3° Congreso Argentino de Neonatologia
Buenos Aeres 1_3 July 2016

PN nutrition in VLBW infants: improvement of postnatal growth using optimal

J Rigo MD PhD

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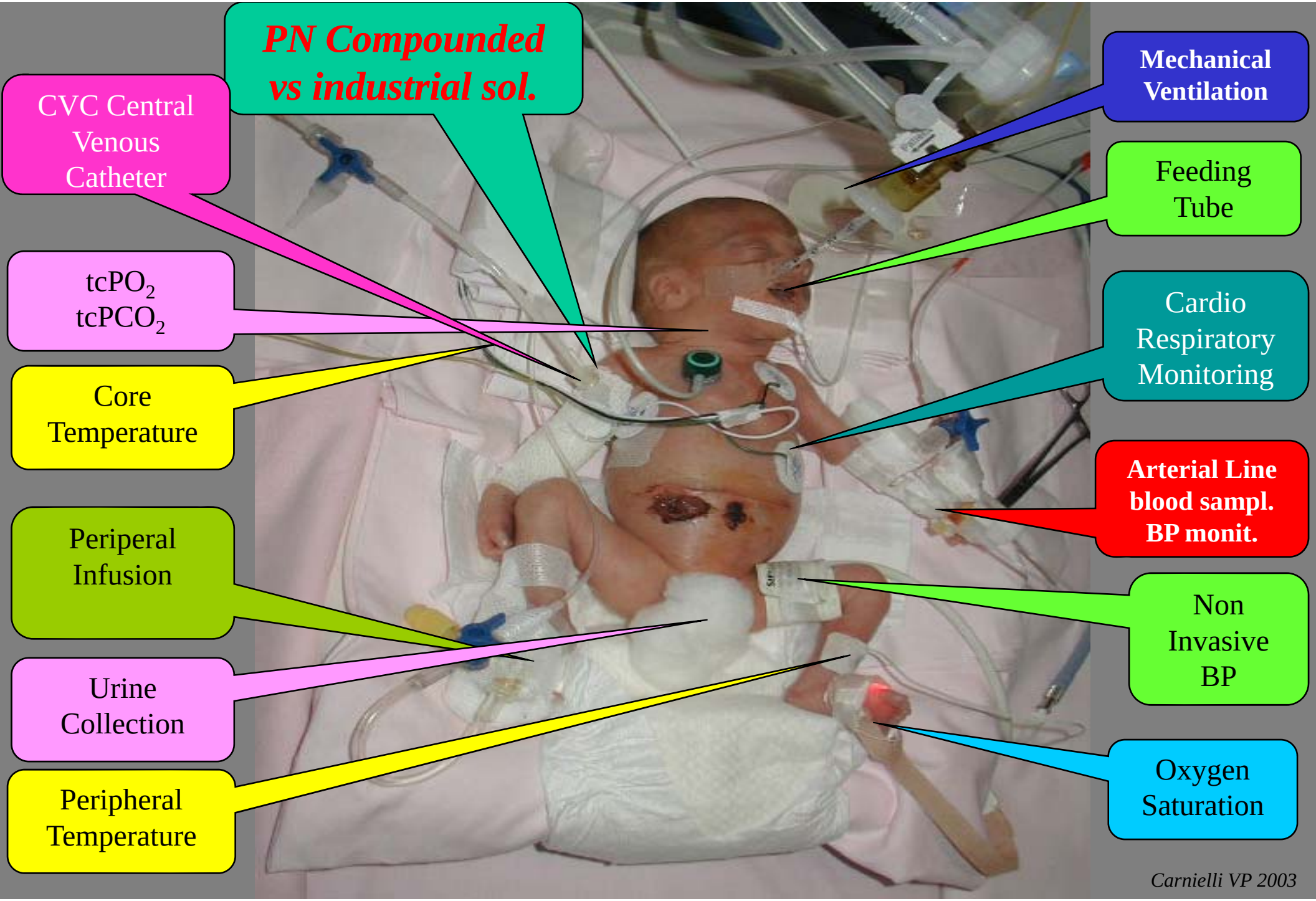
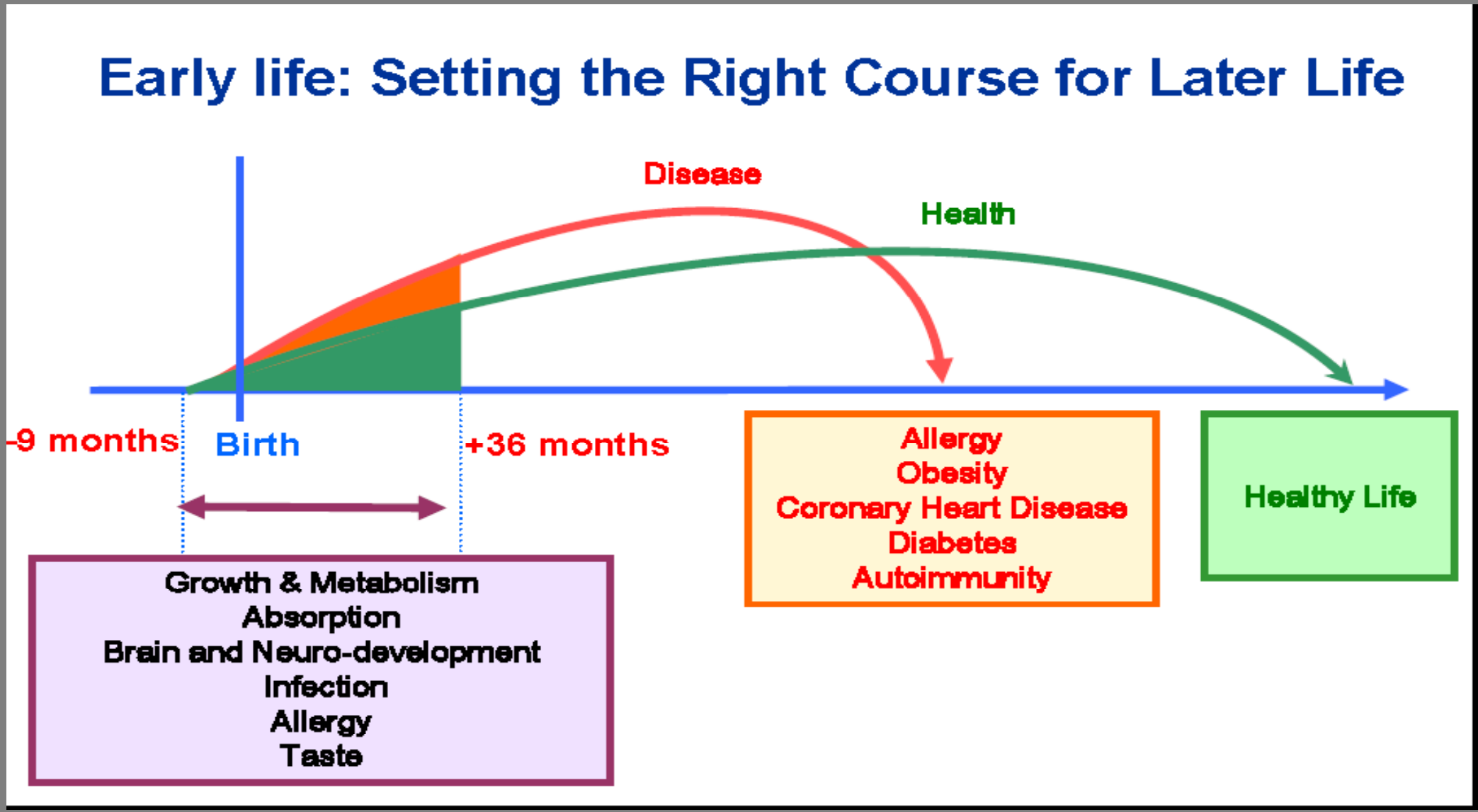
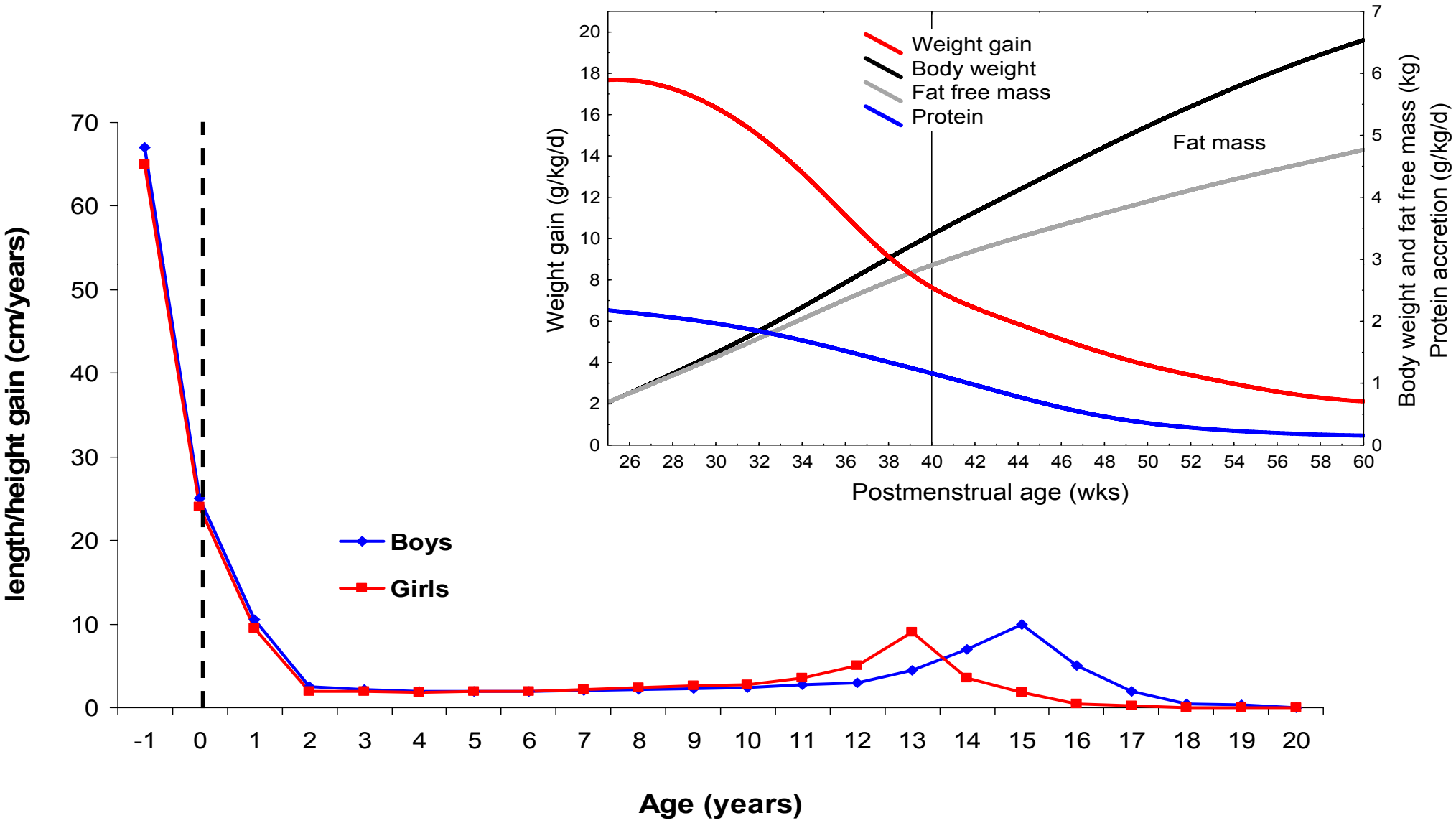

PN Compounded vs industrial sol.
CVC Central Venous Catheter
tcPO2
tcPCO2
Core Temperature
Peripheral Infusion
Urine Collection
Peripheral Temperature
Mechanical Ventilation
Feeding Tube
Cardio Respiratory Monitoring
Arterial Line blood sampl. BP monit.
Non Invasive BP
Oxygen Saturation
Carnielli VP 2003

