Protein Recommendations: Time for an Update?

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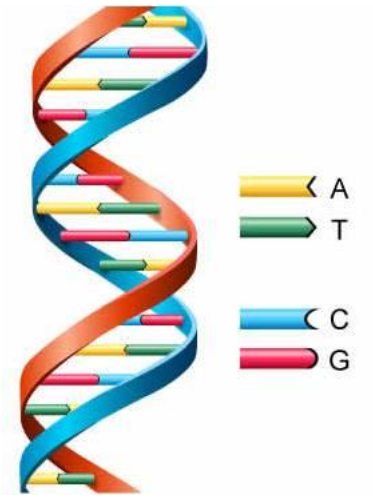
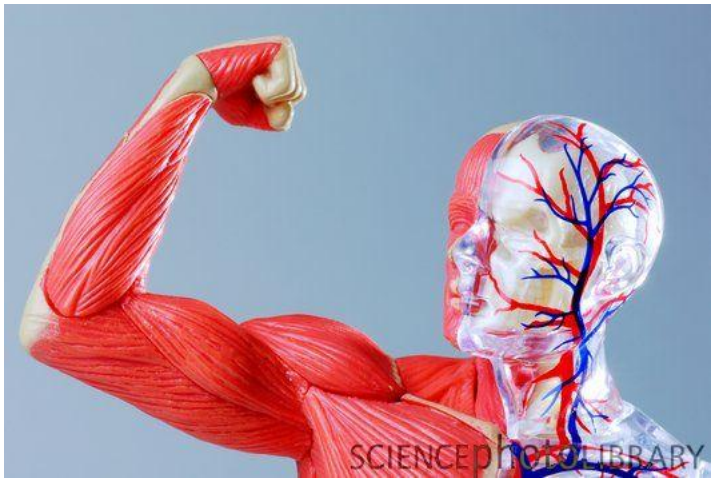
Protein

- *Proteos* which means ‘primary’ or ‘taking first place’
- Function as enzymes, transport carriers, and as hormones
- Nutritional importance of protein is because of their constituent 20 amino acids





Amino Acids

Essential

Lysine, Methionine, Threonine

Tryptophan, Phenylalanine, Histidine

Leucine, Isoleucine, Valine

Conditionally Essential

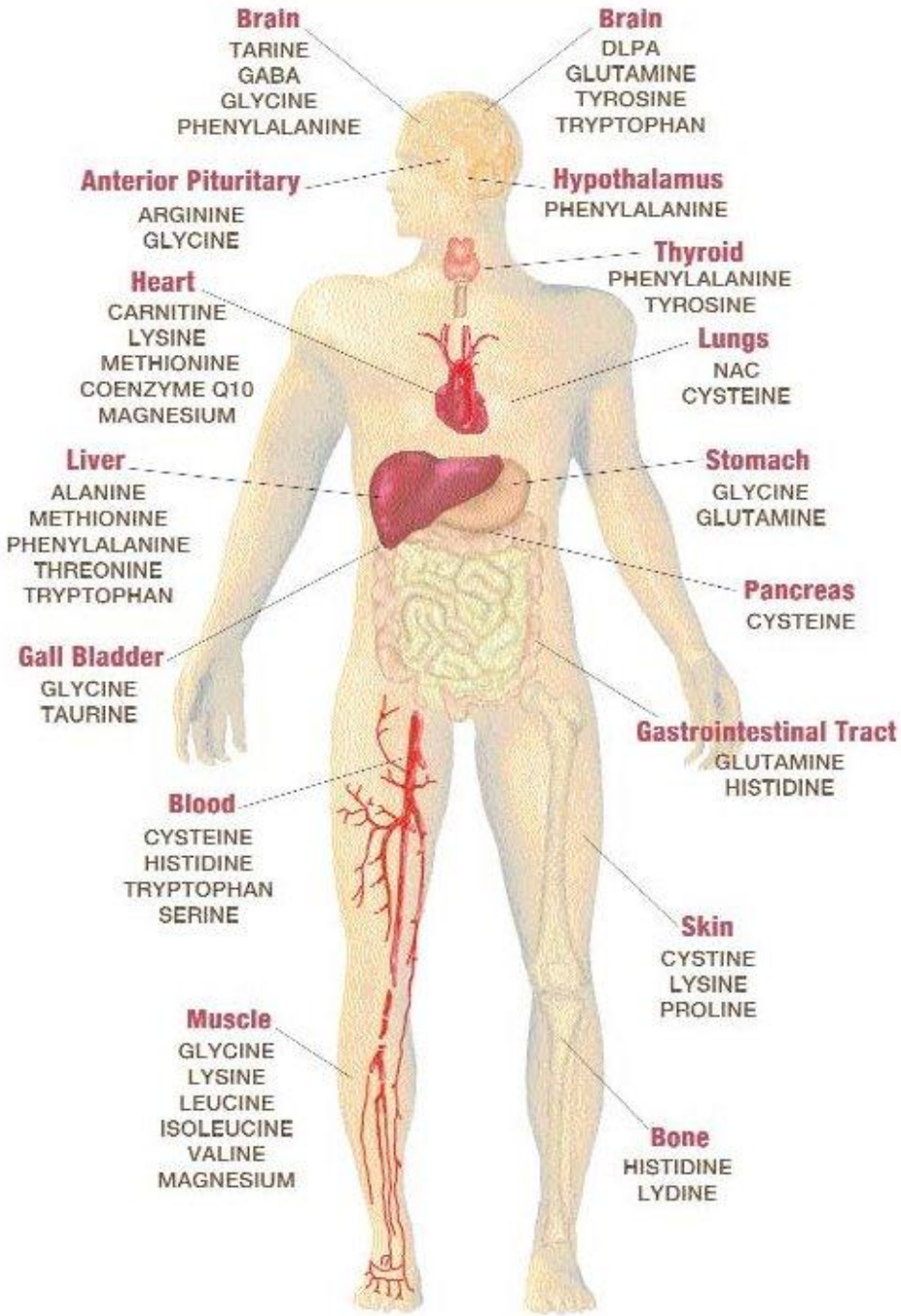
Tyrosine, Cysteine, Arginine

Glycine, Proline, Glutamine

Non Essential

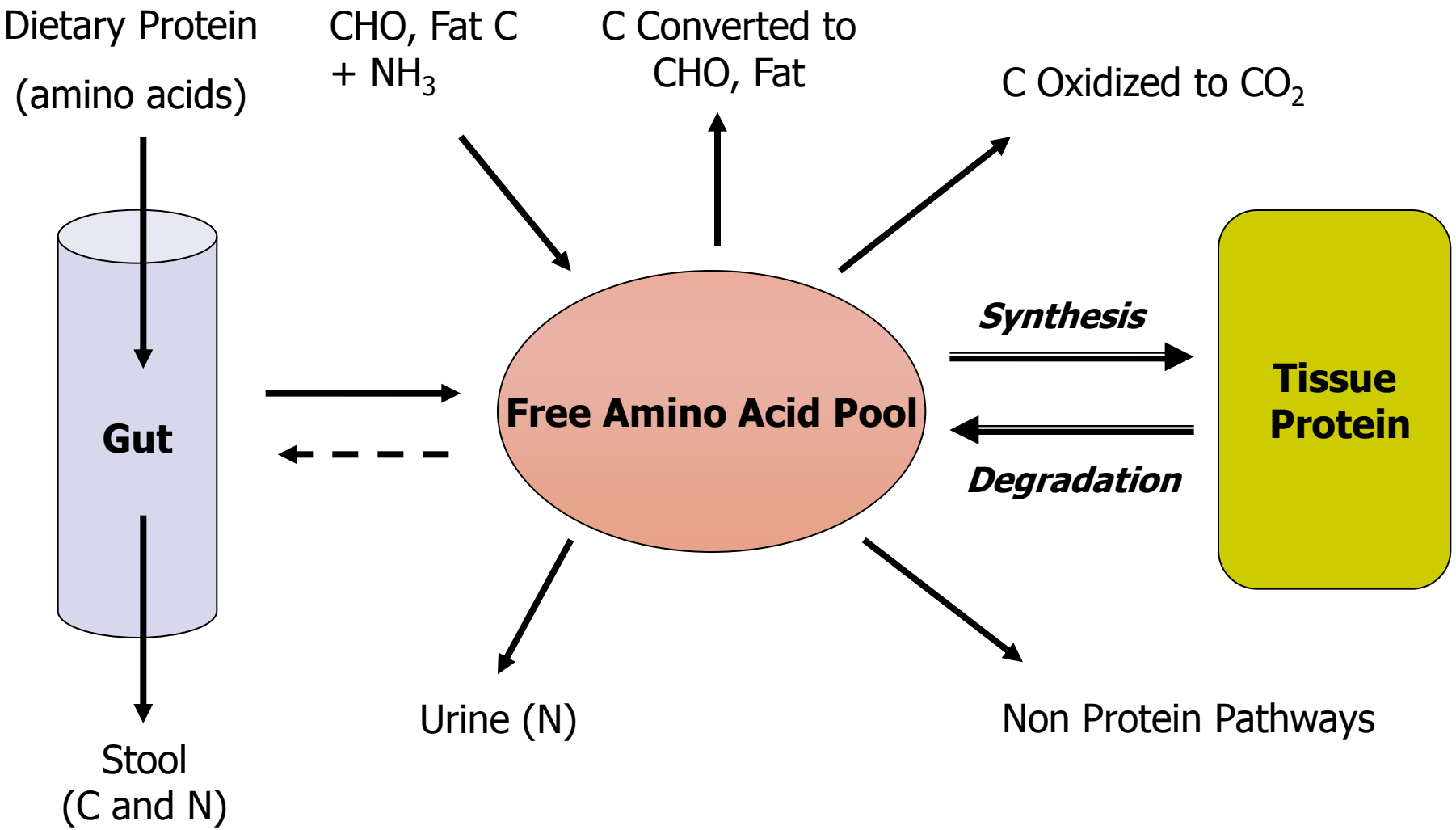
Alanine, Asparagine, Serine

Aspartate, Glutamate



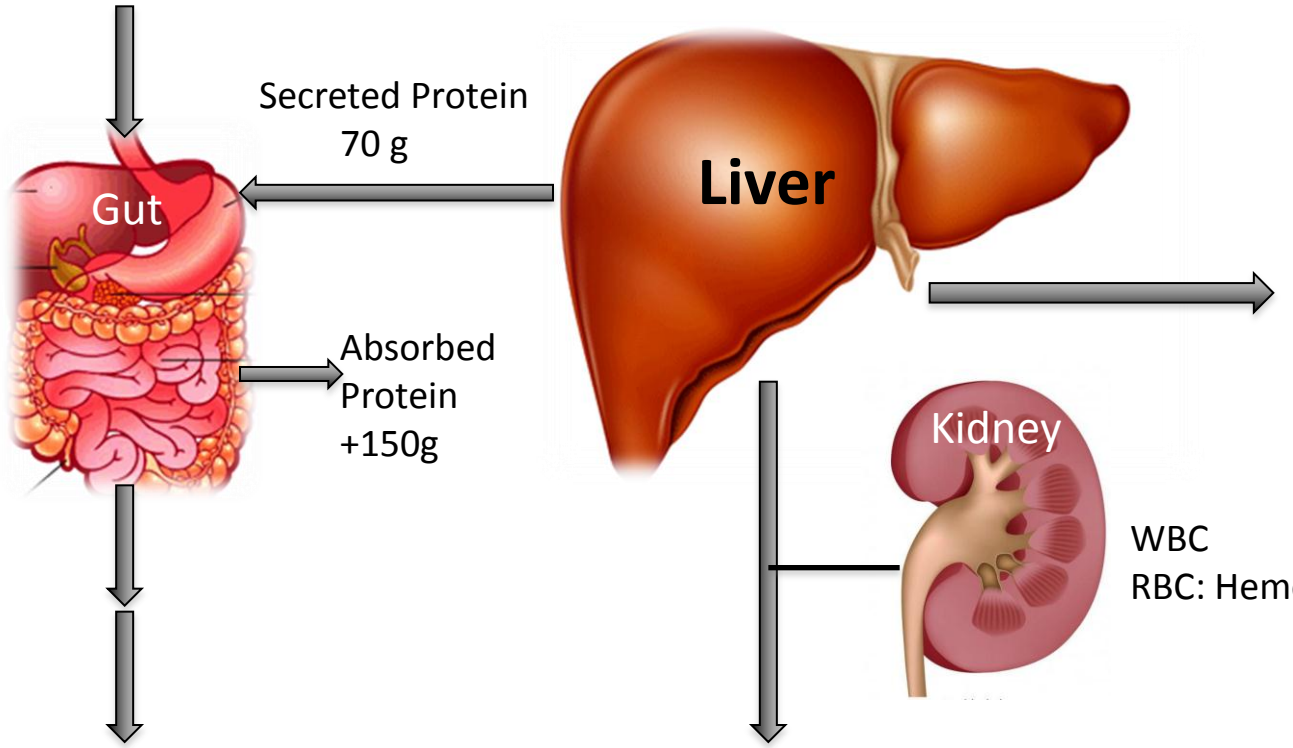
Source: *Healing with Amino Acids*, Pain and Stress Publications 1998.

