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ESPEN LLL Course
Topic 18 - Nutritional Support in Intensive Care Unit Patients

Education and Culture DG
Lifelong Learning Programme

Energy in the ICU

Module 18.1

M. Hiesmayr, MD, MSc

Outline: Energy

- **Energy production in human**
  - - quantitative physiology
  - - regulation & storage
  - - sensing of deprivation

- **Effects of critical illness**
  - •ATP
  - •Mitochondria & respiratory chain:
  - •Substrates

- **Measurement & strategic**
  - •Estimation
  - •Measurement
  - •Kcal & RQ
  - •special conditions: renal replacement, ECMO

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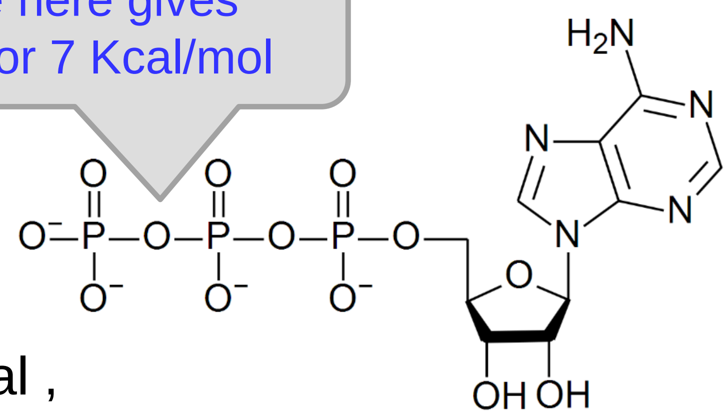
Energy = ATP

- ATP
  - Exclusive form of energy in humans supported by FADH2, NADH & Creatine Phosphate
  - generated from glycolysis, β–oxidation and oxydative phosphorylation
  - All macronutrients (glucose, lipids, amino acids) are possible substrates but also alcohol and some infused substances like lactate, acetate, malate and citrate
  - 1 mol= 507.18 g
- Units
- Joule: 1 Newton. 1 meter
  - Kcal= 4.18 kJ
  - Watt= 1 J/second
    (climbing a stair 200 W = 172 Kcal ,
    at rest 80 W = 70 Kcal)

Cleavage here gives
30 KJ/mol or 7 Kcal/mol



ATP content in ICU patients

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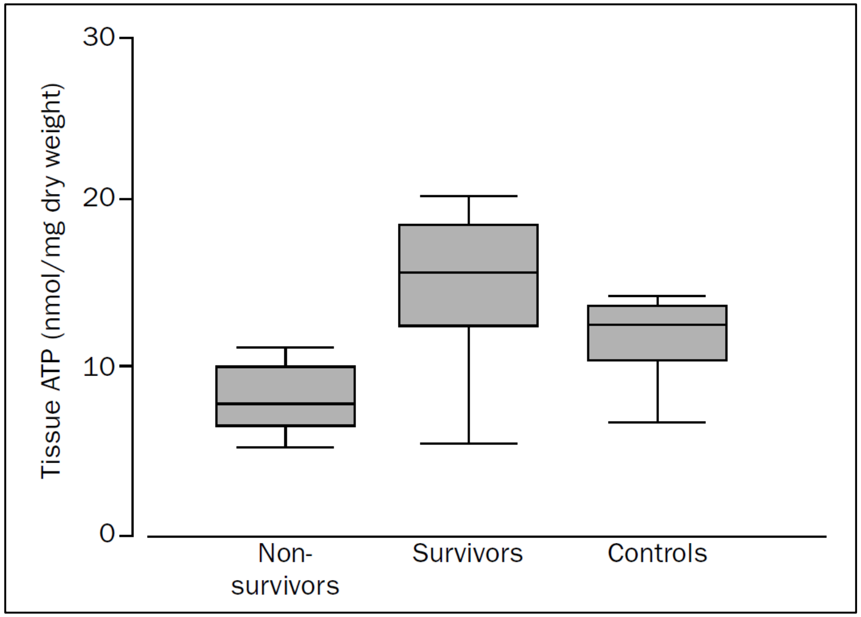
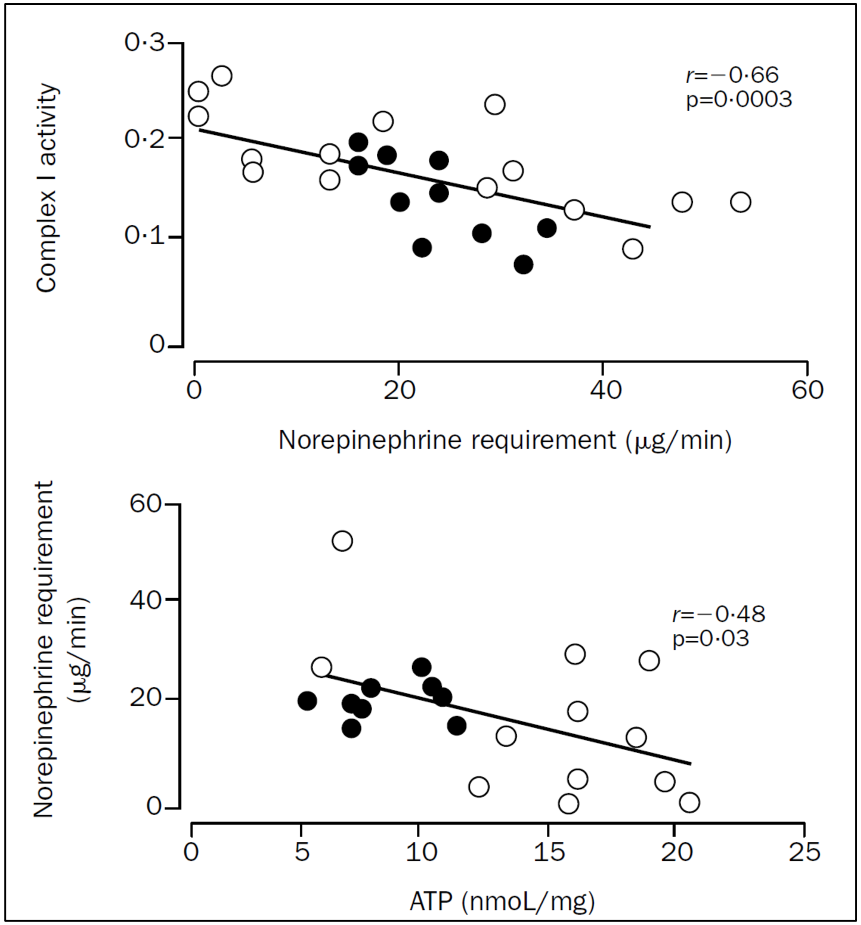
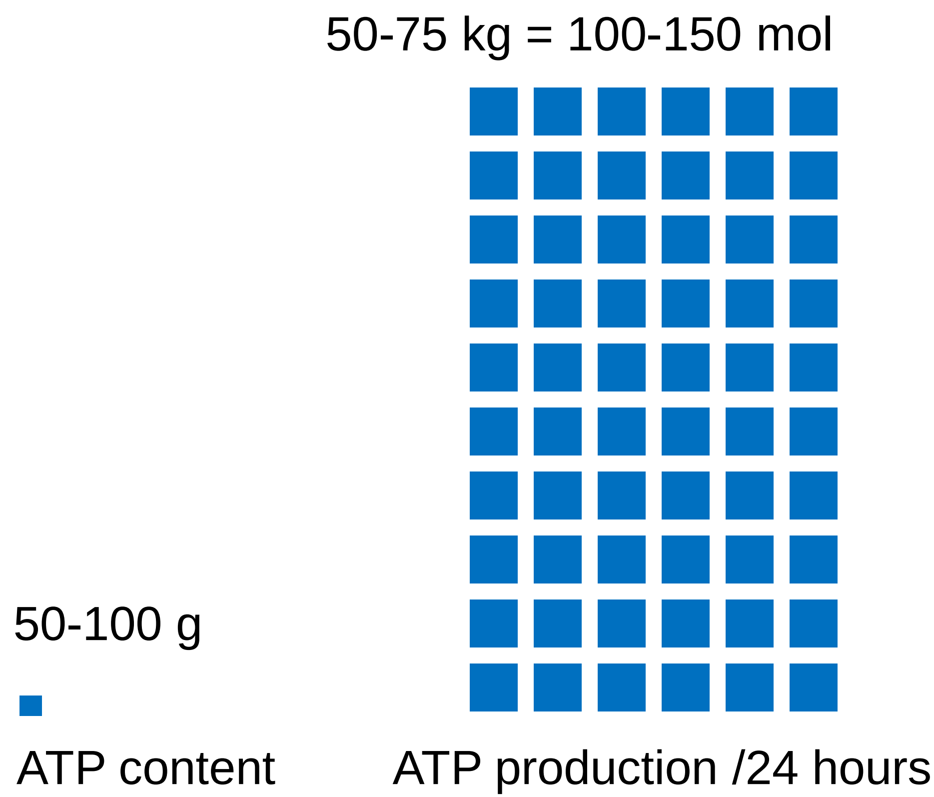




- **correlates with severity (norepinephrine)**

Brealey D et al (M.Singer) Lancet 2002; 360: 219-23

ATP & ADP in adult human



- ATP very fast recycling!
- Any disturbance of oxydative phosphorylation affects cellular energy availability

- ATP: ADP ratio in tissue 200:1 ??

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Relative contribution of processes to whole body energy consumption

• **Protein turnover**	**20-30%**
• Na+/K+ ATPase	20-28%
• **Mitochondrial proton leak**	**20-25%**
• Triacylglycerol turnover	<3%
• Calcium cycling	4-10%
• Gluconeogenesis	5-10%
• Ureagenesis	<3%
• Actinomyosin ATPase	<8%
• **DNA/RNA turnover**	**<2%**
• Substrate cycling	<5%

ICU patients: Flat batteries = **less essential** processes reduced

Rolfe DF, Brown GC. Physiol Rev 1997; 77: 731-58.
Singer M Crit Care 2017; 21 (Suppl 3): 309

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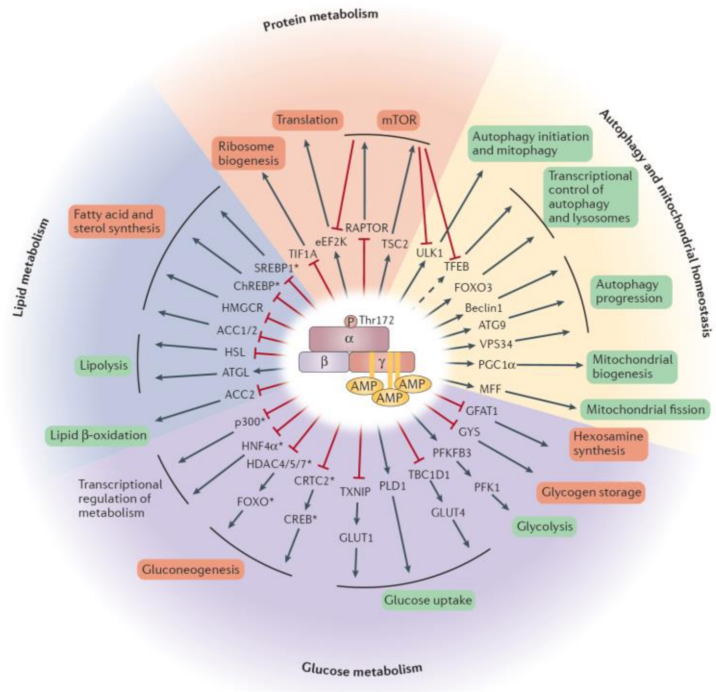
Body sensing & Adaptation

