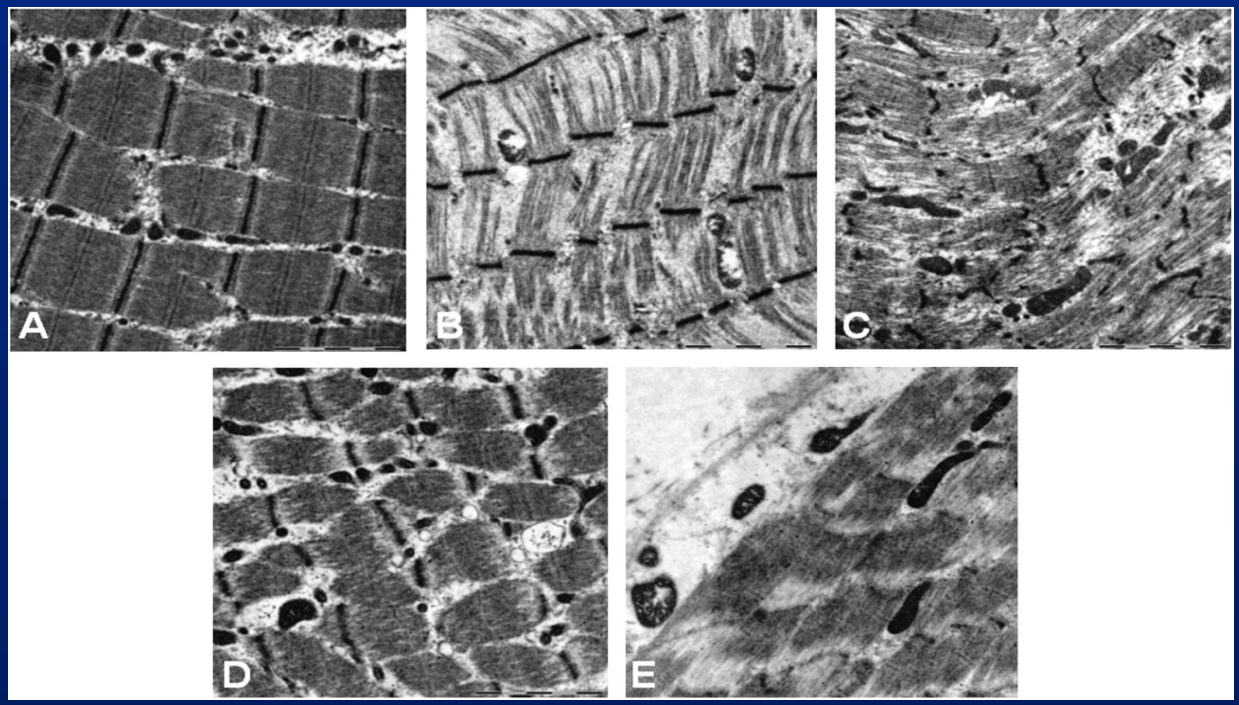




Plank Ann. Surg. 1998; 228: 146

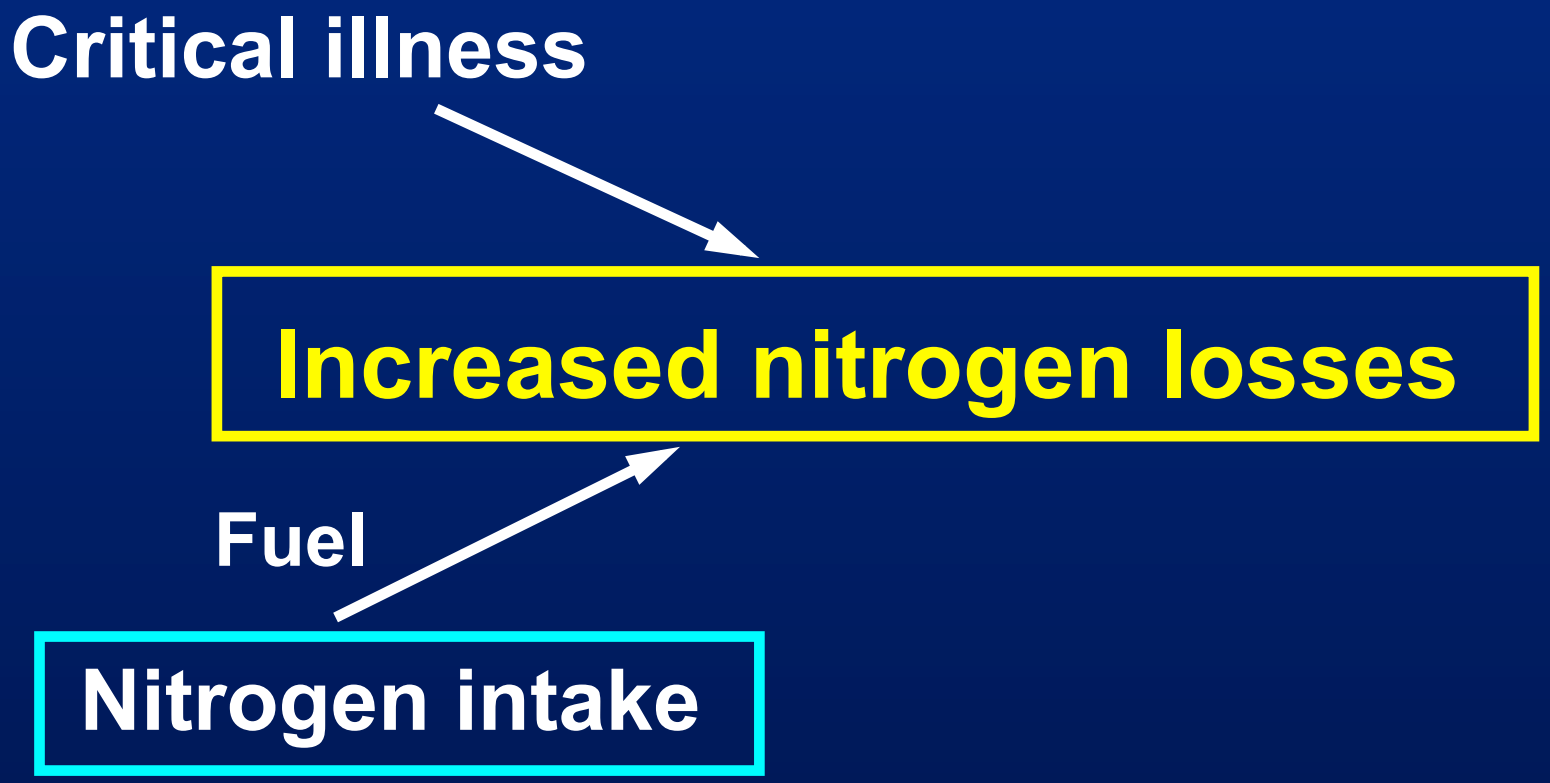
Survival in Critical Illness Is Associated with Early Activation of Mitochondrial Biogenesis

Carré et al AJRCCM 2010;182:745



Ultrastructural features of muscles and their mitochondria. (*A*) Control muscle showing well-aligned sarcomeres with well-defined A, I, and M bands and Z lines. Clusters of dense mitochondria are seen between fibers. (*B* and *C*) Muscle from a sepsis survivor showing focal breakdown of muscle morphology with loss of sarcomere structural integrity and swollen or damaged mitochondria. (*D* and *E*) Muscle from a nonsurvivor showing that mitochondrial changes affect the subsarcolemmal and interfiber regions. *Bar* = 2 μm in all cases