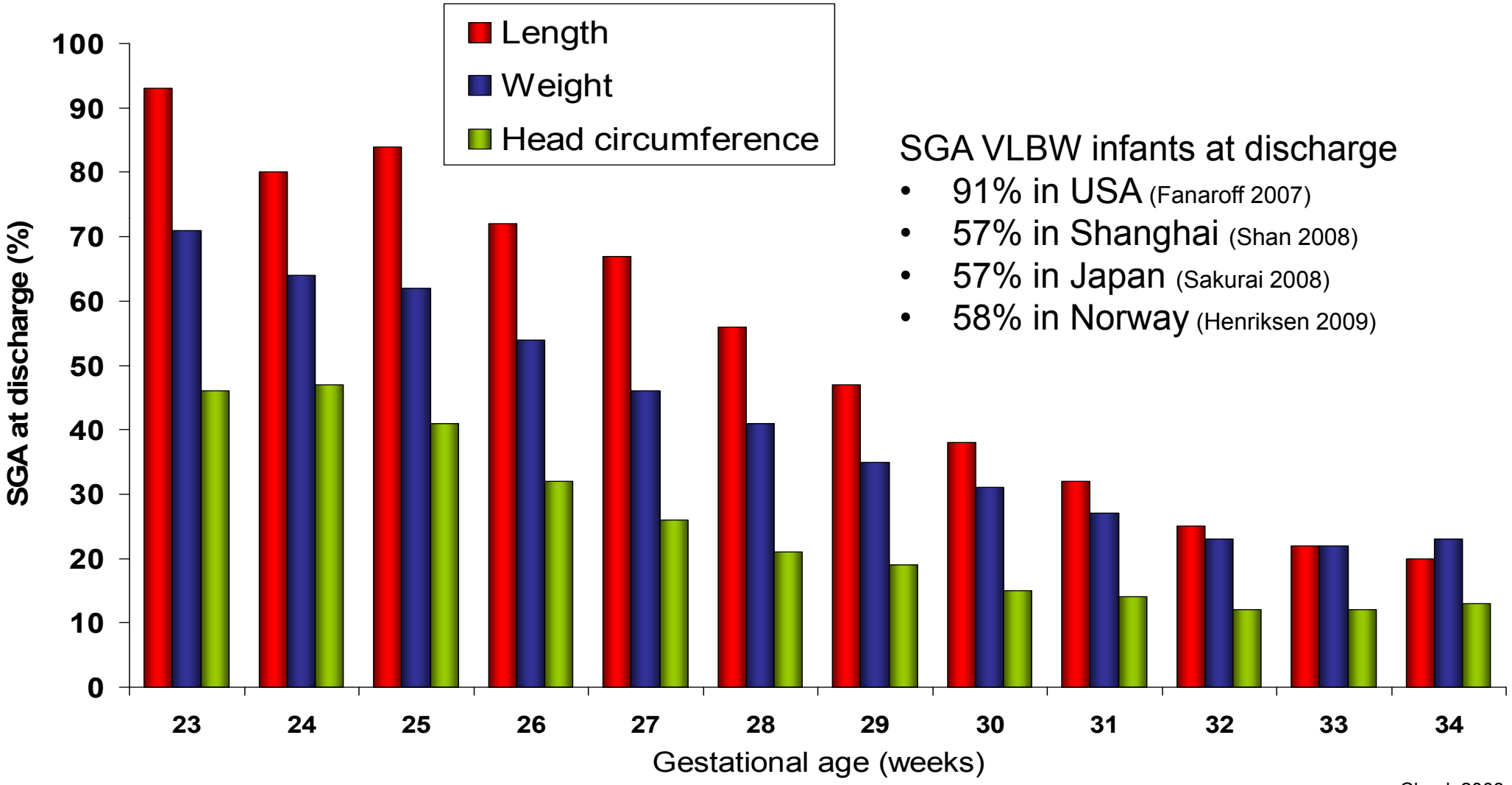
Growth similar to intrauterine growth; Myth or Reality?



Growth rate according to age



Postnatal growth restriction in preterm infants



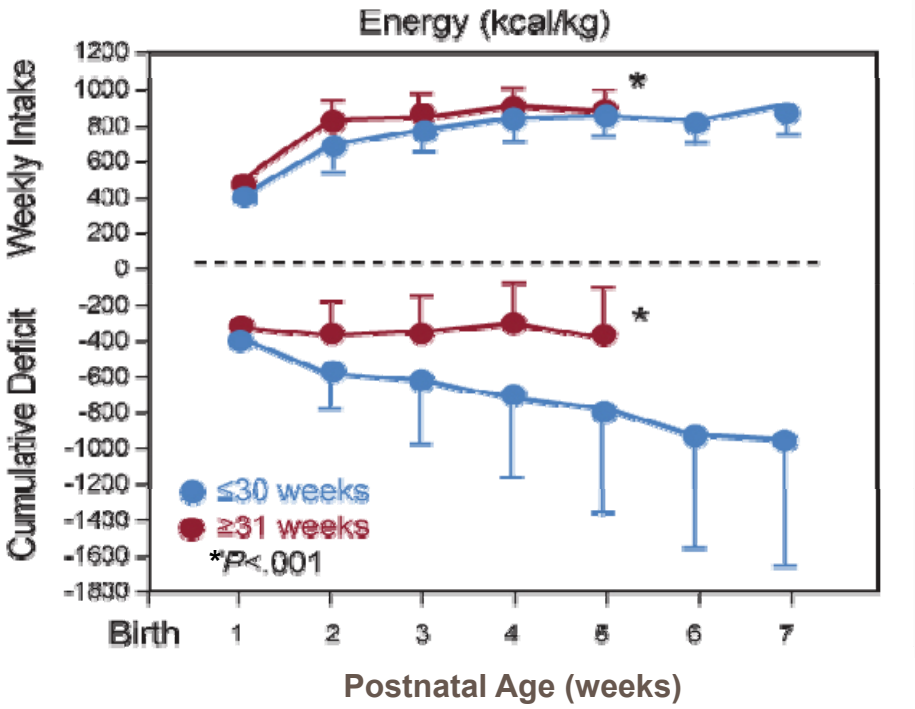
SGA VLBW infants at discharge

- 91% in USA (Fanaroff 2007)
- 57% in Shanghai (Shan 2008)
- 57% in Japan (Sakurai 2008)
- 58% in Norway (Henriksen 2009)

Clarck 2003

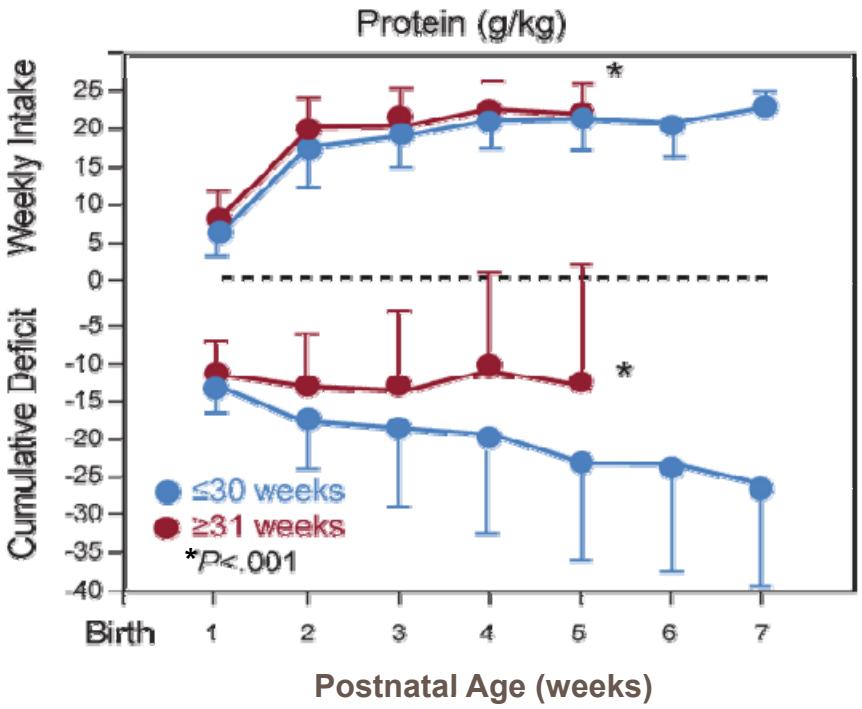
Failure to Achieve Nutritional Goals Produces Nutritional Deficits

Energy Intake and Cumulative Energy Deficit



Energy goal = 120 kcal/kg/d

Protein Intake and Cumulative Protein Deficit



Protein goal = 3 g/kg/d

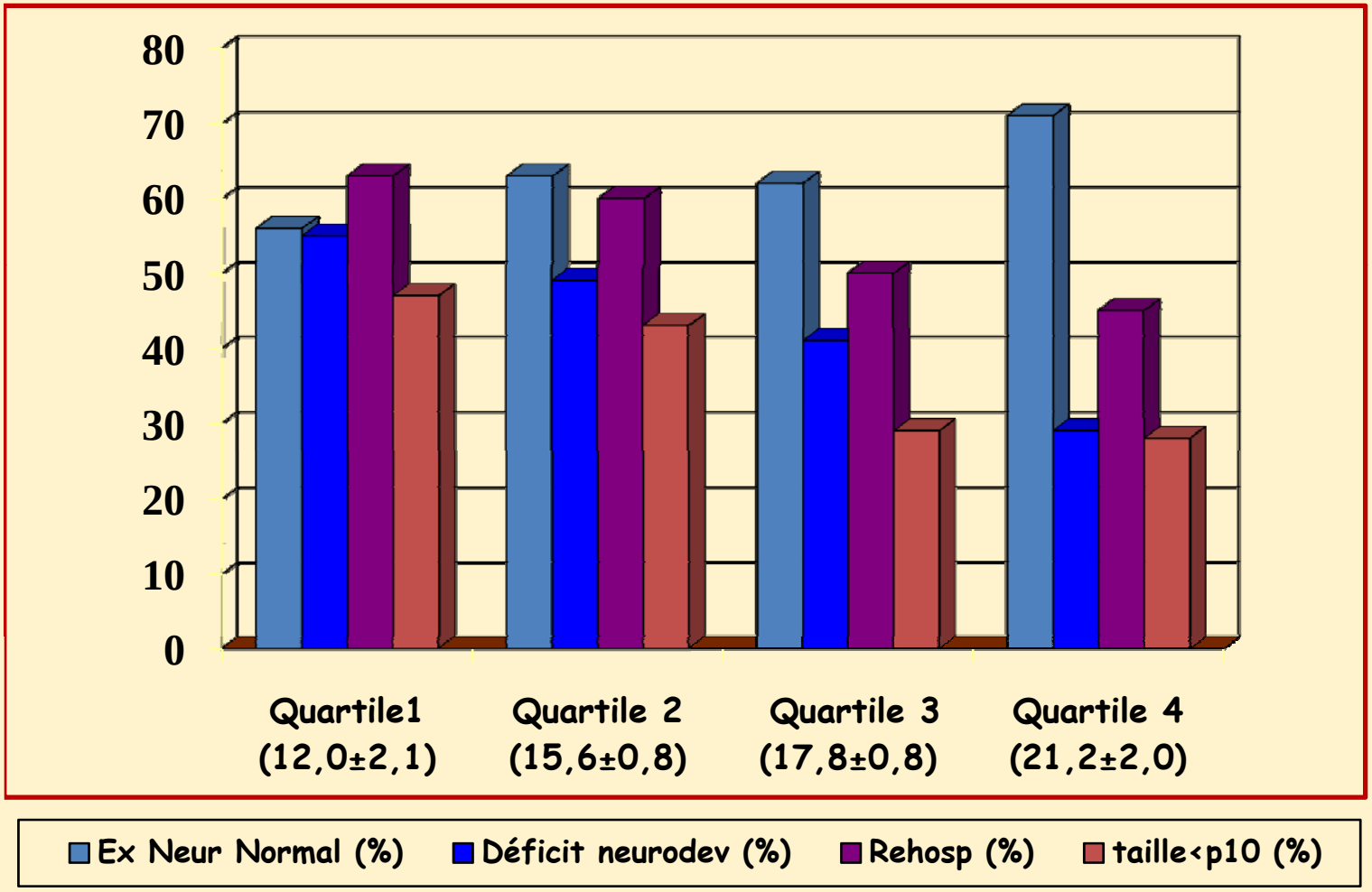
N=105 preterm infants ≤34 weeks GA and a birth weight ≤1750 g

Actual recommendations: Energy goal = 120 kcal/kg/d
Protein goal = ± 4.0 g/kg/d

Embleton NE, et al. *Pediatrics*. 2001;107:270-273.

