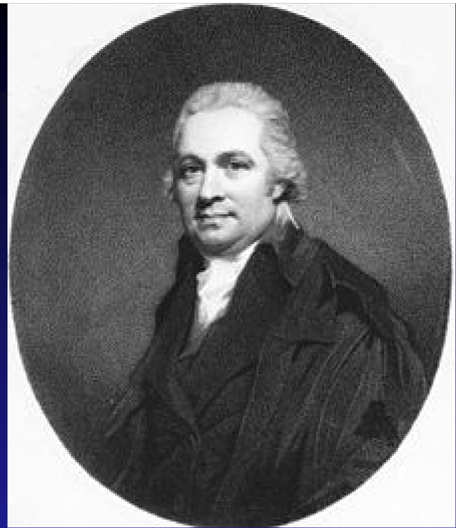
Protein: i går – i dag – i morgen

- Historie
- Nitrogen balance
- Metabolisme & anabolt drive: genopbygning efter natlig faste, fysisk aktivitet, hungersnød og sygdom
- Essentielle aminosyrer
- Protein og funktion
  AA og ikke-krops-protein funktioner
- Patienter

Daniel Rutherford (1749-1819)

Discovered nitrogen in 1772



Gerardus Johannes Mulder (1802 – 1880)

Described the chemical composition of albumin and fibrin i 1839.
The substance is present in all constituents of the animal body and in the plant kingdom.

Jöns Jacob Berzelius (1779 – 1848)

Suggested the name *protein* from πρωτειος, *primarius*

Antoine Lavoisier (1743-1794)

Organic compunds consist predominantly of carbon, hydrogen and oxygen.

Animal matter always contains nitrogen.

Used a calorimeter to estimate the heat evolved per unit of CO_2 produced, eventually finding the same ratio for a flame and animals, indicating that animals produced energy by a type of combustion reaction.

Matter can change its state in a chemical reaction, the total mass of matter is the same at the end as at the beginning of every chemical change

Edward Smith (1819-1874)

Food surveys in 100’s of poor families: nitrogen and carbon.

Criteria for recommendations:
Absence of anaemia; firmness of muscle; elasticity of spirits; capability for exertion.
280 g of carbon & 13 g nitrogen (avg. male)

Two students climbed the Swiss Alps after removing protein entirely from their diet.
The chemical energy required for muscular effort does not come from consumed protein but from fats and carbohydrates.
Urea excretion reflects protein intake, not physical activity

Wilbur Olin Atwater (1844-1907)

TABLE 1

Mean protein and energy intakes of men in Atwater's studies compared with his own and present-day standards

Measure	Nutrient intake[1]	
	Protein	Energy
	g	*kcal*
Type of worker		
Professional men	104	3325
Mechanics	103	3465
Farmers	97	3515
University boat crews	155	4085
Degree of muscular work[2]		
Light	112	3000
Moderate	125	3500
Heavy	150	4500
Current Recommended Dietary Allowances[3]	52	Variable

…where people have sufficient means to make a free choice of diet, their intakes will correspond to their needs for protein as well as for calories.

Carpenter KJ.
J Nutr 1986;116:1364-70.

Chittenden RH (1904) Hindhede M (1913)

…men could maintain their health and sporting prowess with one half of Atwater's standard intake of protein.

Chittenden RH (1904)

…observing good health and vigor among people living habitually on a relatively low protein diet.

Hindhede M (1913)

Carpenter KJ.
J Nutr 1986;116:1364-70.

Peter Ludvig Panum (1820-1885)

In 1866, Panum published 'Contribution to the Examination of the Nutrient Value of Foods’

Food was evaluated for its appetizing value, its respiratory value and its histogenetic value.

He wrote about the importance of foods in malnutrition.
He recommended 'blood flour’ (a powder prepared from pork's blood) as staple food and tried to prepare dietary recommendations for hospitals.

Anders Møller, Danish Food Information

A Gjedde 1977

Figure 1. Peter Ludvig Panum (1820-1885), 1867. Courtesy: Medical Museion, University of Copenhagen.

In 1855-1856, professor in physiology Peter Ludvig Panum (1820-1885) performed a series of remarkable experiments on “putrid poison”.

Dogs were given intravenous infusions of putrefying solutions purified from dog’s meat in distilled water, which had been left to decompose at room temperature, until it was strongly malodorous….
…resulted in characteristic sepsis symptoms and signs, which only started after a delay of half an hour.
…the toxic principle was a solid substance, soluble in water, but insoluble in alcohol, and with preserved activity after long-term boiling.

…it is fair to conclude that “putrid poison” was endotoxin, and as such he deserves credit for being the first to have described endotoxin.

Panum published his observations twice, in Danish in 1856, and in German in 1874.

H. J. Kolmos Dan Med Bull 2006;53:450-2

Genom/Proteom

- Bananfluer: 13.062 gener
- Orme: 19.099 gener
- Mennesker: ≈ 26.000
- Ca. 5.000 forskellige proteiner i hver celle
- Kun en mindre del af proteinerne er identificeret

FC Nielsen Ugeskrift f Læger 2003; 165: 773-776

Evolution

4.5 mia år	Jorden opstår
3.8 - 4.0 mia. år	Thioestre/Peptider t-RNA Protocelle
3.8-3.7 mia. år	Éncellet bakterie (stromatolitter & C^{12}/C^{13})
700-600 mio. år	Flercellede dyr (fossiler)

Cytokrom C: ca. 100 AA	
Art	≠ humant
Rhesus abe	1 AA
Hund	11 AA
Tun	21 AA
Hvede	43 AA
Gær	45 AA

Christian de Duve: Vital Dust p. 3-10. BasicBooks 1995

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- …requirement is the lowest level of dietary protein intake that will balance the losses of nitrogen from the body, and thus maintain the body protein mass…
- …nitrogen balance does not necessarily identify the optimal intake for health, which is less quantifiable.
- There is emerging information on the apparently beneficial effect of protein intakes in excess of the safe level for lowering blood pressure, reducing risk of ischaemic heart disease and improving bone health. Causal relationships?
- The task is to identify protein intakes that enable long-term health and well-being

Pages 24, 250-251

N balance

Nitrogen balance = $N_{in} - N_{out}$

N_{in} = Protein intake/6.25 ≈ protein contains 16 wt% N

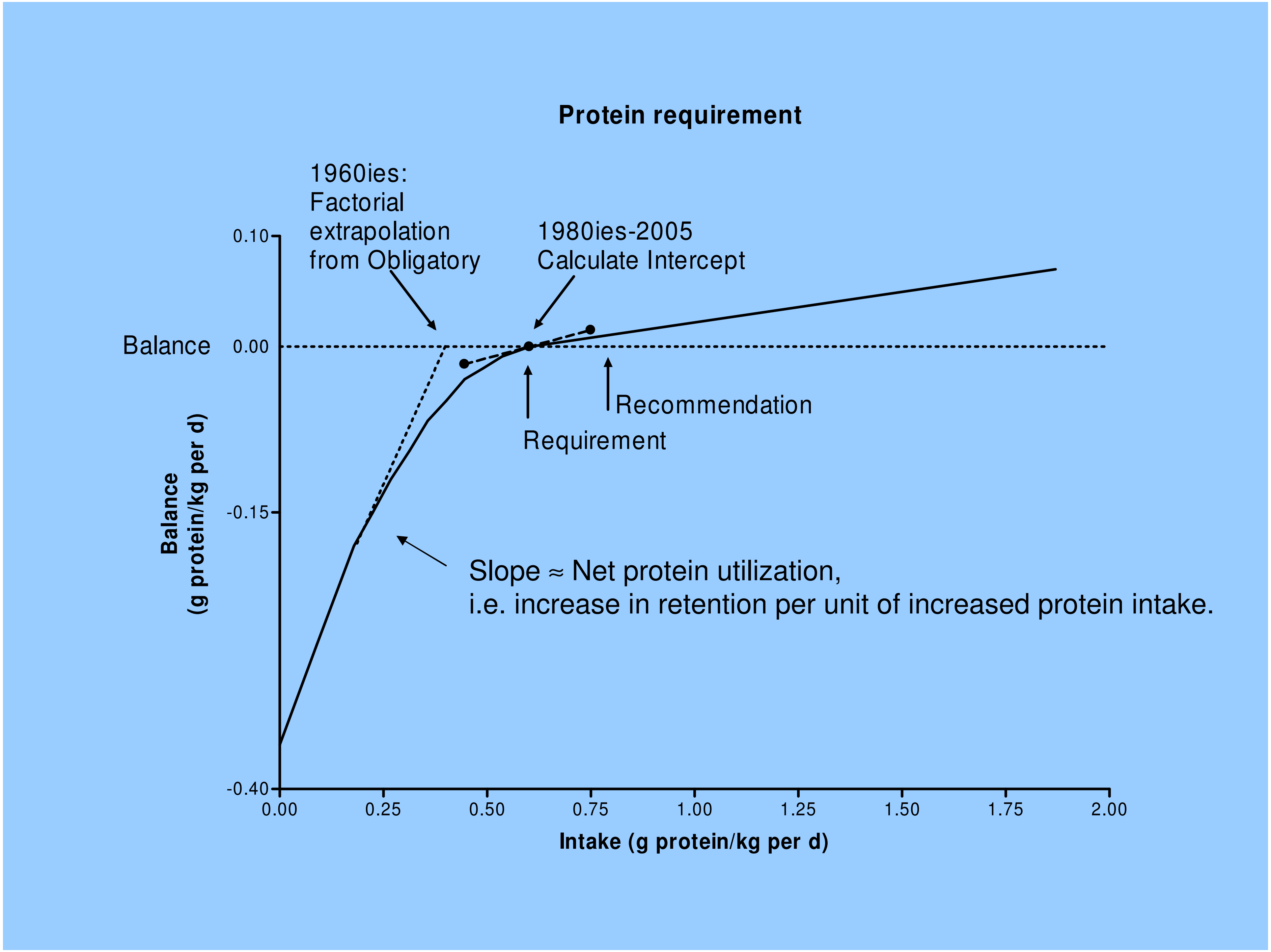
N_{out} = 24h-U-N + 24h-F-N + miscellaneous (skin, secreta)

24h-U-N: urinary nitrogen excretion per 24 h
24h-F-N: fecal nitrogen excretion per 24 h

Obligatory Nitrogen Losses by Adult Men on a Protein-Free Diet

	Daily Nitrogen Loss	
	As Nitrogen (mg N/kg/day)	As Protein Equivalent (g protein/kg/day)
Urine	37	0,23
Feces	12	0,08
Cutaneous (sweat)	3	0,02
Other	2	0,01
Total	54	0,34
Upper Limit (+2 standard deviations)	70	0,44

Shils Table 2.10.


Protein requirement
1960ies:
Factorial
extrapolation
from Obligatory
1980ies-2005
Calculate Intercept
Balance
0.10
0.00
-0.15
-0.40
Recommendation
Requirement
Balance
(g protein/kg per d)
Slope ≈ Net protein utilization,
i.e. increase in retention per unit of increased protein intake.
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
Intake (g protein/kg per d)

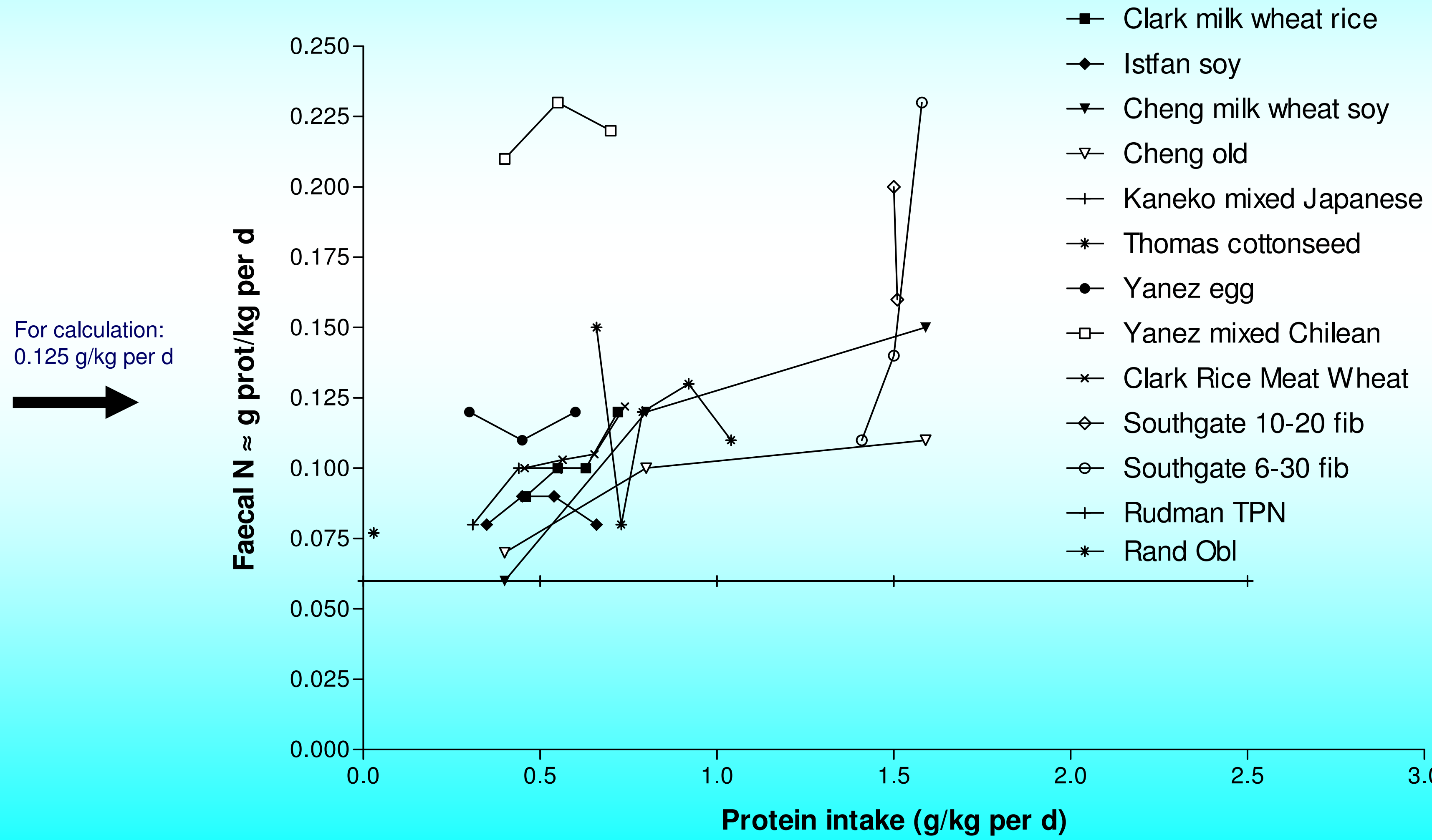
Fecal N

Rand's meta-analysis: Fecal N *vs.* P intake

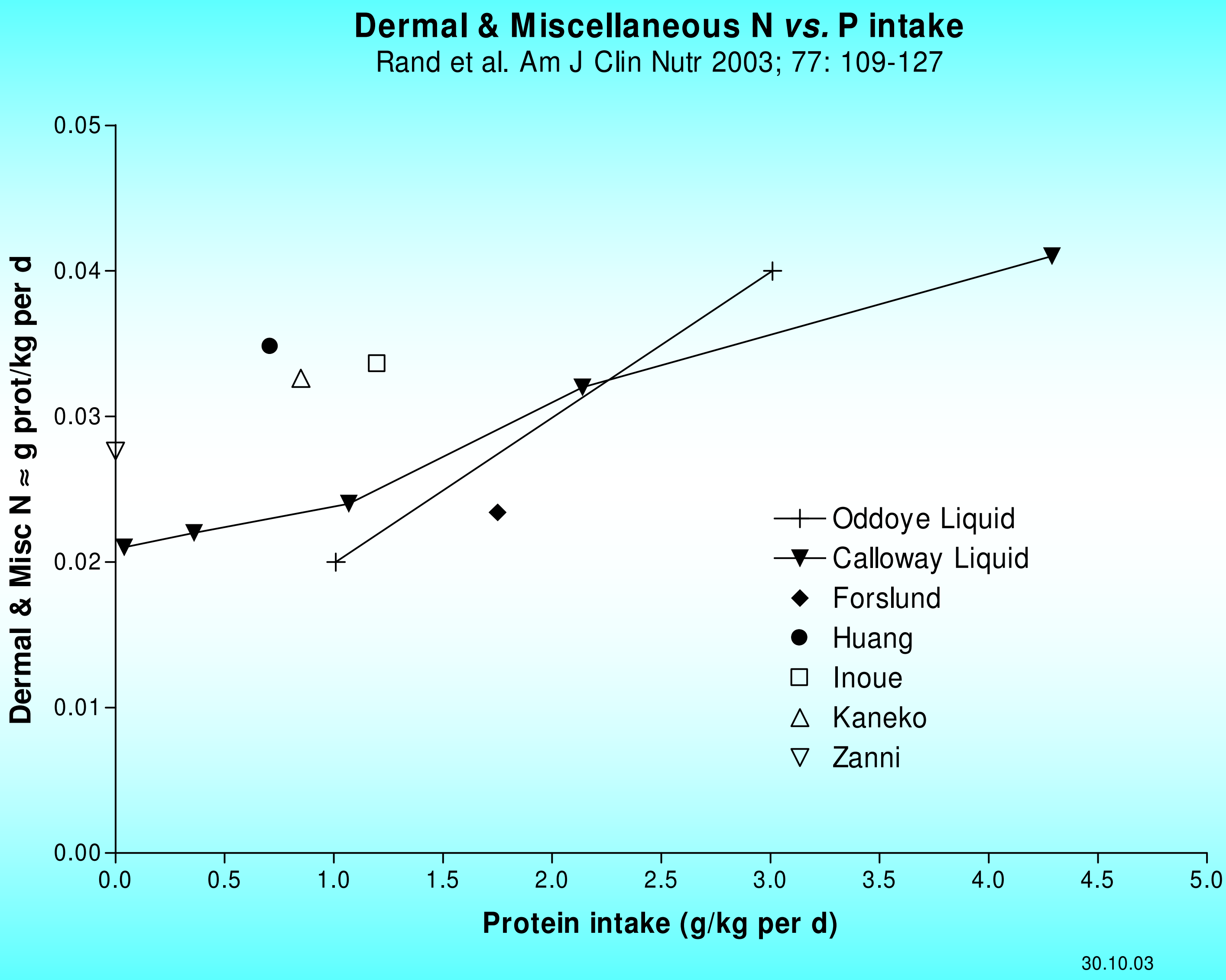
Rand et al. Am J Clin Nutr 2003; 77: 109-127