Overview of Protein Metabolism



Overview of Protein Metabolism

In: Protein intake
90g



Muscle
Viscera
Brain, lung
Plasma
Proteins (Albumin etc)

Out: Fecal Protein
10g
(1.6g N)

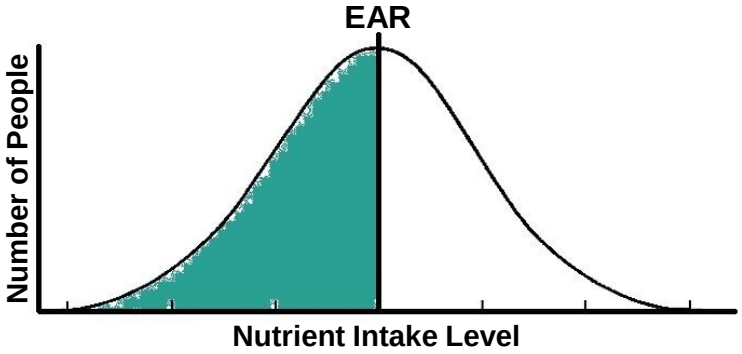
Urinary Nitrogen
75g
(12g N)

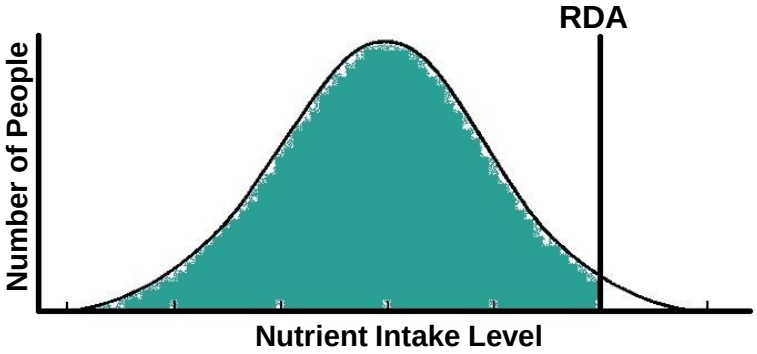
Other Losses
5g
(0.8g N)

Nutrient Intake Recommendations

- Dietary Reference Intakes (DRI)
  - Recommendations - North Americans
- FAO/WHO
  - Recommendations – worldwide/global

- Estimated Average Requirement (EAR)
- Recommended Dietary Allowance (RDA)





Dietary Reference Intakes (DRI) 2005

We can put a man on the moon, but…..

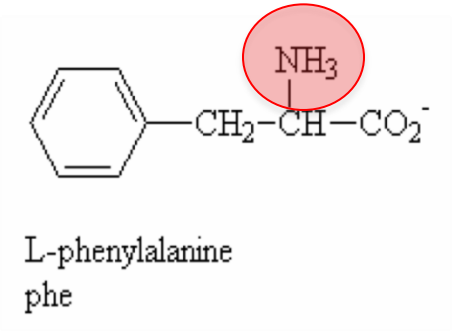
Cannot come to a consensus on how much protein to give him on Earth!

Adult Protein Recommendations (g Pr/kg/d)

Year	***Organization***	***RDA/Safe Intake***
1936	League of Nations	1
1957	FAO	0.66
1965	FAO/WHO	0.89
1973	FAO/WHO	0.57
1985	FAO/WHO/UNU	0.75
2005	DRI	0.8
2007	FAO/WHO/UNU	0.83

Traditional Method to Define Requirements

- Nitrogen metabolism synonymous with protein metabolism



- Assumption is Nitrogen Balance = body needs for protein

- Nitrogen Balance = Nitrogen Intake - Excretion

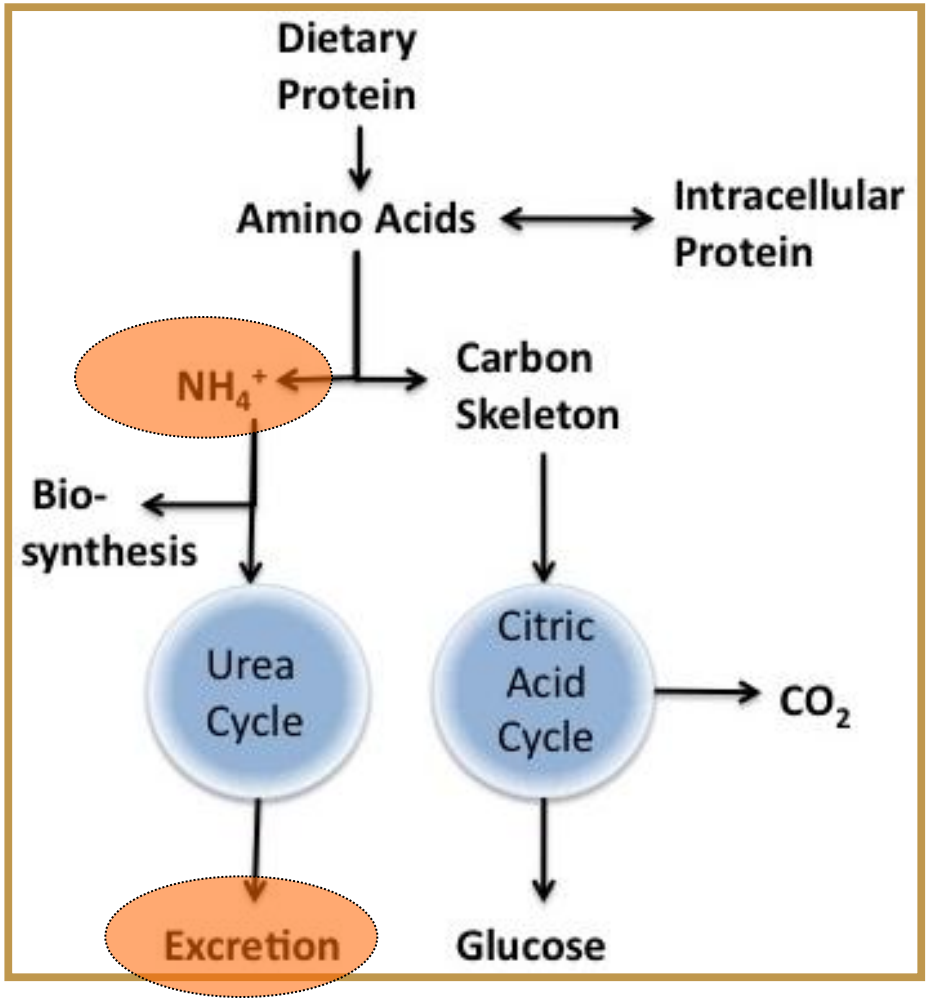
Dietary Reference Intakes (DRI) 2005

Traditional Method to Define Requirements

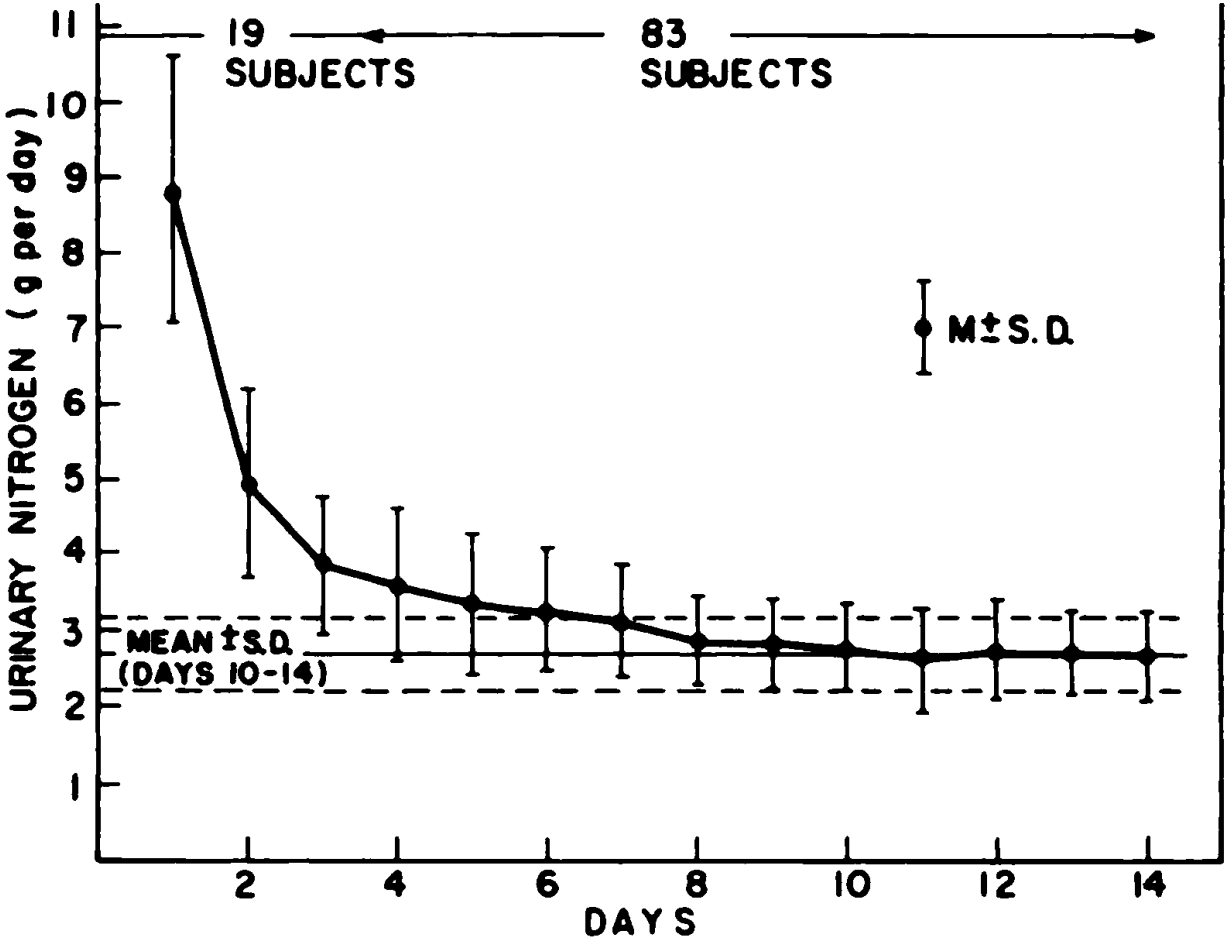
Body Nitrogen Balance

$$B = I - (U + F + S)$$

B = N balance
I = Total N intake
U = Urine N loss
F = Fecal N loss
S = Dermal N loss