Growth similar to intrauterine growth; Myth or Reality?

Early Growth and Long Term Development



RA. Ehrenkranz & al Pediatrics 2006

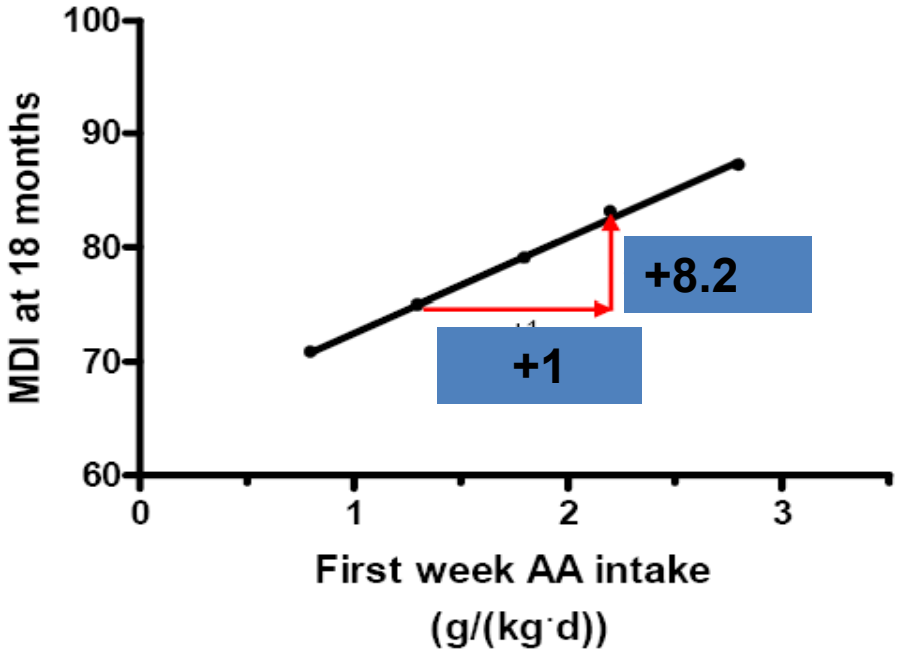
Intra-uterin growth; Myth or Reality?

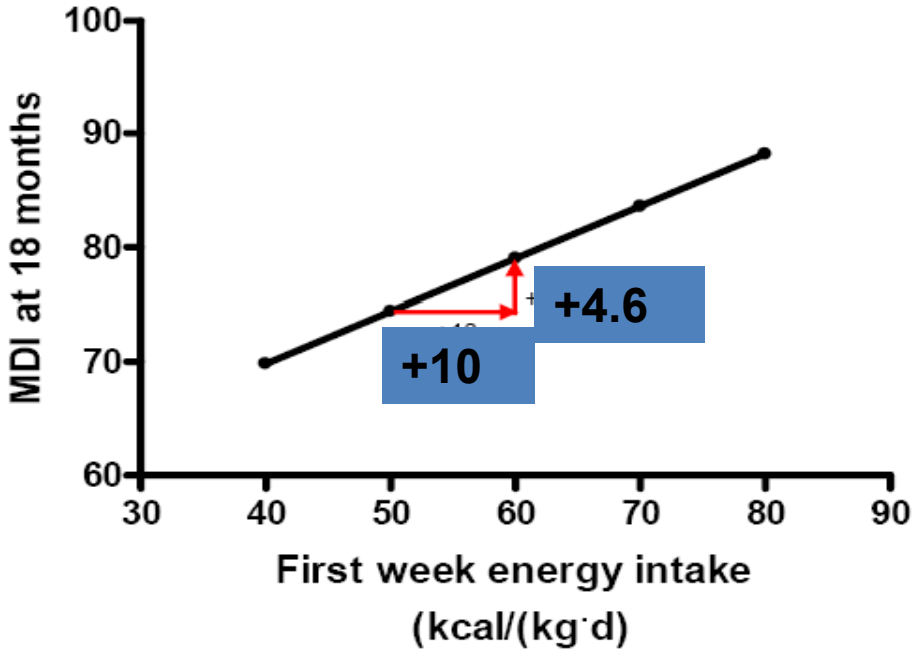
First week protein and energy intakes associated with 18-months developmental outcome in ELBW infants

Day 1 : 0.4 g AA /kg*day and 31 kCal/kg*day

Day 7 : 2.9 g AA /kg*day and 81 kCal/kg*day

Stephens BE, 2009





Nutritional approach for the VLBW infants

- Growth similar to intra-uterin growth: Myth or Reality?
- Did we need mineral's and electrolyte's supplies from the first day
- Potential side effect of early high AA intake. Is there a risk of protein overload?

Growth similar to intrauterine growth; Myth or Reality?

Is it possible to reduce post natal growth restriction in ELBW and VLBW infants?

Senterre T and Rigo J. *Acta Paediatrica.* 2012;101(2):e64-70

Role of an early aggressive nutritional programme using a premixed ready-to-use parenteral solution

Senterre T and Rigo J. *J Pediatr Gastroenterol Nutr.* 2011;53(5):536-42.

Need for a Balanced Parenteral Solution from the First Day of Life in VLBW Infants

a) <u>AA & energy intakes:</u>

1. Early “aggressive” nutrition reduces cumulative nutritional deficit and improves early postnatal growth in VLBW infants
2. AA intake >2.5g kg^{-1} d^{-1} and energy intake >40 kcal kg^{-1} d^{-1} on the first day induces positive nitrogen balance and promotes LBM deposition
3. Appropriate fluid intake 50 to 80 ml kg^{-1} d^{-1} and the limitation of water loss (evaporation, perspiration) to limit the weight loss to between 5 and 10% improves electrolyte homeostasis during the first few days of life
4. Early AA (prot) and energy intakes to reach 4.0 g AA and 120 kcal/kg*d

Growth similar to intrauterine growth; Myth or Reality?

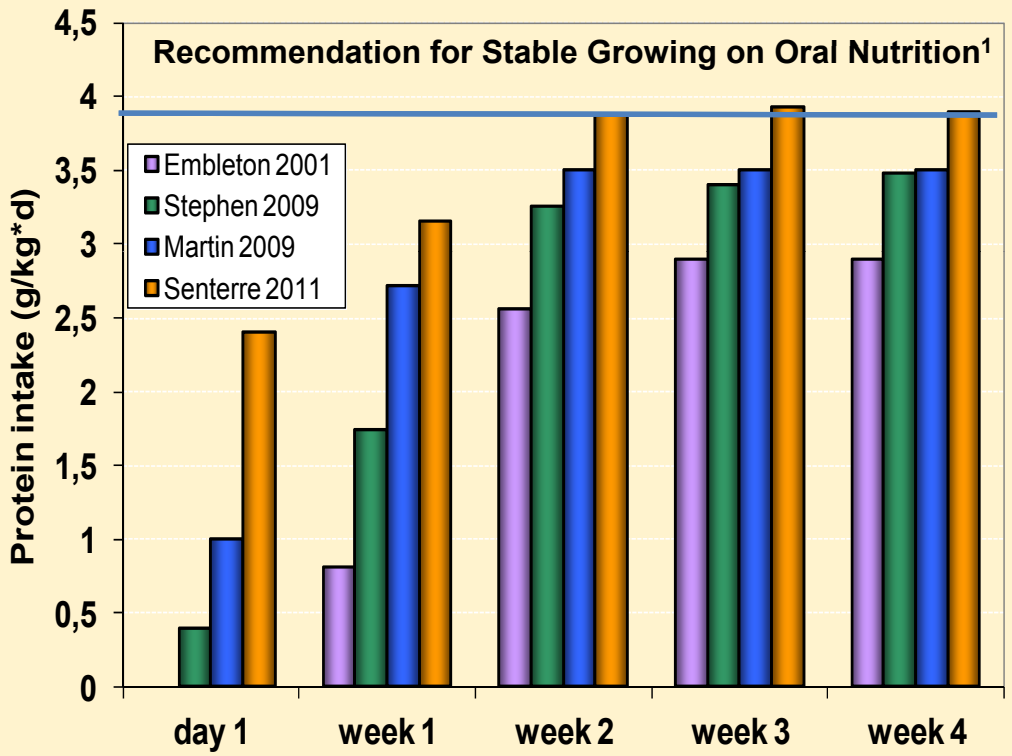
How to provide adequate intakes during the transitional period to enteral nutrition

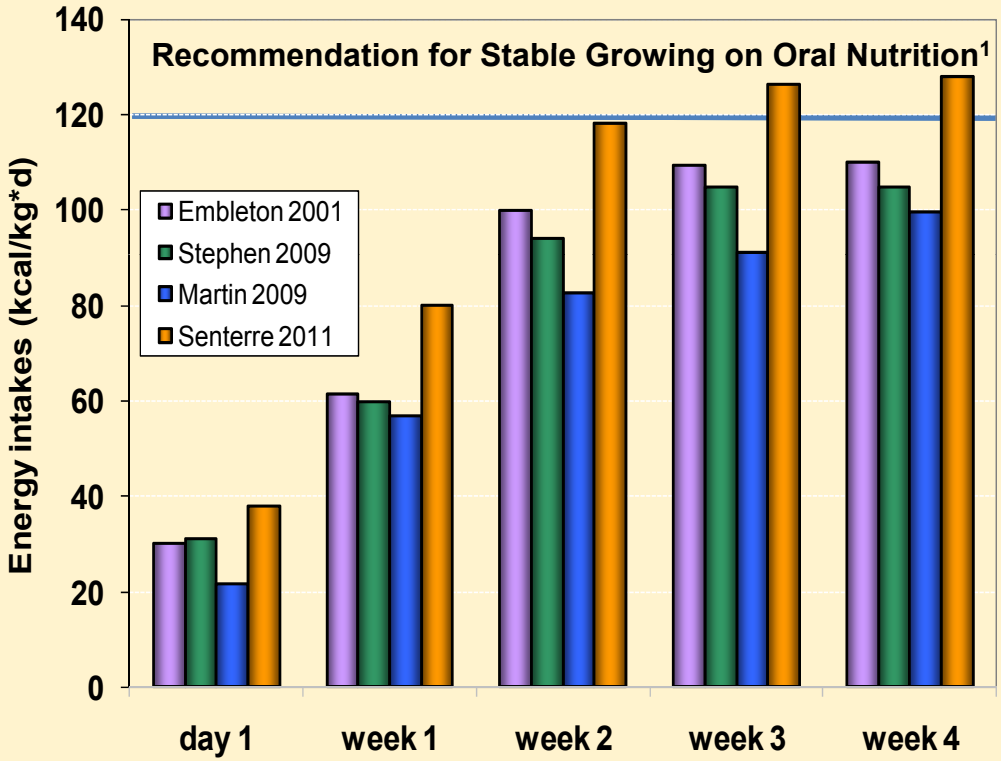
- Enteral feeding was initiated on the first or the second day of age with HM, OMM or banked HM
- First 20 ml/kg was not considered in protein and energy count.
- HM Fortification was initiated at 50 ml/kg*d
- Individual fortification were performed in some preterm infants to compensate the low fat content of OMM and to provide 4.3 g of protein/kg*d
- When HM was not available , VLBW infants received a PTF with a high P/E ratio 3.3 to 3.6 g/100 kcal

Intra-uterin growth; Myth or Reality?

Significant improvement during the first week of life

Recommendations are meet at the end of the first week





Senterre T and Rigo J. *Acta Paediatrica.* 2012;101(2):e64-70 .