Primary studies (19 studies with 237 subjects):
1) ≥ 3 levels of intake near purported balance
2) each level given for 10-14 days
3) Urinay and fecal N determined for 5 last days

For calculation:
0.125 g/kg per d



Dermal N



For calculation:
0.03 g/kg per d

Meta-analysis of N balance to estimate protein requirements

Rand et al. Am J Clin Nutr 2003; 77: 109-127

The protein requirement in healthy adults is defined as the continuing intake of dietary protein that is sufficient to achieve body nitrogen equilibrium (zero balance)…

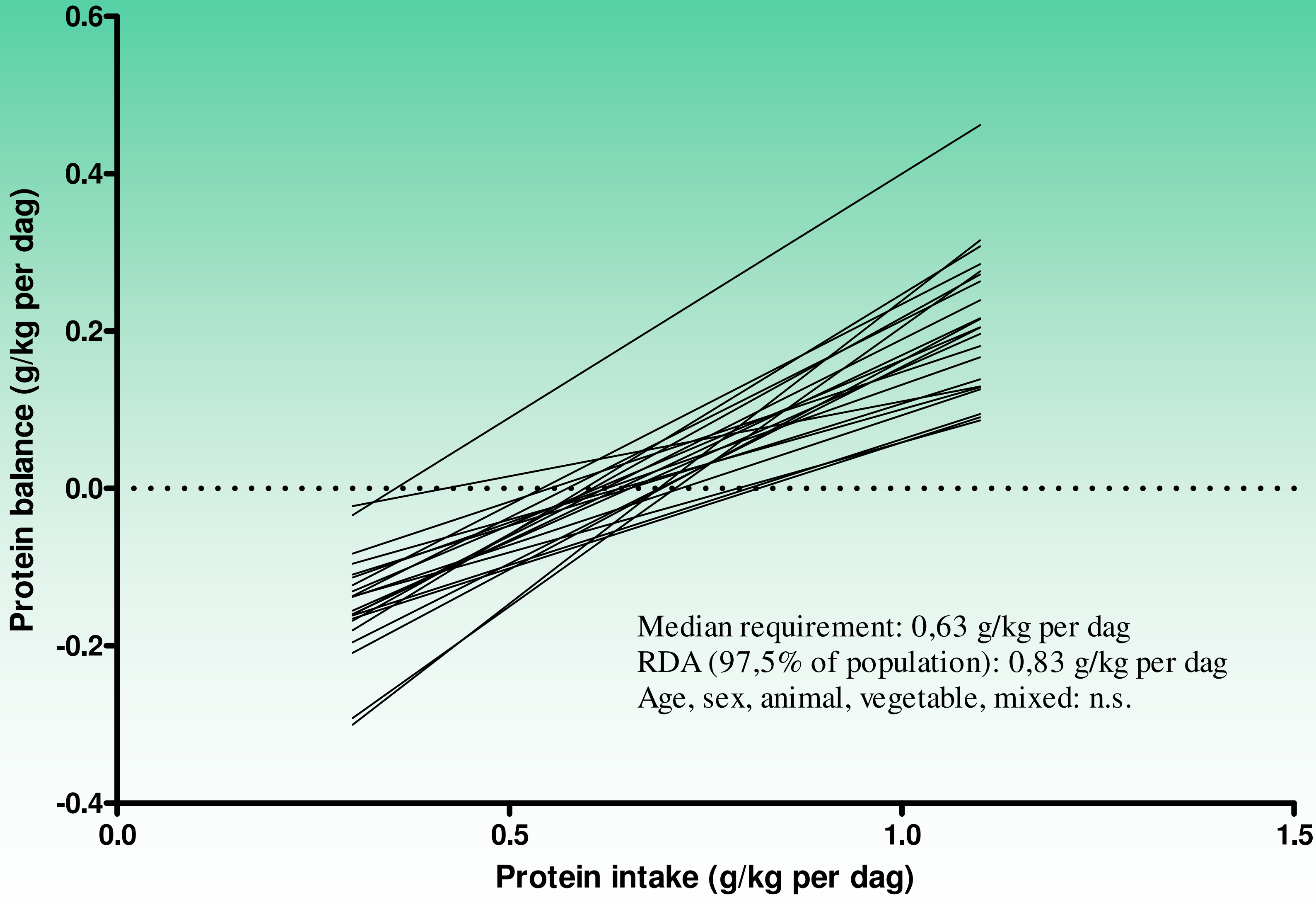
This method remains the primary approach for determining protein requirements in adults, in large part because there is no validated or accepted alternative.

Rand req

Protein requirement and recommendation

Requirement = Y intercept after linear regression analysis of ≥3 levels of protein intake

Rand et al Am J Clin Nutr 2003; 77:109-127



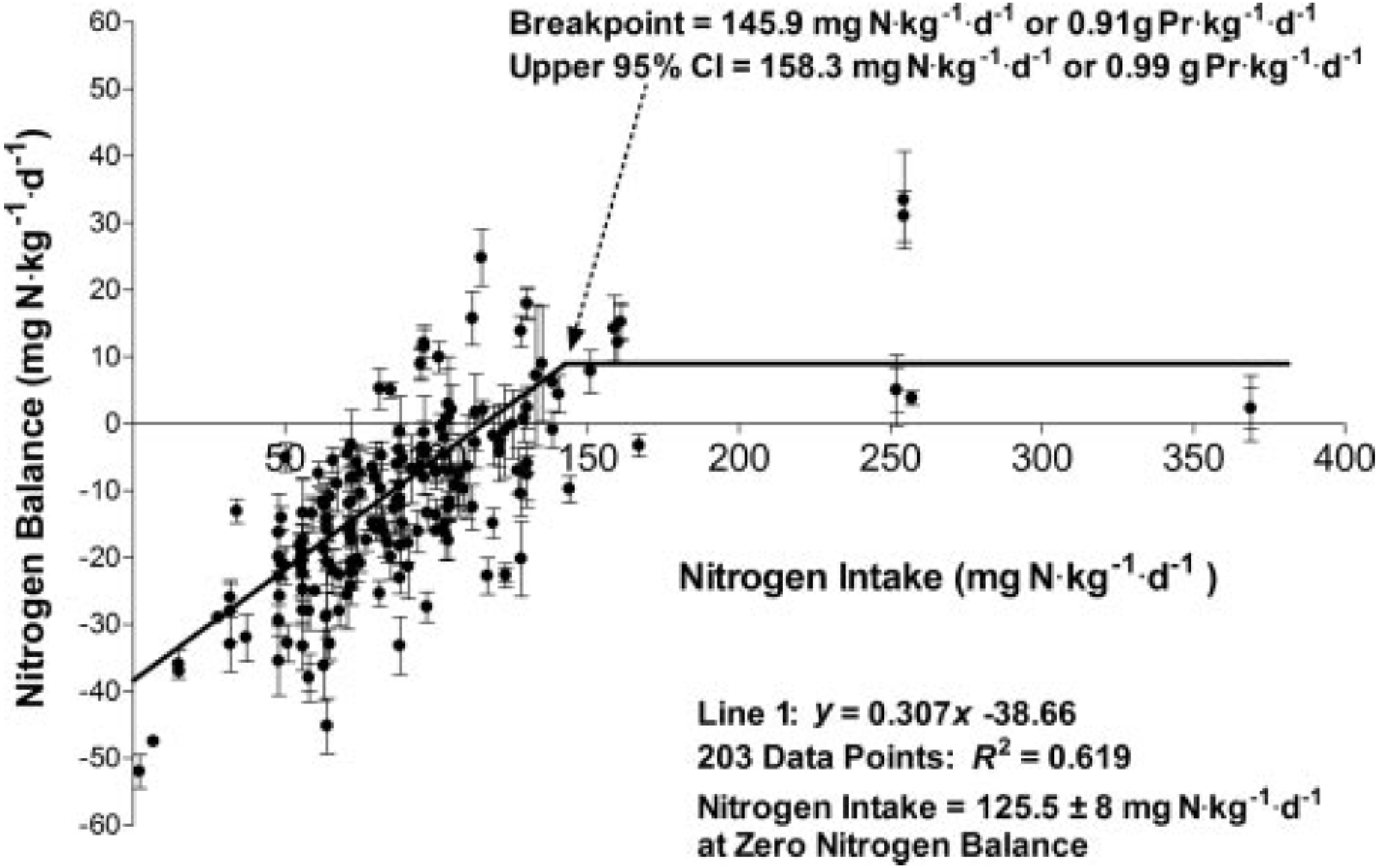


FIGURE 2. Relation between various nitrogen intakes and the mean nitrogen balances from 28 nitrogen balance studies (data from references quoted in Table 3). Values are $\bar{x}$ ± SE. The breakpoint estimates the mean nitrogen

Humayun et al. Am J Clin Nutr 2007;86:995–1002

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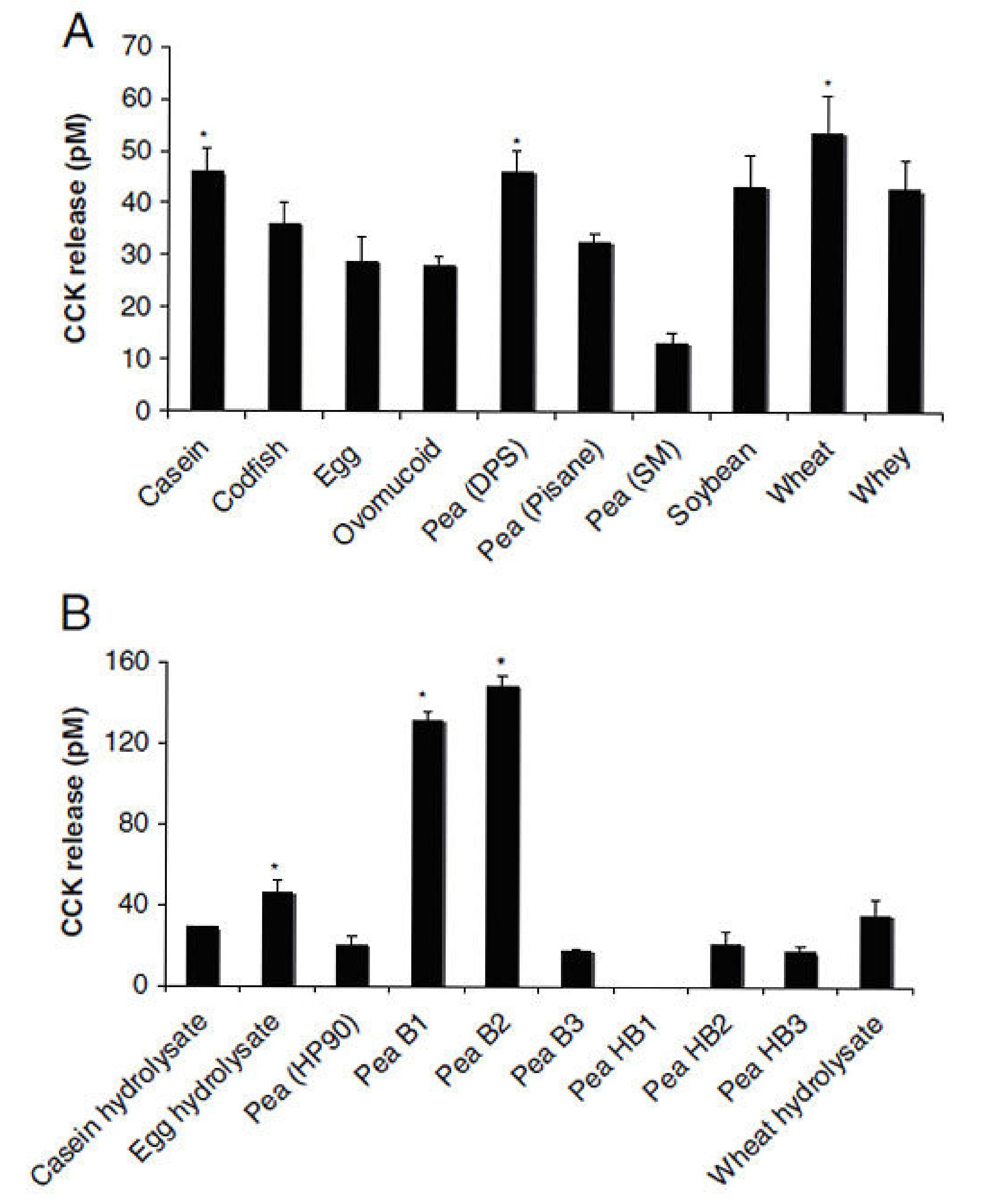
Absorption