Urinary Nitrogen Excretion -Low Protein Test Intakes



Scrimshaw et al, J Nutr 1972

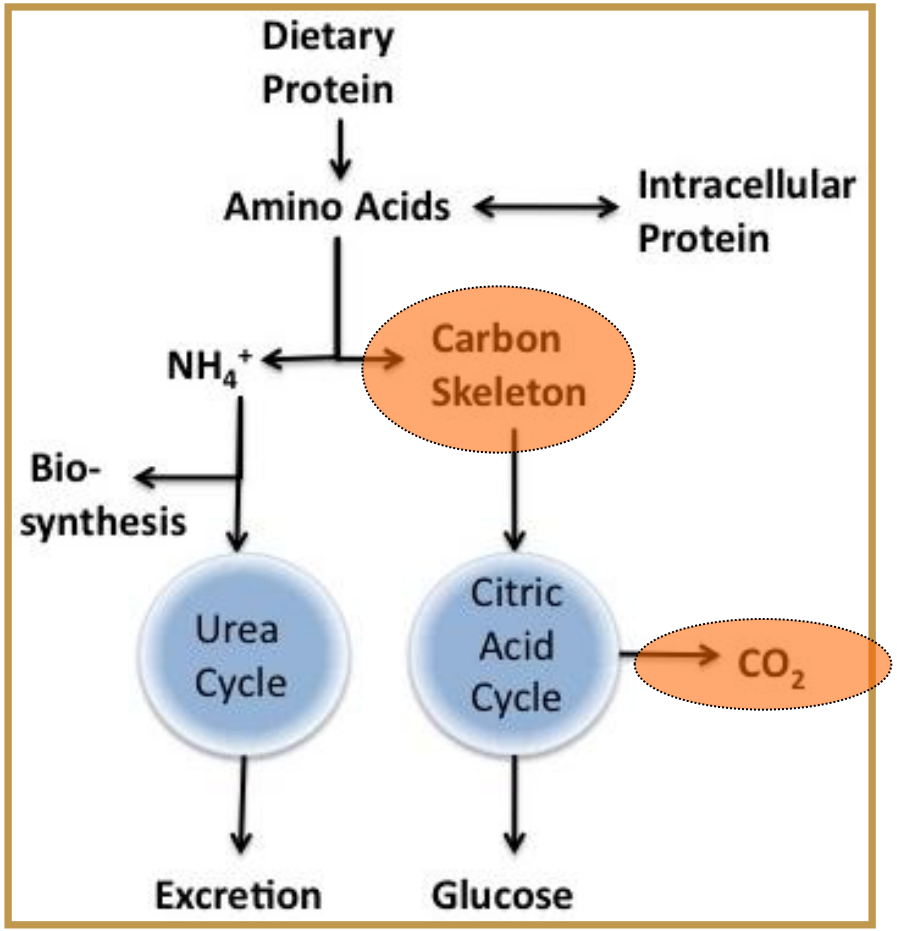
Limitations of Nitrogen Balance Method

- The rate of urea turnover to test protein is slow (3-7d)
- Accurate measurement of N balance is difficult: Overestimate intake, Underestimate excretion
- Therefore falsely positive nitrogen balances may be obtained
- Unethical to apply in children, elderly and in disease.

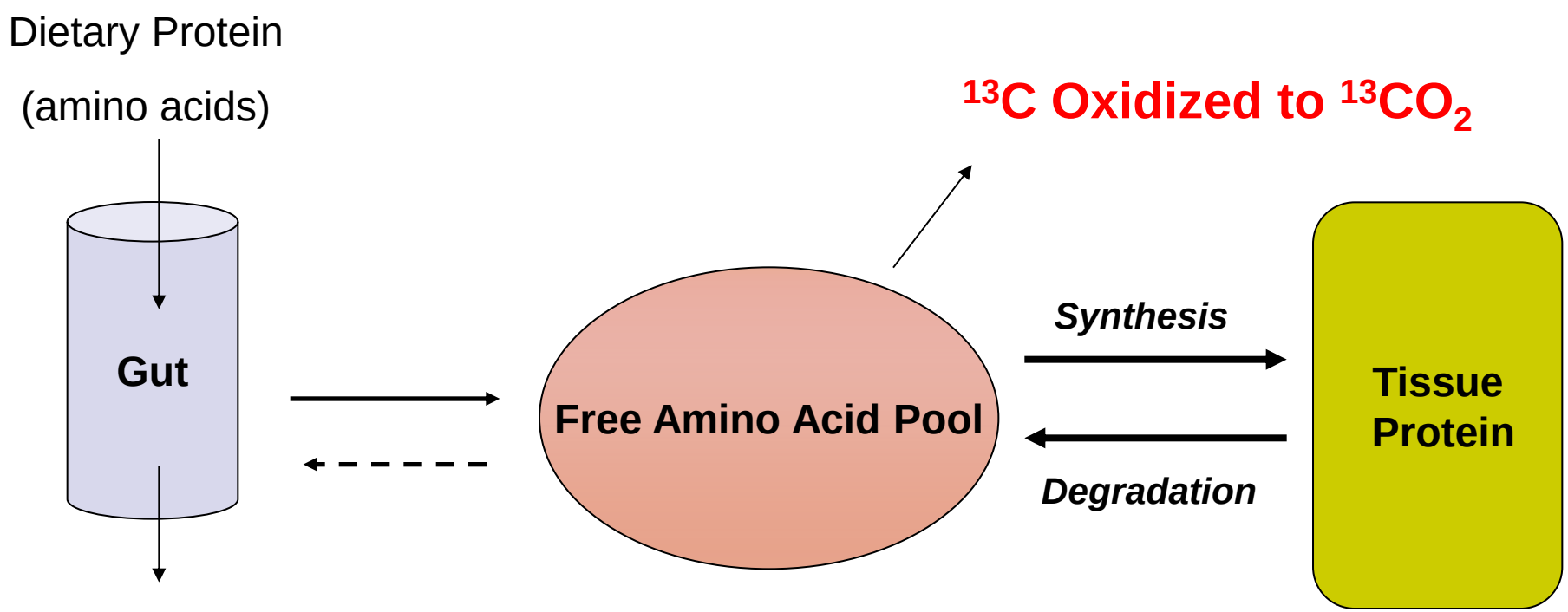
Dietary Reference Intakes (DRI) 2005

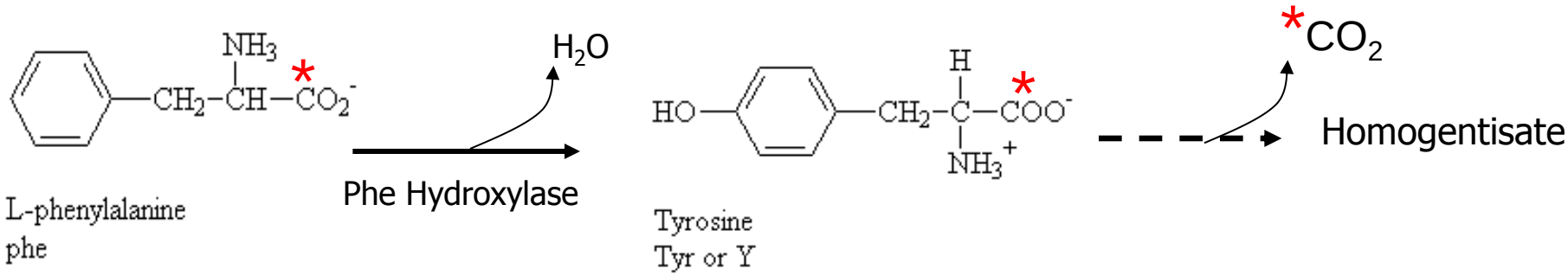
New Method to Define Requirements

- Indicator Amino Acid Oxidation (IAAO)
- Rapid and quick and ethical to apply in vulnerable populations such as pregnancy, childhood