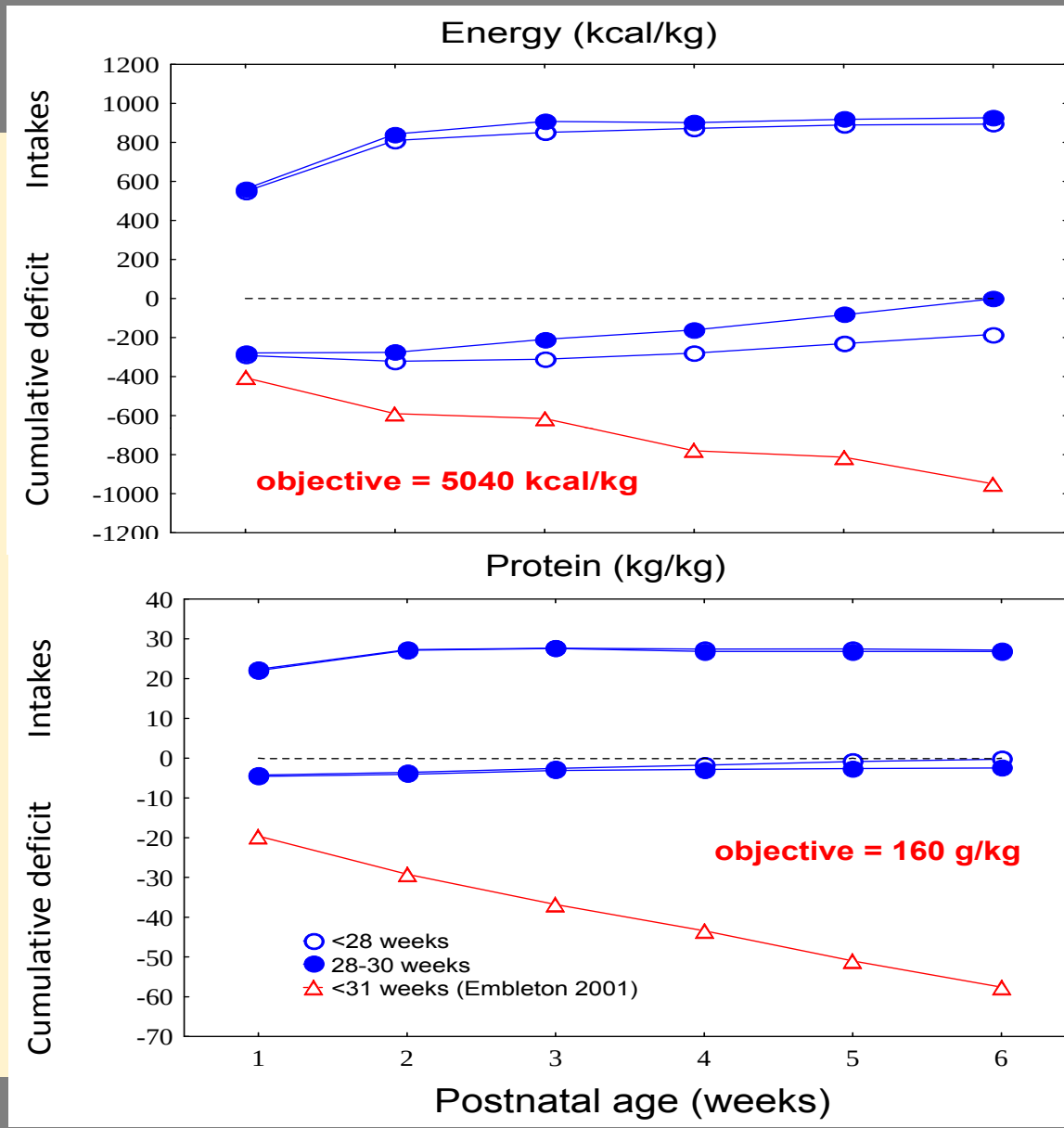
Senterre T and Rigo J. *J Pediatr Gastroenterol Nutr.*. 2011;53(5):536-42. .

Intra-uterin growth; Myth or Reality?

Cumulative nutritional deficit

- ● <28 weeks
- ○ 28-30 weeks
- △ <31 weeks (Embleton 2001)

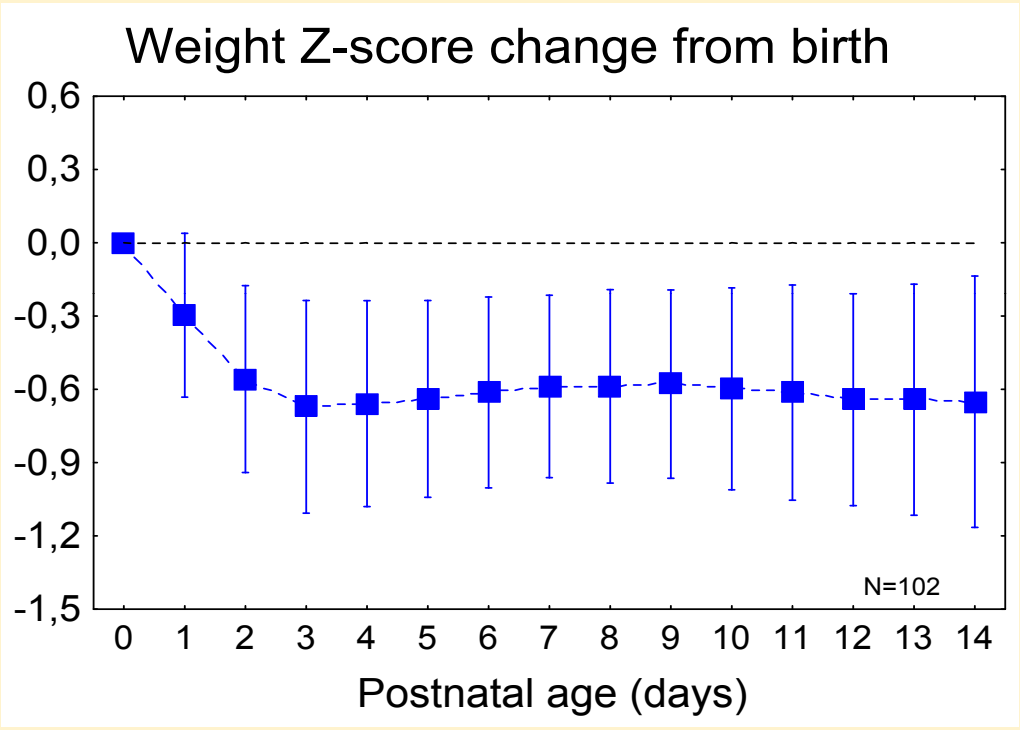
At 6 weeks

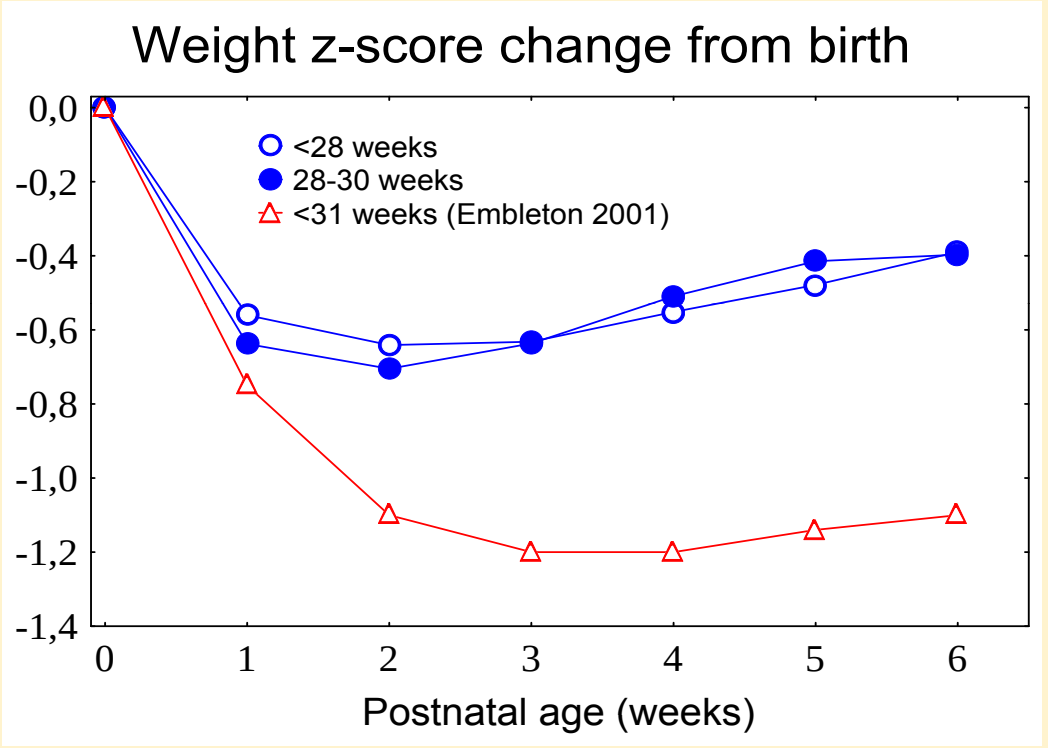


Th Senterre & J Rigo 2011

Intra-uterin growth; Myth or Reality?