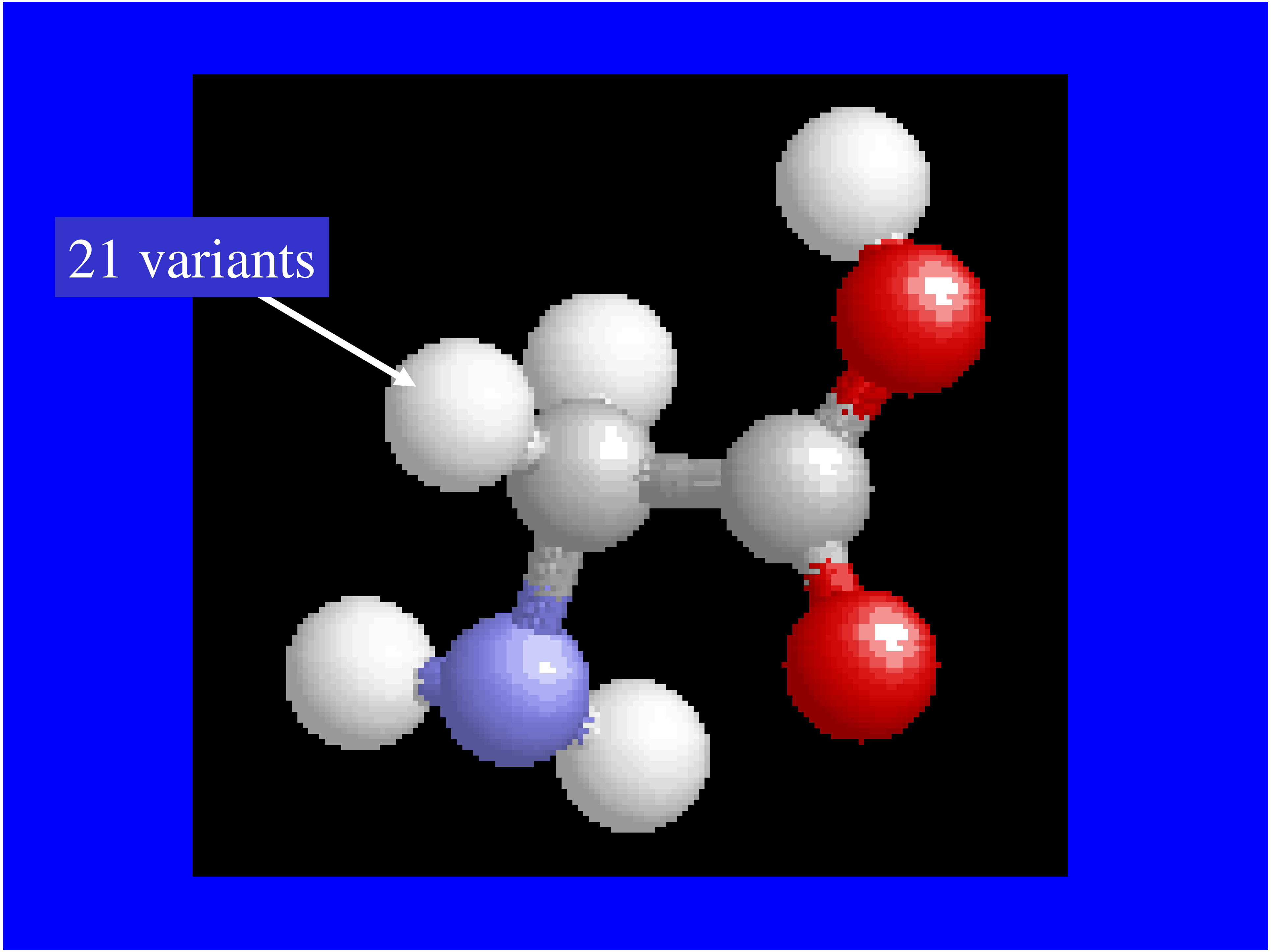
Tissue	Active agent	Action
Stomach	HCl	Destroys tertiary structure → **peptide-bonds exposed**
		Pepsinogen → Pepsin
	Pepsin	Protein → **Peptides and AA**
Duodenum		Peptides and AA → **CCK** ↑ → bile secretion ↑
	Bile	Duodenal enterokinae secretion ↑
	Enterokinase	Activates trypsinogen to trypsin
Pancreas	Trypsinogen/Trypsin	Splits peptide-bonds at lys and arg; activates other proteases
	Chymotrypsin	Splits peptide-bonds at aromatic and neutral AA
	Elastase	Splits peptide-bonds at aliphatic AA (BCAA)
	Carboxypeptidase A	Splits peptide-bonds from carboxyterminal end at aromatic AA
	Carboxypeptidase B	Splits peptide-bonds from carboxyterminal end at arg and lys
	Result: **70 % of protein-AA is oligopeptides (2-6 AA) and 30% is free AA**	
Duodenum	Surface aminopeptidases	Splits oligopeptides to di-and tripeptides and AA
Duodenum Jejunum	Membrane transporters	**60-70% absorbed as di- & tripeptider, 30-40% as free AA**. 60% of all AA/peptides aborbed in duodenum.
	Cytsolic peptidases	Splits peptides → **90% AA and 10% peptides in portal blood**

Shils page 1137-1138

Effect of intact and hydrolyzed proteins on secretion of satiety hormones in murine STC-1 cells.

Geraedts et al 2011. Mol. Nutr. Food Res. 2011, 55, 476–484




21 variants

Glutamate: aminotransferases

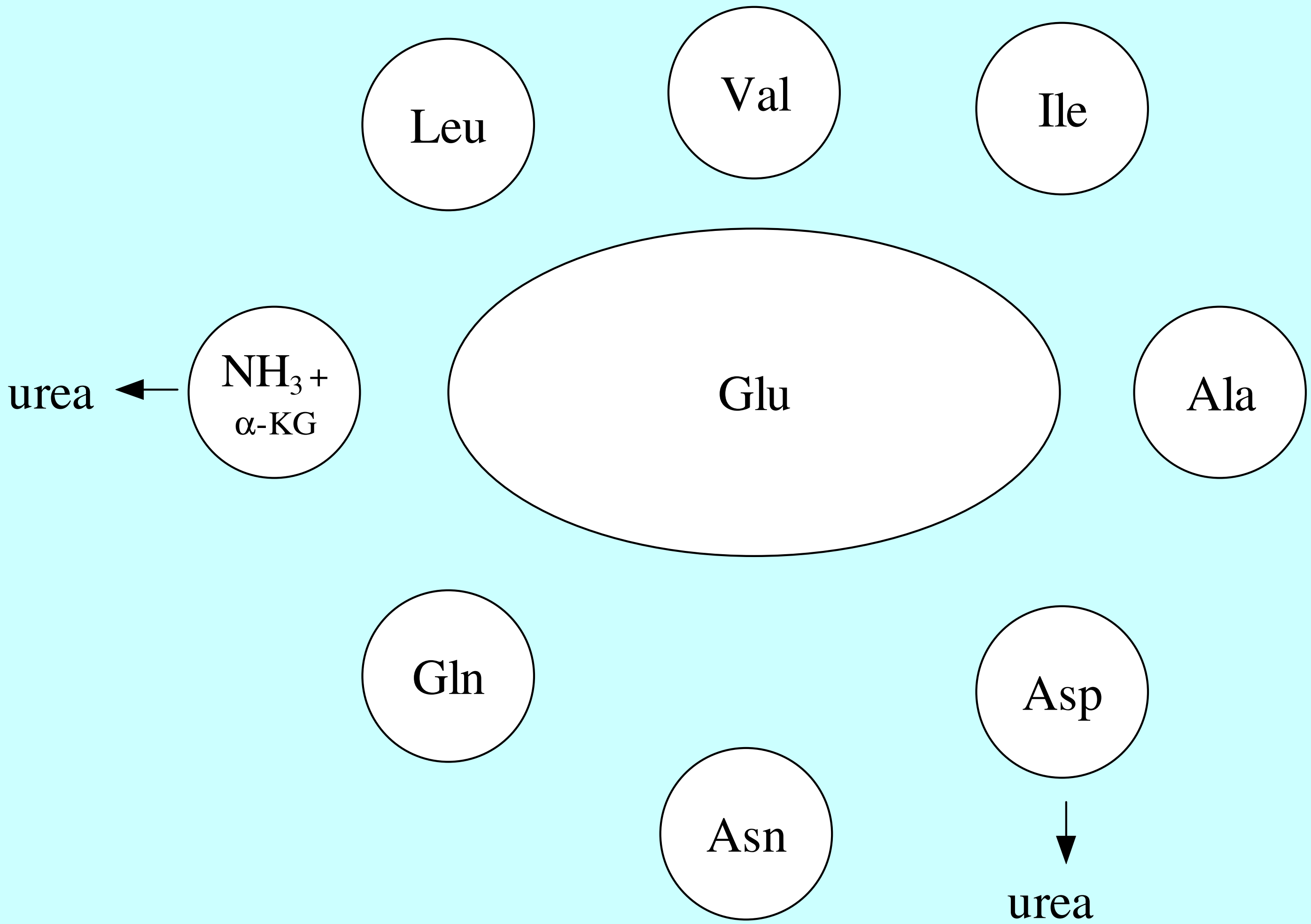


Table 2.2.

Name	Abbreviation	Molecular weight
Essential amino acids		
Isoleucine	Ile	131
Leucine	Leu	131
Valine	Val	155
Lysine	Lys	146
Methionine	Met	149
Phenylalanine	Phe	165
Threonine	Thr	119
Tryptofane	Trp	204
Histidine	His	117
Non essental amino acids		
Alanine	Ala	89
Arginine	Arg	174
Aspartate	Asp	133
Asparagine	Asn	132
Glutamate	Glu	147
Glutamine	Gln	146
Glycine	Gly	75
Proline	Pro	115
Serine	Ser	105

Shils Table 2.2.

Name	Abbreviation	Molecular weight
Conditionally essential amino acids		
Cysteine	Cys	121
Tyrosine	Tyr	181
Non-protein amino acids		
Citrulline	Cit	175
Ornithine	Orn	132
Homocysteine		135
Hydroxylysine	Hyl	162
Hydroxyproline	Hyp	131
3-Methylhistidine		169

Amino acid pool sizes

Pool	Size liter/kg	Concentration mg N/l	Total N g/kg	Turn-over per day
ECW	0.2	55	0.01	84 x
ICW	0.4	800	0.32	
Tissue protein			28	0.03 x

Shils

Amino acids i.c./plasma Table 2.4

Amino Acid		Concentration (mM) Plasma	Muskel i.c.	Muskel i.c./Plasma
Alanin	NE	0,33	2,34	7,1
Arginin	NE	0,08	0,51	6,4
Asparagin	NE	0,05	0,47	9,4
Aspartat	NE	0,02		
Glutamat	NE	0,06	4,38	73,0
Glutamin	NE	0,57	19,45	34,1
Glycin	NE	0,21	1,33	6,3
Ornithin	NE	0,06	0,30	5,0
Prolin	NE	0,17	0,83	4,9
Serin	NE	0,12	0,98	8,2
Taurin	NE	0,07	15,44	221,0
Histidin	E	0,08	0,37	4,6
Isoleucin	E	0,06	0,11	1,8
Leucin	E	0,12	0,15	1,3
Lysin	E	0,18	1,15	6,4
Methionin	E	0,02	0,11	5,5
Phenylalanin	E	0,05	0,07	1,4
Threonin	E	0,15	1,03	6,9
Valin	E	0,22	0,26	1,2
Cystein	CE	0,11	0,18	1,6
Tyrosin	CE	0,05	0,10	2,0
Total		2,78	49,56	17,8

Shils Table 2.5

System	Amino Acid Transported	Tissue Location	pH Dependence
Sodium dependent			
A	Most neutrals (Ala, Ser)	Ubiquitous	Yes
ASC	Most neutrals	Ubiquitous	No
B	Most neutrals	Intestinal brush border	Yes
N	Gln, Asn, His	Hepatocytes	Yes
N^m	Gln, Asn	Muscle	No
Gly	Gly, sarcosine	Ubiquitous	
X_{AG-}	Glu, Asp	Ubiquitous	
Sodium independent			
L	Leu, Ile, Val, Met, Phe, Tyr, Trp, His	Ubiquitous	Yes
T	Trp, Phe, Tyr	Red blood cells, hepatocytes	No
Y^+	Arg, Lys, Orn	Ubiquitous	No
asc	Ala, Ser, Cys, Thr	Ubiquitous	Yes

Neutrals: gly, ser, ala, val, leu, ileu, thr

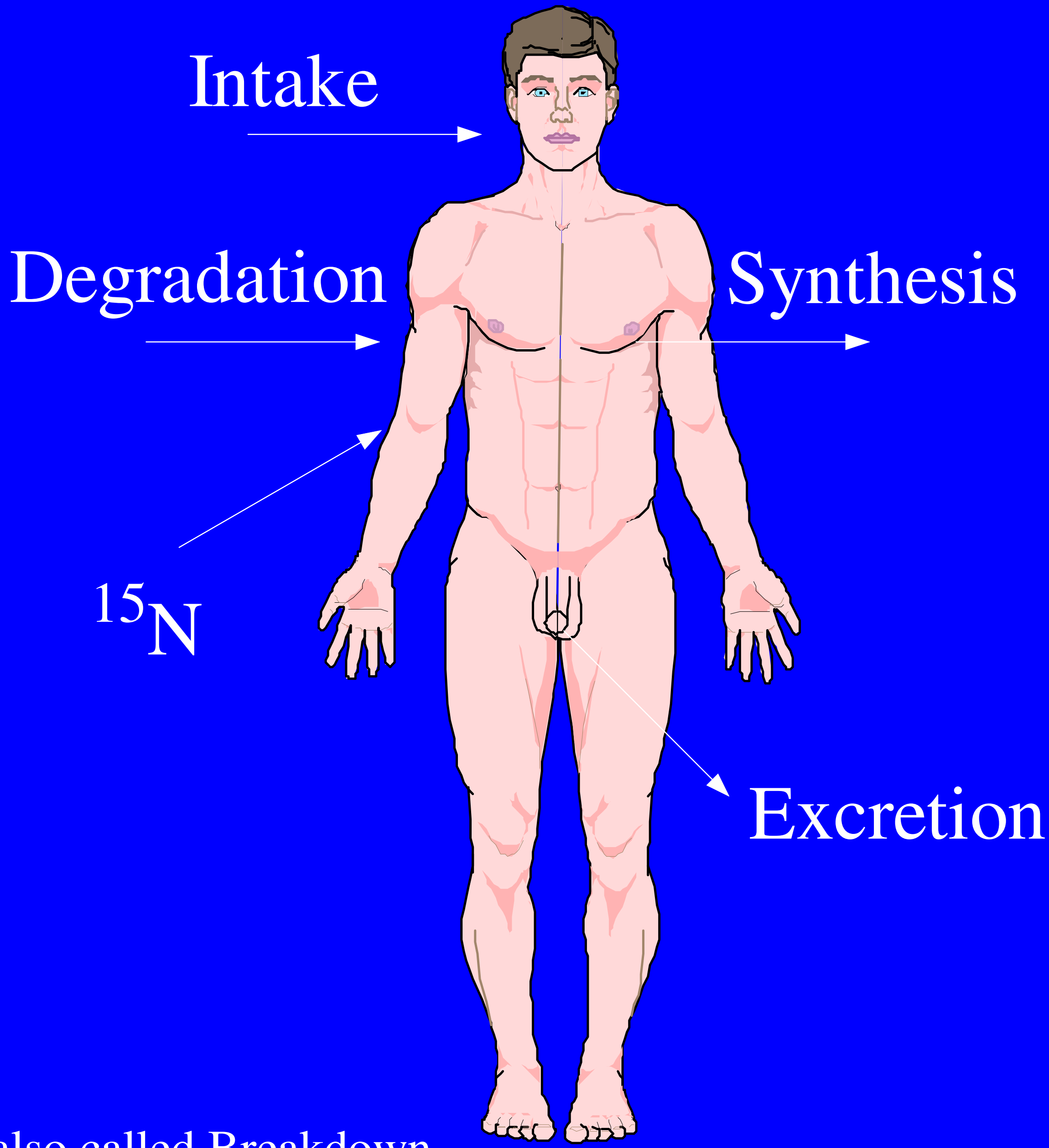
Amino acid synthesis

Metabolic Pathway	Important Enzymes	Nitrogen End-Products	Other Substrates
Amino acids converted to other amino acids			
Glutamate $+NH_3$	Glutamin synthetase	Glutamine	
Aspartate $+NH_3$	Asn synthetase	Asparagine	
Glutamate	…	Ornithine	
Ornithine	…	Citrullin	…
Citrullin	…	Arginine	…
Phenylalanine	Phenylalanine hydroxylase	Tyrosine	
Glutamate		Proline	
Serine		Glycin	
Methionine + serine		Cysteine	
Transamination from glutamate			
Glutamate		Alanine	Pyruvate
Glutamate		Aspartate	Oxaloacetate
Glutamate		Serin	Glucose
Other pathways			
α-ketoglutarate + NH_3		Glutamat	