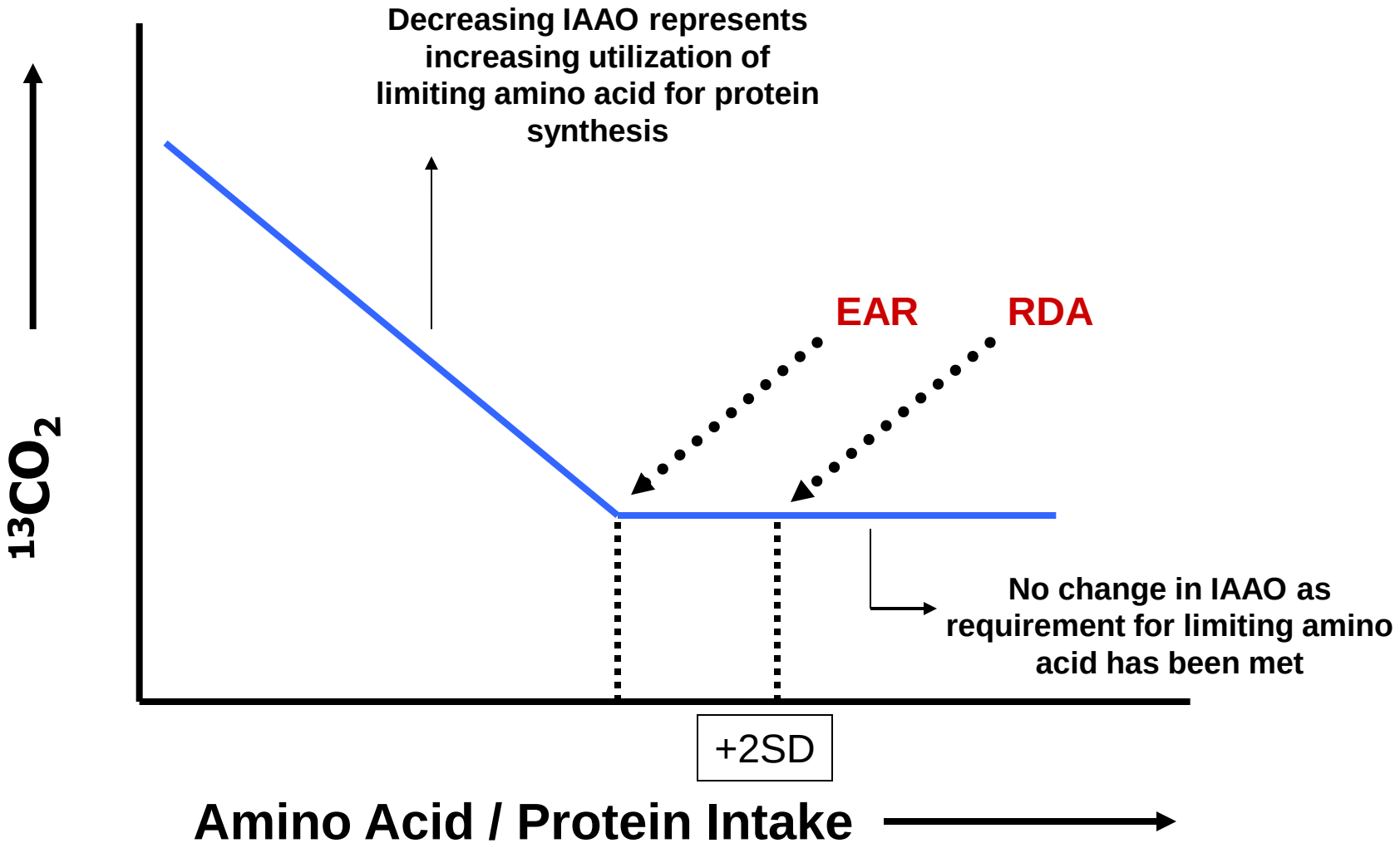


End Product of Protein Metabolism





Indicator Amino Acid Oxidation: Concept

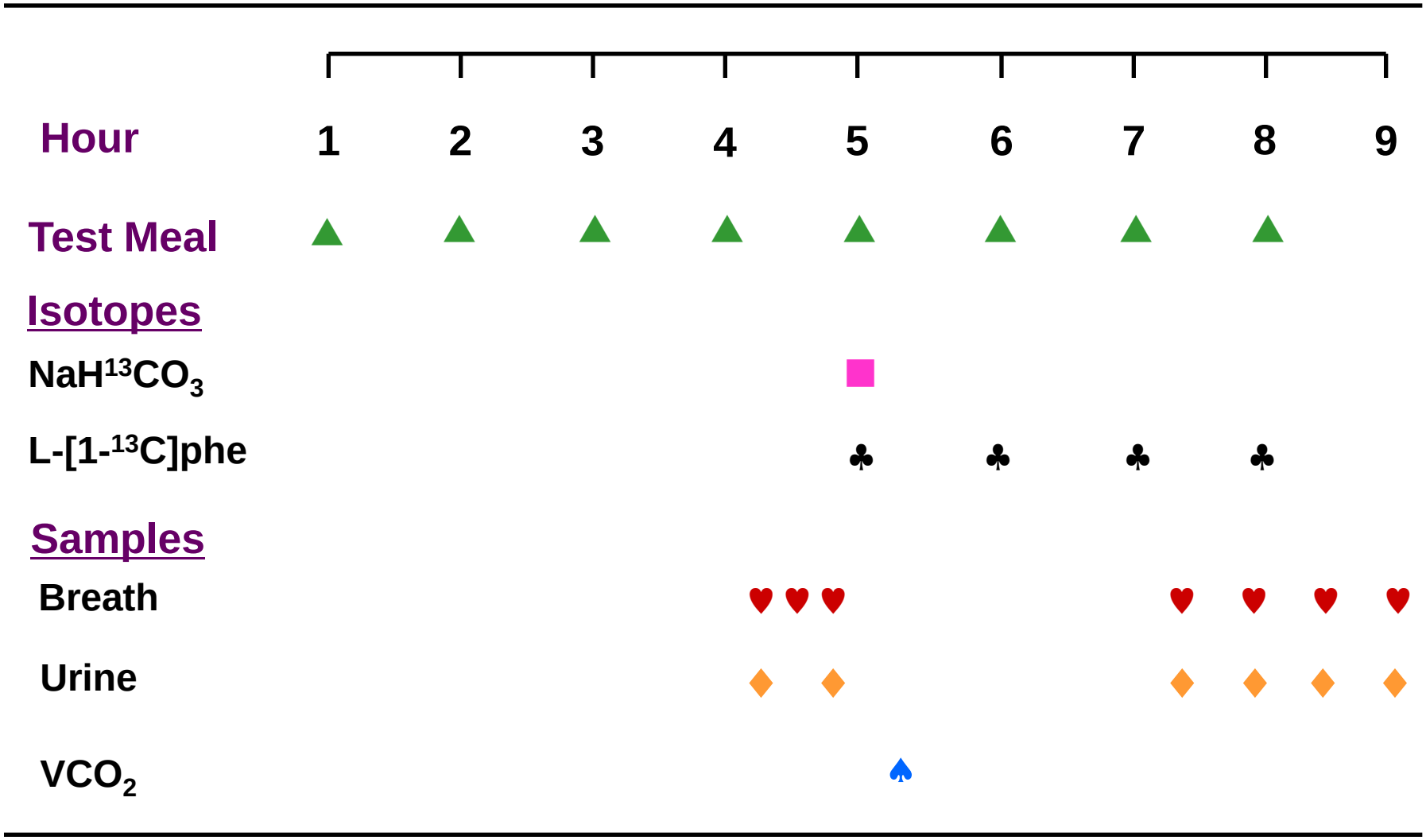


Elango et al. J Nutr 138:243-246, 2008

Minimally Invasive Technique

- Indicator Amino Acid Oxidation (IAAO)
  - Single study day adaptation
    - *Elango et al. J Nutr 139: 1082-1087, 2009*
  - Oral Stable Isotope delivery
    - *Kriengsinyos et al J Nutr 132:2251-7, 2002*
  - Measurement of $^{13}CO_2$ in breath and urine
    - *Bross et al J Nutr 128:1913-9, 1998*

Typical Study Day Protocol



Method: Pre-study assessment

Indirect Calorimetry

Calipers

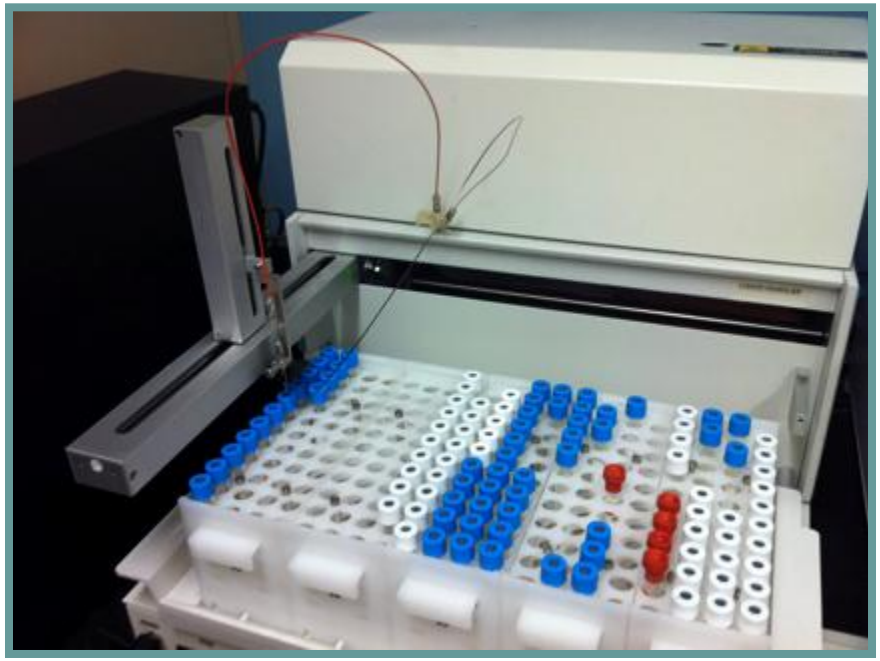
Bioelectric Impedance Analysis

- Medical and diet history, anthropometrics

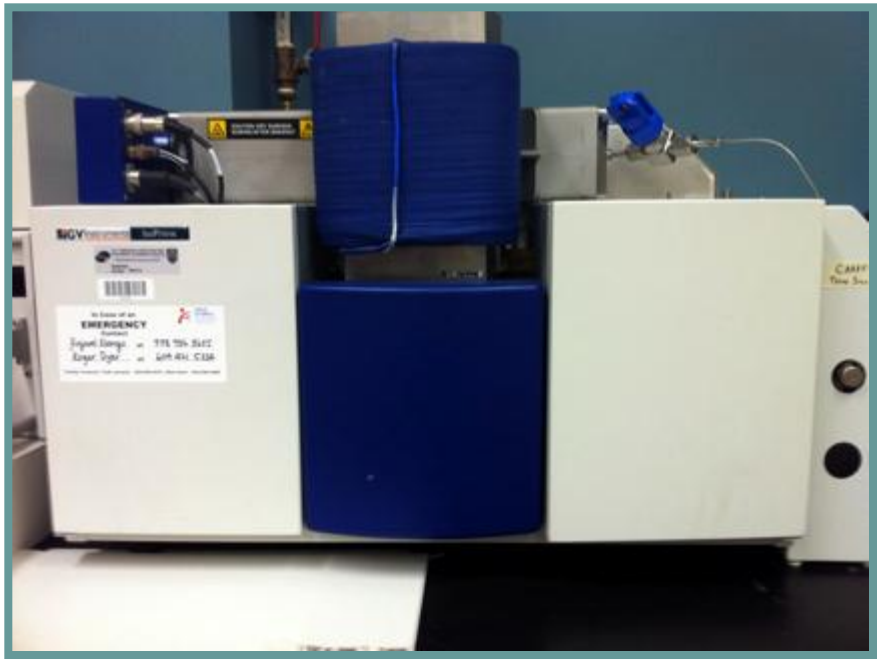
Diet, Sample Collection

Breath and Urine Sampling

Sample Analysis



Multi-flow



Continuous Isotope Ratio Mass Spectrometer

❖Urine analysis by LC Tandem Mass Spectrometry

Summary of Adult Human Amino Acid Requirements (1993 – 2006)

Requirement estimates in mg/kg/d

Amino Acid	FAO 1985	IAAO	FAO 2007	IAAO Reference
Histidine	8-12	-	11	Kriengsinyos et al (2002)
Isoleucine	10	42	15	Riazi et al (2003)
Leucine	14	55	34	Riazi et al (2003)
Lysine	**12**	**35**	**31**	Kriengsinyos et al (2002), Zello et al(1993)
Methionine	13	13	15	Di Buono et al (2001)
Phenylalanine	14	42	27	Hsu et al (2006)
Threonine	**7**	**19**	**16**	Wilson et al (2000)
Tryptophan	3.5	4	4	Lazaris-Brunner et al (1998)
Valine	10	47	19	Riazi et al (2003)
Total BCAA	-	144	-	Riazi et al (2003)

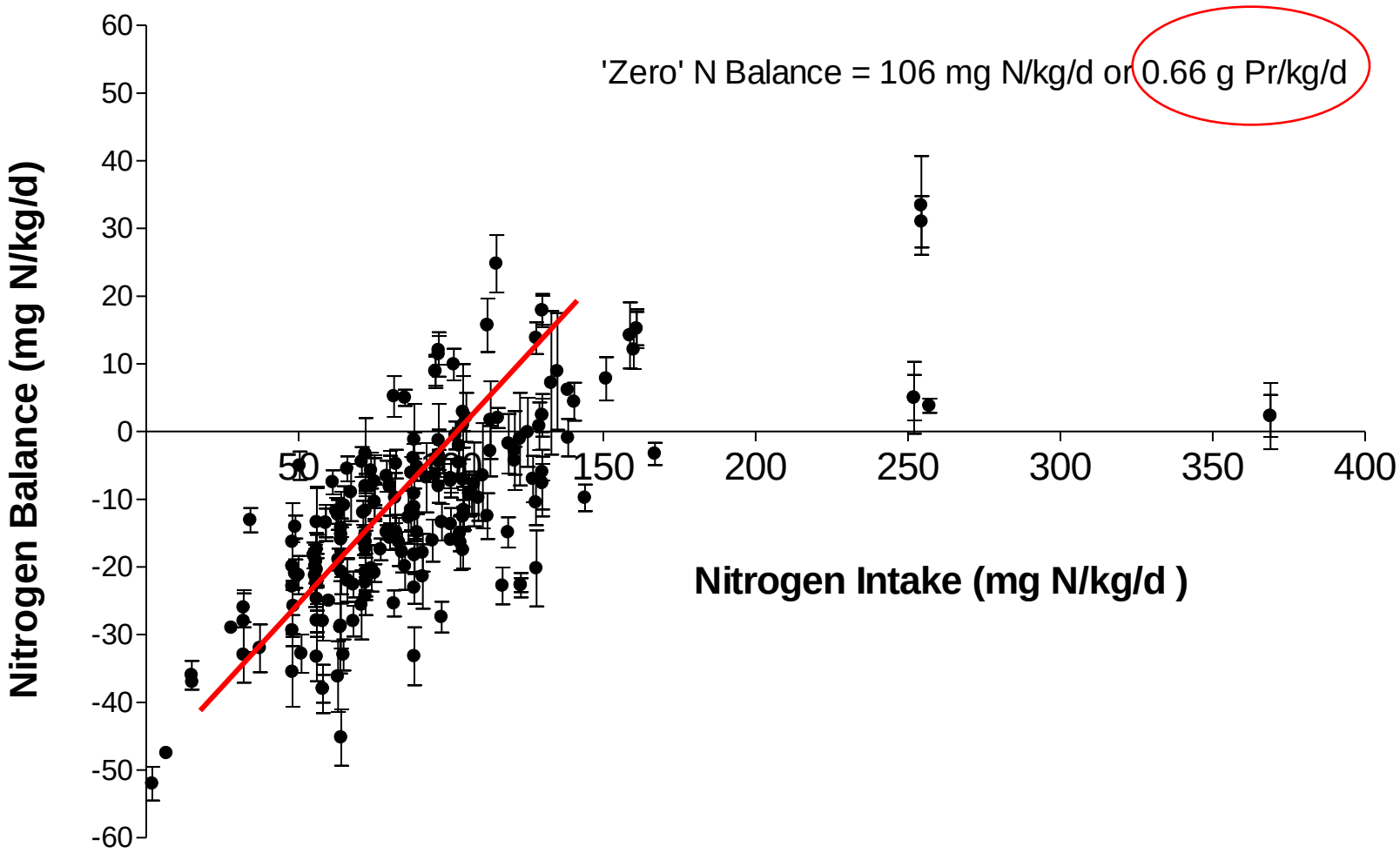
Elango et al. Curr Opin Clin Nutr Metab Care 11:34-39, 2008

Current Recommendations for Protein Intake in Humans

- ADULTS
  - EAR = 0.66 g/kg/d
  - RDA = 0.80 g/kg/d
- Results based on Nitrogen Balance