Standardized PN in the NICU Can Meet Guidelines



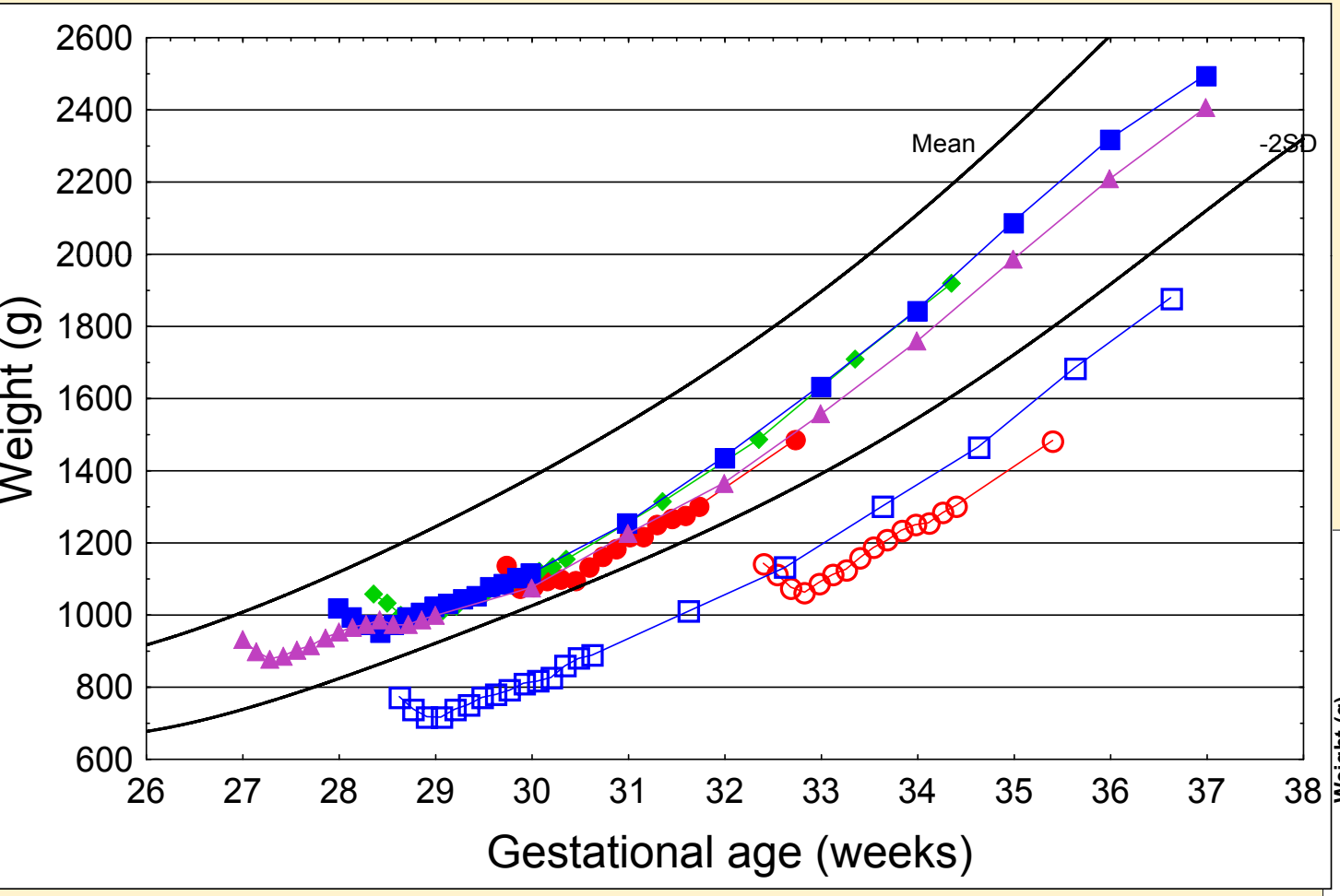


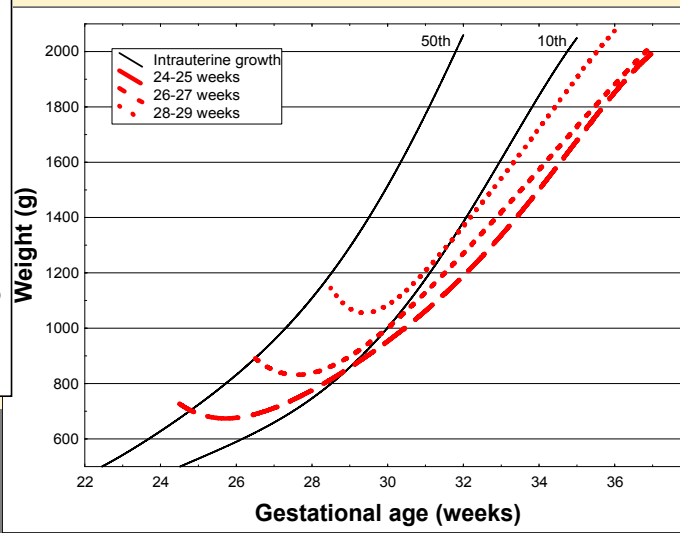
- Growth restriction limited to the first three days of life by contrast with earlier studies
- Growth similar to intrauterine growth after first 3 days of life

Senterre T and Rigo J. *Acta Paediatrica.* 2011—in press.

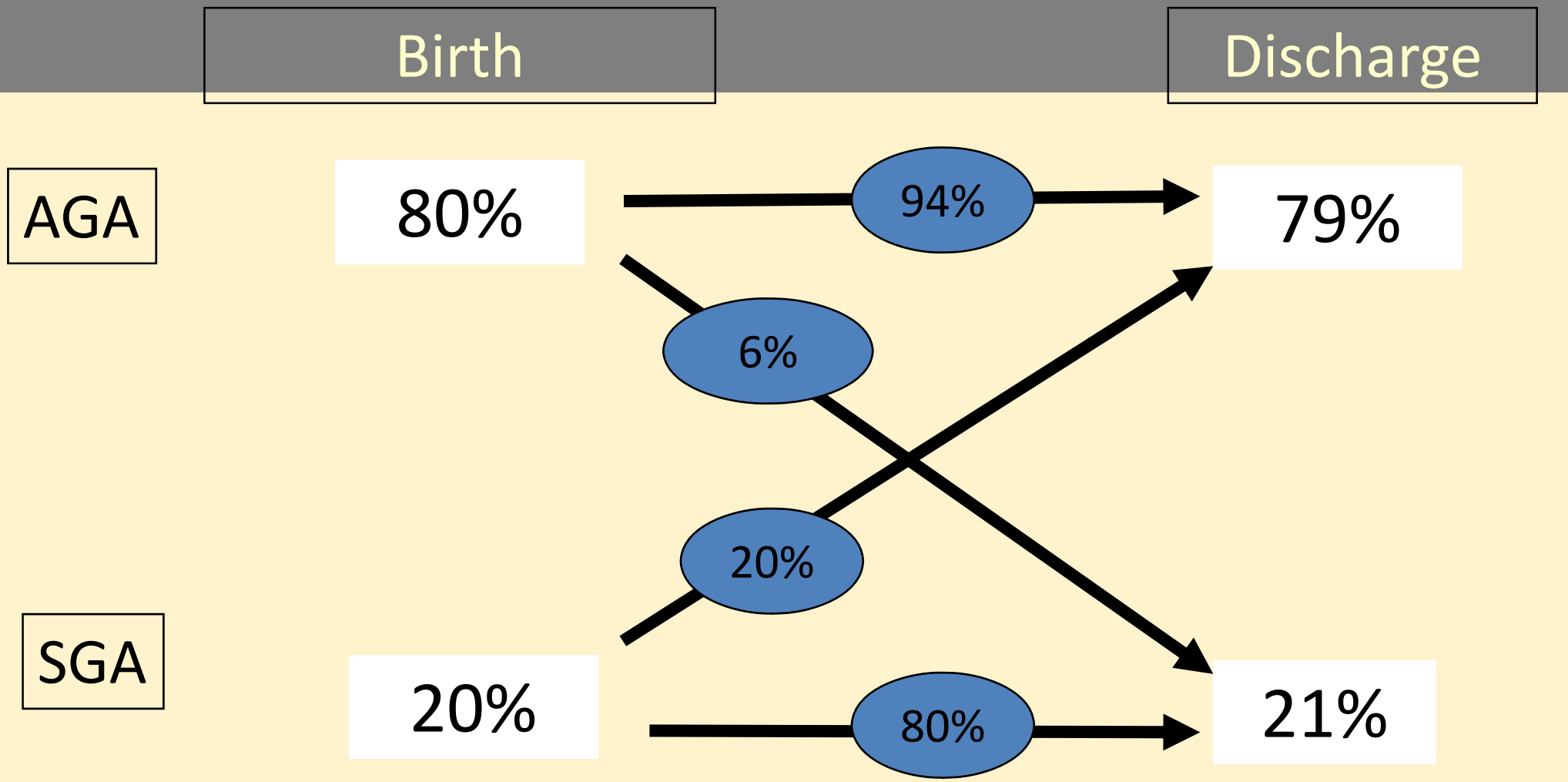
Intra-uterin growth; Myth or Reality?

Is it possible to abolish Post Natal Growth Restriction?





Growth similar to intrauterine growth; Myth or Reality?



Usher & McLean

Litterature

40-90%

Conclusions

1. *Optimal nutrition from birth in the range of the recent guidelines allows to reduce initial weight loss, to induce early positive nitrogen balance and to promote early weight gain in the range of the intra-uterine growth rate.*

2. *Early HM fortification <50ml/kg, adequate HM fortification to provide at least 4.3g/kg*d of protein and 130 kcal/kg*g and the use of preterm formula with high Prot/energy ratio allow to maintain an adequate growth rate >17g/kg*d and to obtain a relative catch up growth before discharge or theoretical term.*

3. *Cumulative nutritional deficit can be abolish and postnatal growth restriction is not an inevitable phenomena in the ELBW infants.*

Nutritional approach for the VLBW infants

- Growth similar to intra-uterin growth: Myth or Reality?
- Did we need mineral's and electrolyte's supplies from the first day
- Potential side effect of early high AA intake. Is there a risk of protein overload?

Parenteral nutrition

Ca & P intakes:

- Ca and P supplies are necessary from the first day of life in VLBW infants on PN

- In parenteral solution, optimal molar Ca/P ratio is close to 1/1 or slightly<1

- Phosphorus need can be estimated from the AA and the Ca intakes provided by the parenteral solution

Need for a balanced parenteral solution

Electrolyte's Homeostasis in VLBW infants

- Extra-Uterin Adaptation = transitional Phase
  - Physiological Water loss : extracellular volume reduction
  - Oliguria during the first 24-48 hours of life
  - Weight loss: 5-10% du BW Term infants, 10-20% preterm <1500g (Fusch 2005)

- Fréquents Electrolytic Disorders in VLBW infants <1500g
  - Hypernatriemia >150 mmol/L : 30-50% (Huston 2007, Gawlowski 2006, Kermorvant-Duchemin 2012)
  - Hyperkaliemia >7 mmol/l : 20-25% (Mildenberger 2002, Thayyil 2008, Yaseen 2009, Iacobelli 2010)

  = Challenge for the Neonatologists

Recommendations :

- No Na and K intakes during the first days of life.

(Fusch 2005, ESPGHAN 2005, Bhatia 2006)

More aggressive nutrition may induce a new metabolic syndrome in VLBW infants

a) Current guidelines

1. By turning the nitrogen balance from negative to positive, AA administration could also minimize the occurrence of water and ions disturbances after birth especially in ELBW infants.
2. In addition P supply cannot be provide without Na or K.

Need for a balanced parenteral solution

Electrolyte's Homeostasis in VLBW infants

c) <u>Na, K & Cl intakes:</u>

1. Phosphorus supply is associated to a Na or K intake
2. LBM accretion requires some P and K retention for the intracellular compartment (10 mg P/160 mg Nitrogen) and Na for the extracellular compartment (1 à 1.5 mmol/10g de LBM).
3. Limitation of the initial weight loss improves electrolyte homeostasis during the first week of life
4. Increase of AA intake reduces or prevents the non-oliguric hyperkaliemia
5. The use of a balanced electrolyte intake improves acid base status ($Na^+ + K^+ - Cl^- > 1\text{-}2$ mmol)

Compounded ready to use or industrial multichamber bag

Kg*d		Estimated optimal parenteral intakes	Senterre & Rigo 2011	New NUMETA G13% 3CB
Fluids	ml/kg/d	-	165	130
Energy	Kcal/kg/d	90-120	118	118
Protein	g/kg/d	3.5-4.0	4.1	4.0
Glucose	g/kg/d	13-18	18.8	17.3
Fat	g/kg/d	2-4	3.0	3.25
Sodium	mmol/kg/d	2-7	2.4	3.25
Potassium	mmol/kg/d	2-5	2.3	2.7
Chloride	mmol/kg/d	2-7	3.0	4.0
Calcium	mmol/kg/d	1.3-4.0	2.7	1.62
Phosphorus	mmol/kg/d	1.0-2.5	2.7	1.63
Magnesium	mmol/kg/d	0.15-0.30	0.25	0.20

Th Senterre & J Rigo 2011; J.Rigo& al 2012

How to use Standardized Parenteral Nutrition in VLBWI

Minimal adaptation allows to provide nutritional recommendations during the early days of life

APP 2	1083*mOsm/L*			**J1**		**J2**			**J3**		**J4**		**J5**	**≥ J6**	
volume	*100*	**ml/kg/d**	**40**	**50**	**60**	**70**	**80**	**90**	**100**	**110**	**120**	**130**	**140**	**150**	**160**
AA	*2,7*	g/kg/d	**1,1**	**1,4**	**1,6**	**1,9**	**2,2**	**2,4**	**2,7**	**3**	**3,2**	**3,5**	**3,8**	**4,1**	**4,3**
glucose	*12,5*	gr/kg/jour	5	6,3	7,5	8,8	10	11,3	12,5	13,8	15	16,3	17,5	18,8	20
Lipid 20%*		gr/kg/jour	1	1	1	1,5	1,5	1,5	2	2	2,5	2,5	3	3	3
energy	*57*	**kCal/kg/d**	**32**	**38**	**44**	**54**	**60**	**65**	**76**	**81**	**92**	**97**	**108**	**113**	**120**
Na+	*1,6*	mmol/kg/d	0,6	0,8	1	1,1	1,3	1,4	1,6	1,8	1,9	2,1	2,2	2,4	2,6
K+	*1,5*	mmol/kg/d	0,6	0,8	0,9	1,1	1,2	1,4	1,5	1,7	1,8	2	2,1	2,3	2,4
Cl-	*2*	mmol/kg/d	0,8	1	1,2	1,4	1,6	1,8	2	2,2	2,4	2,6	2,8	3	3,2
Ca++	*72*	mg/kg/d	28,8	36	43,2	50,4	57,6	64,8	72	79,2	86,4	93,6	100,8	108	115,2
P	*55*	mg/kg/d	22	27,5	33	38,5	44	49,5	55	60,5	66	71,5	77	82,5	88