Shils

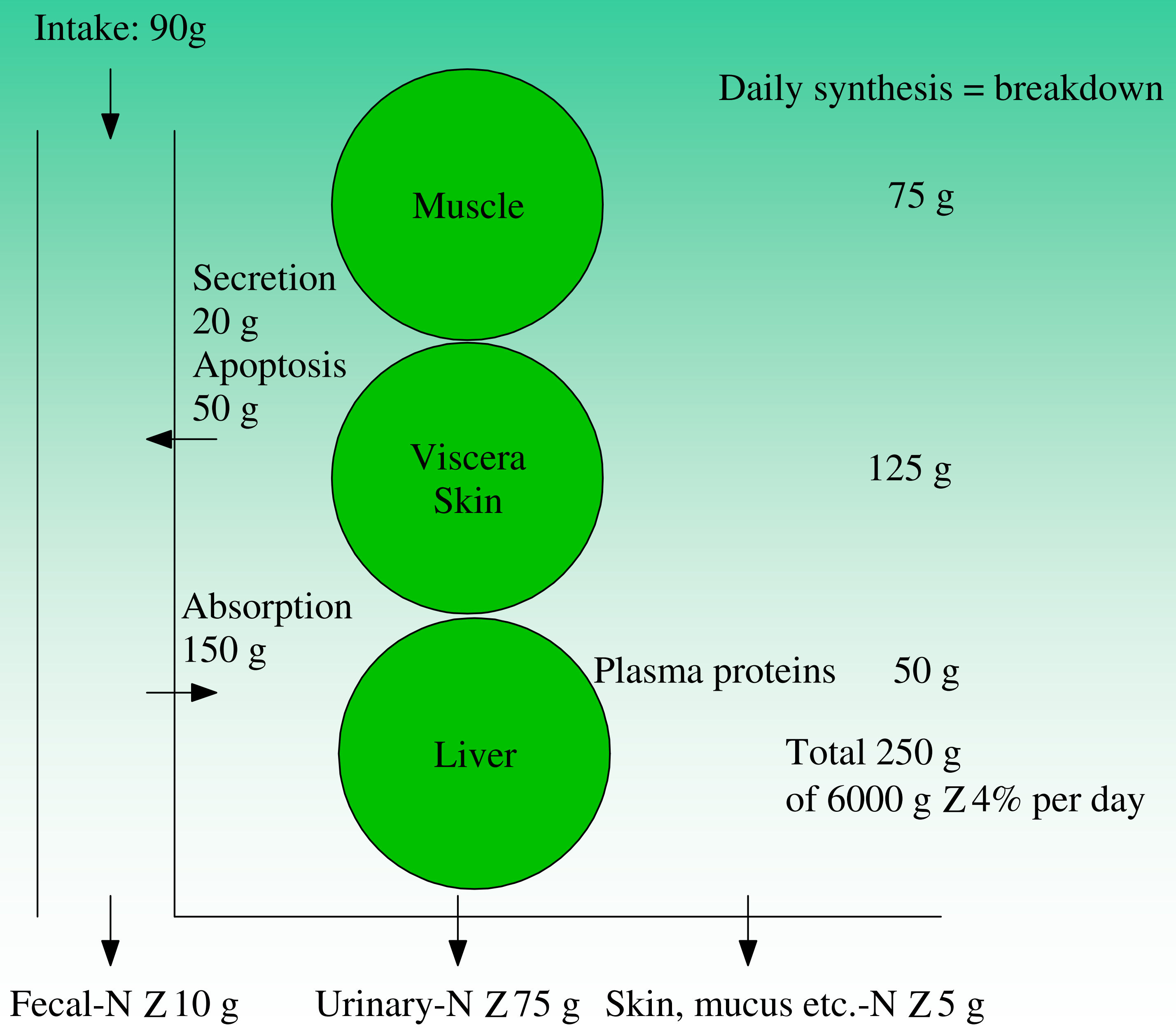
Amino acid catabolism   Shils Table 2.6

Metabolic Pathway	Important Enzymes	Nitrogen End-Products	Other End-Products
Transamination to form glutamate			
Alanine		Glutamate	Pyruvate
Aspartate		Glutamate	Oxaloacetate
Leucine		Glutamate	Ketones
Isoleucine		Glutamate	Succinate + Ketones
Valine		Glutamate	Succinate
Ornithine		2 Glutamate	α-ketoglutarate
Tyrosine		Glutamate	Ketone + Fumarate
Cysteine		Glutamate	Pyruvate + SO_4^{2-}
Amino acids converted to other amino acids			
Asparagine	Asparaginase	Aspartate + NH_3	
Glutamine	Glutaminase	Glutamate + NH_3	
Arginine	Arginase	Ornithine + urea	
Phenylalanine	Phenylalanine hydroxylase	Tyrosine	
Proline		Glutamate	
Cysteine		Taurine	



Degradation is also called Breakdown
Excretion is also called Catabolism

Protein turn-over

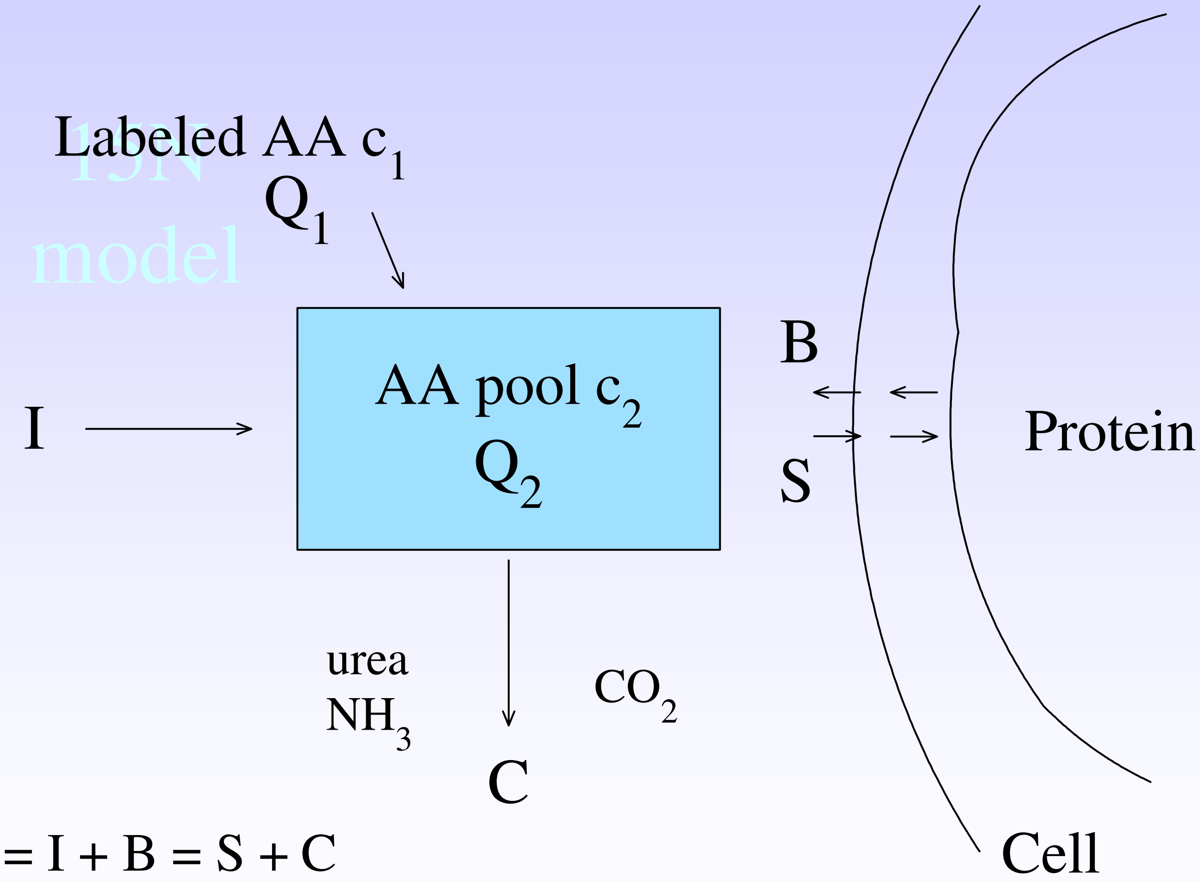


Dilution equation:

$c_1 \times v_1 = c_2 \times v_2$ □ $v_2 = c_1/c_2 \times v_1$

Fick's principle:

$c_1 \times Q_1 = c_2 \times Q_2$ □ $Q_2 = c_1/c_2 \times Q_1$



$Q_2 = I + B = S + C$

I = Intake; C = catabolism;

B = Breakdown; S = Synthesis

Q: ^{15}leu > ^{15}gly > ^{15}glu □ ^{14}leu

Millward: Anabolic drive ≈ NPU

Healthy volunteers investigated at a low, normal and high protein intake (milk protein).
NPU calculated as Δ leu balance/Δ leu intake.
Volunteers divided into high and low NPUs.

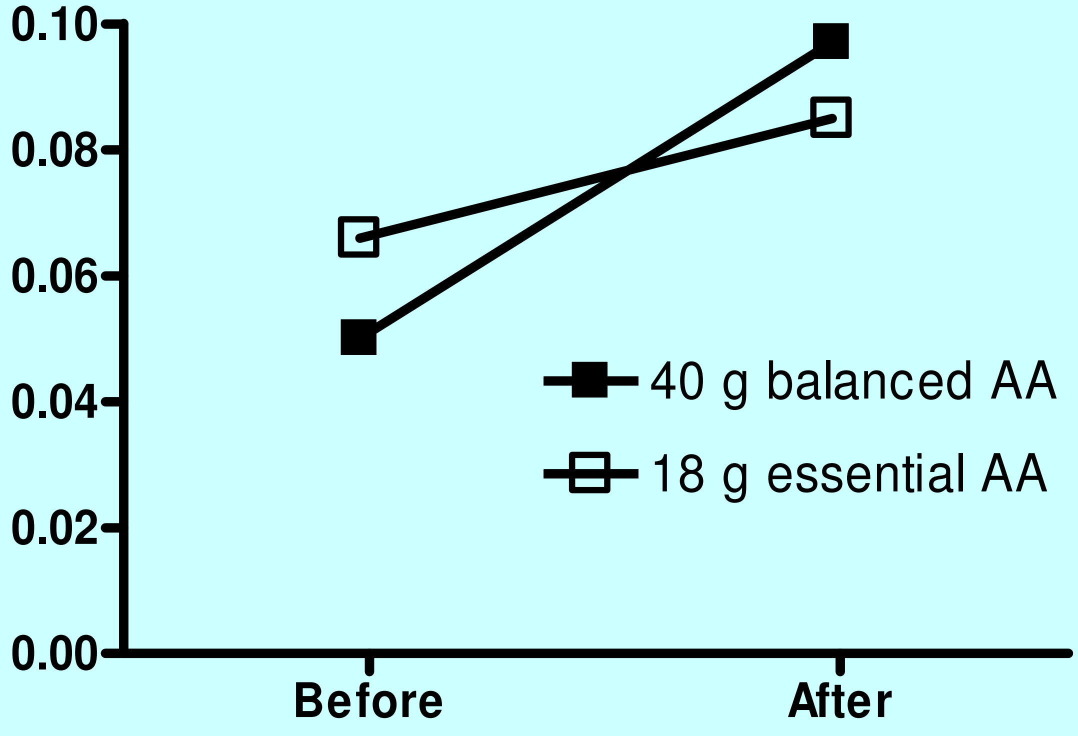
Changes in protein metabolism (μmol/h per kg) from low to high intake:		
	High NPU	Low NPU
Protein Synthesis	0	20
AA Oxidation	2	18
Protein Degradation	-70	- 30
Plasma AA	lower	

Effects probably mediated via AA & insulin
→ a food protein has different effects in different individuals
Also different effects of different proteins?

Fereday et al. 1998: Clin Sci 95:725-733; Millward et al. 1996; Baillière's Clin Endocrin Metabol 10: 533-549

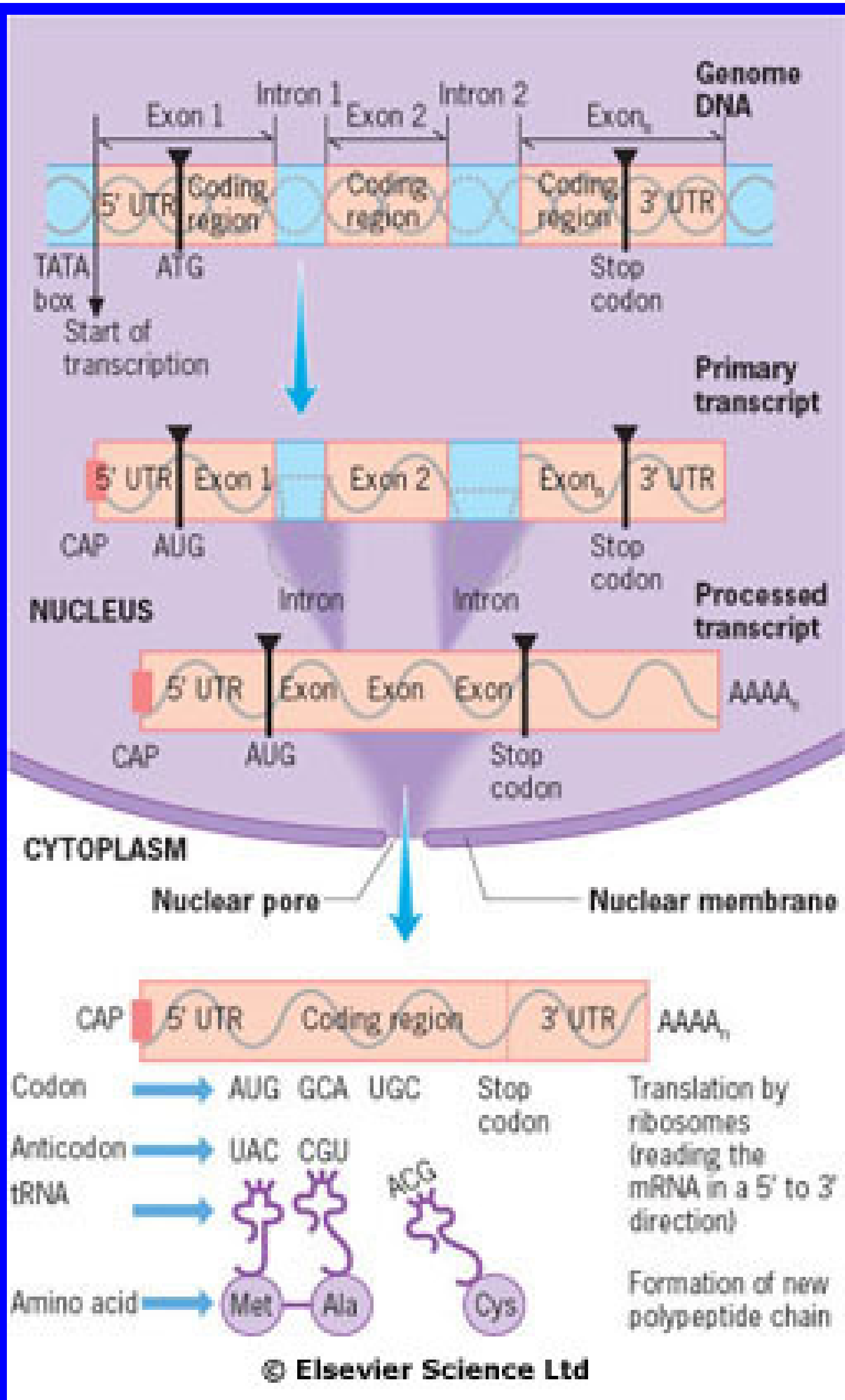
Effect on fractional synthesis rate in muscle

Volpi et al. Am J Clin Nutr 2003; 78:250-258



Essential AA responsible for postprandial stimulation of protein synthesis transcription

translation



Regulation

- SYNTHESIS
  - Leucine stimulates mRNA (i.e. transcription) for ribosomal protein
  - Leucine stimulates translation via initiation factors
  - Insulin stimulates leucine's effect on translation
- BREAKDOWN
  - BCAA (muscle) og Aromatic AA (liver) inhibit protein degradation
  - Insulin inhibits protein degradation

Anthony et al. Am J Physiol Endocrinol Metab 2001;281:E430-E439
Layman. Can J Appl Physiol 2002;27:646-662.
Nagasawa et al. J Nutr Biochemistry 2002; 13: 121-127

Synthesis of erythrocyte glutathione in healthy adults at 1.1 or 0.6 g prot/kg per day

Jackson et al. Am J Clin Nutr 2004;80:101-107

Synthesis of albumin in healthy adults at 1.4 or 0.6 g prot/kg per day

Jackson et al. Am J Physiol 2001;281:1179-87

Table 3. *The concentration, FSR, and ASR of plasma albumin in 6 normal adults before and following consuming a diet that provided a marginal level of protein for 7 days*

	Concentration, g/l	FSR, %/day		ASR, $mg \cdot kg^{-1} \cdot day^{-1}$	
		Plasma	VLDL-apoB-100	Plasma	VLDL-apoB-100
Study 1	39.4 ± 1.11	8.50 ± 0.96	13.7 ± 1.02	151 ± 14	258 ± 25
Study 2	37.9 ± 1.20	5.1 ± 0.56*	8.22 ± 0.61*	91 ± 8*	155 ± 15*