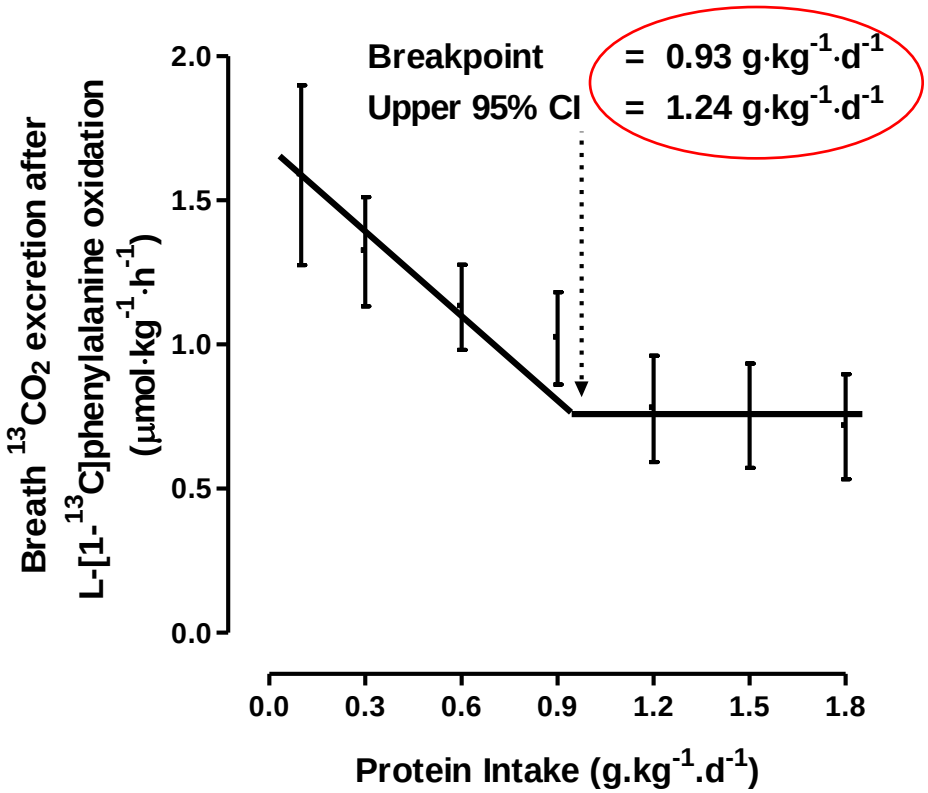
Dietary Reference Intakes (DRI) 2005; FAO/WHO/UNU 2007

N Balance Studies in Young Men



Rand et al AJCN;73:109-27, 2003; Dietary Reference Intakes (DRI) 2005

Protein Requirements – Adult Men



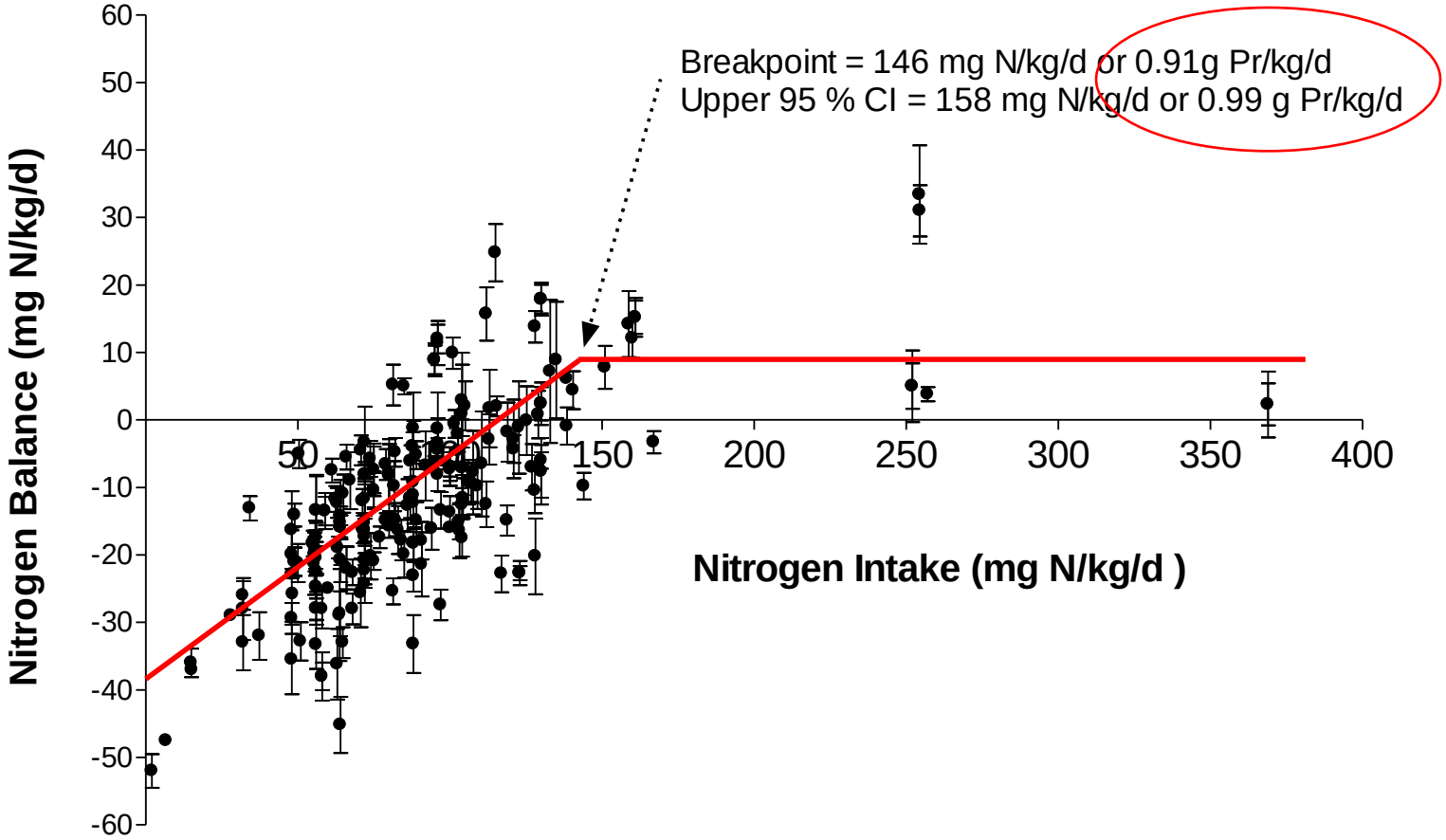
Current DRI (2005)

EAR = 0.66 g/kg/d
RDA = 0.8 g/kg/d

Current recommendations are ~30% underestimated

*Humayun, **Elango,** et al Am J Clin Nutr;86:995-1012, 2007*

Reanalysis of N Balance Studies in Young Men



*Rand et al AJCN;73:109-27, 2003; Humayun, **Elango** et al AJCN;86:995-1012, 2007*

Current Recommendations for Protein Intake in Children (6-10y)

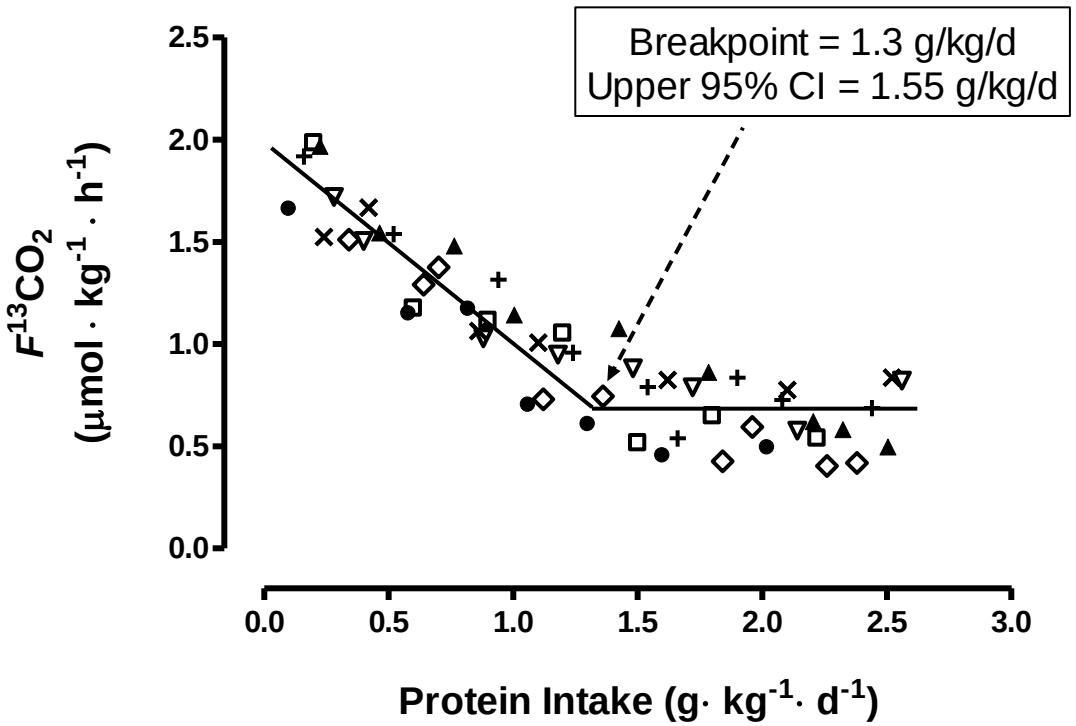
- CHILDREN
  - EAR = 0.76 g/kg/d
  - RDA = 0.95 g/kg/d

- Results based on a Factorial Method
  - Maintenance + Growth (Deposition/Efficiency)

- Where 'maintenance' = Adult Nitrogen Balance values

Dietary Reference Intakes (DRI) 2005; FAO/WHO/UNU 2007

Protein Requirements - 6-10 y Children



Current DRI (2005)

EAR = 0.76 g/kg/d
RDA = 0.95 g/kg/d

Current recommendations are ~70% underestimated

***Elango** et al Am J Clin Nutr, 94: 1545-52, 2011*

Summary I – Protein Requirements

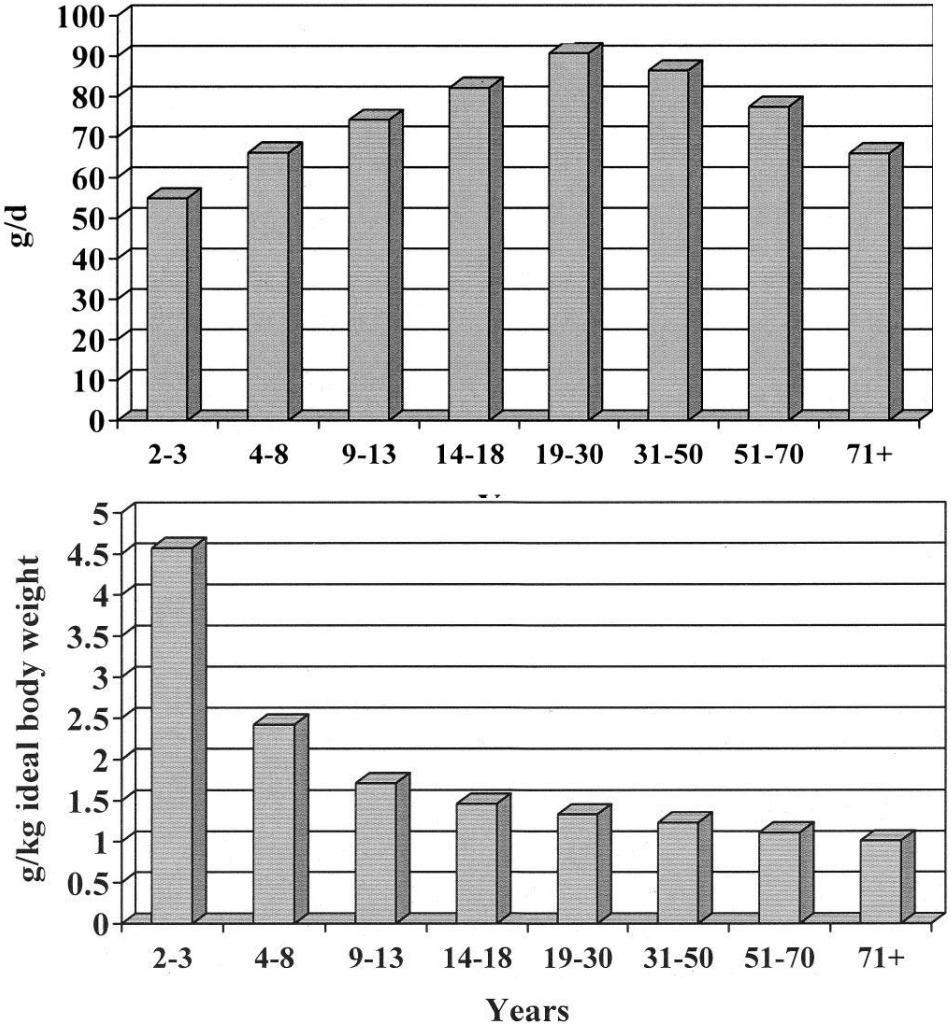
- Protein Requirements (g Pr/kg/d)