Primene 10%

A.A	*1*	g/kg/d	1	1	1	0,5	0,5	0,5	0	0	0	0	0	0	0
volume	*10*	**ml/kg/d**	**10**	**10**	**10**	**5**	**5**	**5**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
energy	*3,75*	kCal/kg/d	3,8	3,8	3,8	1,9	1,9	1,9	0	0	0	0	0	0	0

TOTAL INTAKES

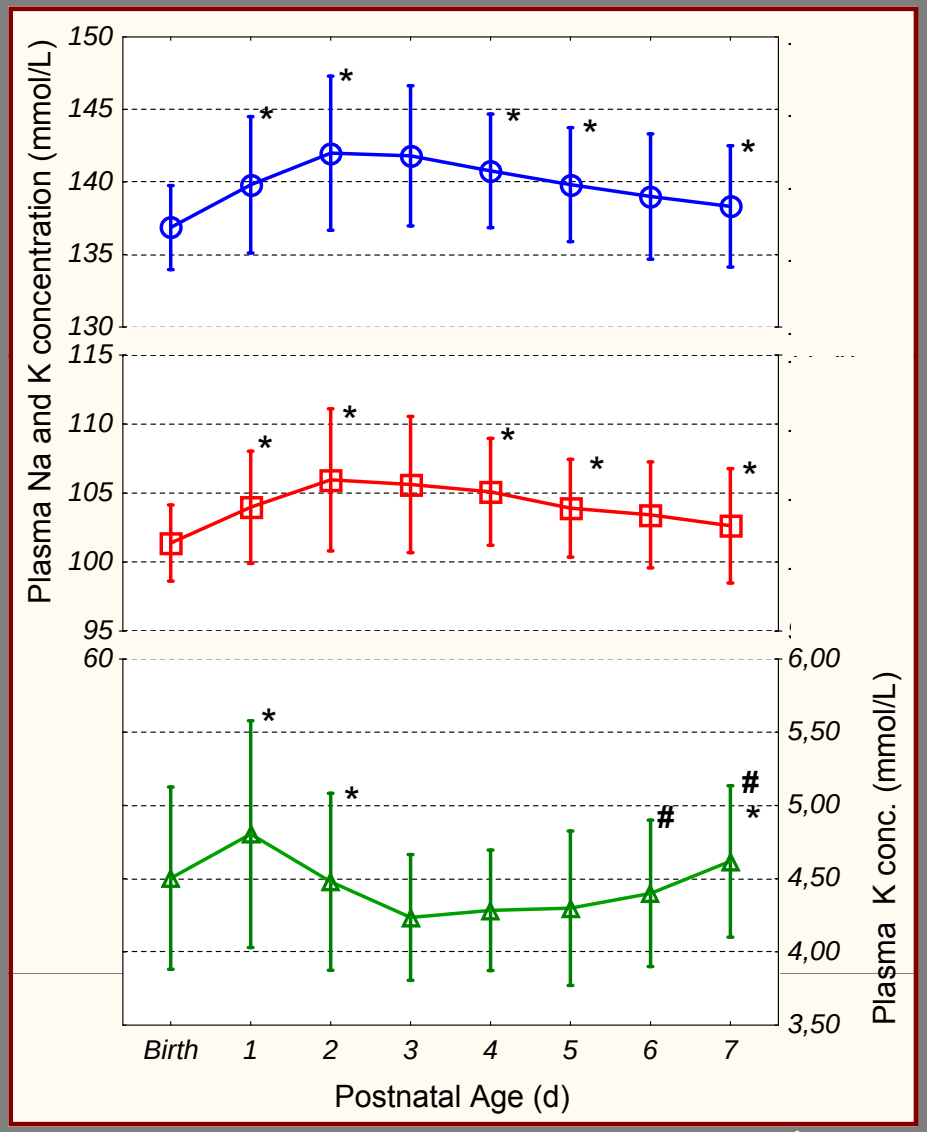
volume	**ml/kg/d**	**55**	**65**	**75**	**82**	**92**	**102**	**110**	**120**	**132**	**142**	**155**	**165**	**175**
AA	**g/kg/d**	**2.1**	**2.4**	**2.6**	**2.4**	**2.7**	**2.9**	**2,7**	**3**	**3,2**	**3,5**	**3,8**	**4,1**	**4,3**
energy	**kCal/kg/d**	**36**	**42**	**48**	**56**	**62**	**67**	**76**	**81**	**92**	**97**	**108**	**113**	**120**

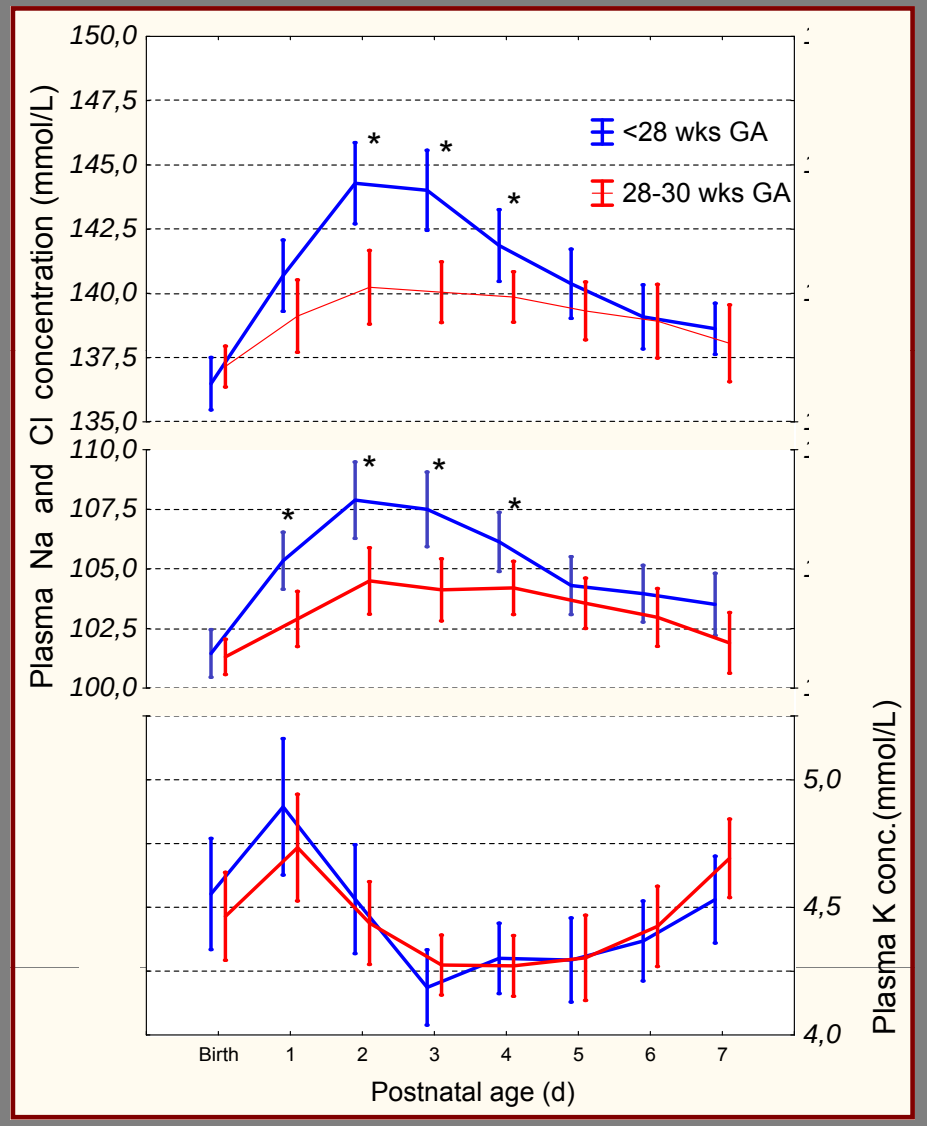
* Added separetely

Energy=AA*3.75+Glu*3.75+lip*9.3 kcal

More aggressive nutrition may induce a new metabolic syndrome in VLBW infants

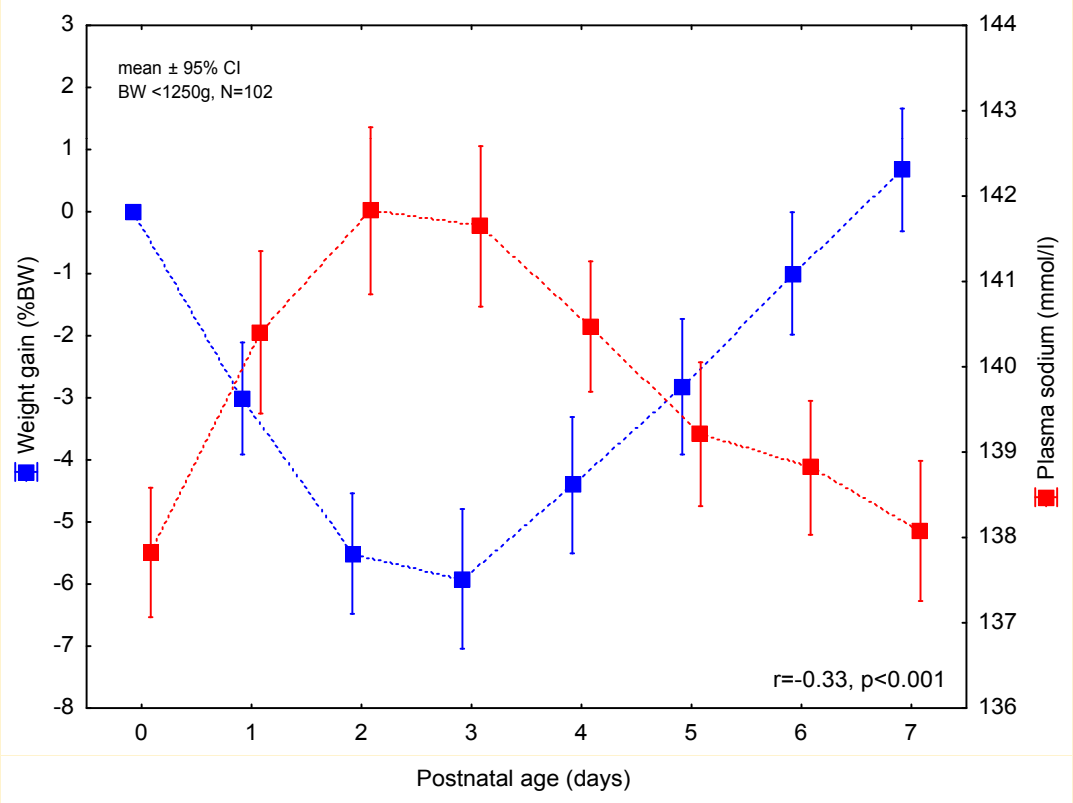
Balanced Parenteral Solution Improves Electrolyte's Homeostasis.