Albumin synthesis during hourly meals

Barber et al. Am J Physiol Endocrinol Metab 2000;279:E707-14

	Healthy	Cancer
Body weight, kg	77	56
Wt loss, %	-	19
S-albumin, g/l	45	42

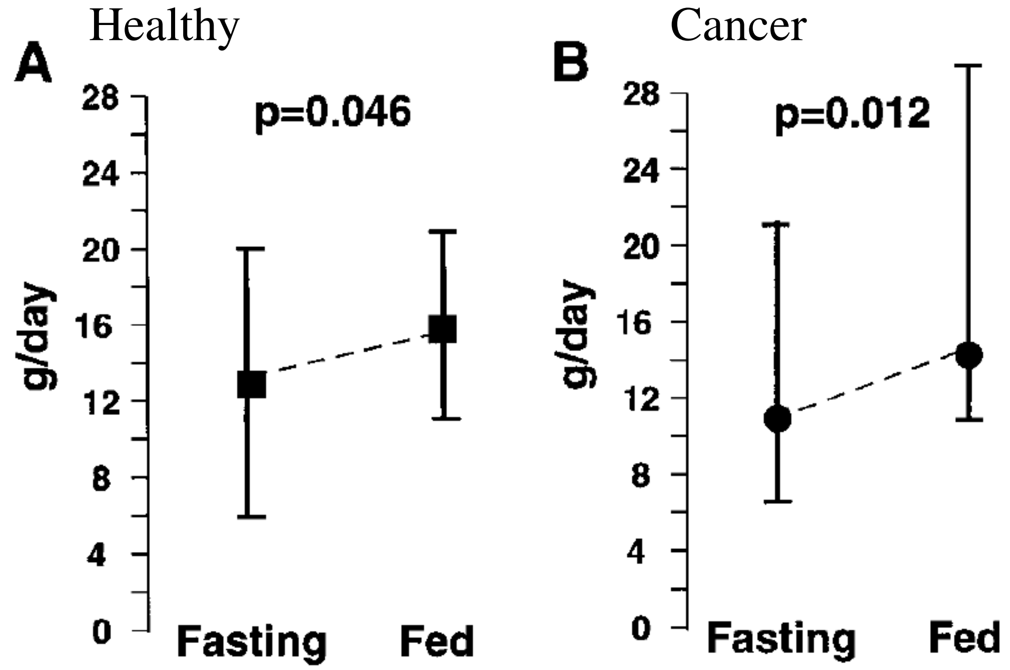


Fig. 3. Albumin total synthesis rates in fasted and fed state in healthy controls (*A*) and weight-losing cancer patients (*B*). Graph presents medians (symbols) and ranges (SE bars). Median rise is 24% for *A* and 29% for *B*. Comparison between fasting and fed values is by the Wilcoxon signed rank test. There was no significant difference between control and cancer patient values by Mann-Whitney *U*-test (P = 0.70 fasting, P = 0.30 fed).

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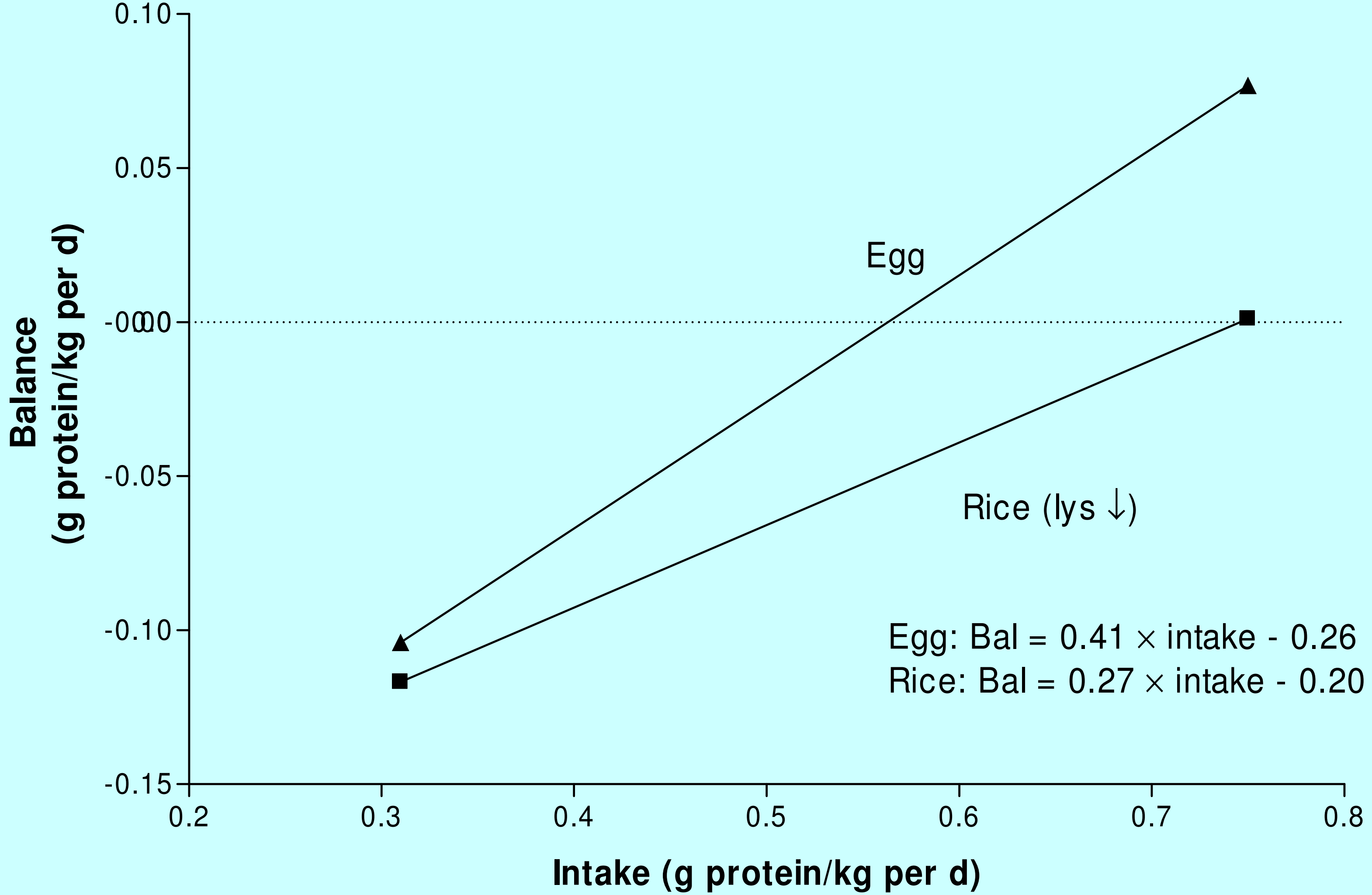
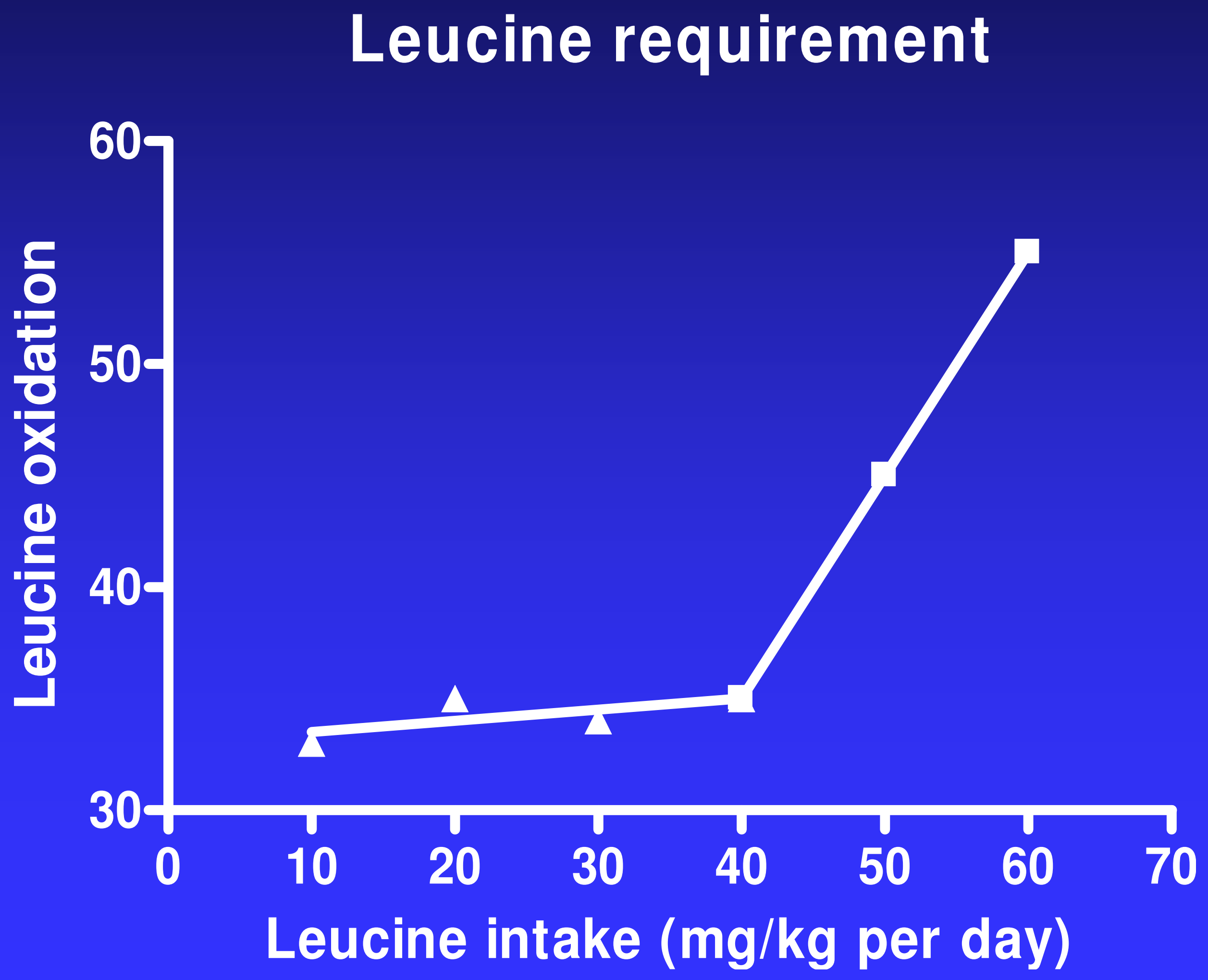
Protein requirement and utilization with rice or egg
Inout et al J Nutr 1973; 103: 1673-1687



Requirement for essential amino acids



Protein and amino acid requirements in human nutrition

Report of a Joint WHO/FAO/UNU Expert Consultation - 2007

	2007	1985
Total protein, g/kg per day	**0.83**	**0.75**
Histidine, mg/kg per day	10	10
Isoleucine, mg/kg per day	20	10
Leucine, mg/kg per day	39	14
Lysine, mg/kg per day	30	12
Methionine & Cysteine, mg/kg per day	15	13
Methionine, mg/kg per day	10	-
Cysteine, mg/kg per day	4	-
Phenylalanine & Tyrosine, mg/kg per day	25	14
Threonine, mg/kg per day	15	7
Tryptophan, mg/kg per day	4	4
Valine, mg/kg per day	26	10
Total essential amino acids, mg/kg per day	**184**	**94**
% of total protein	**22**	**13**

Protein and amino acid requirements in human nutrition

Report of a Joint WHO/FAO/UNU Expert Consultation - 2007

Table 24

Distribution of amino acids in food proteins and diets

	Percentage of requirement pattern[a]											
	Egg	**Beef**	**Milk**	**Soya**	**Potato**	**Rice**	**Maize**	**Wheat**	**Cassava**	**Yam**	**UK diet[b]**	**Indian diet[c]**
Lys	139	203	158	144	121	**86**	**58**	**57**	**92**	**91**	140	**87**
Tryp	293	213	417	217	240	224	117	217	192	213	211	293
Threo	223	202	191	191	167	153	157	127	115	157	177	143
SAA	225	182	164	114	131	176	132	203	124	125	174	182
BCAA	168	144	151	136	120	146	177	122	**79**	116	143	132
TAAA	301	275	271	281	243	305	314	306	135	265	311	317

Lys, lysine; Tryp, tryptophan; Threo, threonine; SAA, sulfur amino acids; BCAA, branched-chain amino acids; TAAA, total aromatic amino acids.

(mg EAA/g dietary prot)/(mg req EAA/g req prot)

Effect of oral leucine on protein synthesis in rats

Crozier et al. J Nutr 2005;135:376-82.

100% = the daily intake (1.35 g leucine/kg body wt)

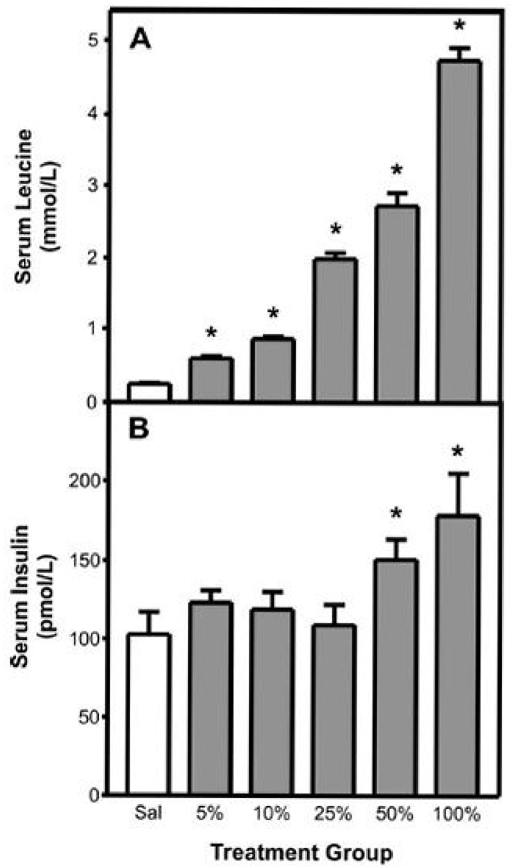


FIGURE 1 Changes in (*A*) serum leucine and (*B*) insulin concentrations following oral leucine administration in rats. Serum leucine and insulin concentrations were measured 30 min following administration of saline or leucine at doses ranging from 0.068 to 1.35 g leucine/kg body wt. Values are means ± SE, n = 8–12. *Different from saline-treated controls, $P < 0.05$.

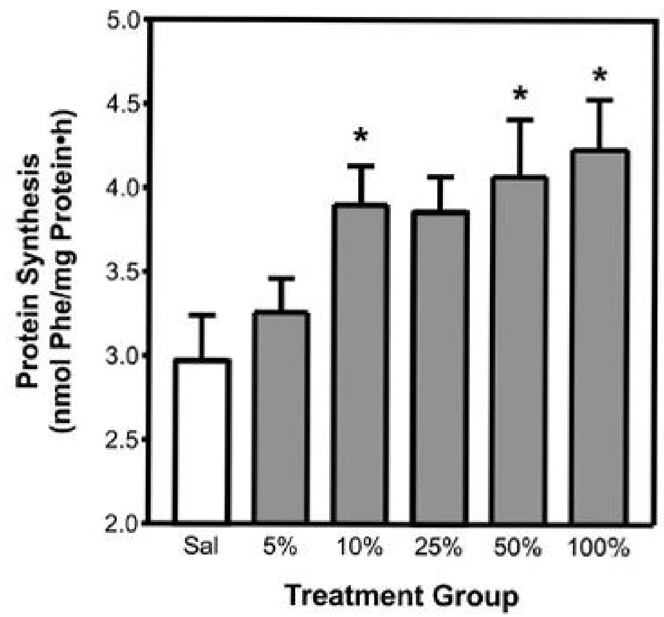


FIGURE 2 Rates of protein synthesis in gastrocnemius muscle of rats following oral leucine administration. Protein synthesis was measured by the incorporation of [^{3}H]phenylanlanine into protein 30 min following administration of saline or leucine at doses ranging from 0.068 to 1.35 g leucine/kg body wt. Values are means ± SE, n = 6–12. *Different from saline-treated controls, $P < 0.05$.

Effect of dietary protein on protein synthesis in rats.