Adults	DRI 2005	IAAO	Increase In Req
EAR	0.66	0.93	29% ↑
RDA	0.80	1.2	33% ↑

Children (6-10y)	DRI 2005	IAAO	Increase In Req
EAR	0.76	1.3	41% ↑
RDA	0.95	1.55	39% ↑

- Protein requirements are significantly underestimated

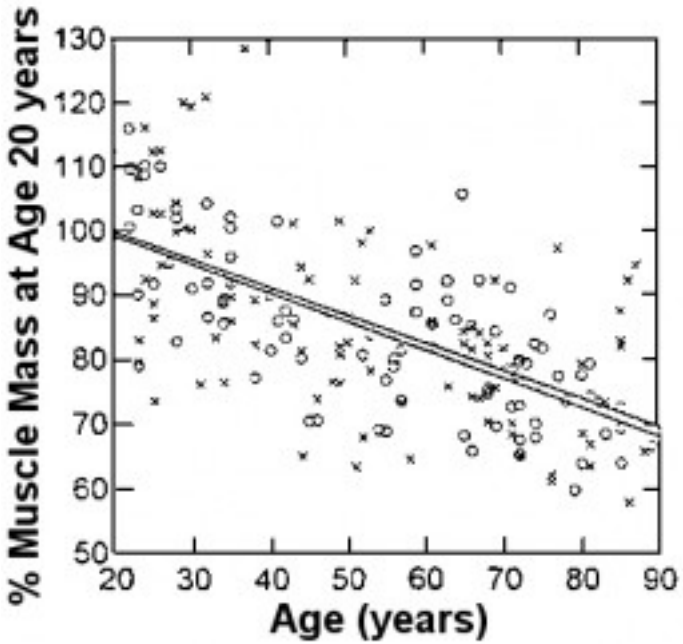
Elderly Protein Intakes

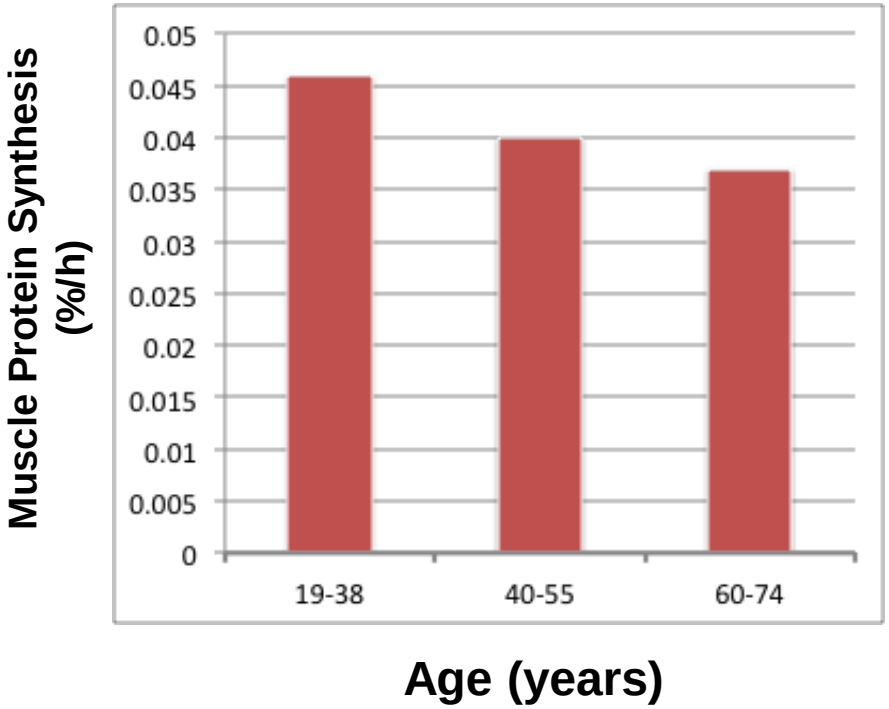


- 71y+ avg intake = 66 g/d
- Clear decline with aging
- Elderly women have lowest protein intake

Fulgoni et al, AJCN 2008; 87:1554s-7s

Muscle Mass and Function Loss with Age

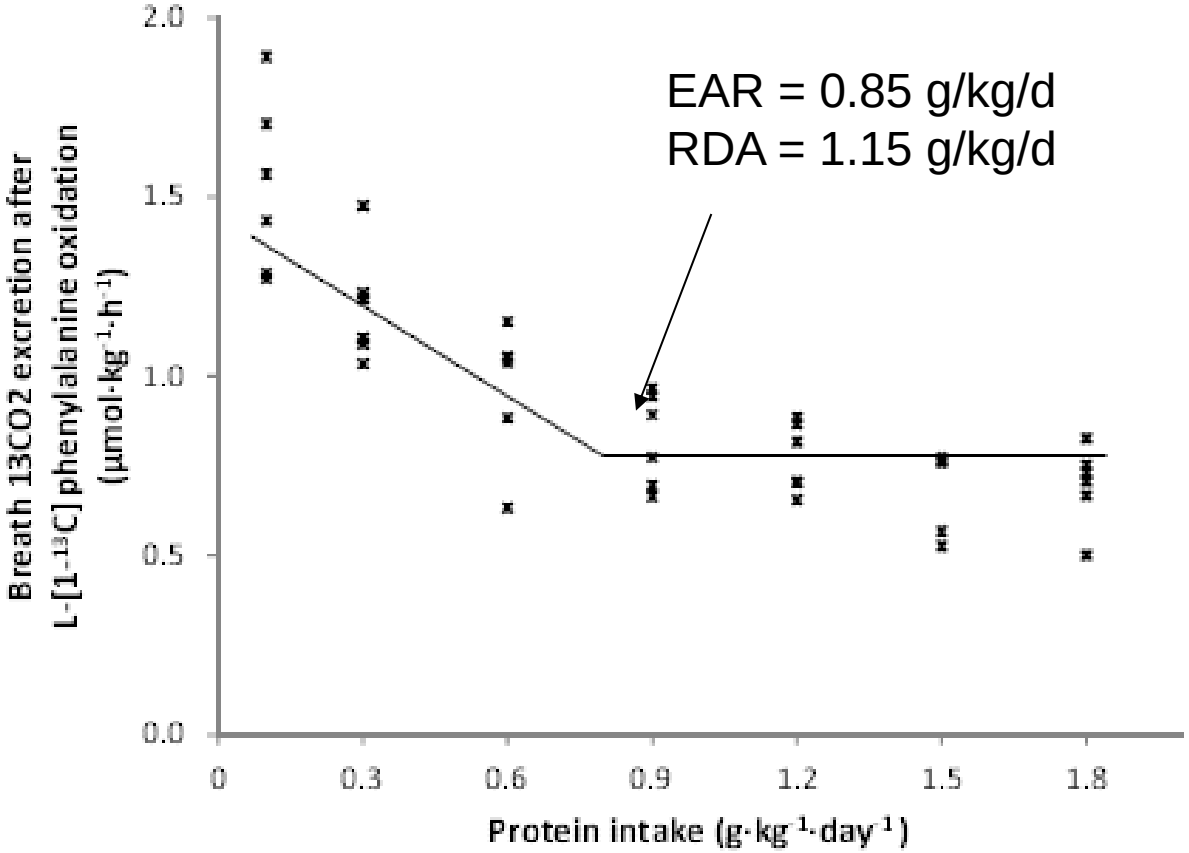




- Muscle mass and muscle protein synthesis decreases with age

Sheen et al, AJCN 2001; 83:1554-7; Short et al AJP 2004; 286, E92-101

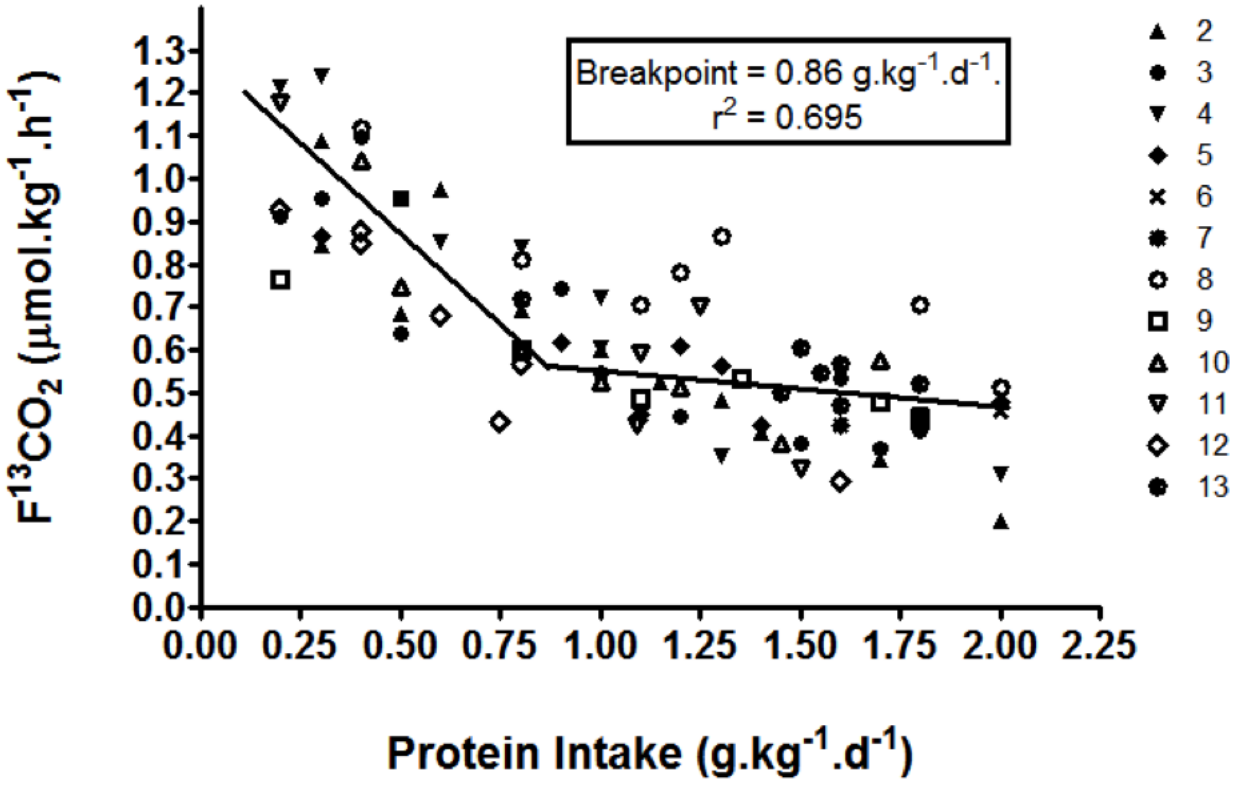
Protein Requirements – 80y Women



Current recommendations are ~30% underestimated

*Tang, **Elango,** Campbell WW et al Faseb J 2012*

Protein Requirements – 65-85y Women



Current recommendations are ~30% underestimated

Rafii, Courtney-Martin, ***Elango,*** *Pencharz et al Faseb J 2013*

Summary II – Protein Requirements

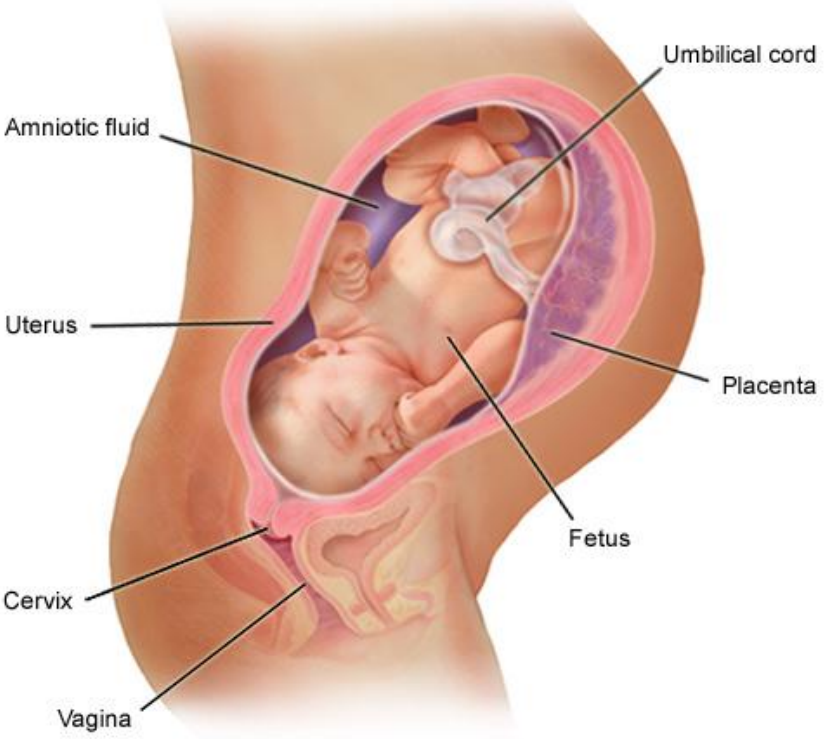
- Protein Requirements (g Pr/kg/d)