Th Senterre JFRN 2012

Electrolyte's Homeostasis



BW <1250g, BW: 1005 ± 157 g

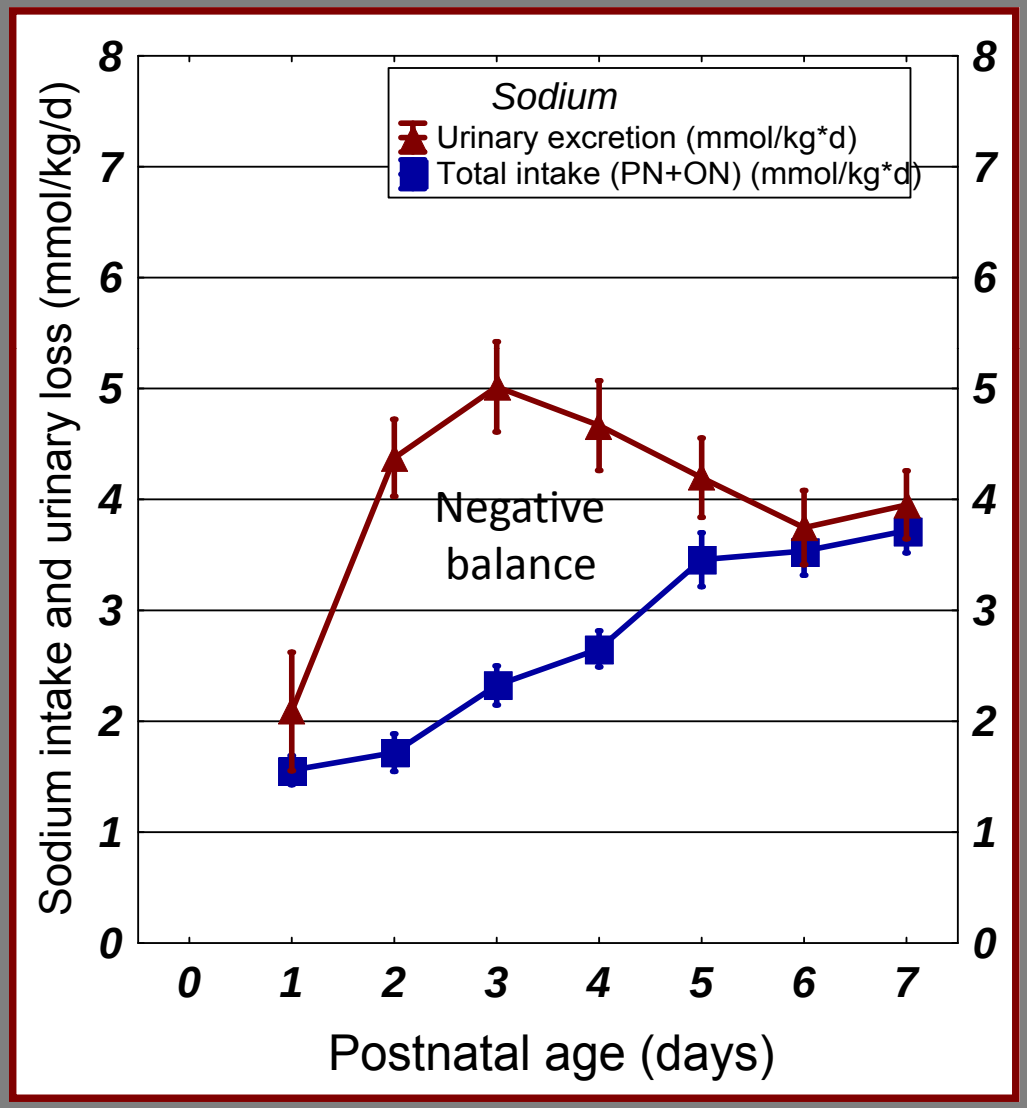
N=102 GA: 28.5 ± 1.9 weeks

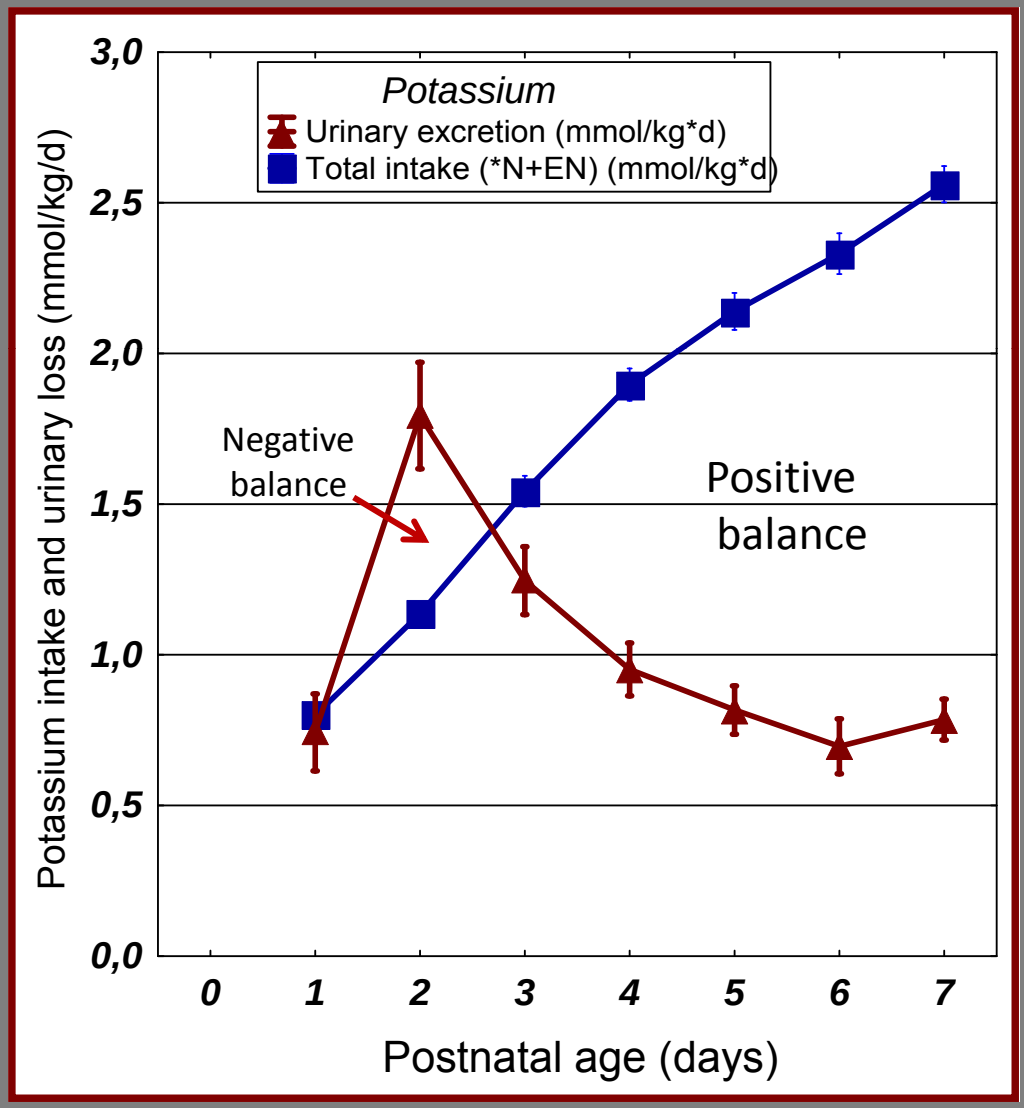
Mean ± SD

	Incidence	Literature
Na >150 mmol/L	16%	30-50%
Na <130 mmol/L	30%	
K >7 mmol/L	0%	20-25%
K <3 mmol/L	9%	

More aggressive nutrition may induce a new metabolic syndrome in VLBW infants

Balanced Parenteral Solution Improves Electrolyte's Homeostasis.