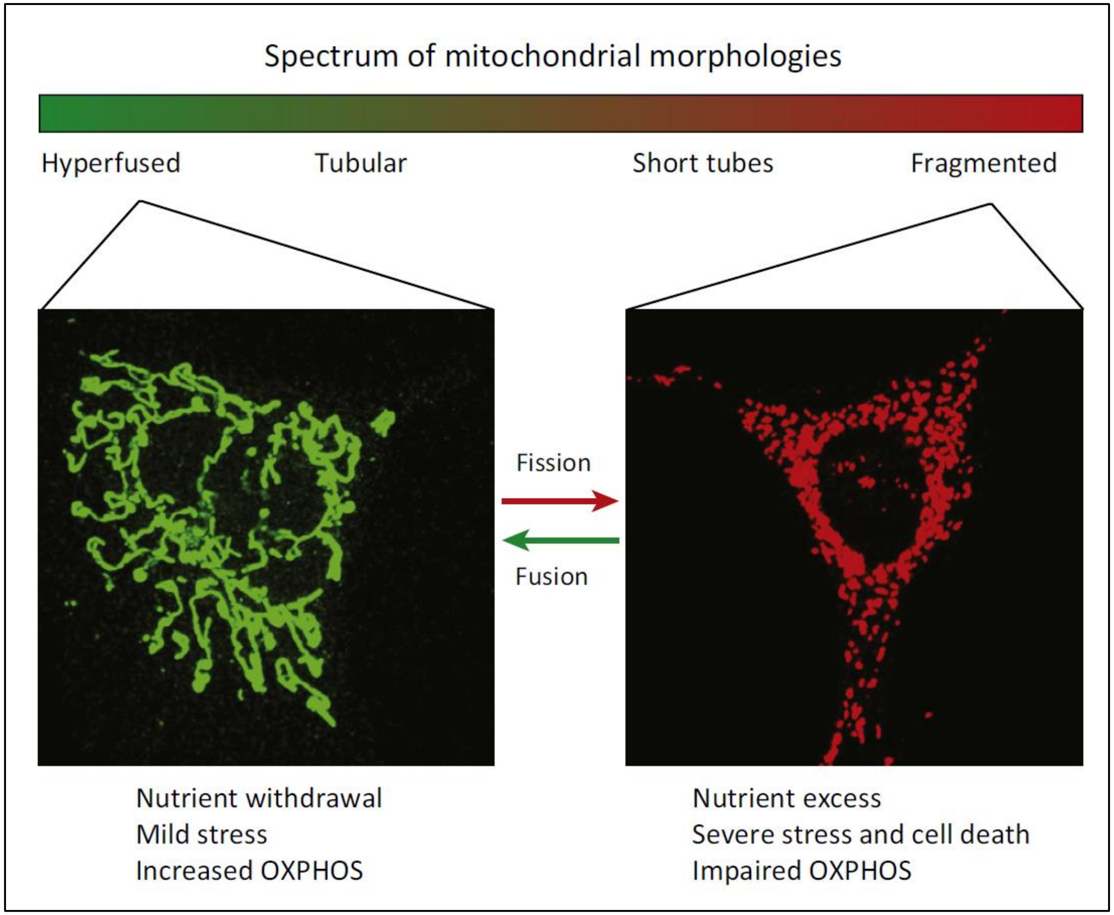
- **Cells are sensing**
  - O_2
  - CO_2
  - H^+ (acidosis)
  - Substrate availability
- **Organs have priorities**
  - Brain: **me first!!**
    - O_2
    - CO_2 removal
    - Glucose 100g/24h
  - Heart
  - Liver
  - GI tract shut down



AMPK: a sensor of ATP deprivation

Herzig & Shaw Nature Reviews: Mol Cell Biol 2018; 19:121

Mitochondria: stress / nutrients & morphology



Wai T , Langer T Trends in Endocrinology and Metabolism 2016; 27:105

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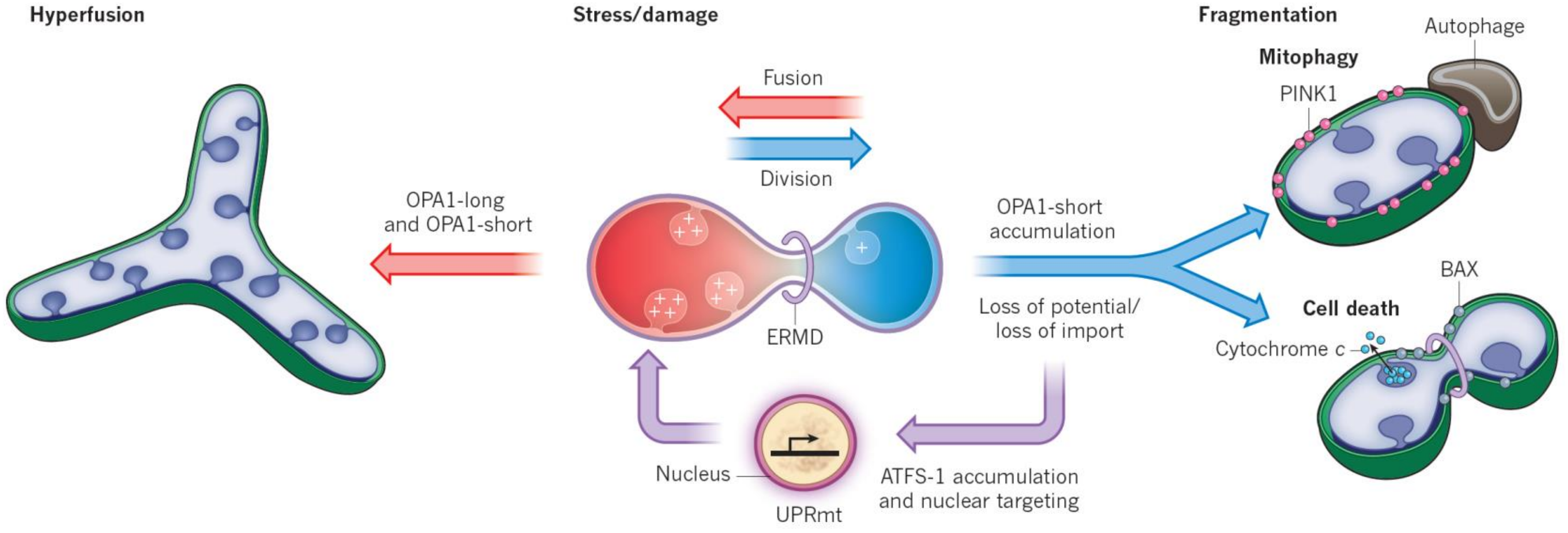
Mitochondria adapt to stress: fusion & fission



- Mitochondria division to recover membrane potential or mitophagy or death

Friedman JR & Nunnari J Nature 2014; 505: 335-343

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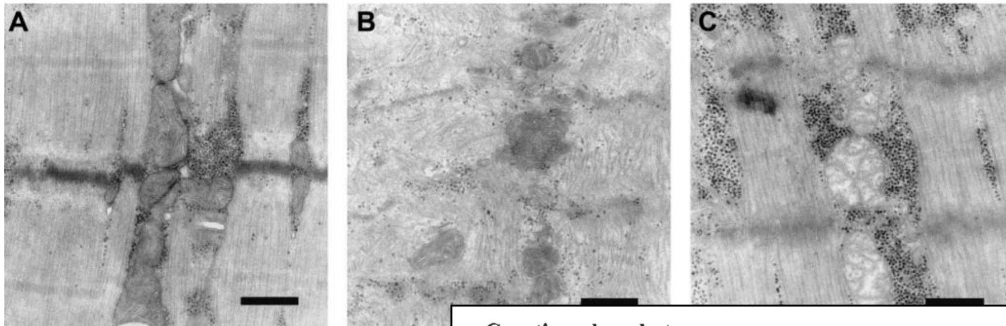
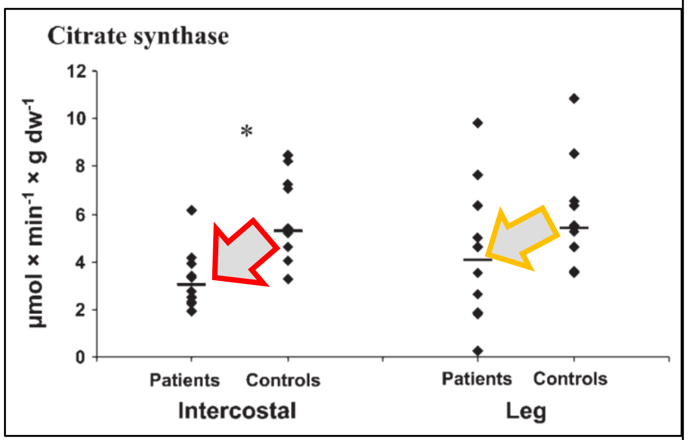
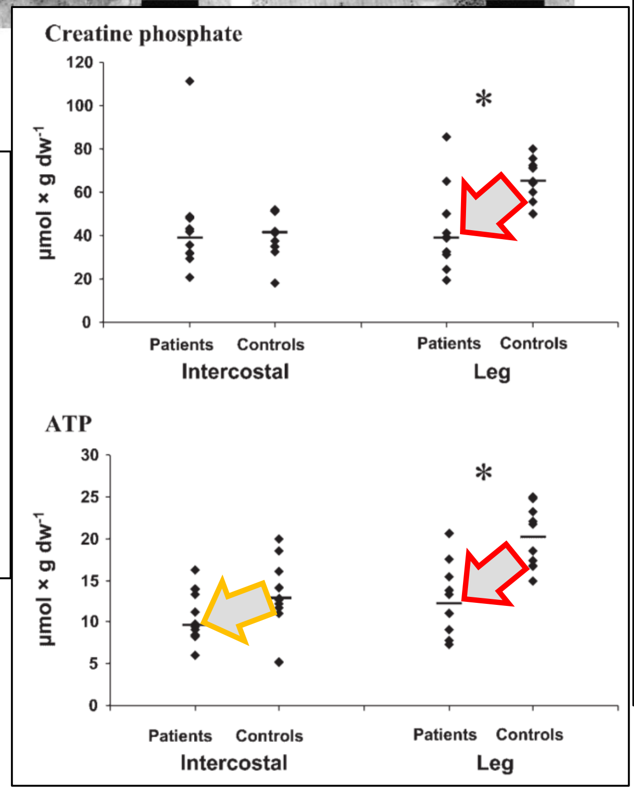
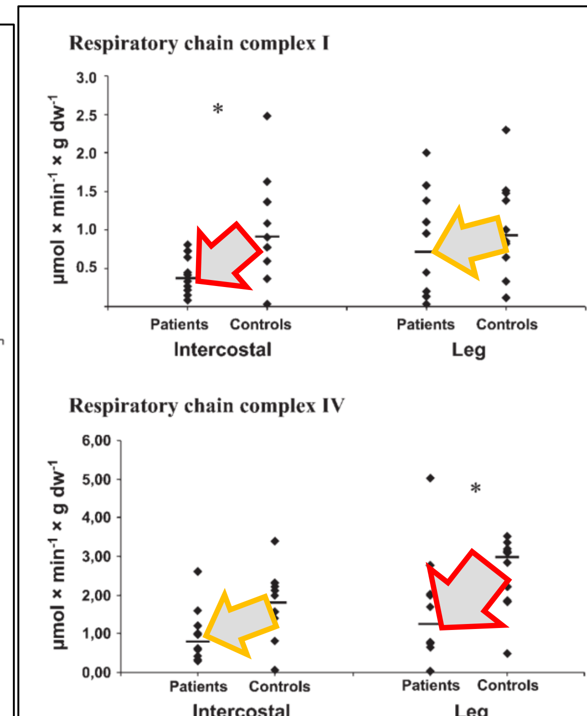
CP – ATP in ICU patients









Hall KD Am J Physiol Endocrinol Metab 2006; 291: E23

Creatine Phosphate – ATP: an dual exercise system

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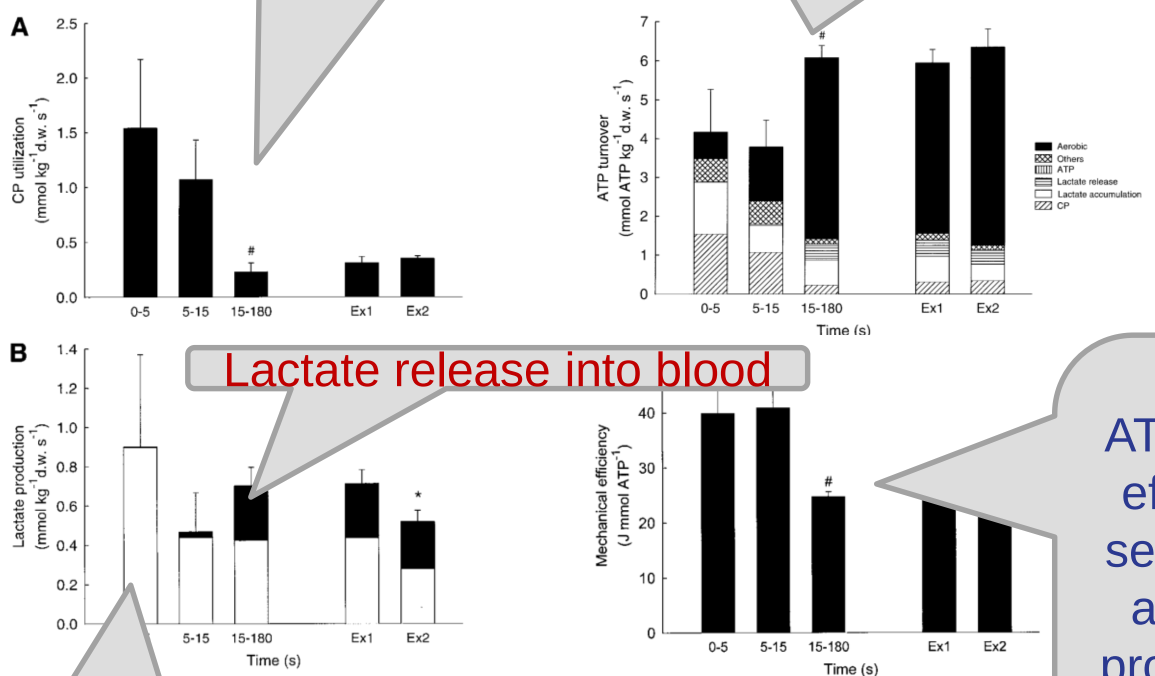
Creatine Phosphate:
A battery for 15 seconds