Whey: 11% leucine; wheat: 7% leucine;

30 E % whey = 0.6 g leucine/kg body weight

Norton et al. J Nutr 2009;139:1103-9

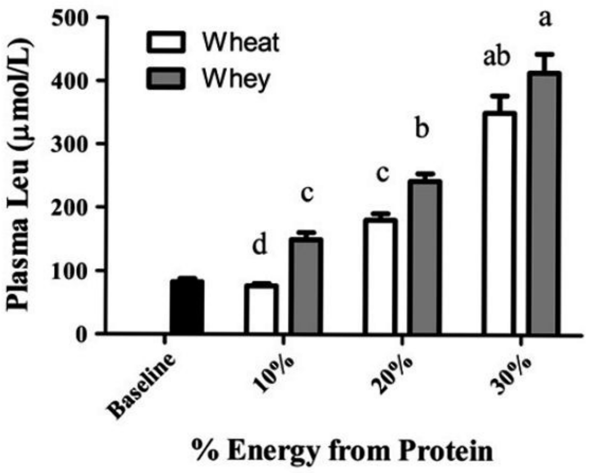


FIGURE 4 Plasma Leu concentrations of rats fed complete meals containing either wheat or whey at 3 different total protein contents (10, 20, or 30% of energy). Data are means ± SEM; $n = 7$–8. Labeled means without a common letter differ, $P < 0.05$. All fed groups except 10% wheat differed from baseline, $P < 0.05$.

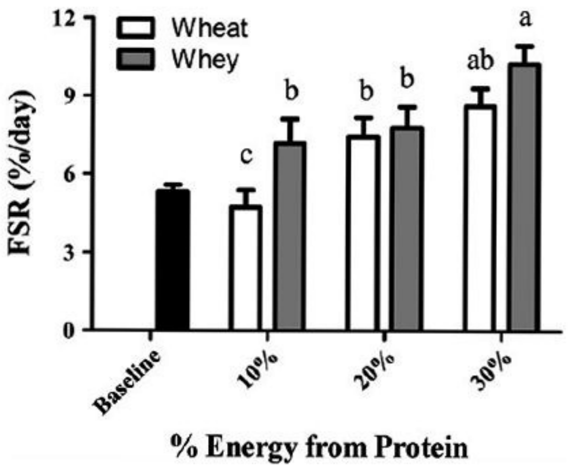


FIGURE 6 Rates of protein synthesis in gastrocnemius muscle of rats fed a complete meal containing either or whey at 3 different total protein contents (10, 20, or 30% of energy). Data are means ± SEM; $n = 7$–8. Labeled means without a common letter differ, $P < 0.05$. All fed groups except 10% wheat differed from baseline, $P < 0.05$.

3 months' AA supplementation in healthy elderly
(12 g: leu, ileu, val, lys, cys, his, thr, met, phe, tyr, try)

Scognamiglio et al. Gerontology 2005; 51:302-308

(2N = 95. Age: 75 yrs. BMI: 27. Usual intake: 1700 Kcal, 62 g protein.

	Control	AA
Max handgrip, kg	14 → 14	15 → 20[1)]
LV ejection fraction, exercise[*)]	56 → 56	55 → 67[2)]
6 min walking, m	212 → 212	215 → 269[1)]
Questionnaire, walking stairs, score	73 → 72	72 → 98[1)]

[*)] 3 min at 40% of Max handgrip

[1)] $P<0.001$ [2)] $P<0.01$

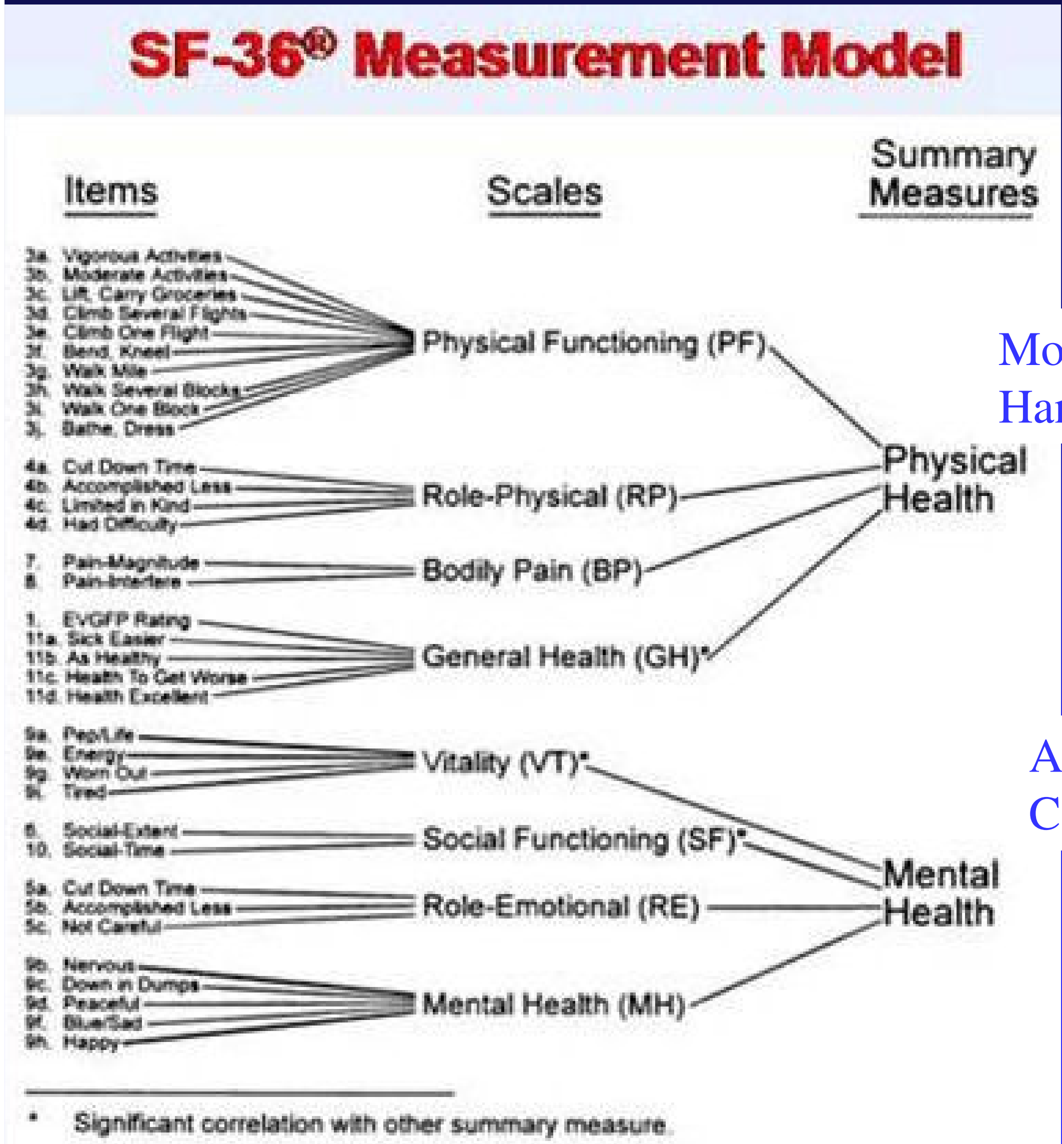
Protein: i går – i dag – i morgen

- Historie
- Nitrogen balance
- Metabolisme & anabolt drive: genopbygning efter natlig faste, fysisk aktivitet, hungersnød og sygdom
- Essentielle aminosyrer
- Protein og funktion
  AA og ikke-krops-protein funktioner
- Patienter

What should we measure for ”long-term health and well-being”?

Recording ≈ Subjective

Measuring ≈ Objective



Mobility (timed-up-and go), **TUG**

Hand grip strength & endurance, **HGS & HGE**

Addenbrooke’s Cognitive examination, **ACE**

Continuous Reaction Time, **CRT**

- requires a lot of validation

Lene Holm Jakobsen

Accomodation to 8 weeks' inadequate protein intake.

2N=12. Castaneda et al. Am J Clin Nutr 1995; 62: 30-39

	Low Prot	Control
Intake, g/kg per d	0.47	0.91
Balance, g/kg per d	-0.03	0.01
LBM-DEXA, kg	41 → 39[1)]	38 → 40
Skin test, n antigens	3.0 → 1.5[1)]	1.7 → 2.5
Muscle relaxation rate	12 → 9[1)]	12 → 10

[1)] Sign ≠ base-line [2)] Sign ≠ ctr [3)] Sign ≠ ctr and 3 weeks

N balance adapted – but loss of function

5 weeks' supplementation with milk protein daily in elderly with hip fracture.

(2N = 62. Age: 82 yrs. BMI: 24. Usual intake: 48 g protein.
Tkatch et al. J Am Col Nutr 1992;11:519-25

	Control Iso E CH	Protein 20 g
Reduced femoral BMD in 7 mths, N	12	6[1)]
Favorable clinical course, % of N	36	79[2)]
Complications incl. death, % of N	80	52[1)]
Length of stay incl. rehab, d	102	69[1)]

[1)] $P<0.05$ [2)] $P=0.02$

6 months' supplementation with milk protein daily in elderly with hip fracture.

(2N = 82. Age: 81 yrs. BMI: 24. Usual intake: 48 g protein.
Schurch et al. Ann Intern Med 1998;128:801-9.

	Control Iso E CH	Protein 20 g
Change in IGF-I, µg/l	24.5	45.1[1)]
Change in femoral BMD, %	-4.7	-2.3[2)]
Length of stay, d	54	33[1)]

[1)] P=0.02 [2)] P=0.03

Supplements in Kenyan schoolchildren

1255 kJ ”with >3 times the recommended level of protein intake” for 23 months

Avg. age: 7 years, 25% stunted, 2% wasted

Grillenberger et al. 2003; J Nutr 133: 3975S-3964S

	Meat	Milk	Energy	Control
Δ weight, kg [1)]	3.9	3.9	3.9	3.5
Δ MAMA, mm^2 [1) 2)]	153	118	116	85
Δ Physical activity [3)]	↑			

[1)] All groups ≠ control

[2)] meat ≠ milk

[3)] significantly greater in meat group (data not published)

MAMA = mid-arm-muscle-circumference

Proteinbalance ved indtag af 1.2 g protein/kg per dag fra hhv. æggehvide og mælk hos børn med kwashiorkor 2N=22

Manary et al Am J Clin Nutr 1997; 66: 643-648

	æggehvide	mælk
Kost Try bidrag til AFP syntese, %	61	71
Urea appearance rate (μmol/kg per h)	195	137[1)]
Leucin oxidation (μmol/kg per h)	21	15[1)]
Protein Degradation (μmol/kg per h)	255	222
Protein Syntese (μmol/kg per h)	266	243
C reaktivt protein (mg/l)	13	30
TNF-α (ng/l)	17	38

[1)] P= 0.048

Tabel 2.7.

Food protein: non-tissue-protein functions

Amino Acid	Incorporated Into
Arginine	Creatine
Aspartate	Purines (A & G) and pyrimidines (C & U)
Cysteine	Glutathione
	Taurine
Glutamate	Neurotransmitters (GABA, glu), Glutathione
Glutamine	Purines and pyrimidines
Glycine	Creatine, Glutathione
	Porphryins (hemoglobin and cytochromes)
	Purines
Histidine	Histamine
Lysine	Carnitine
Methionine	One-carbon methylation/transfer reactions
	Creatine
	Choline
Serine	One-carbon methylation/transfer reactions
	Ethanolamine and choline
Tyrosine	Neurotransmitters (catecholaminer)
Tryptophan	Neurotransmitters (serotonin)

Shils Table 2.7

Protein: i går – i dag – i morgen

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  AA og ikke-krops-protein funktioner
- Patienter

Protein and amino acid requirements in human nutrition

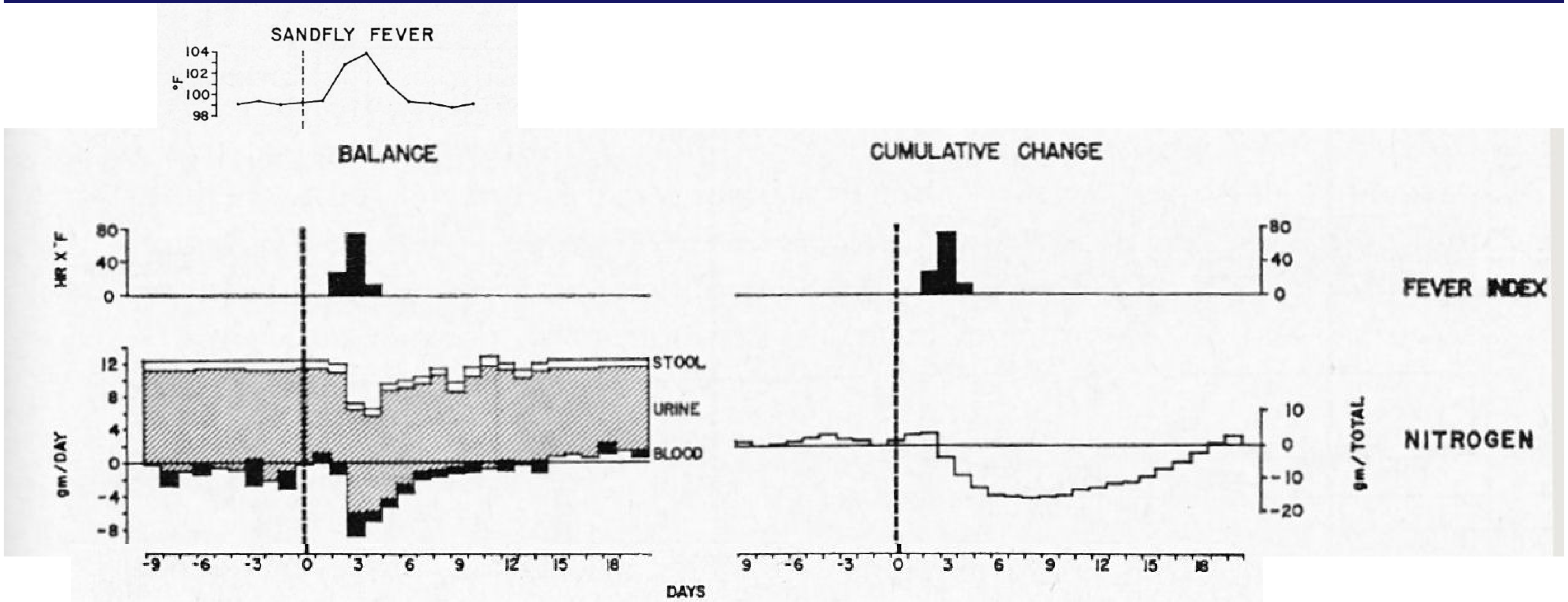
Report of a Joint WHO/FAO/UNU Expert Consultation - 2007

Patients…

Protein and amino acid requirements in human nutrition

Report of a Joint WHO/FAO/UNU Expert Consultation - 2007

Chapter 11: Influence of infection on protein and amino acid requirements



Effect of 3 days' sandfly fever in healthy volunteers.

35% of cumulative nitrogen loss due to decreased intake

Beisel et al. Ann Intern Med 1967; 67:744-779; Powanda & Beisel. Review. J Nutr 2003;133:322S-327S.