Nitrogen balance in ICU patient

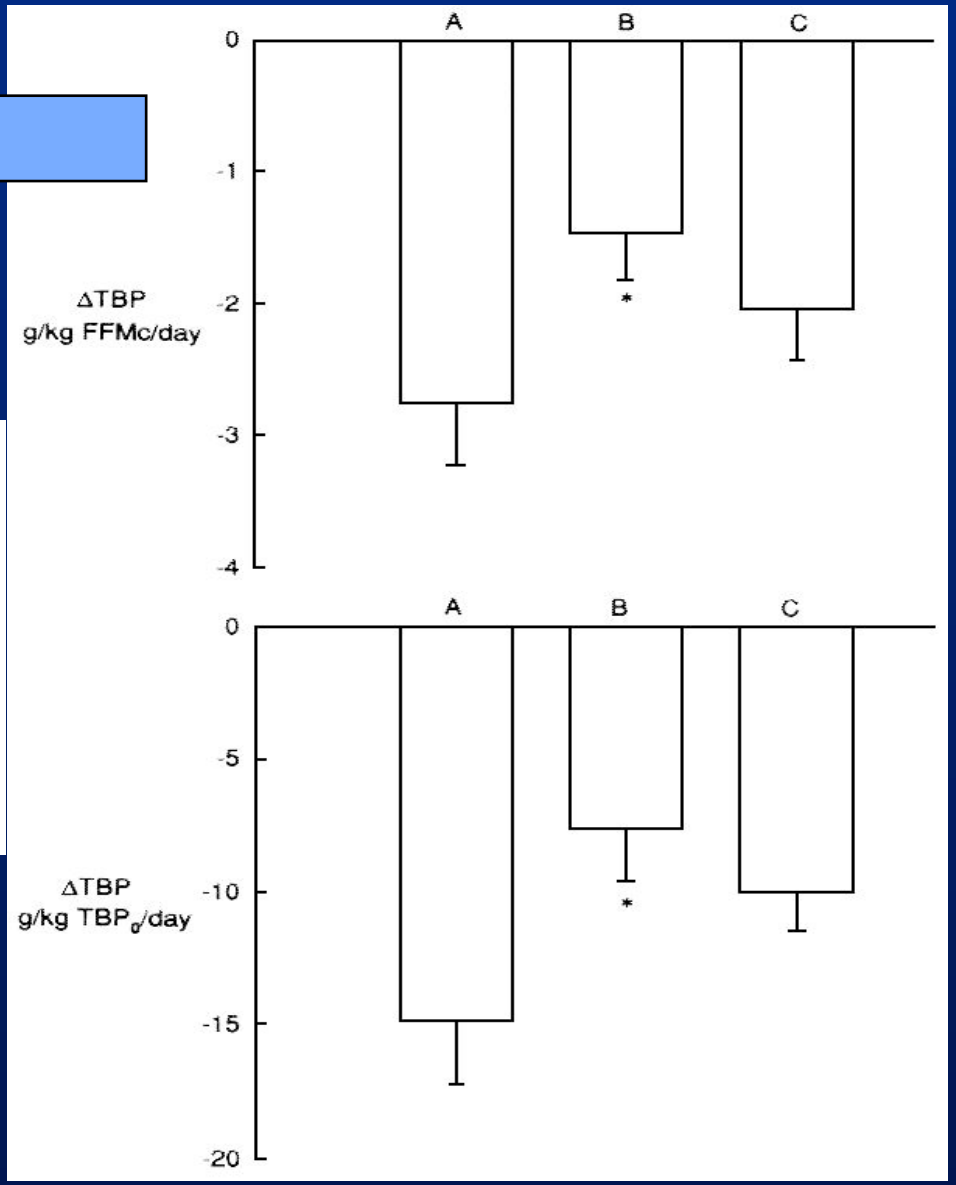


HOW MUCH PROTEINS?

Ishibashi N, et al. Crit Care Med 1998; 26: 1529-35.

Patient Group	Protein (g/kg/day)	Dextrose (kcal/kg/day)	Lipid (kcal/kg/day)	Nonprotein Calorie Intake (kcal/kg/day)
A (n = 7)	1.14 ± 0.13[a,b]	18.3 ± 2.1	8.9 ± 7.9	27.3 ± 8.2
B (n = 8)	1.47 ± 0.11[b]	20.4 ± 1.4[c]	7.0 ± 5.4	27.4 ± 5.4
C (n = 8)	1.86 ± 0.14[b]	24.7 ± 2.3[c]	6.6 ± 3.4	31.3 ± 2.5
p[d]	<.001	<.001	NS	NS

[a]Mean ± SD; [b]$p < .001$ for all pairwise comparisons; [c]$p < .001$ for comparison with group A; [d]analysis of variance.