ATP Production plateau:
After 15 seconds



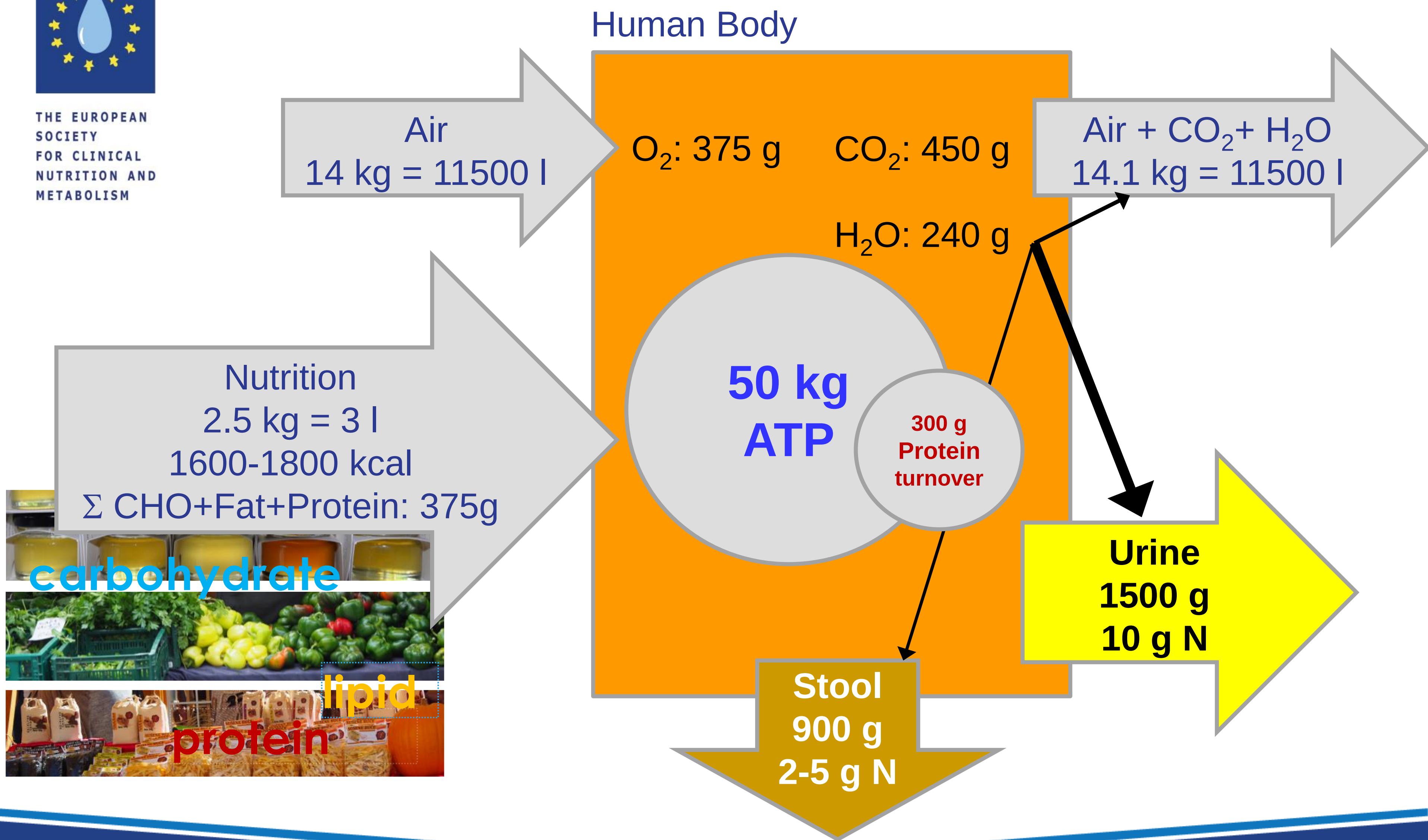
Lactate release into blood

ATP appears less efficient after 15 seconds because another energy provider (CP) was used initially

Lactate in muscle

Bangsbo J et al Am J Physiol Endocrinol Metab 280; E956

Body mass balance



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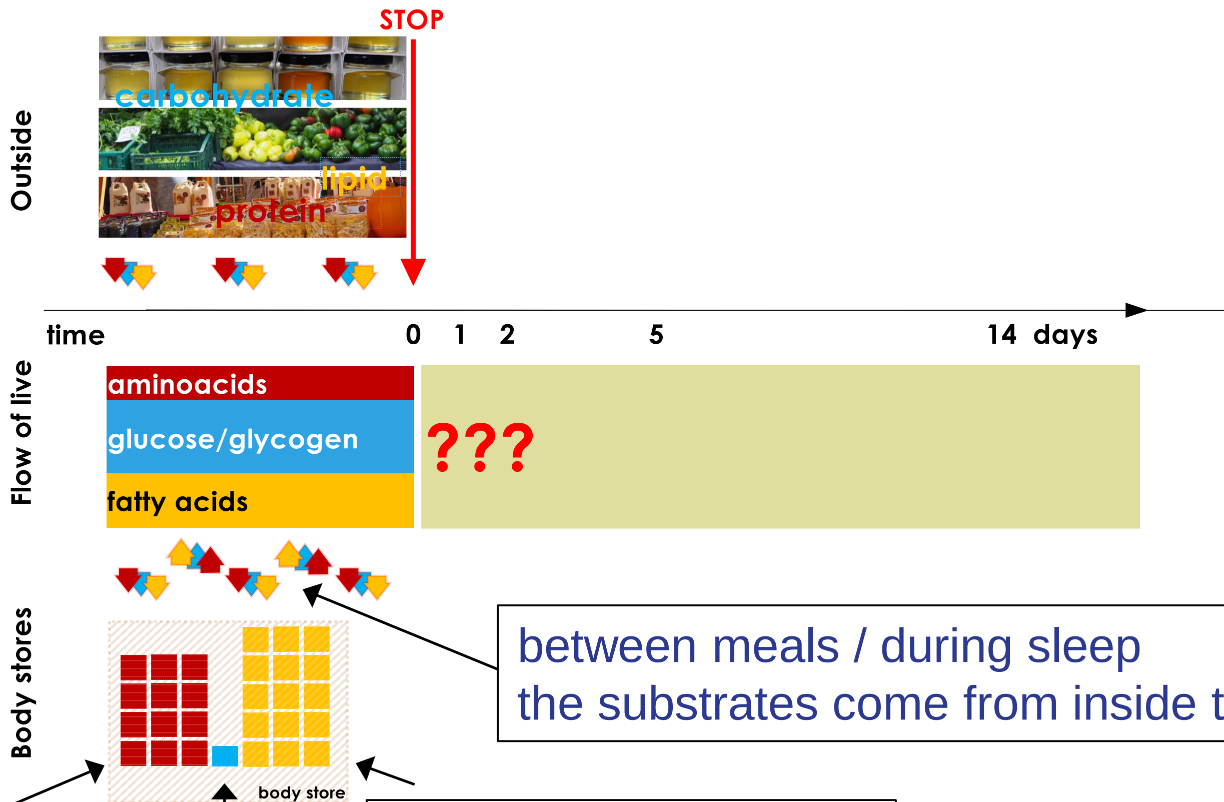
Phase 1: in daily life the body has reserves



= 1 kg

between meals / during sleep
the substrates come from inside the body

Functional protein

Stored & functional fat

Glycogen stores decrease by ≈ 50% within 24 hours without food

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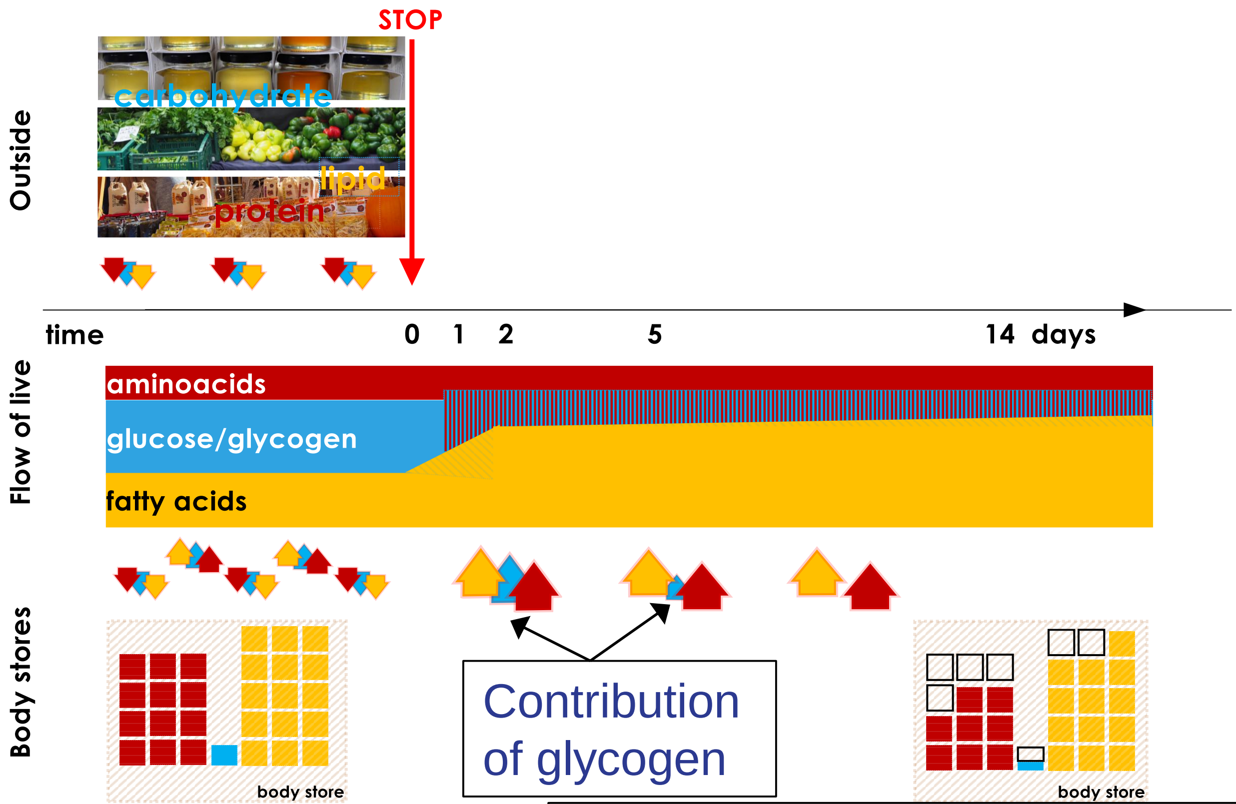
Phase 2: feeding from inside



After 2 weeks without food: Glycogen store empty

- 4 kg functional protein lost
- 2 kg fat lost

Hiesmayr M (2018)

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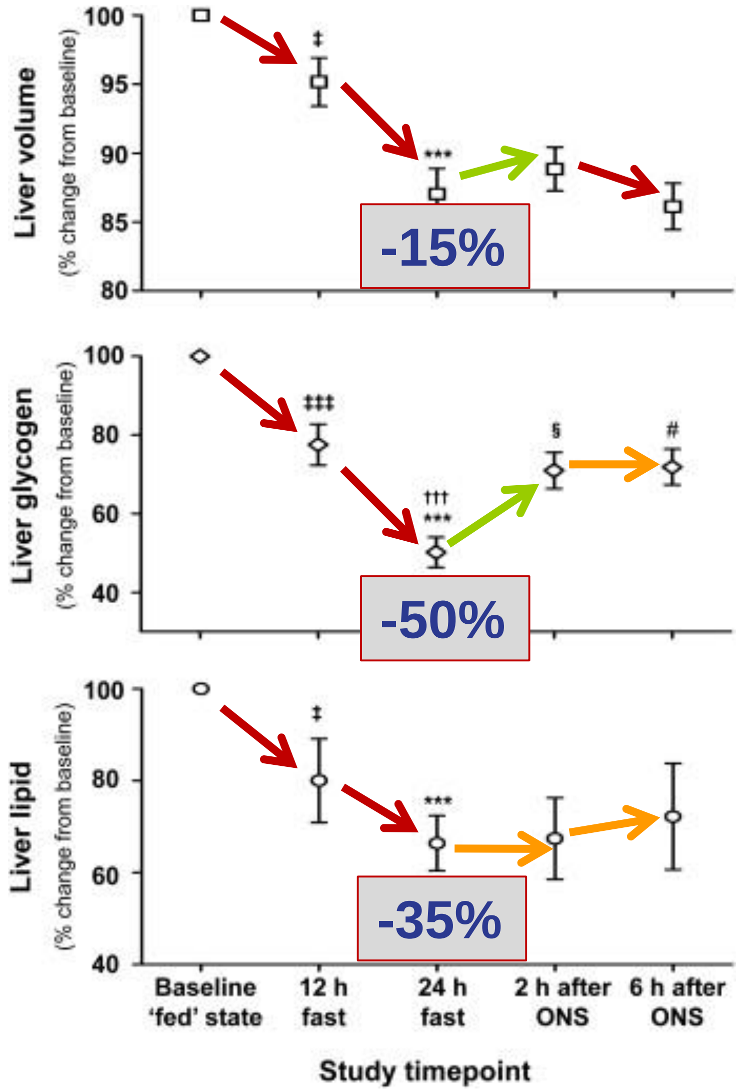
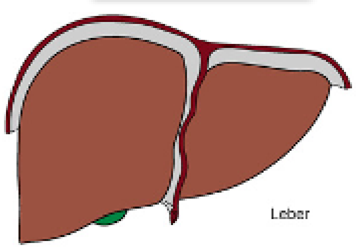
24 h Fasting & Refeeding