Intake in at-risk patients

2 N = 212 patients at risk (NRS-2002) in 3 hospitals from multiple specialities were randomized to standard treatment or a daily follow-up care by a team of nurse and dietitian. Mean ± SD

Intake (mean ± SEM)	Control N=99	Team N=103
Energy intake, kJ/kg per d	106 ± 5	126 ± 5[1)]
Protein intake, g/kg per d	0.9 ± 0.04	1.1 ± 0.04[1)]
Energy, % of requirement	84 ± 3	99 ± 3[1)]
Protein, % of requirement	66 ± 3	83 ± 3[1)]
Protein, % ptt ≥ 75% of req.	36	62[2)]
Protein, % ptt ≥ 75% of req.[a)]	46	81[3)]

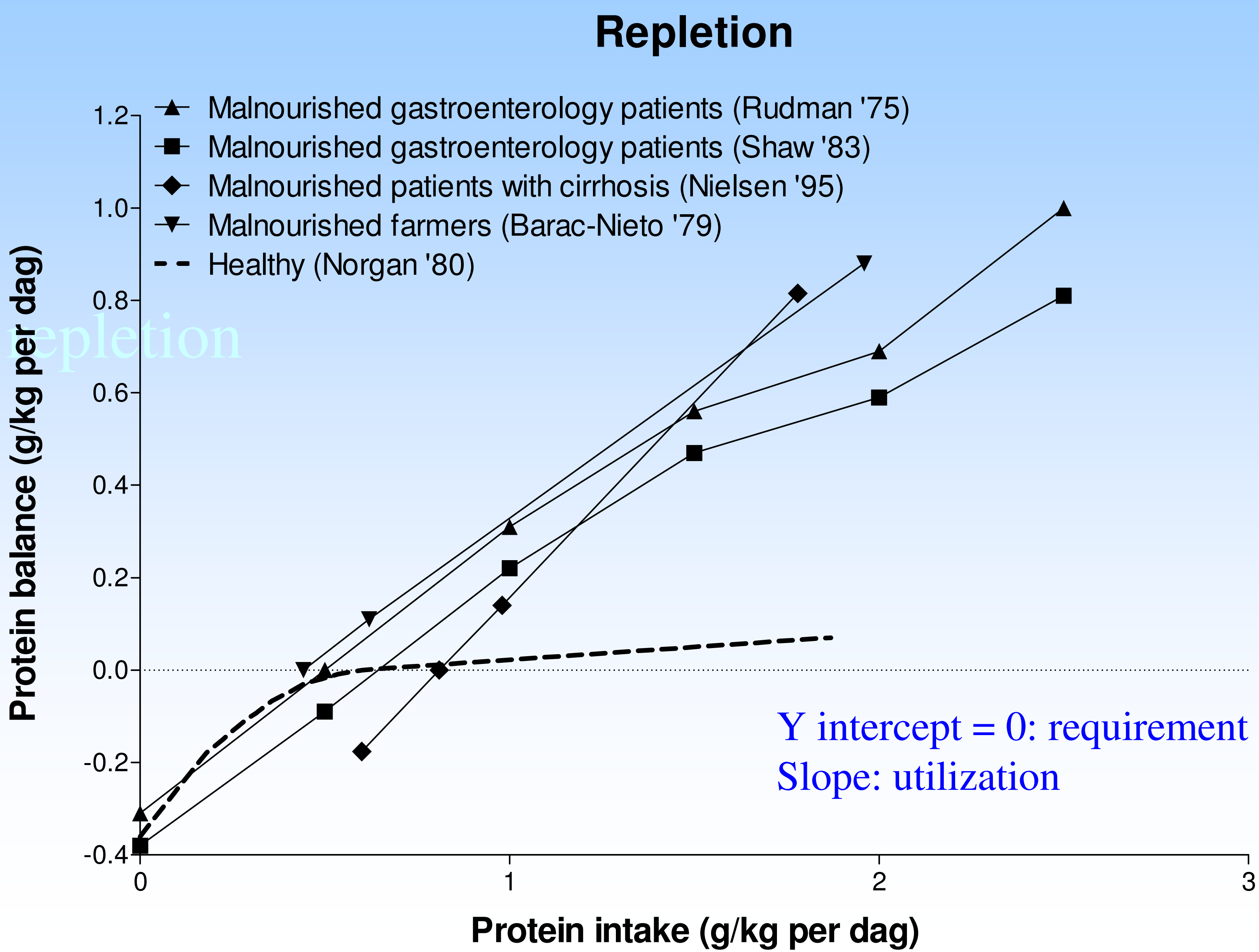
[a)] ≥4days, not terminally ill, not starving due to procedures

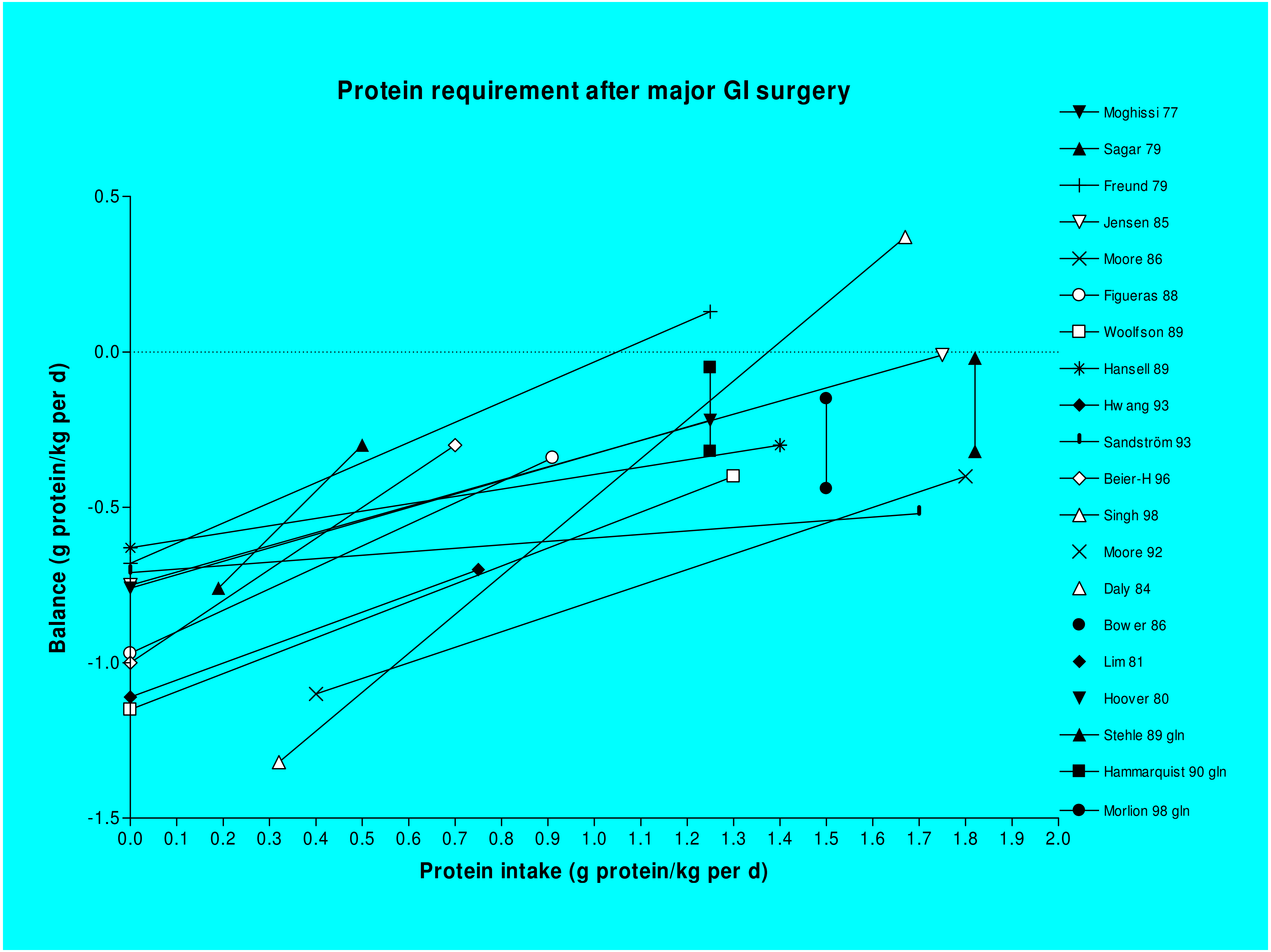
[1)] P < 0.005 [2)] P = 0.0004 [2)] P < 0.0001

Johansen N et al. Clin Nutr 2004; 23:539-550

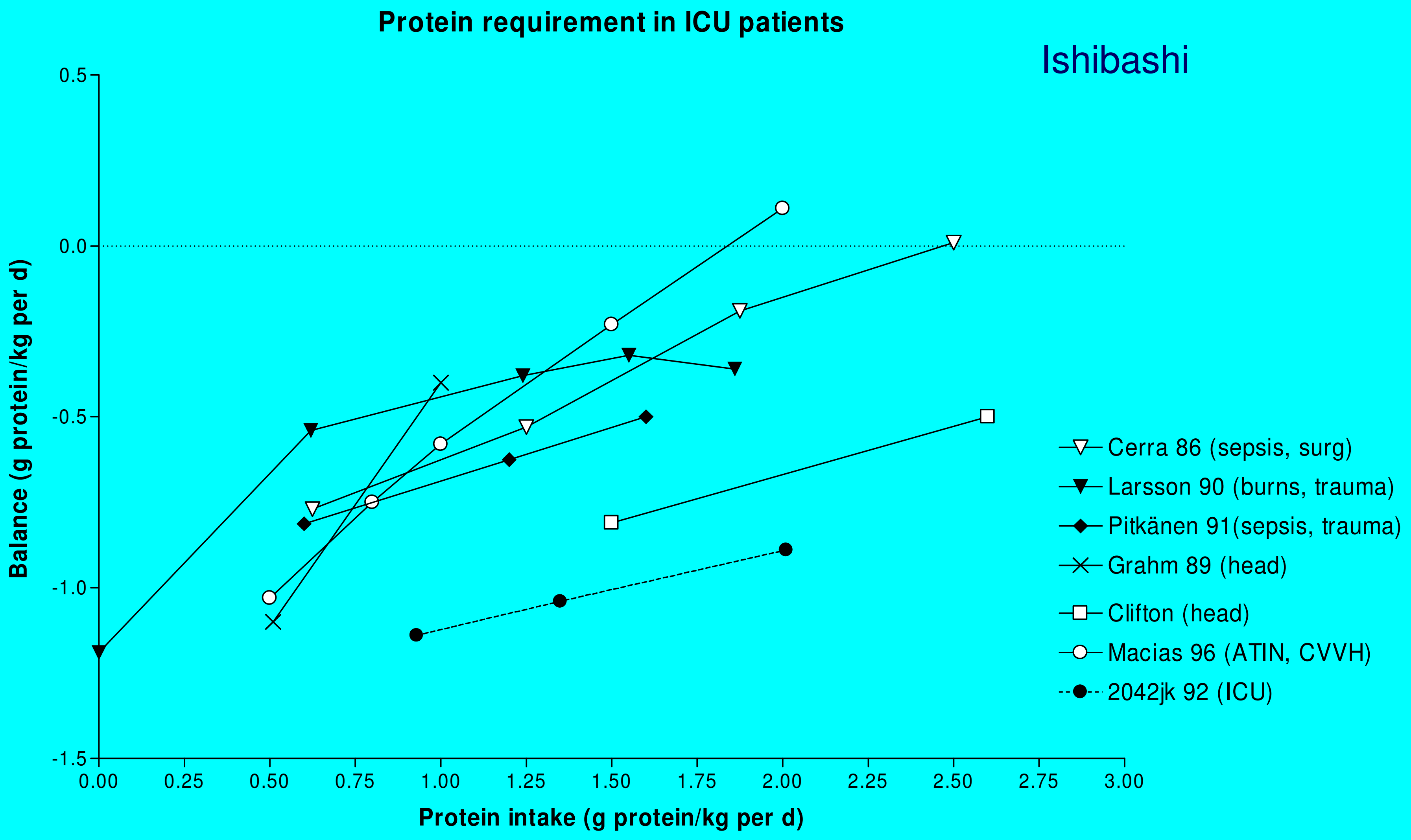
Anabolic drive ≈ NPU.

Results from balance between whole body protein synthesis and breakdown





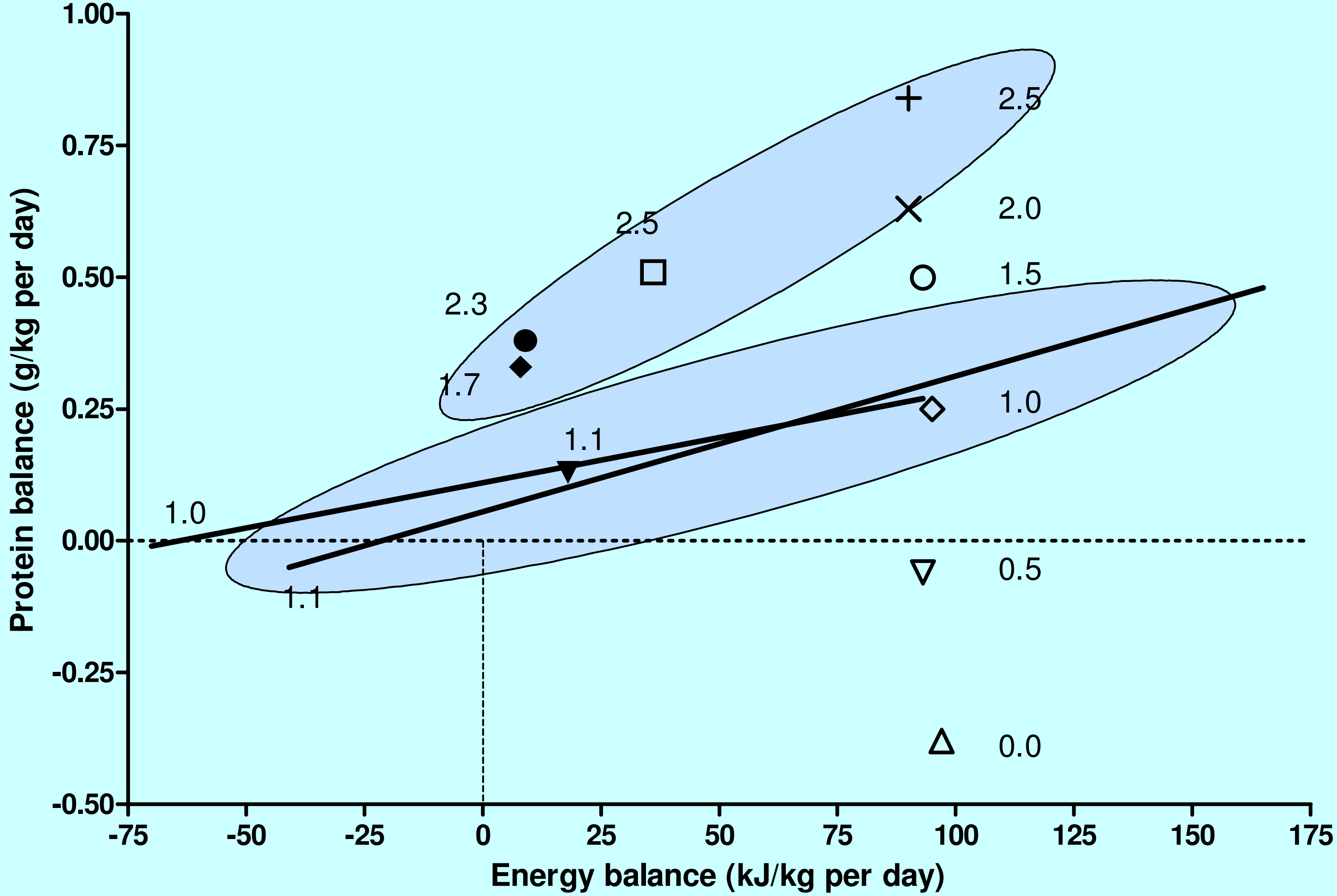
Protein requirement after major GI surgery
Balance (g protein/kg per d)
Protein intake (g protein/kg per d)
0.5
0.0
-0.5
-1.0
-1.5
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8 1.9 2.0
Moghissi 77
Sagar 79
Freund 79
Jensen 85
Moore 86
Figueras 88
Woolfson 89
Hansell 89
Hw ang 93
Sandström 93
Beier-H 96
Singh 98
Moore 92
Daly 84
Bow er 86
Lim 81
Hoover 80
Stehle 89 gln
Hammarquist 90 gln
Morlion 98 gln