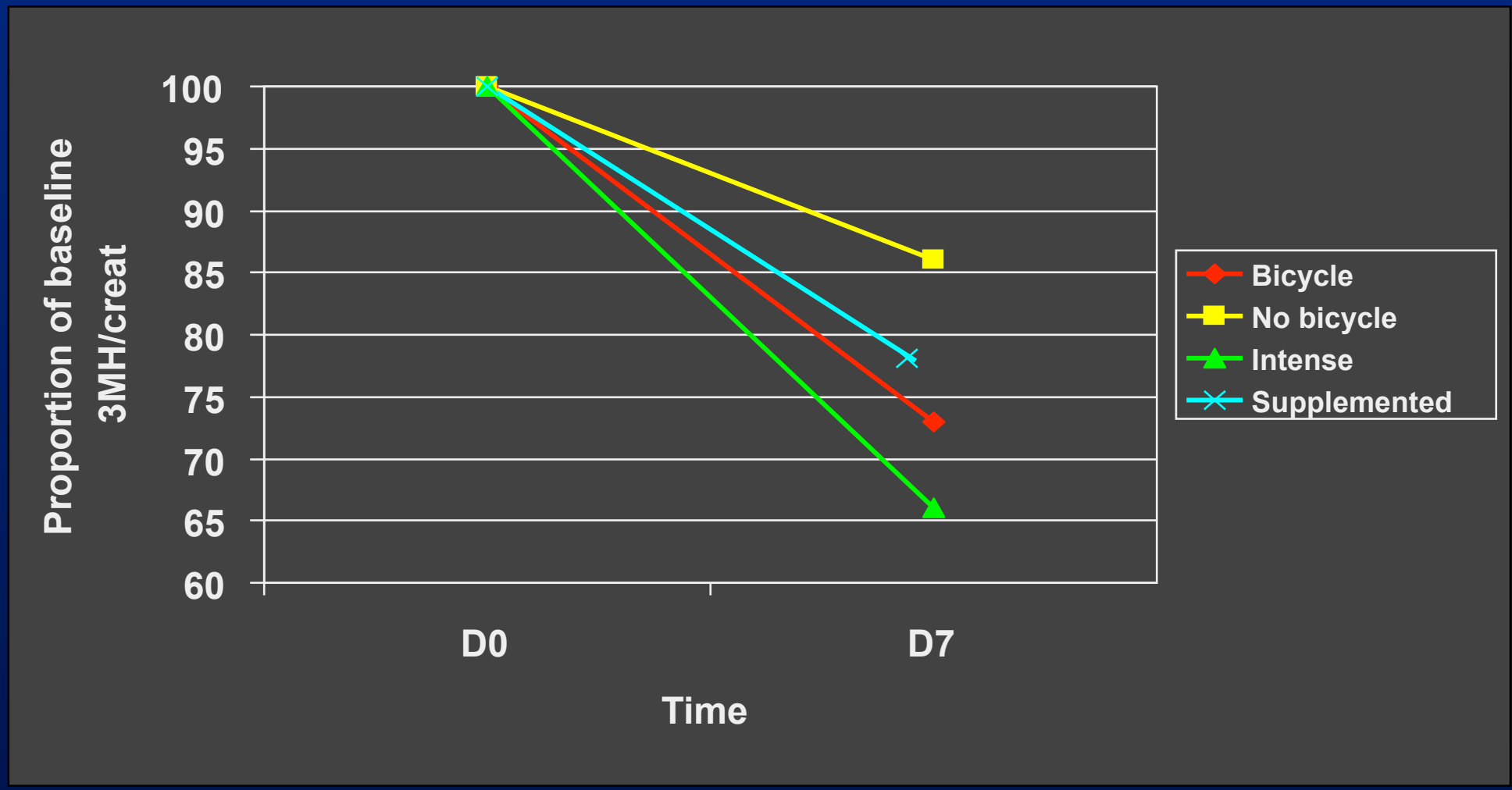


ΔTBP : loss of Total body protein (in vivo neutron Activation)