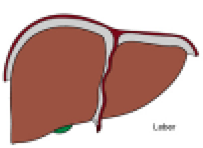
Volume

Glycogen

Lipid







Awad et al Clin Nutr 2010: 29: 538

3 days no nutrition:
induced insulin resistance

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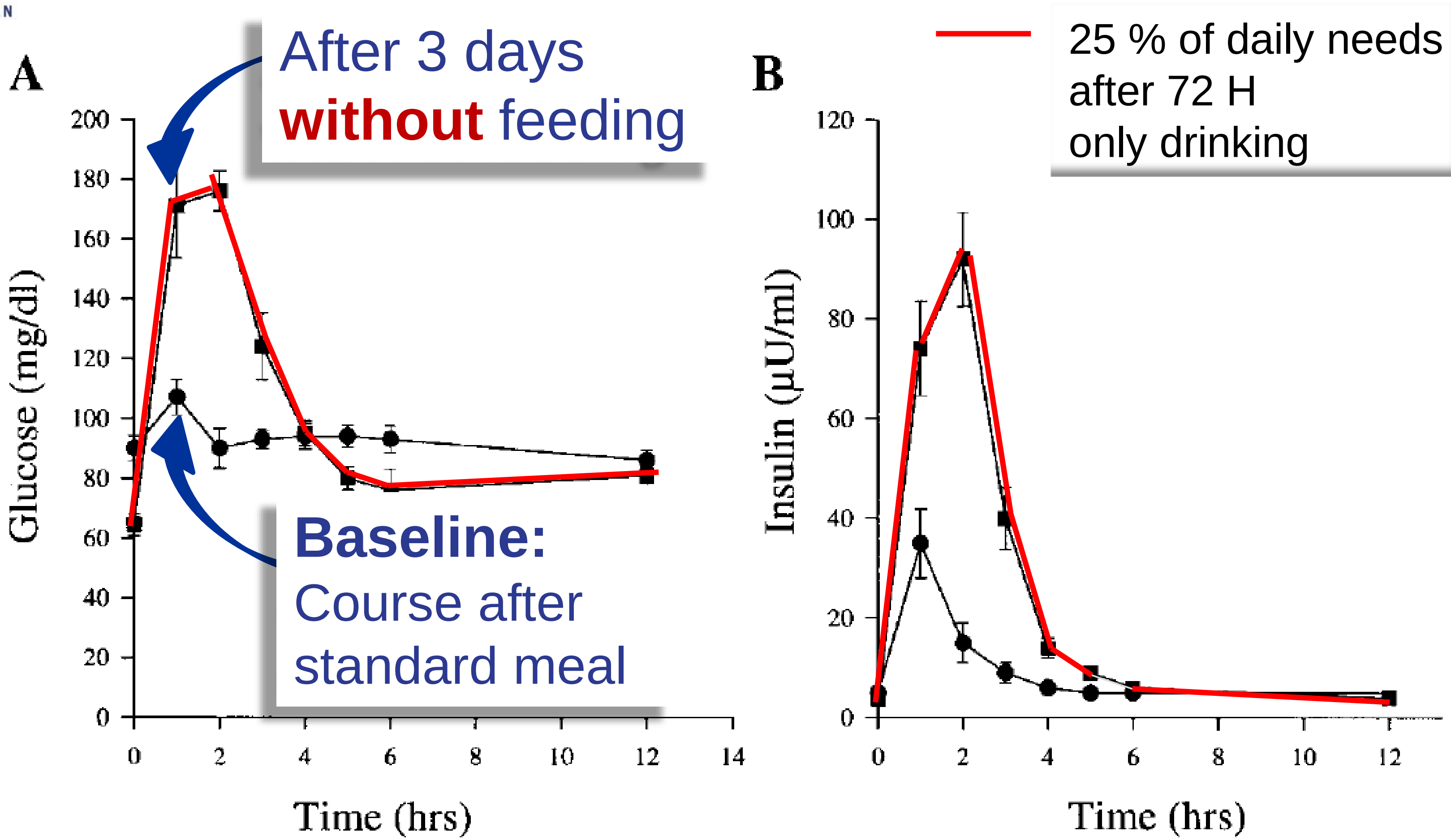

Horton et al. JAP 2001; 90:155-163

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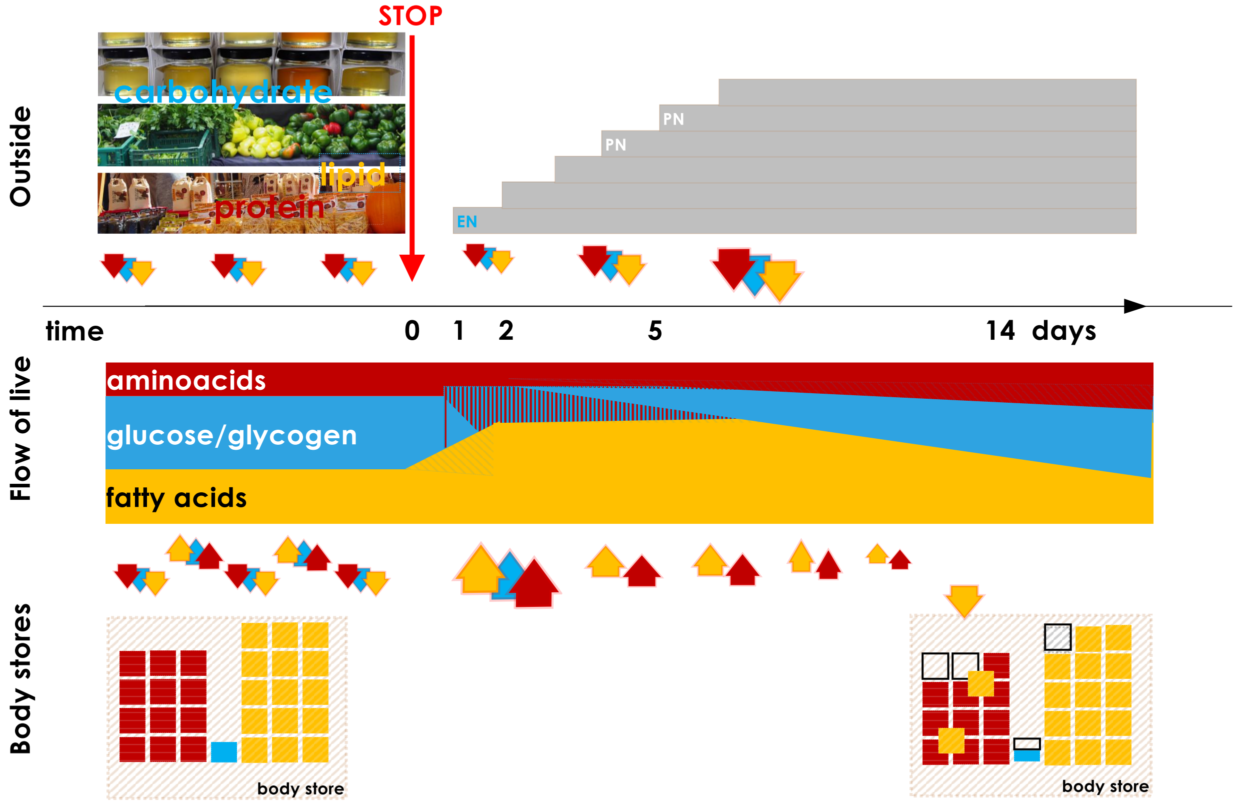
Step 3: ICU adaptive nutrition



With progressive „artificial nutrition“ (EN/PN) the feeding from inside the body program is progressively reduced and body loss is reduced

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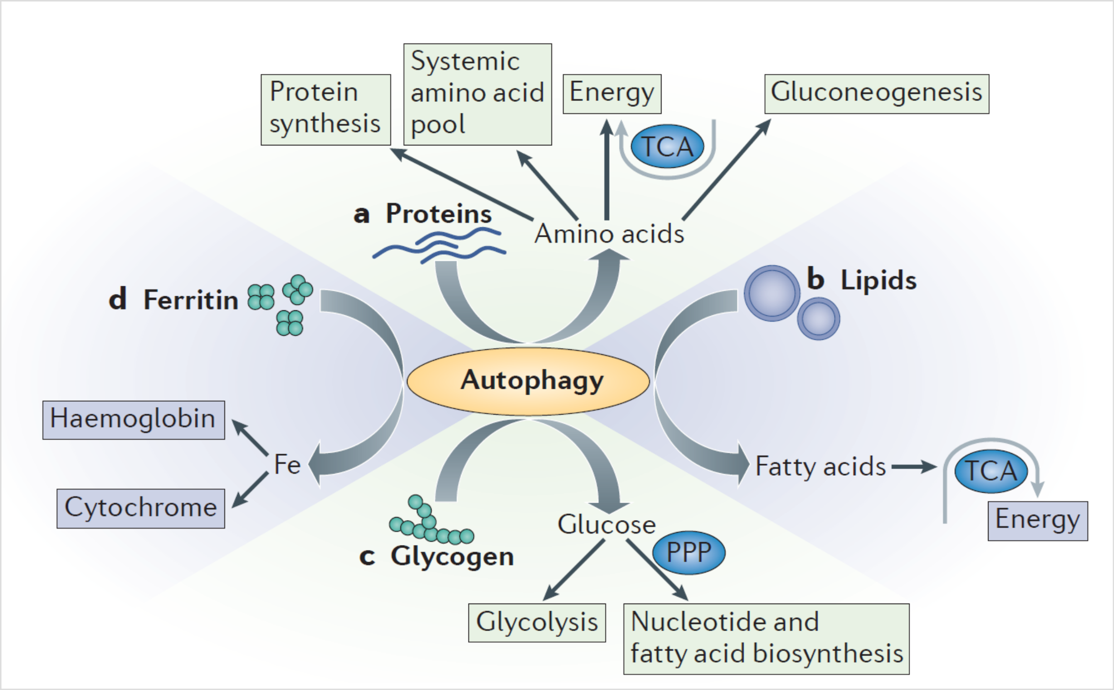
CELL DEATH AND AUTOPHAGY

Autophagy at the crossroads of catabolism and anabolism

Jasvinder Kaur and Jayanta Debnath



NATURE REVIEWS | MOLECULAR CELL BIOLOGY VOLUME 16 | AUGUST 2015

From substrate to energy

- **Glucose (180 g/mole)**
  $C_6H_{12}O_6 + 6\ O_2 = 6\ CO_2 + 6\ H_2O + 4$ kcal/g
  RQ = 6/6 = 1 kcal/O_2= 120
- **Fat (Palmitic acid 256 g/mole)**
  $C_{16}H_{32}O_2 + 23\ O_2 = 16\ CO_2 + 16\ H_2O + 9$ kcal/g
  RQ = 16/23 = 0.7 kcal/O_2= 100
- **Aminoacids (89-204 g/mol Alanin 89 g/mole)**
  $2(C_3H_7O_{2N}) + 6\ O_2 = 5\ CO_2 + 5\ H_2O + CH_4ON_2$ 4 kcal/g
  RQ = 5/6 = 0.83 kcal/O_2= 104

PHA RQ =17/23=0.74 kcal/O_2= 57

- Citrate RQ = 1.33
- Alcohol RQ = 0.67

Formulae in evolution

Harris Benedict 1919	♂: 66.4730 + (13.7516 x W) + (5.0033 x H)-(6.7550 x A) ♀: 655.0955 + (9.5634 x W) +(1.8496 x H)-(4.6756 x A)
Harris Benedict 1984	♂: 88.362 + (13.397 x W) + (4.799 x H)-(5.677 x A) ♀: 447.593 + (9.247 x W) +(3.098 x H)-(4.33 x A)
Faisy-Fagon	(8 x W) + (14 x H) + (32 x Vm) + (94 x T)-4834
Ireton-Jones 1992	1925-(10 x A) + (5 x W) + (281 if ♂) + (292 if trauma present) + (851 if burns present)
Ireton-Jones 1997	1784-(11 x A) + (5 x W) + (244 if ♂) + (239 if trauma present) + (840 if burns present)
Penn State 1998	(1.1 x value of HBE) + (140 x Tmax) + (32 x V_E)-5340
Penn State 2003	(0.85 x value of HBE) + (175 x Tmax) + (33 x V_E)-6433
Penn State 2003b	Mifflin (0.96) + Tmax (167) + Ve (31)-6212 Mifflin: Men: 10(W) + 6.25(H)-5(A) +5
Penn State 2010	Mifflin (0.71) + VE (64) + Tmax (85)-3085 Women: 10(W) + 6.25(H)-5(A)-16
Swinamer	(945 x BSA) – (6.4 x A) + (108x T) + (24.2 x RR) + (817 x V_T)-4349
American College of Chest Physicians (ACCP) recommendation	25 × W – if BMI 16-25 kg/m² use usual body W – if BMI > 25 kg/m² use ideal body W – if BMI < 16 kg/m² use existing body W for the first 7-10days. then use IBW
ESICM '98 statement	Caloric target = caloric need × corrected IBW Formula for calculating IBW ♂: 50 + [0.91x (H-152.4)] ♀: 45.5 + [0.91x (H-152.4)]

Corrected IBW	
If BMI < 18.5	(IBW + actual body W) /2
If BMI 18.5 – 27	IBW
If BMI > 27	IBW x 1.2

Caloric need (kcal/kg/day)	♀	♂
A ≤ 60 years	30	36
A > 60 years	24	30

♂: male; ♀: female; W: weight (kg); H: height (cm); A: age (years); Vm: minute ventilation (L/min); T: body temperature (°C); BSA: body surface area (m²); HBE: Harris Benedict equation; T_{max}: maximum body temperature in the past 24 h (°C); RR: respiratory rate (breaths/min); IBW: ideal body weight (kg); BMI: body mass index (kg/m²); V_E: minute volume (L/min); V_T: tidal volume (L).