Elderly Women (80+y)	DRI 2005	IAAO	Increase In Req
EAR	0.66	0.85	22% ↑
RDA	0.80	1.15	30% ↑

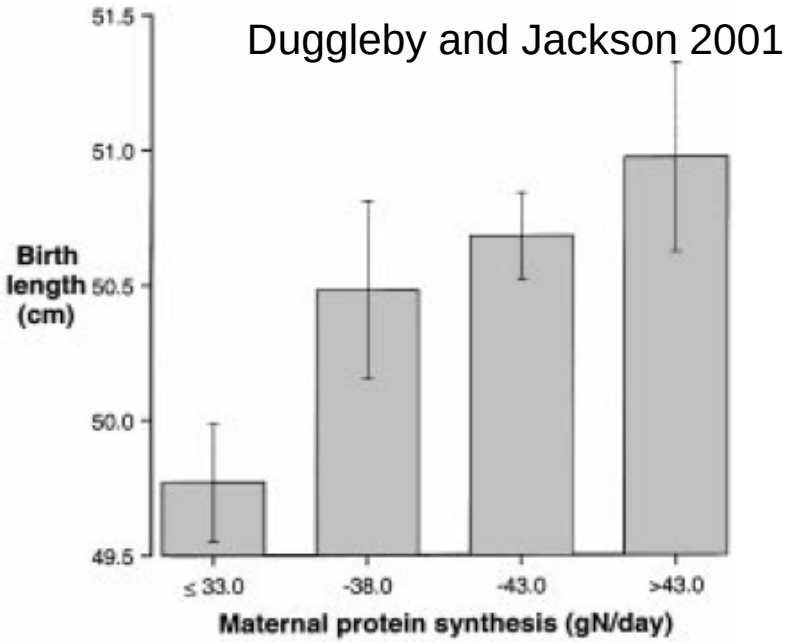
- Currently follow up studies in men 65+y are ongoing

Quote: “You are what you eat”

Perhaps: “You are what your mother ate”



Role of Protein in Infant Birthweight



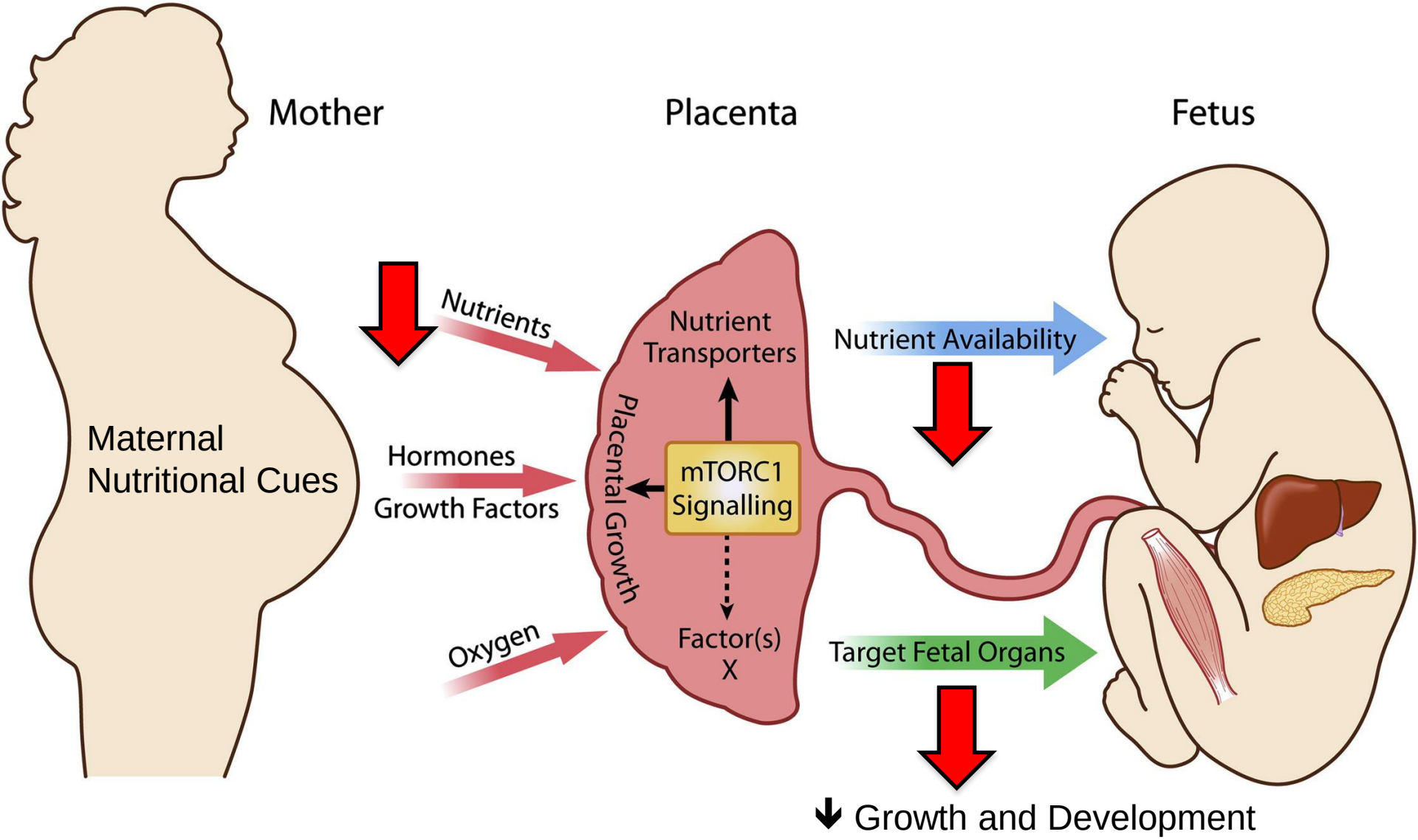
Association of maternal protein intake before conception and throughout pregnancy with birth weight

G. CUCÓ[1], V. ARIJA[1], R. IRANZO[2], J. VILÀ[2], M. T. PRIETO[1] & J. FERNÁNDEZ-BALLART[1]

Acta Obstetricia et Gynecologica. 2006; 85: 413–421

A 1g increase in protein intake preconception, 10th, 28th and 36th wk of pregnancy leads to 8-11 g increase in birthweight

Maternal – Fetal Nutrition

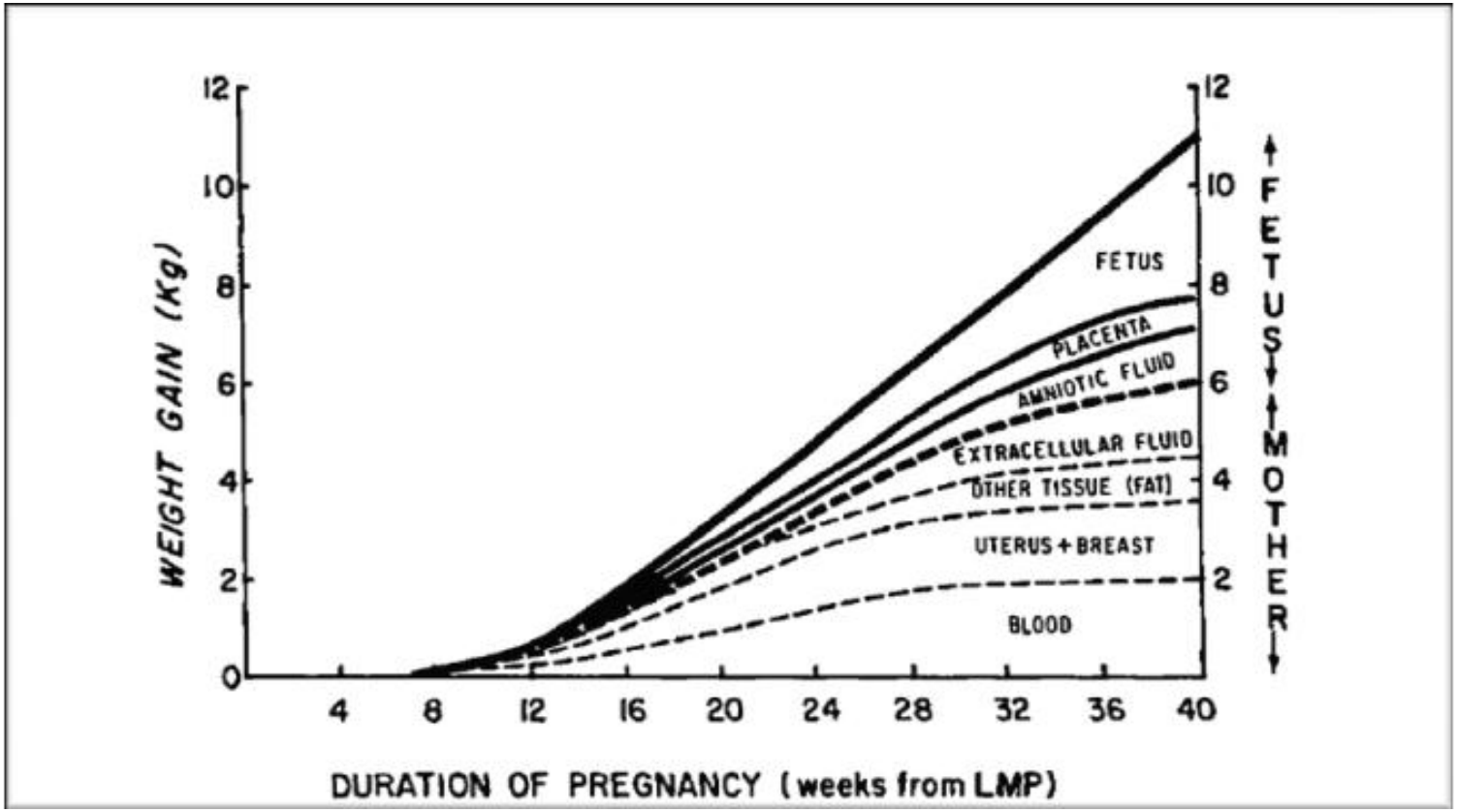


Pregnancy
Recommendations vs Requirement

	DRI 2005 Recommendation	For a 60 kg Pregnant Woman
	g/kg/d	g/d
EAR	0.88	53
RDA	1.1	66

- Non-Pregnant adult protein needs + protein deposition
- Increasing protein intake (68 g/d to 101 g/d) improved birth weight of siblings - Montreal Diet Dispensary (1976-1986)