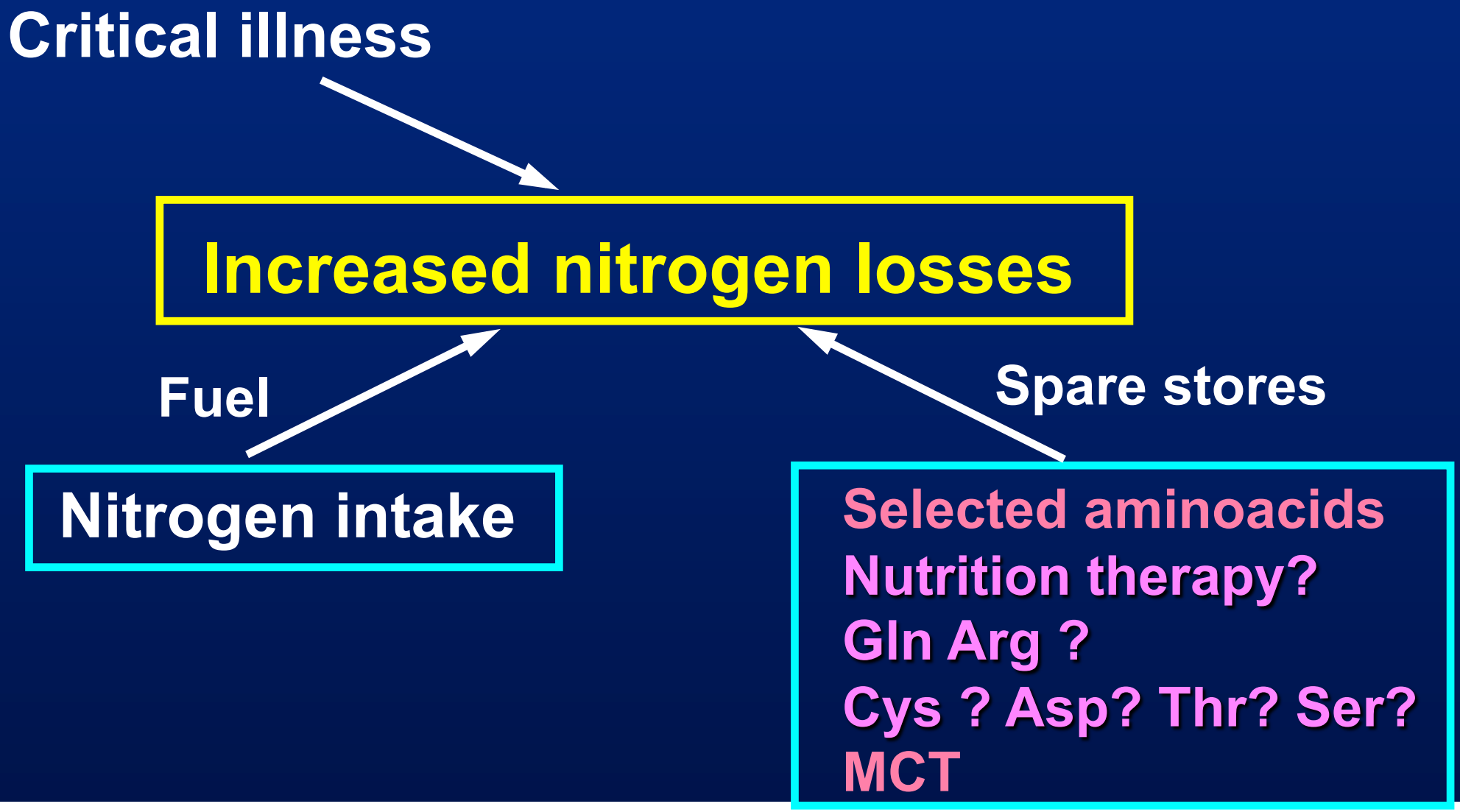
Réduction du catabolisme protéique

De Prato Nutr Clin Metab 2008 (abstract)

Effects of exercise on muscle protein catabolism



Nitrogen balance in ICU patient



TAKE-HOME MESSAGES

- No hyper alimentation
- In the absence of prior severe malnutrition
  - Target on day 3-5 : 20-25 kcal/kg BW /day
  - Anabolic – recovery phase 25-30 kcal/kg BW /day
- Carbohydrate/lipid ratio 60-70/30-40%
- Protein intake 1.2-1.8 g/kg BW /day