Multiple formula cannot overcome the problem that weight in ICU patients does not represent the mix of activity and „shut down“ of organs & tissues

De Waele E et al. Minerva Anestesiologica 2015; 81: 272-82

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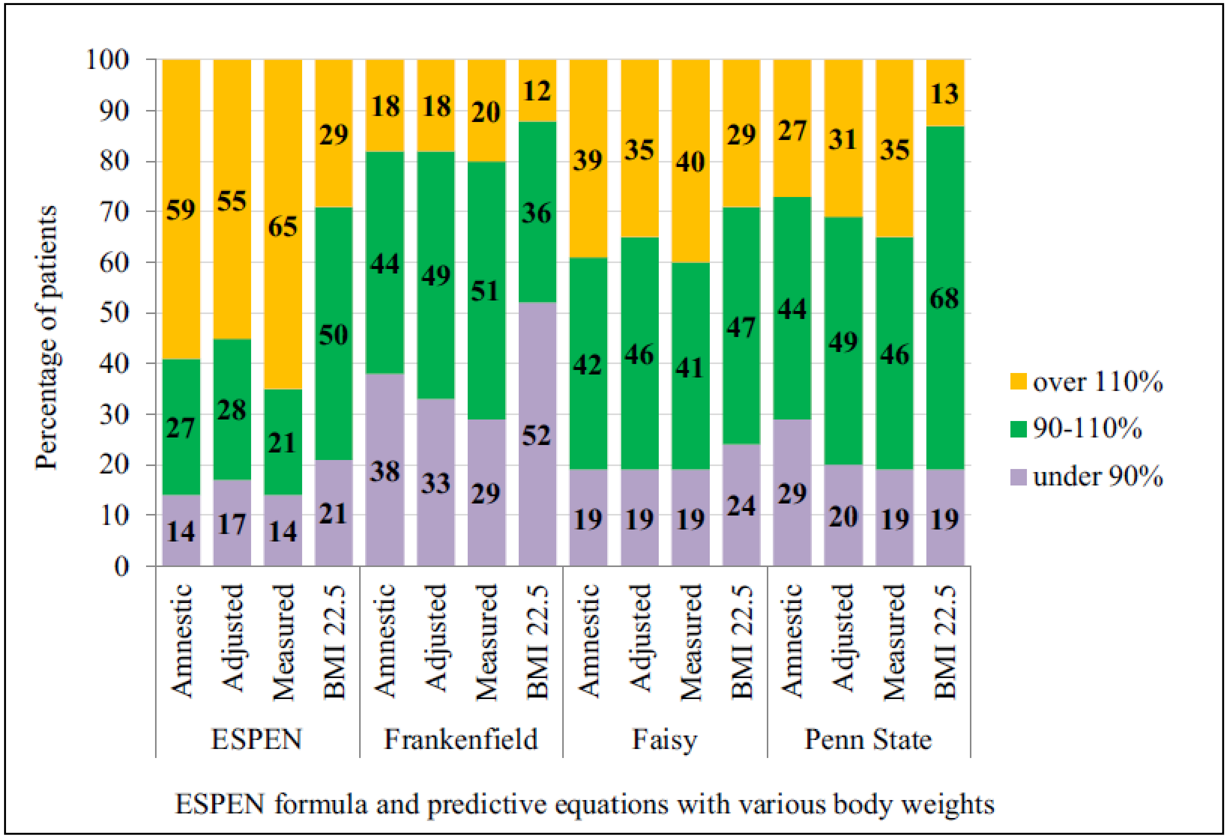
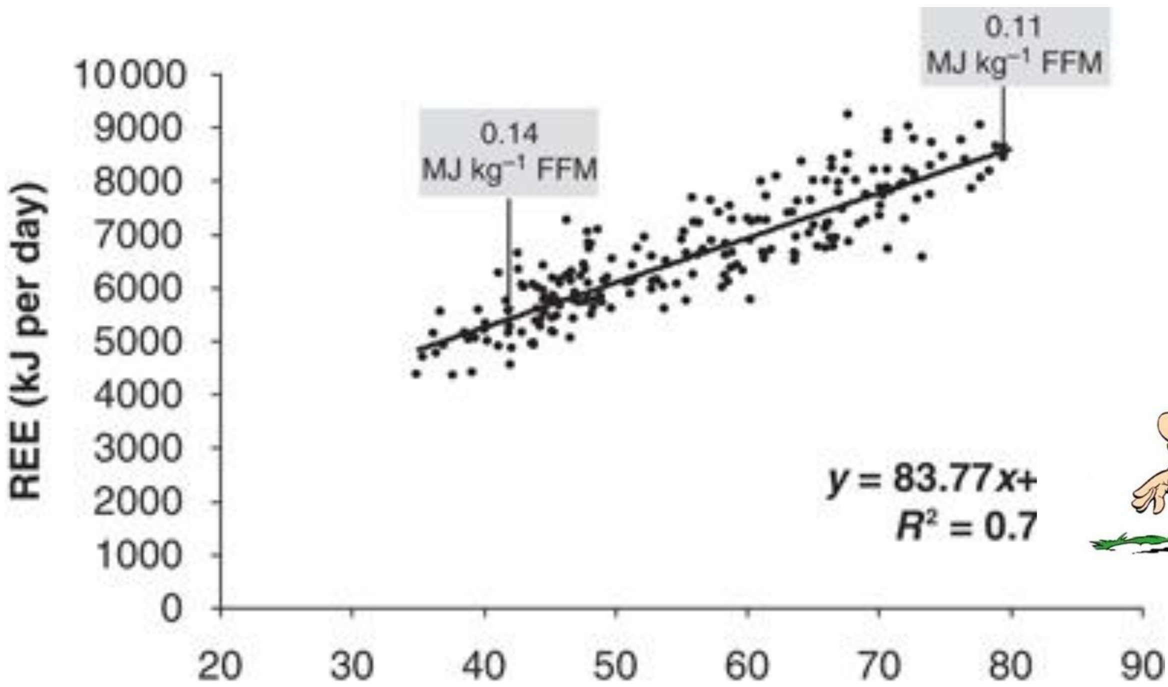
Formula & weight: a trick to be more precise



Whatever „trick“ is applied > 50% of energy estimates are out of range.

Graf S et al. Clin Nutr 2017; 36: 224-28

FFM & REE:



Muscle mass

Organ mass

FFM	30–40 kg	40–50 kg	50–60 kg	60–70 kg	70–80 kg
MM (kg)	16.74	20.83	26.57	31.59	36.05
OM (kg)	2.53	2.82	3.05	3.37	3.64
MM/OM	6.59	7.44	8.09	9.43	9.94

Müller MJ et al. EJCN 2009; 63: 1045-56

How much energy consumes an intact organ?

	organ REE	organ weight
• heart	x 440 (Kcal/kg)	x 0.3 = 150 Kcal
• kidneys	x 440	x 0.3 = 150
• **brain**	**x 240**	**x 1.3 = 330**
• liver+	x 200	x 2.0 = 400
• muscle	x 13	x 20.0 = 300
• rest mass	x 7	x 20.0 = 140
• fat	x 4.5	x 20.0 = 90
• Bones	x 2.0	x 8.0 = 16
		Σ = 1576

5% of body weight

66% of total energy

Leibel et al. Metabolism 1984; 33:164-170 & Wang et al. Am J Physiol Endocrinol Metab 2000; 279: E539-E545

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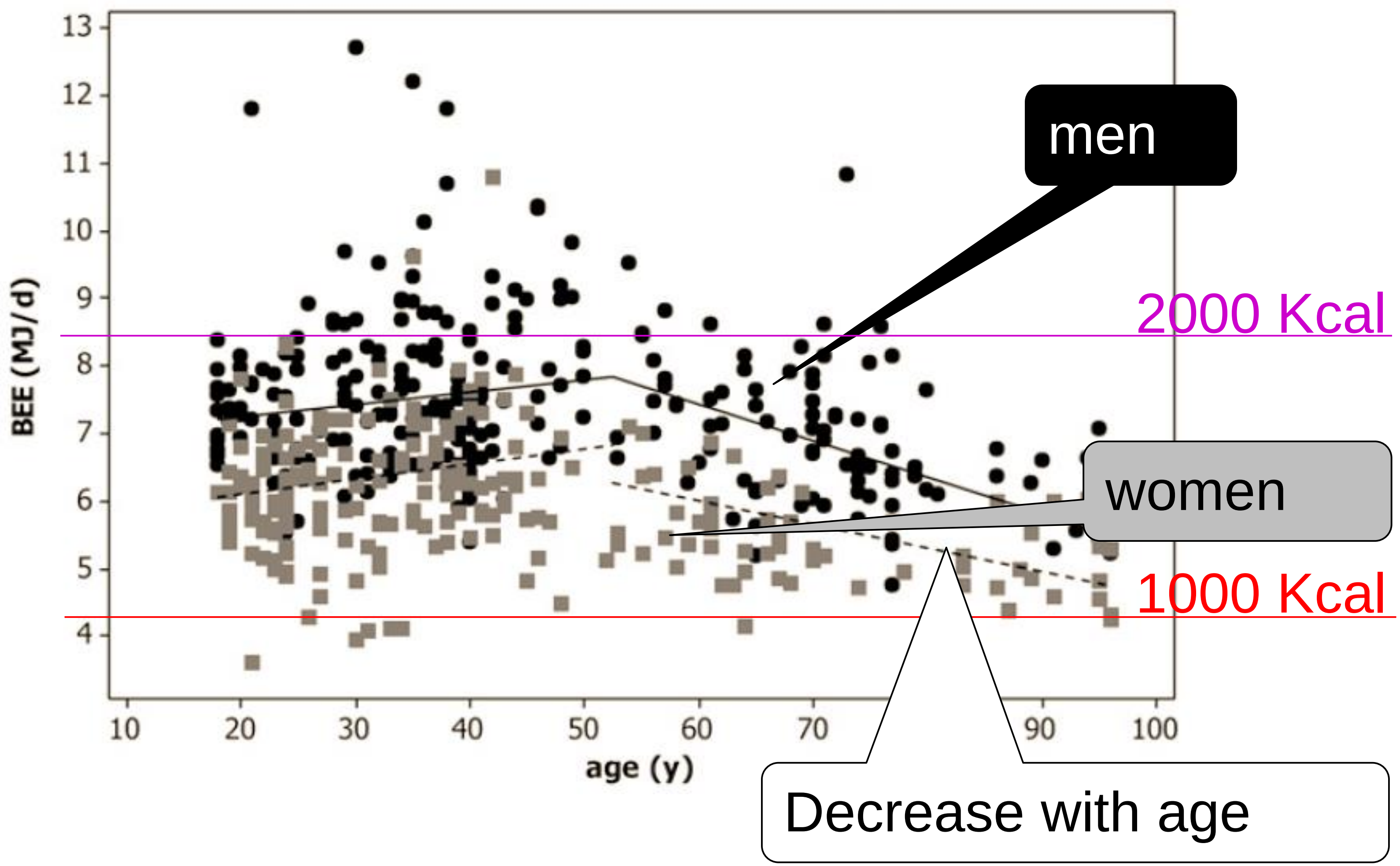
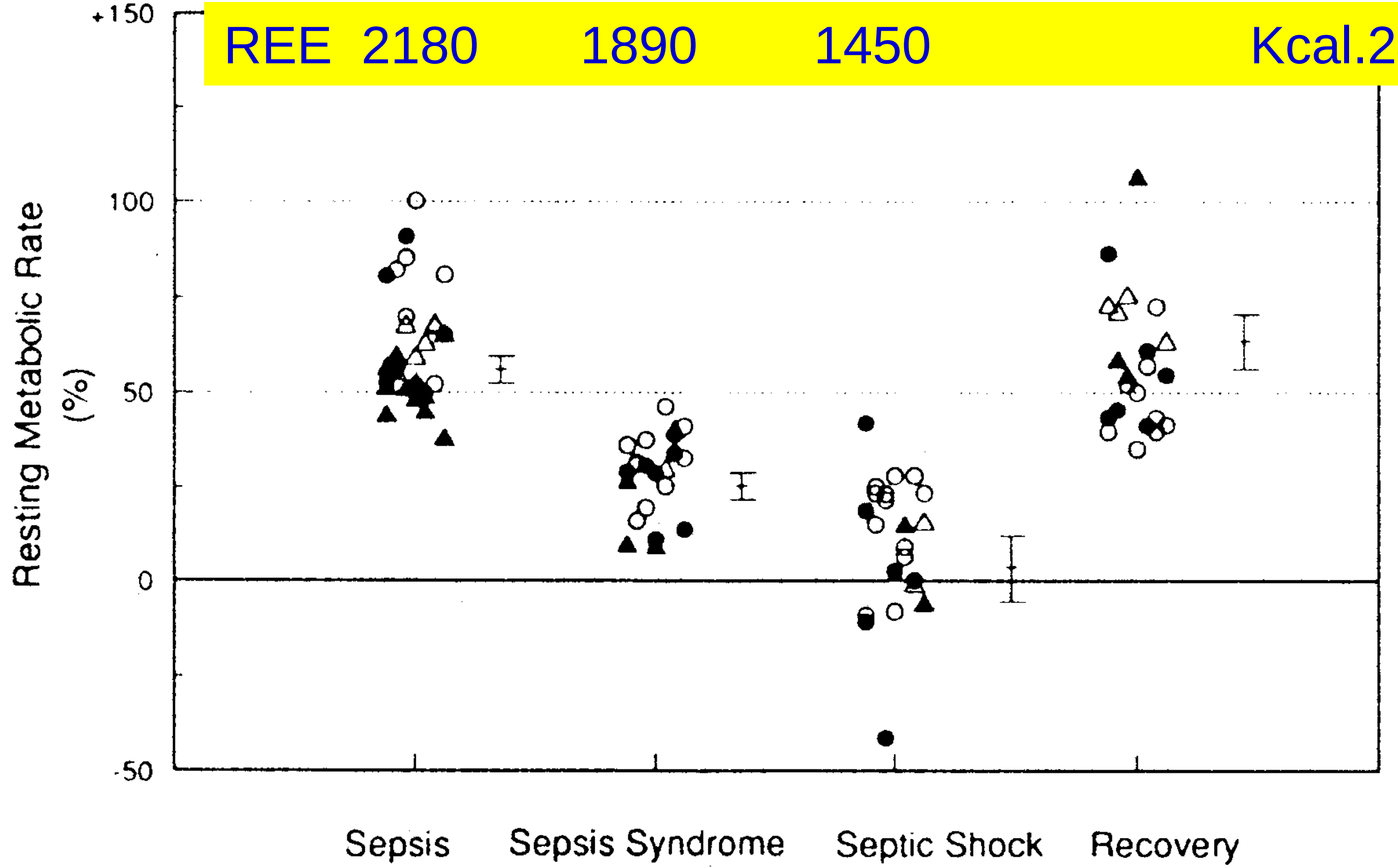
Basal energy use versus age & gender