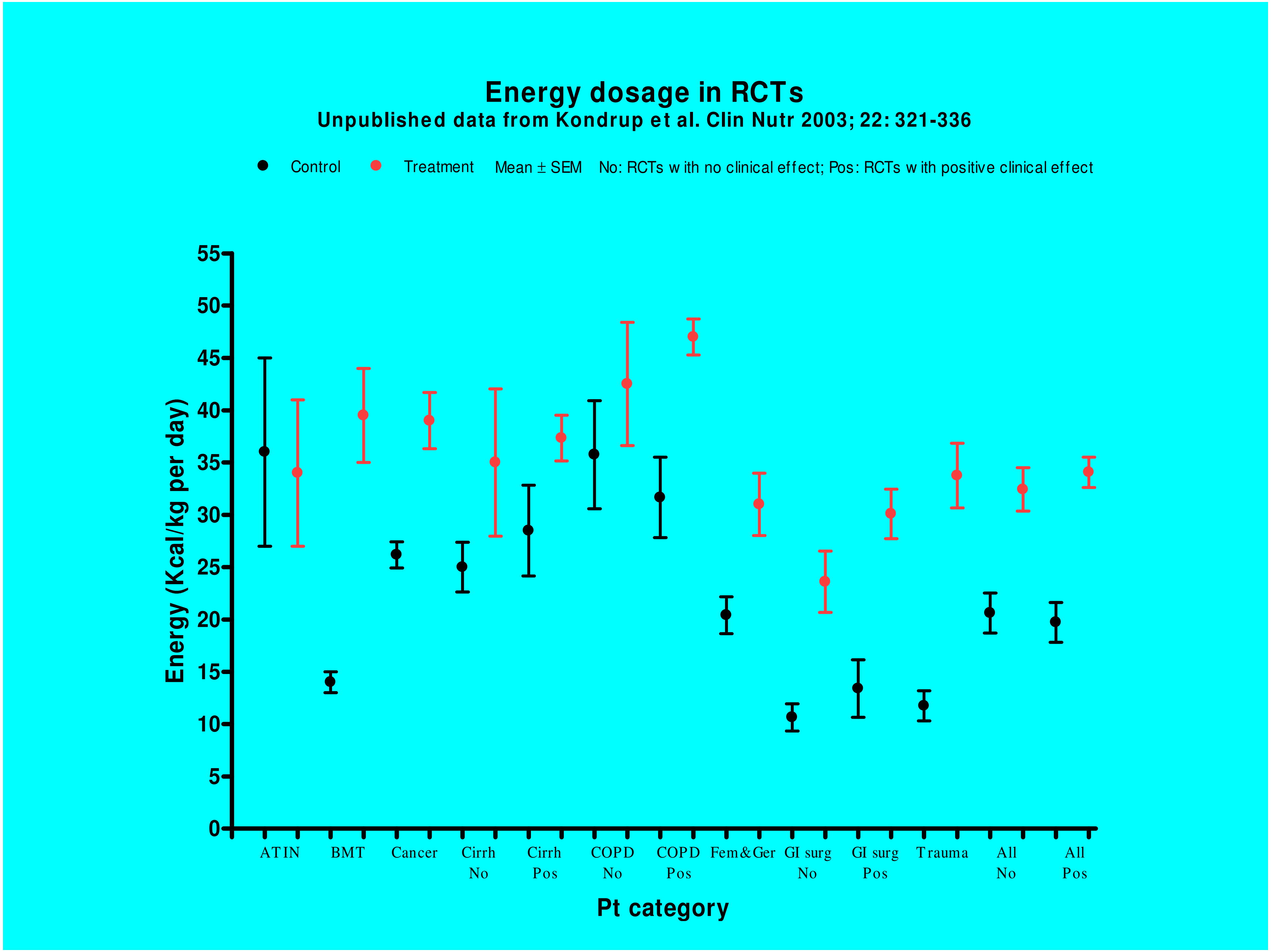

Protein requirement in ICU patients
Ishibashi
Balance (g protein/kg per d)
Protein intake (g protein/kg per d)
0.5
0.0
-0.5
-1.0
-1.5
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
2.25
2.50
2.75
3.00
Cerra 86 (sepsis, surg)
Larsson 90 (burns, trauma)
Pitkänen 91(sepsis, trauma)
Grahm 89 (head)
Clifton (head)
Macias 96 (ATIN, CVVH)
2042jk 92 (ICU)

Protein balance & Energy balance in depleted patients

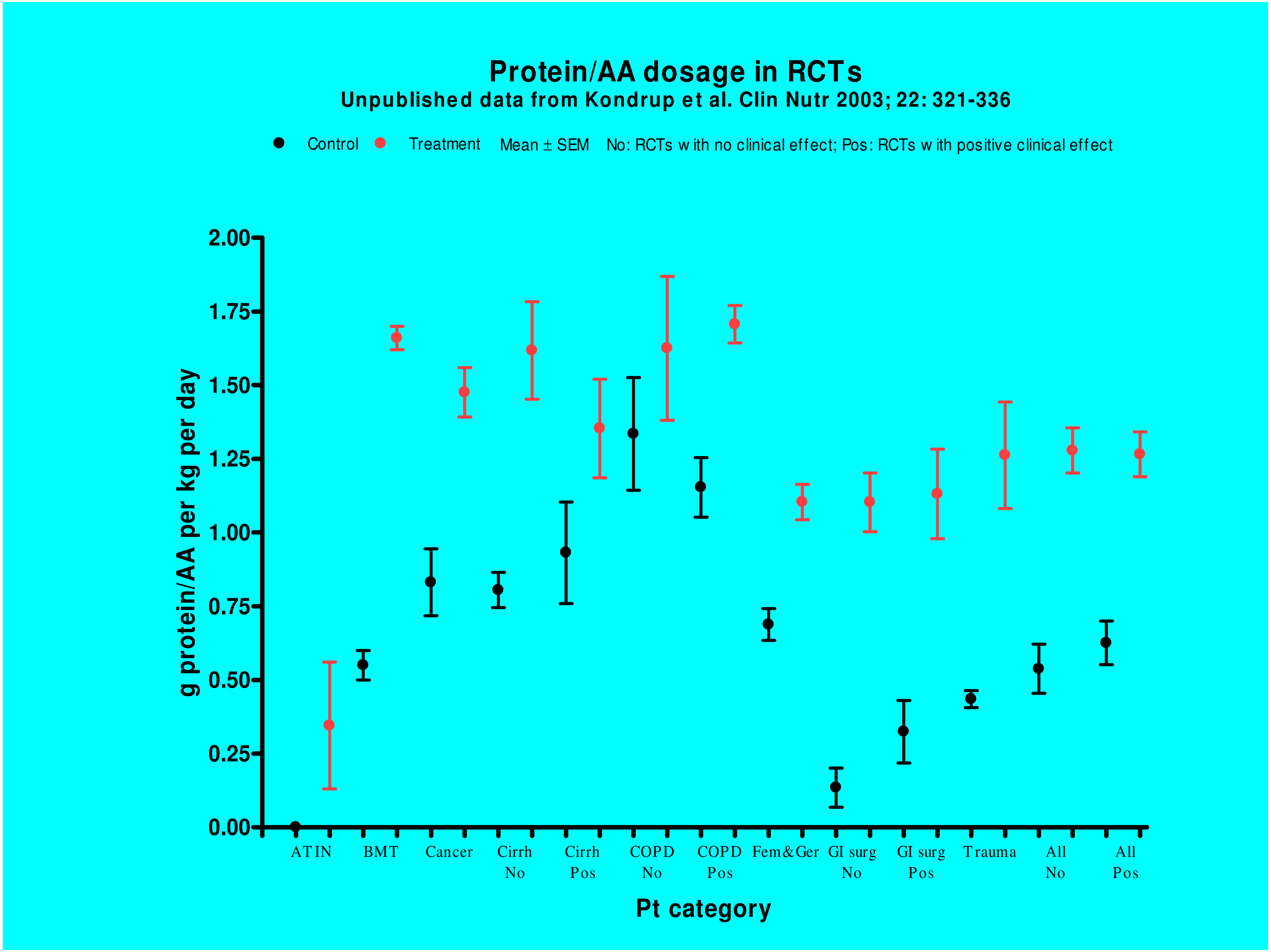
Chikenji et al. Clin Sci 1987; 72: 489-501

Numbers: protein intake (g/kg per day)



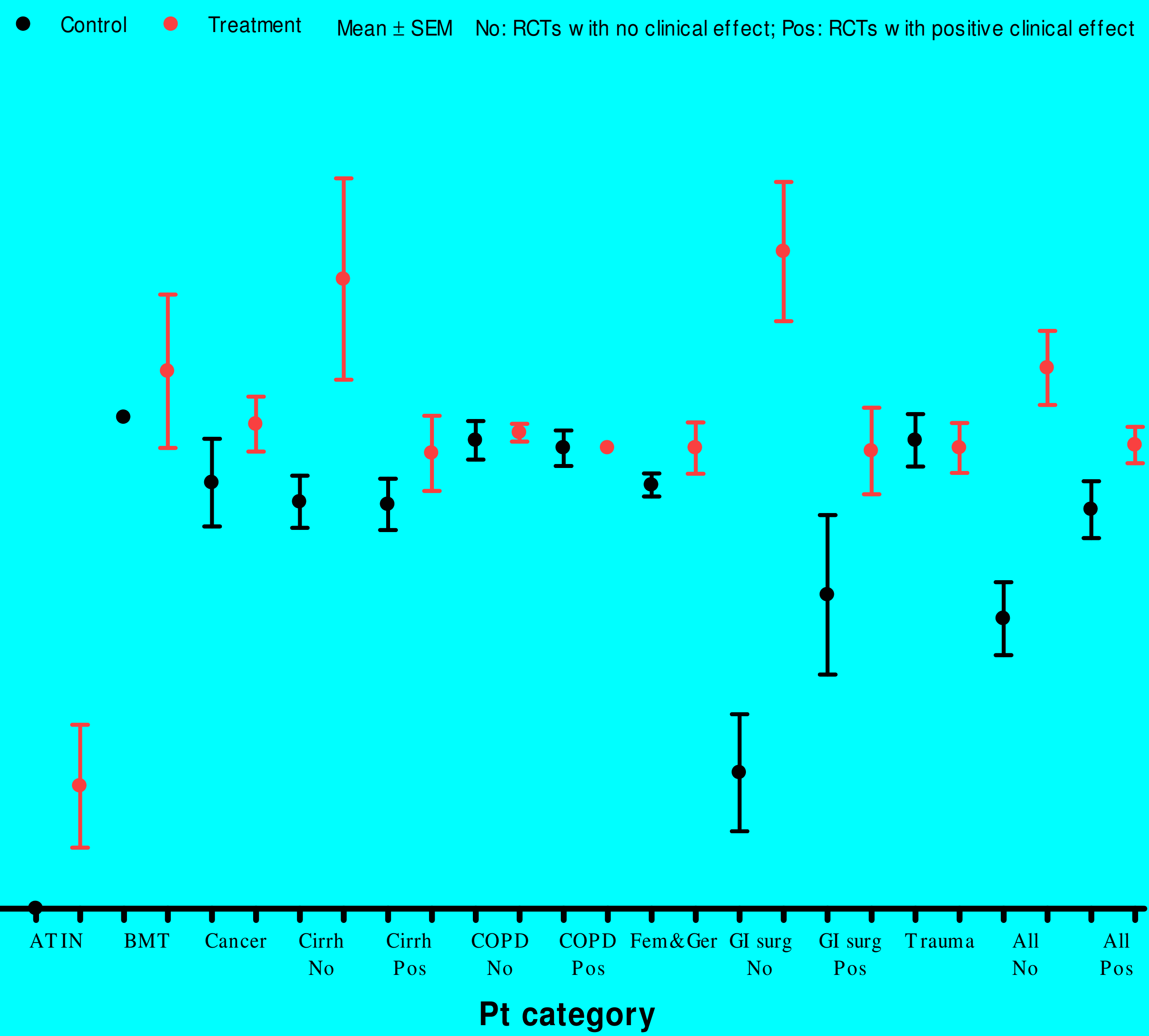


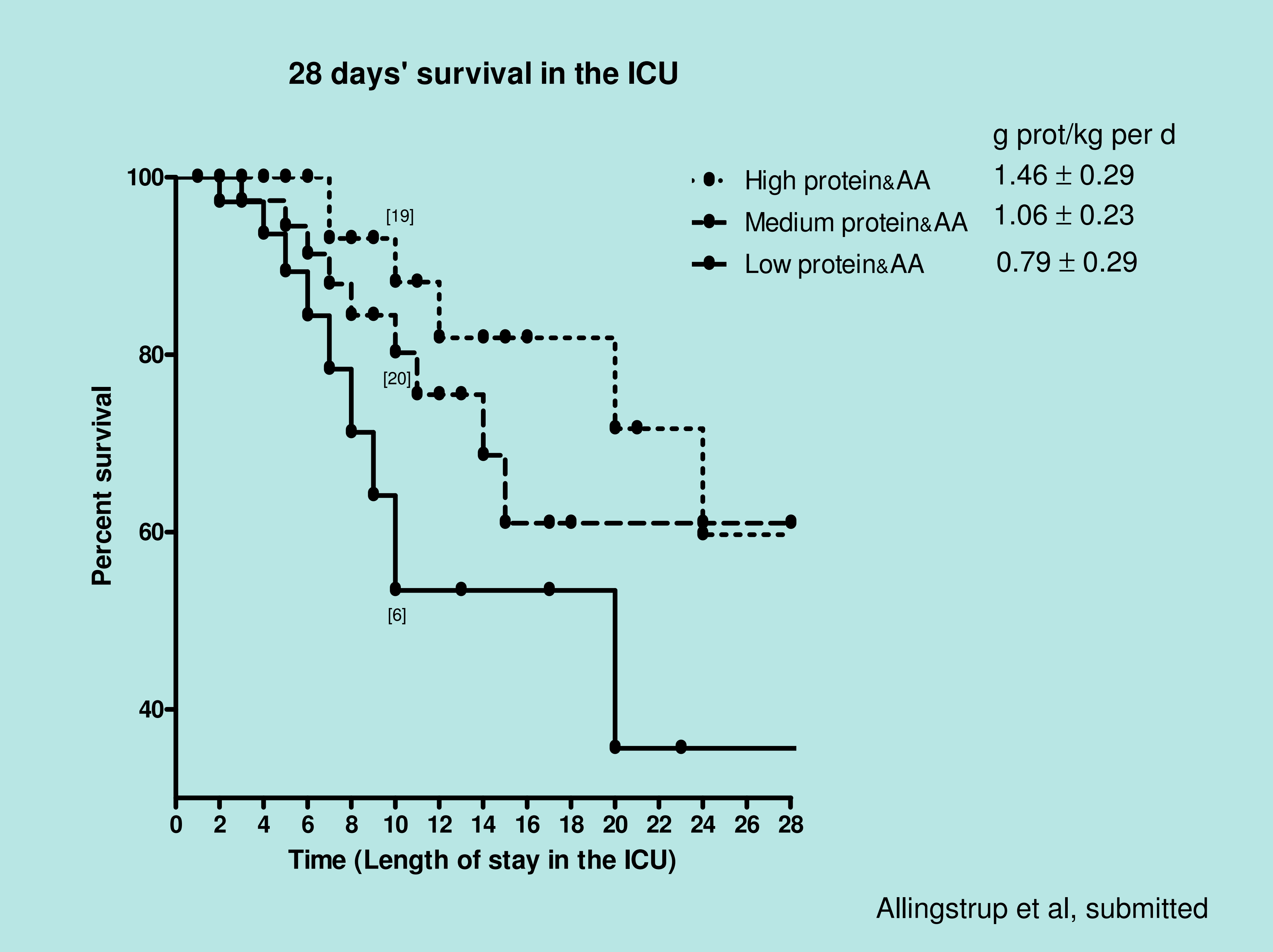
Energy dosage in RCTs
Unpublished data from Kondrup et al. Clin Nutr 2003; 22: 321-336
Control
Treatment
Mean ± SEM
No: RCTs with no clinical effect; Pos: RCTs with positive clinical effect
Energy (Kcal/kg per day)
55
50
45
40
35
30
25
20
15
10
5
0
ATIN
BMT
Cancer
Cirrh No
Cirrh Pos
COPD No
COPD Pos
Fem&Ger
GI surg No
GI surg Pos
Trauma
All No
All Pos
Pt category


Protein/AA dosage in RCTs
Unpublished data from Kondrup et al. Clin Nutr 2003; 22: 321-336
Control
Treatment
Mean ± SEM
No: RCTs with no clinical effect; Pos: RCTs with positive clinical effect
g protein/AA per kg per day
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
ATIN
BMT
Cancer
Cirrh No
Cirrh Pos
COPD No
COPD Pos
Fem&Ger
GI surg No
GI surg Pos
Trauma
All No
All Pos
Pt category

Protein/AA Energy% in RCTs

Unpublished data from Kondrup et al. Clin Nutr 2003; 22: 321-336




28 days' survival in the ICU
g prot/kg per d
High protein&AA
1.46 ± 0.29
Medium protein&AA
1.06 ± 0.23
Low protein&AA
0.79 ± 0.29
Percent survival
100
80
60
40
[19]
[20]
[6]
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Time (Length of stay in the ICU)
Allingstrup et al, submitted