Protein Deposition in Pregnancy

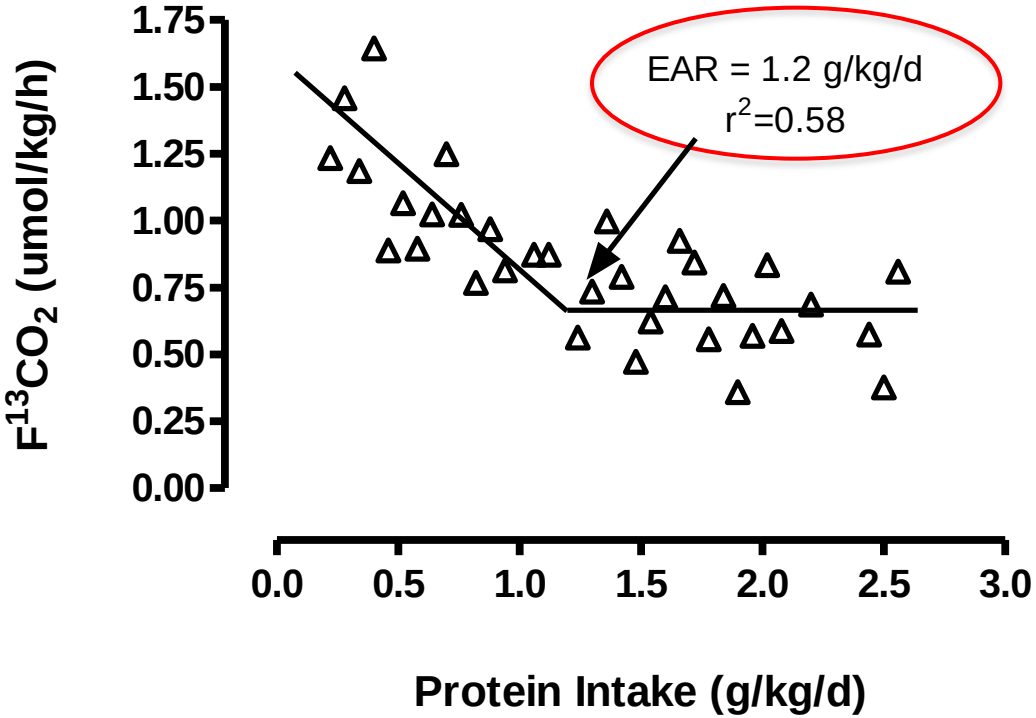


	T1	T2	T3
Protein synthesized per day:	1.2 g/d	6.1 g/d	10.7 g/d

Pitkin (1976) Clinical Obstetrics and Gynecology 19(3):489-513

Early Gestation 11-20 wks

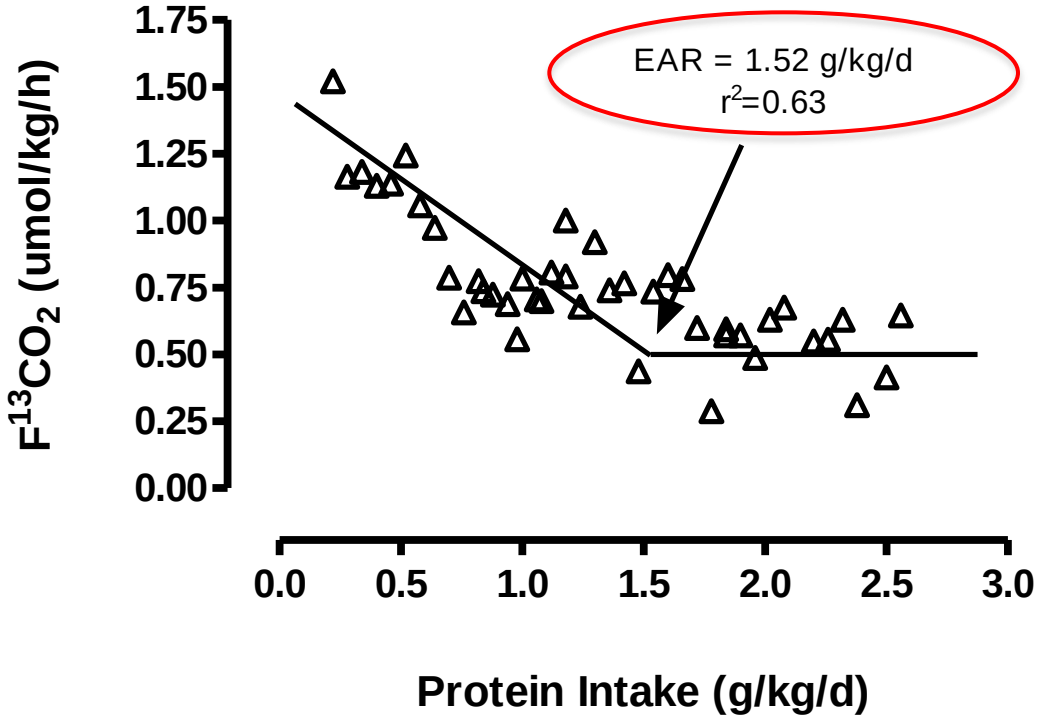
- Early gestation: n=34; Age=23-34y; singleton pregnancies



*Stephens, **Elango** et al Faseb J 2012*

Late Gestation 30-38 wks

- Late gestation: n=43; Age=24-35y; singleton pregnancies



*Stephens, **Elango** et al Faseb J 2012*

Summary II – Protein Requirements

- Protein Requirements (g Pr/kg/d)

Pregnant Women	DRI 2005	IAAO Early Gestation	IAAO Late Gestation
EAR	0.88	1.2	1.52
RDA	1.1	_	_

- Currently Lysine requirement studies are ongoing

Children Living in Developing Countries

World Health Organization

FAO FIAT PANIS

Sets Recommendations

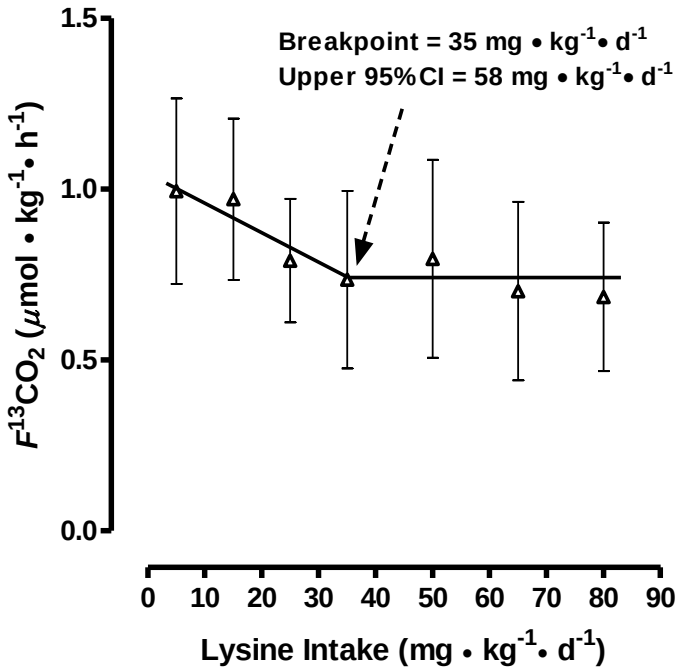
© 2005 Wadsworth - Thomson

- Grain & Cereal based diet
- Limiting in ‘Lysine’, an essential amino acid

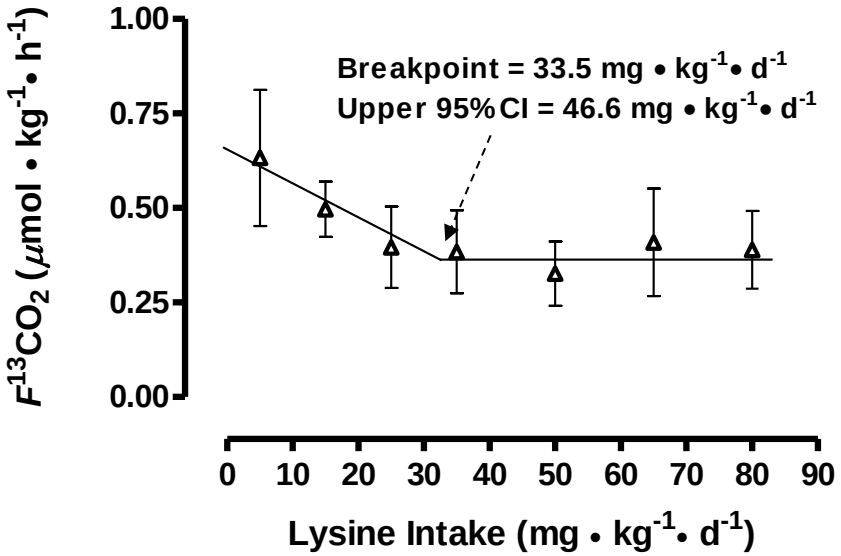
- General Hypothesis: body has undergone adaptation and accommodation to survive on lower protein and energy

- Collaboration with St. John’s Research Institute, Bangalore, India [2005 – current]
  - Malnourished school-aged children

Lysine Requirements:
Canadian Vs. Indian Children



EAR = 35 mg/kg/d

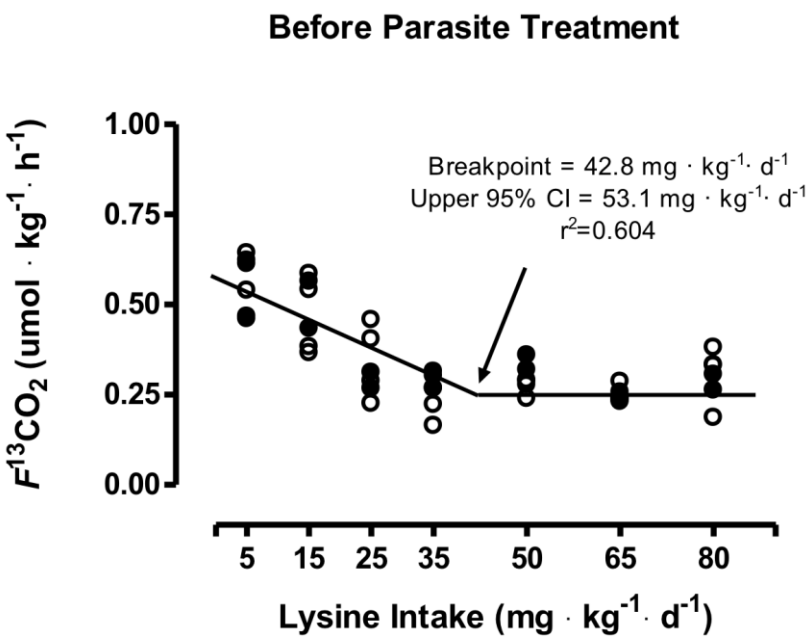


EAR = 33.5 mg/kg/d

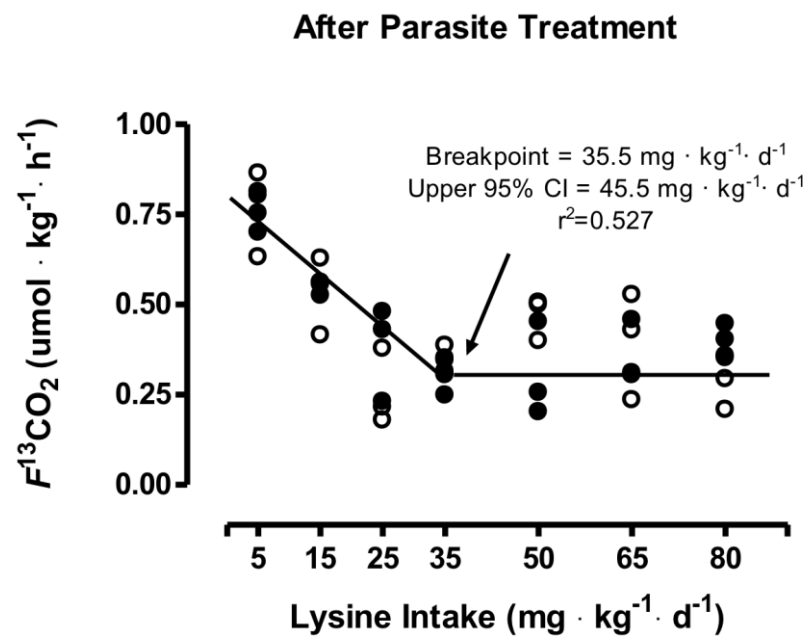
Elango et al. AJCN 86:360-5, 2007

*Pillai, **Elango** et al. J Nutr. 140:54-9. 2010*

Lysine Requirements: Malnourished Children



EAR = 42.8 mg/kg/d



EAR = 35.5 mg/kg/d

*Pillai, **Elango** et al. Dietary Protein for Human Health, Proceedings, 2011*

Summary III – Protein and Amino Acid Requirements

- Global lysine children requirements could be similar
- Earlier studies by Young & Kurpad in adult Indian men confirmed the same
- Protein requirements must be considered in the context of
  - Amino acid composition
  - Dietary energy
  - Parasite infestation

Conclusions

- Current protein intake recommendations inadequate
- 'Optimal' protein and amino intakes could have health benefits
- Local implications –
  - Elderly Care Homes, Hospital Nutrition Services

Meals on Wheels

- Global implications -

WFP United Nations World Food Programme

World Health Organization

FAO FIAT PANIS

Acknowledgements

- Study participants
- Canadian Institutes for Health Research (CIHR) Grant Support
- Mead Johnson Nutritionals (Canada)
- Ajinomoto Co Inc., Japan
- St. John's Research Institute, Bangalore

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BC CHILDREN'S HOSPITAL
An agency of the Provincial Health Services Authority

CHILD & FAMILY RESEARCH INSTITUTE

Questions?