Speakman & Westerterp, Am J Clin Nutr 2010; 92: 826-834

Metabolic rate in sepsis

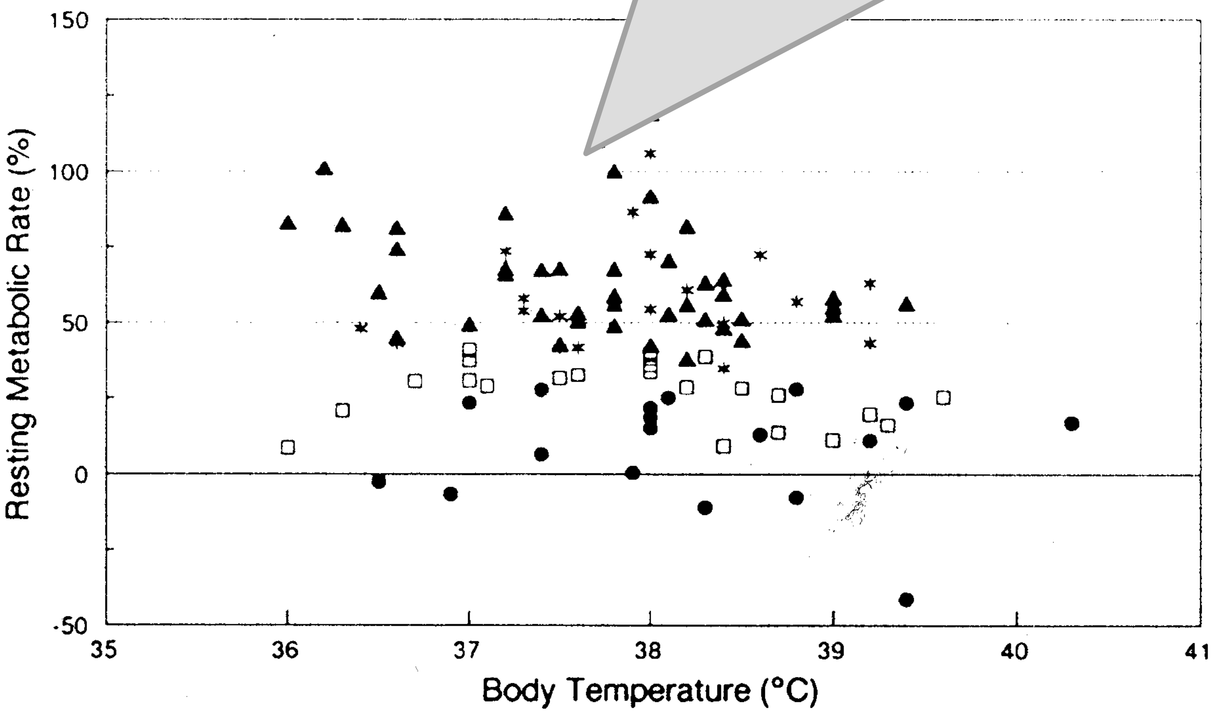
	Sepsis	Sepsis Syndrome	Septic Shock	
VO_2	180	156	120	$ml.min^{-1}.m^{-2}$
REE	2180	1890	1450	$Kcal.24h^{-1}$



Kreymann et al. Crit Care Med 1993; 21: 1012-19

Metabolic rate & temperature in sepsis

None of the sepsis states was associated with an increase of REE when temperature increased
2 factors: centralisation / proton leakage



Kreymann et al. Crit Care Med 1993; 21: 1012-19

ICU treatment modifies energy production/consumption: level of sedation

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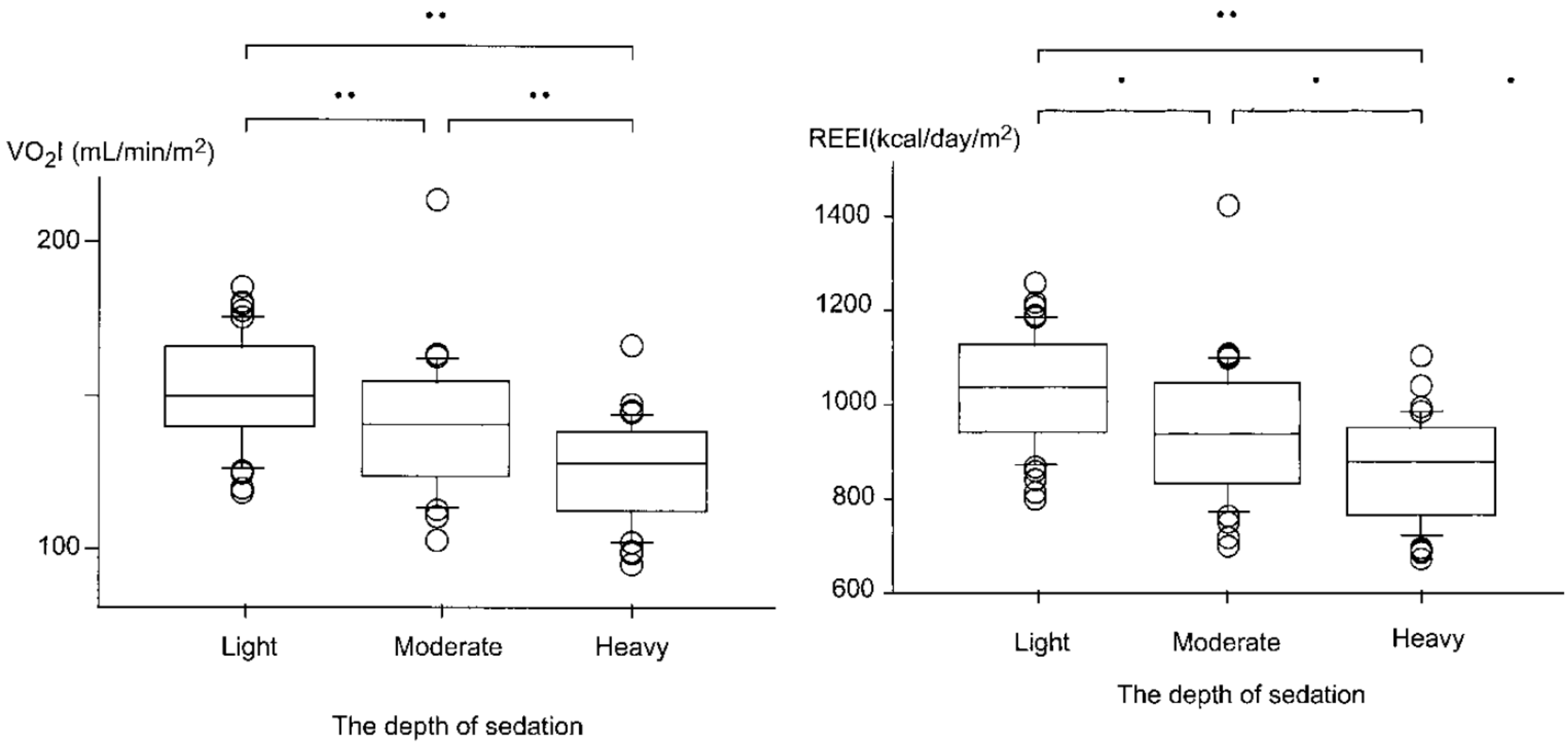
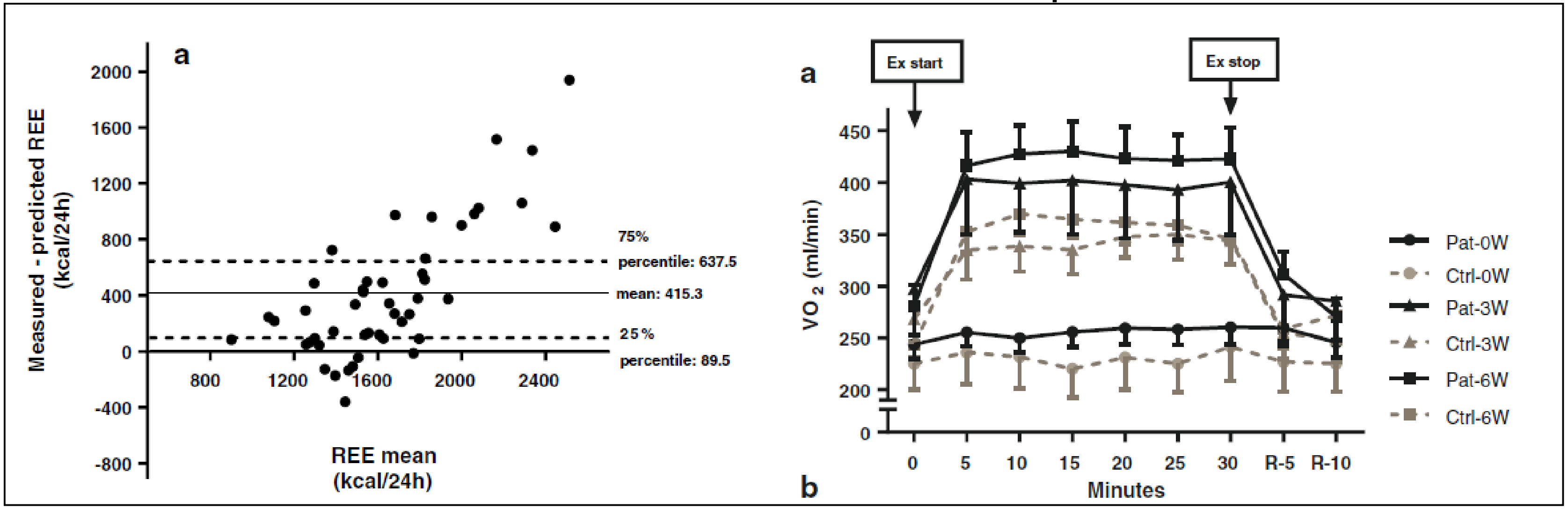


Terao Y et al Crit Care Med 2003; 31: 830-3.

Exercise increases energy consumption

Comparison with HBE



Minimal exercise (3/6W) necessitates
more energy than in controls
Extra energy of 30 min exercise: 4.5 l VO_2 or 30 Kcal

Exercise in ICU is often of short duration (fatigue)

Hickmann CE et al Intens Care Med 2014; 40: 548-555

A complex city as an analogy

Activity (metabolic) can be determined by observing how much fuel is transported in and what remains on the train on the way out. Alternatively you observe the waste (smoke). Observing exported products ignores internal activity.

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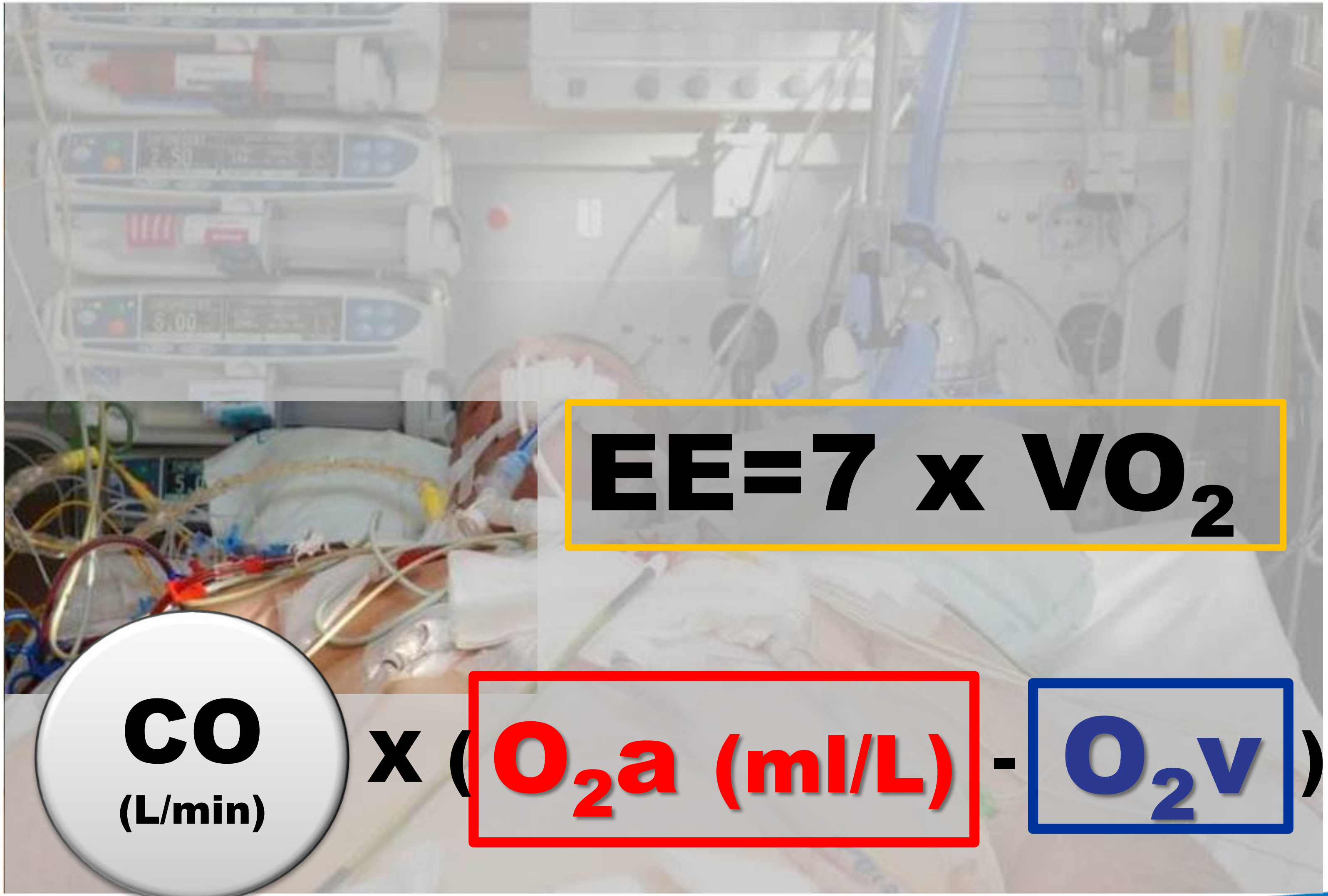
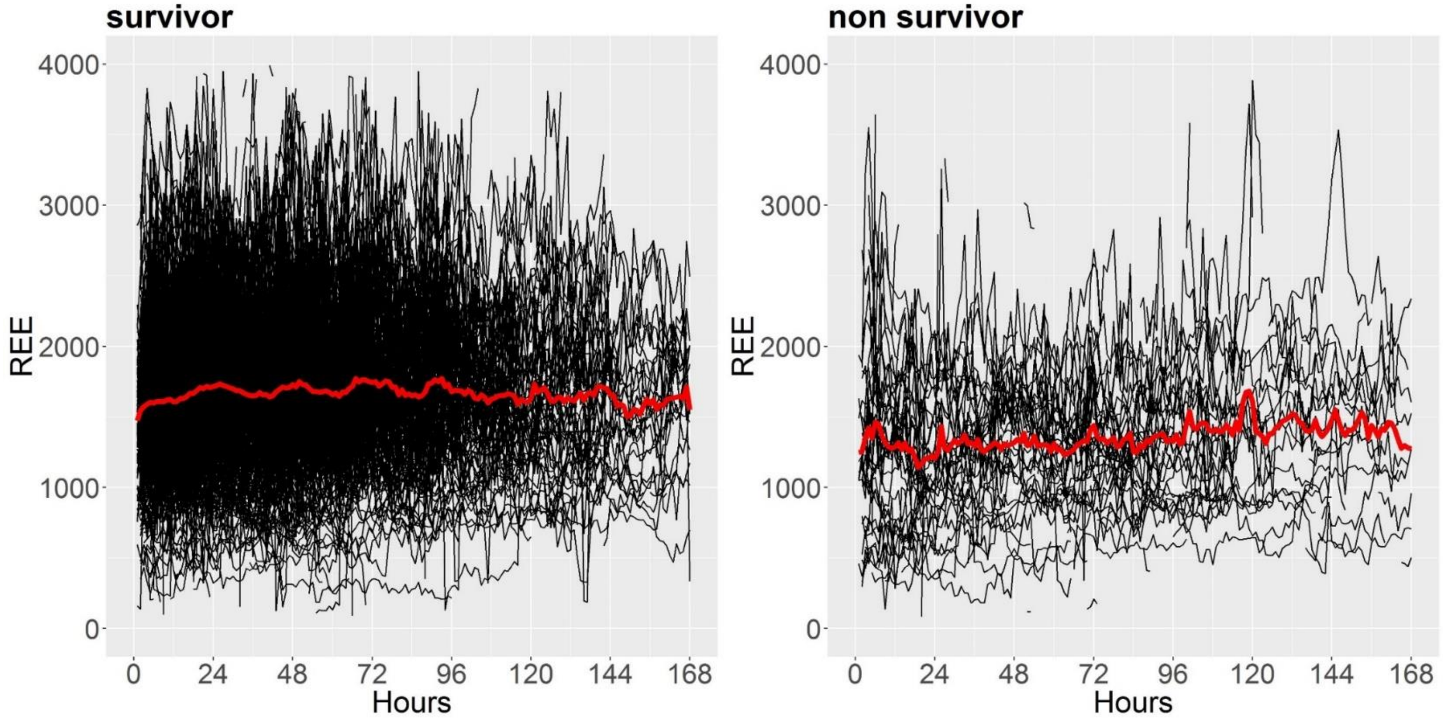
USE of the Swan-Ganz catheter for metabolic orientation



$$EE = 7 \times VO_2$$

$$CO\ (L/min) \times (O_2a\ (ml/L) - O_2v)$$

REE (…VO_2 from PulmArtCath) after major cardiac surgery in ICU



Nearly stable energy consumption during the first week in ICU, small fluctuations with a period of 24 hours indicating phases of more/less rest

Hiesmayr M (personal communication 2018)

USE of a specific device for metabolic measurement

V_E

F_ECO_2

F_IO_2 & F_EO_2

VE is determined either with a mixing chamber or with a flowmeter breath by breath.
The difficulty is the synchronisation of the measured gas concentrations with the expiratory flow.
FiO2 appears to fluctuate in some ventilators.

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Indirect calorimetry: the calculations

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CO_2 fast infrared sensor
Only 1 Volume

$V\,CO_2 = V_E.F_ECO_2$ easier measurement

$V\,O_2 = (V_I.F_IO_2 - V_E.F_EO_2)$ difficult measurement!

O_2 slow sensor, 2 concentrations (F_iO_2 & F_eO_2), usually with one sensor
2 gas volumes necessary: V_I estimated via Haldane transformation

Respiratory indirect calorimetry (Weir):

$$\textbf{EE} = 1.44\,(\,3.94 \times VO_2 + 1.11 \times VCO_2 - 2.17 \times N_{loss}$$

[ml/min] [ml/min]) [g]

!!! ***(FiO2 < 0.6, Flow exp < 40 [80] l/min)*** **Error 5-8%**

estimate EE = $1.44\,(4.86 \times RQ^{-1} \times VCO_2\,) \approx 8 * VCO_2$ **Error variable (?) 20 %**
(from ventilator measurements)

REEE: IC vs VCO_2 (ventilator: volumetric capnography)

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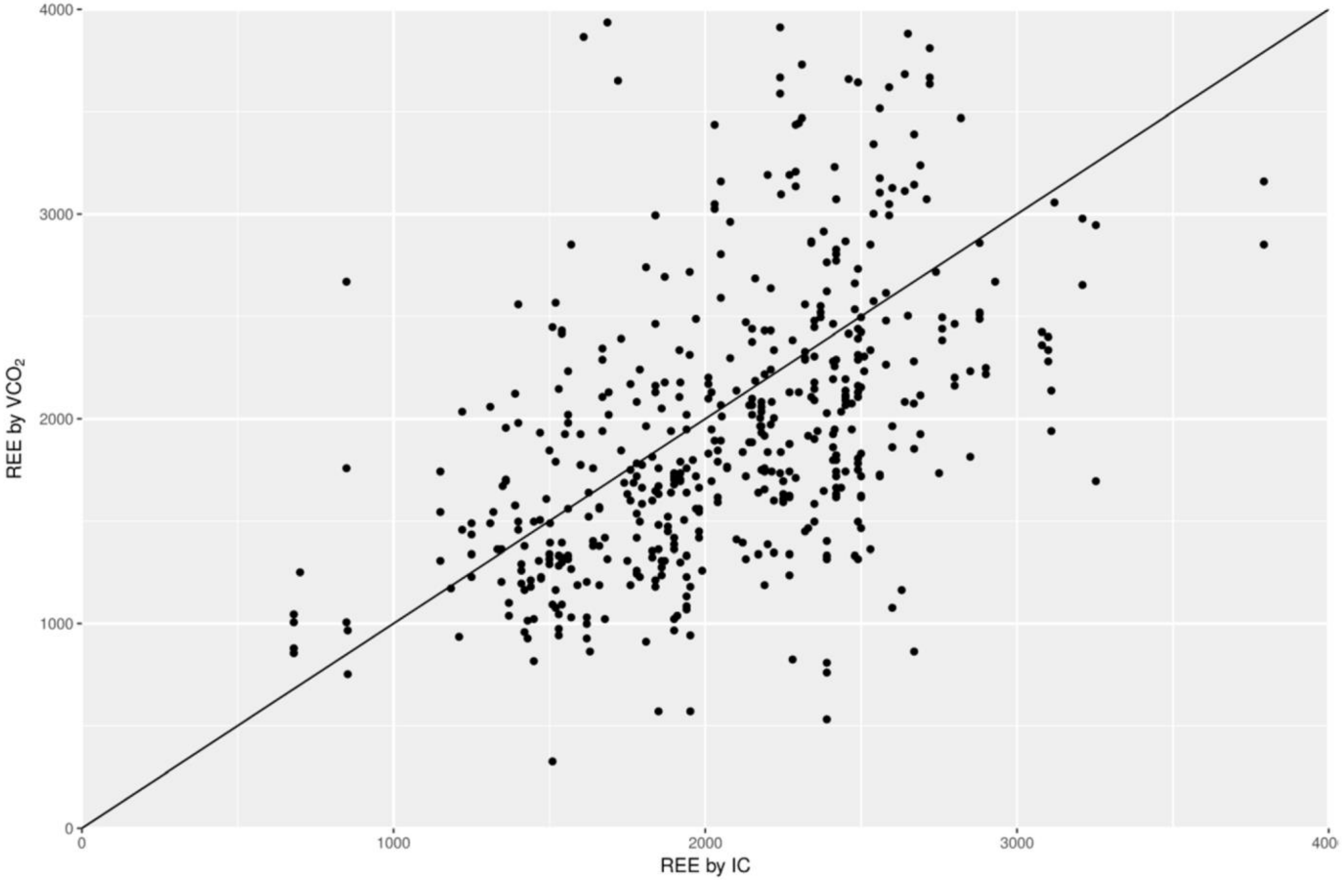

Kagan I et al Crit Care 2018; 22: 186

3100 Kcal on indirect calorimetry

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- Patient: male 80 kg 185 cm 72 a temp 37.3°C ruptured AAA repair with large transfusion
  - Day 6 in ICU
  - Arousable on minimal continuous opiods
  - CRP 12 falling
  - Pressure support (11mbar) ventilation 9 Liter/‘
  - Ileus / IAP 15 mbar / GRV 450 ml
  - Nearly anuric / CRRT
  - Trophic feeding + PN 1500 Kcal/24 hours
- **Impossible!**

Indirect Calorimetry: conditions?

- Stability for 30 minutes
- No change in drugs(all ?)
  - Vasoactive
  - Sedation/pain
  - Fluid
- Postprandial/fasted?
- $FiO_2 < 0.6$
- PEEP <14 (PIP???)
- No leak
- No CRRT ? 1.5-4% underestimation?
- No ECMO ?

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ECMO: full double IC calorimetry for the patient & the ECMO circuit

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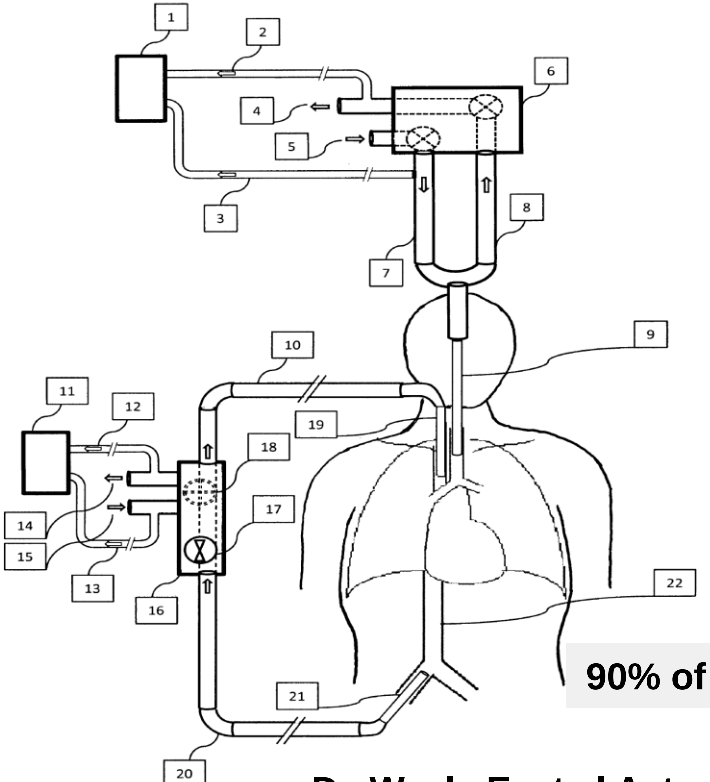

Applying the Weir formula on the combined data produced a $REE_{composite}$ of 1703 kcal/day. Implementing the manual-derived VO_2 and VCO_2 membrane oxygenator characteristics into the Weir formula retrieved a REE of 1729 kcal/day. The Faisy–Fagon and Harris–Benedict equations yielded REE values of 1373 and 1563 kcal/d. Application of the ESPEN guideline estimated REE in our patient at 1675 kcal/d.

90% of gas exchange via ECMO

De Waele E. et al Acta Anaesth Scand 2015; 59: 1296-1305

ECMO:
IC + Calculation

ESPEN

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MEEP – Measuring Energy expenditure (EE) in Extracorporeal lung supp

Lung measurement

- Use indirect calorimetry to measure
  - $VO2_{lung}$ [ml/min] by the lung
  - $VCO2_{lung}$ [ml/min] by the lung

ECMO calculatio

- Take **BGAs** from blood stream **pre and post** the ECMO membrane
- Use the **model published by Dash and Bassingthwaighte** to determine O2 and CO2 content in blood pre and post ECMO membrane
  - Dash available from: www.physiome.org (model 0149)
  - O_2 difference [ml/l] = O_2Dash (BGA_{post}) – O_2Dash (BGA_{pre})
  - CO_2 difference [ml/l] = CO_2Dash (BGA_{pre}) - CO_2Dash (BGA_{post})
- $VO2_{ECMO}$[ml/min] = O_2 difference [ml/l] x ECMO blood flow [l/min]
- $VCO2_{ECMO}$[ml/min] = CO_2 difference [ml/l] x ECMO blood flow [l/min]

ulate the total O_2 uptake and total CO_2 elimination:

$VO2_{total}$[ml/min] = $VO2_{lung}$[ml/min] + $VO2_{ECMO}$[ml/min]

$VCO2_{total}$[ml/min] = $VCO2_{lung}$[ml/min] + $VCO2_{ECMO}$[ml/min]

- Use $VO2_{total}$ and $VCO2_{total}$ to calculate EE per day by Weir:
  - **EE** [kcal/d] = **(3.9 x $VO2_{total}$**[ml/min] **+ 1.1 x $VCO2_{total}$**[ml/min] **) x 1.44**

Wollersheim T et al. Clin Nutr 2018; 37: 301-7

REE vs substrate provision: outcome at 60 days

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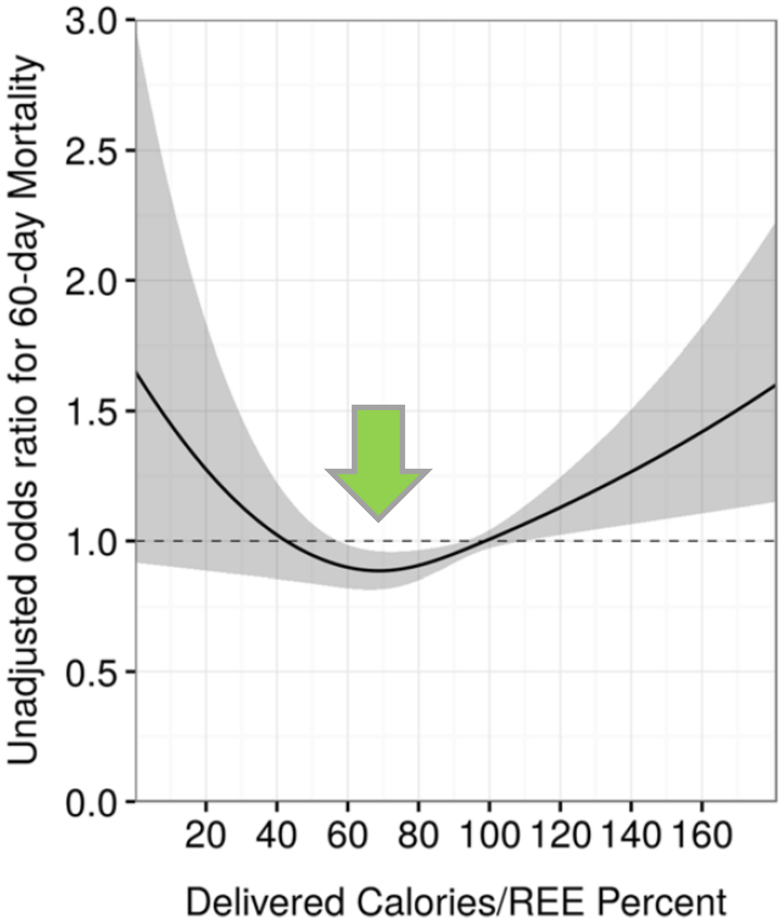


Best outcome at substrate supply for 70% of measured REE
means that 30% of substrates are endogenously produced in the critically ill and are not suppressed at this stage of illness
by artificial nutrition provided at REE.

Zusman et al. Crit Care 2016; 20: 367

ICU: energy factors

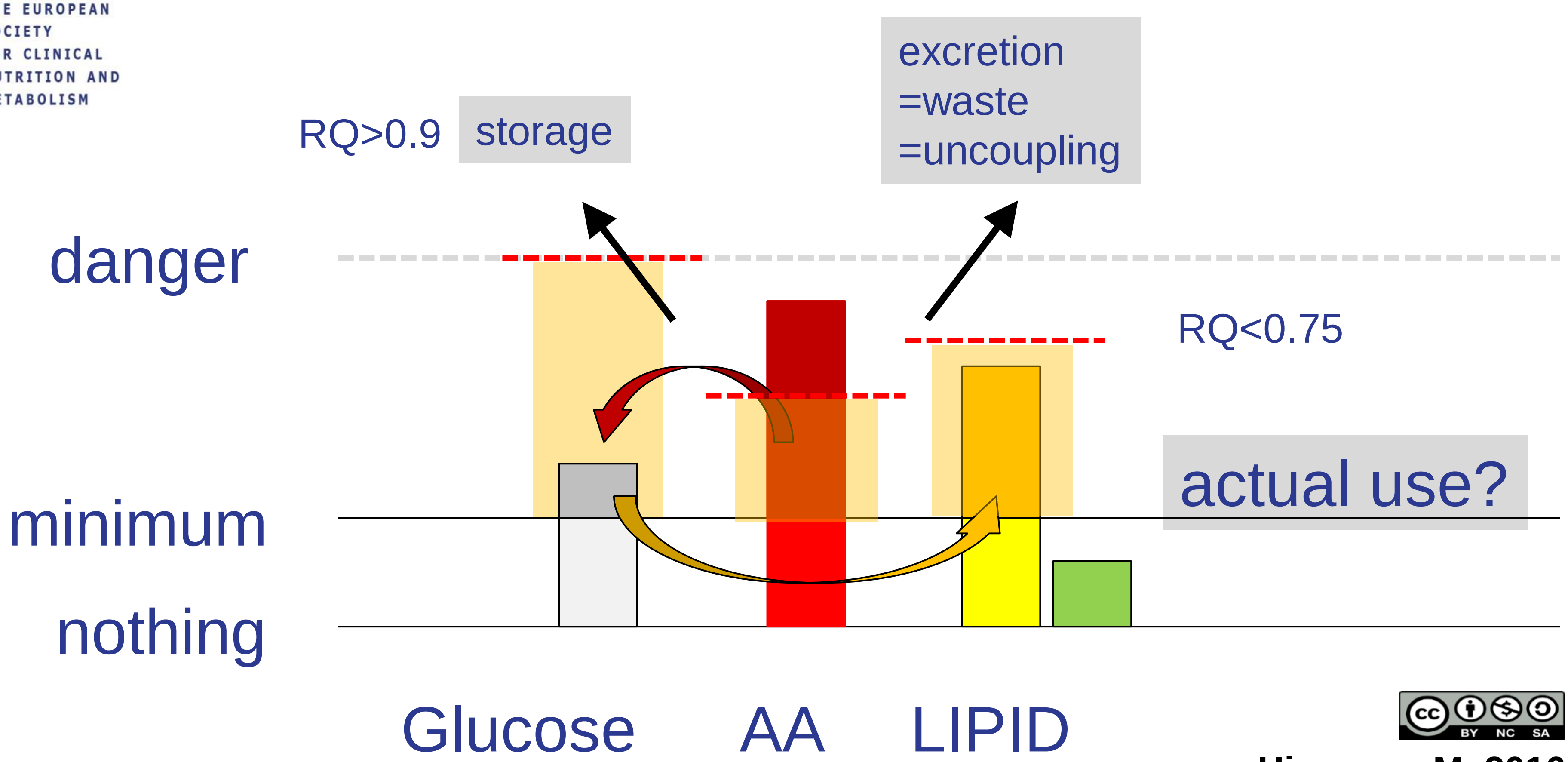
- Sedation
- Pain treatment
- Muscle relaxants
- Antiphlogistic
- Antipyretic

- Shock
- Vasoconstriction
- Organ loss
- Organ dysfunction

- Awakening
- Dyspnea
- Weaning
- Shivering
- Seizures
- Delirium

- Inflammation
- Fever
- Wounds
- Organ repair
- Physiotherapy

Correct amount of macronutrients in disease states?



Hiesmayr M 2016

Singer P Hiesmayr M et al. Clin Nutr 2014; 33: 246-51

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Conclusion

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Energy = ATP production is depressed in ICU patients.

Substrates (CHO/Lipid/Protein(AA)) are the fuel to produce ATP in oxydative phosphorylation

Many factors modify energy consumption in ICU: treatments and organ priorities

Measurement is better than all formula but does only suggest the amount of fuel needed in the actual clinical state

Extreme amount of fuel can impair endogenous repair mechanism (mitophagy/autophagy)