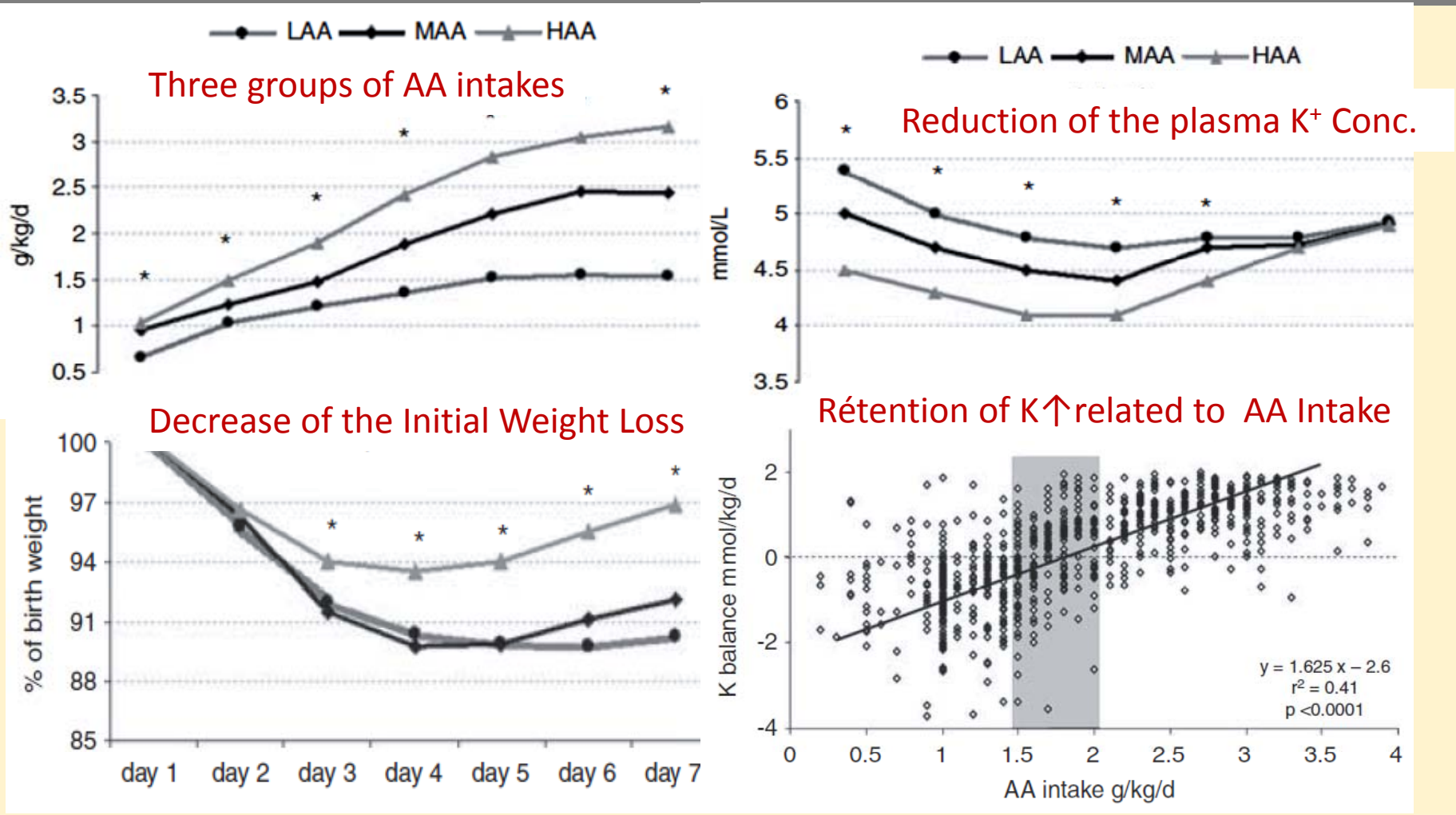




Th Senterre JFRN 2012

More aggressive nutrition may induce a new metabolic syndrome in VLBW infants

Effect of AA intake on Initial weight loss and Plasma K^+

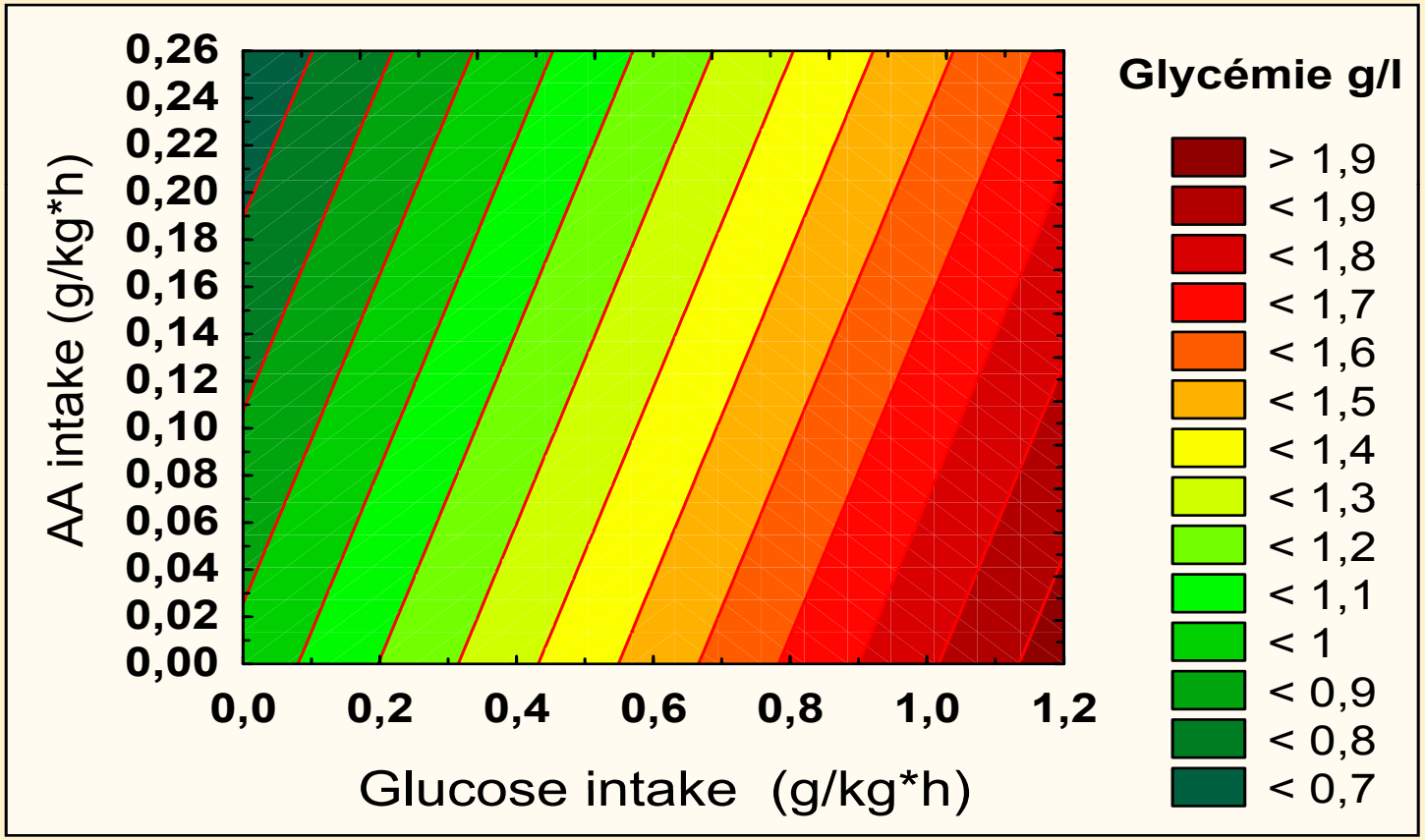


Bonsante F Iacobelli S& al Eur. J Clin Nutr. 2011;65:1088-93

Nutritional approach for the VLBW infants

- Growth similar to intra-uterin growth: Myth or Reality?
- Did we need mineral's and electrolyte's supplies from the first day
- Potential side effect of early high AA intake. Is there a risk of protein overload?

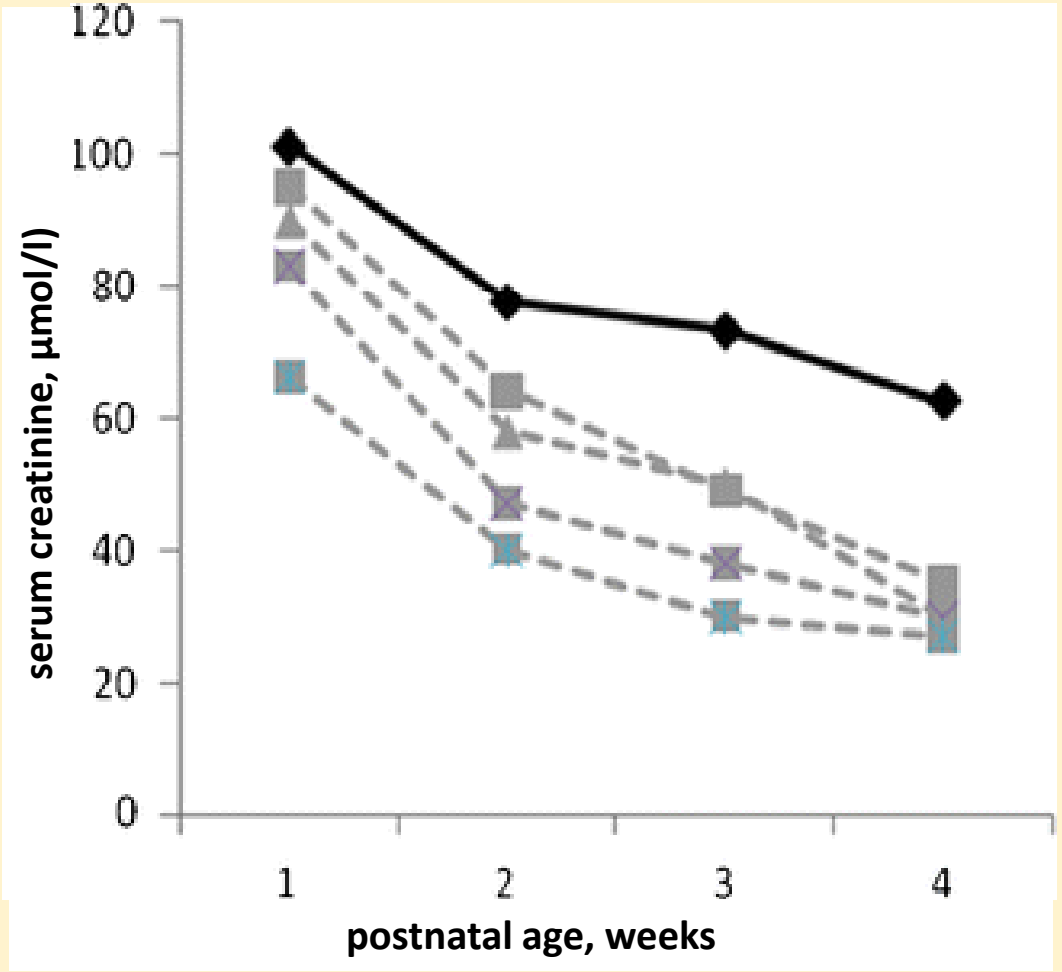
Influence of AA intakes on glucose tolerance



Blood glucose = 0.85* glucose intake – 1.23* AA intake + 0.93

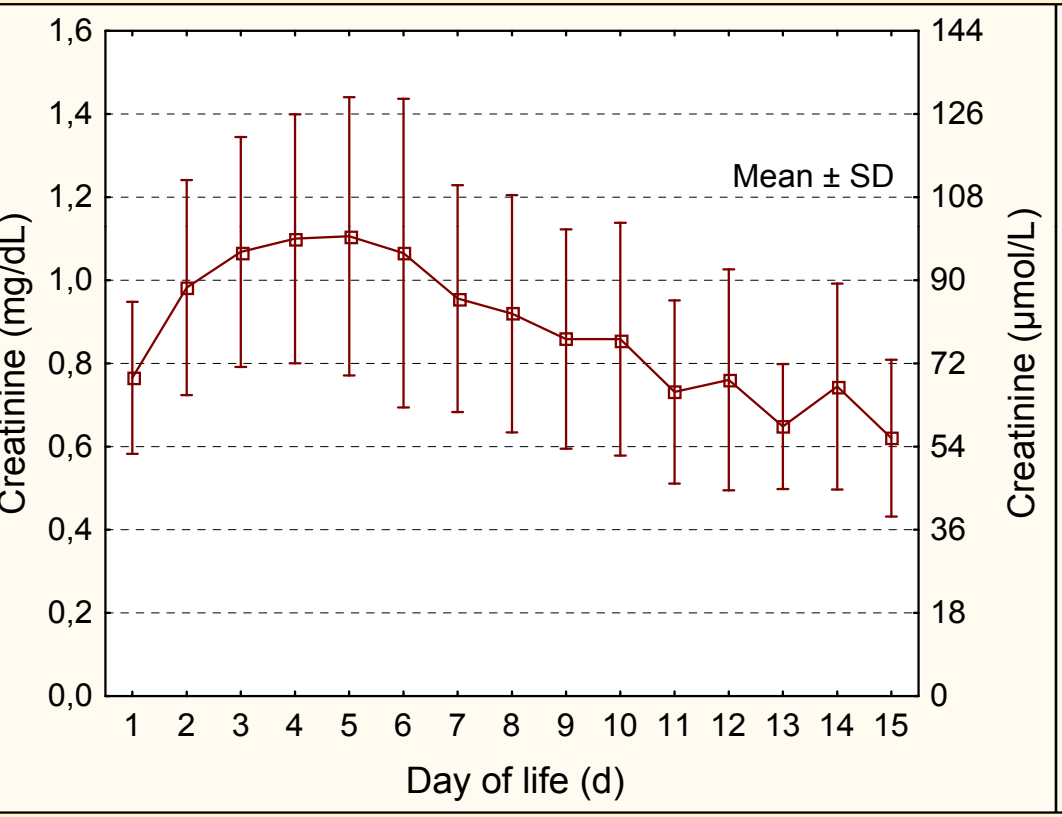
Consequences of aggressive nutitional approach in VLBW infants

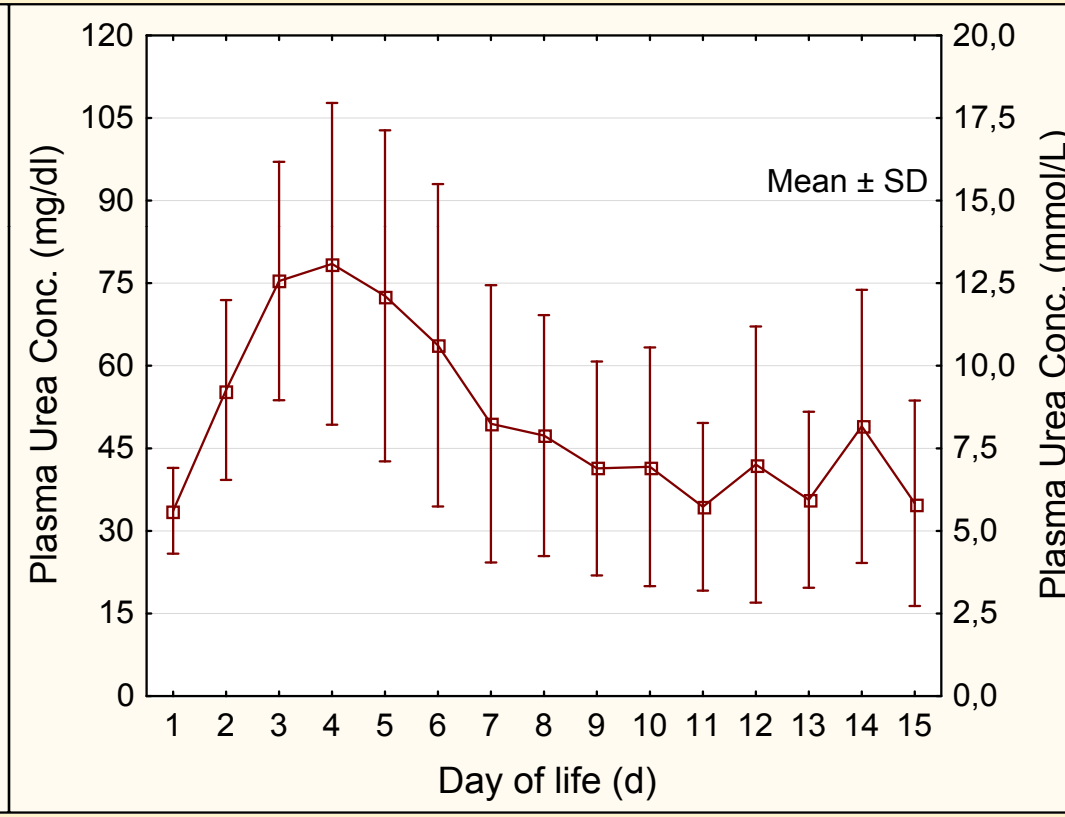
Median creatinemia levels in low birth weight neonates from peak creatinemia until the fourth week of postnatal life (1,000–1,500 g, 1,501–2,000 g, 2,001–2,500 g, and term neonates were extracted from the paper of Guignard- *grey discontinuous line*), the observations in ELBW neonates (i.e., <1,000 g) (*black continuous line*)



George I et al, Pediatr Nephrol 2011, 26: 1843-9

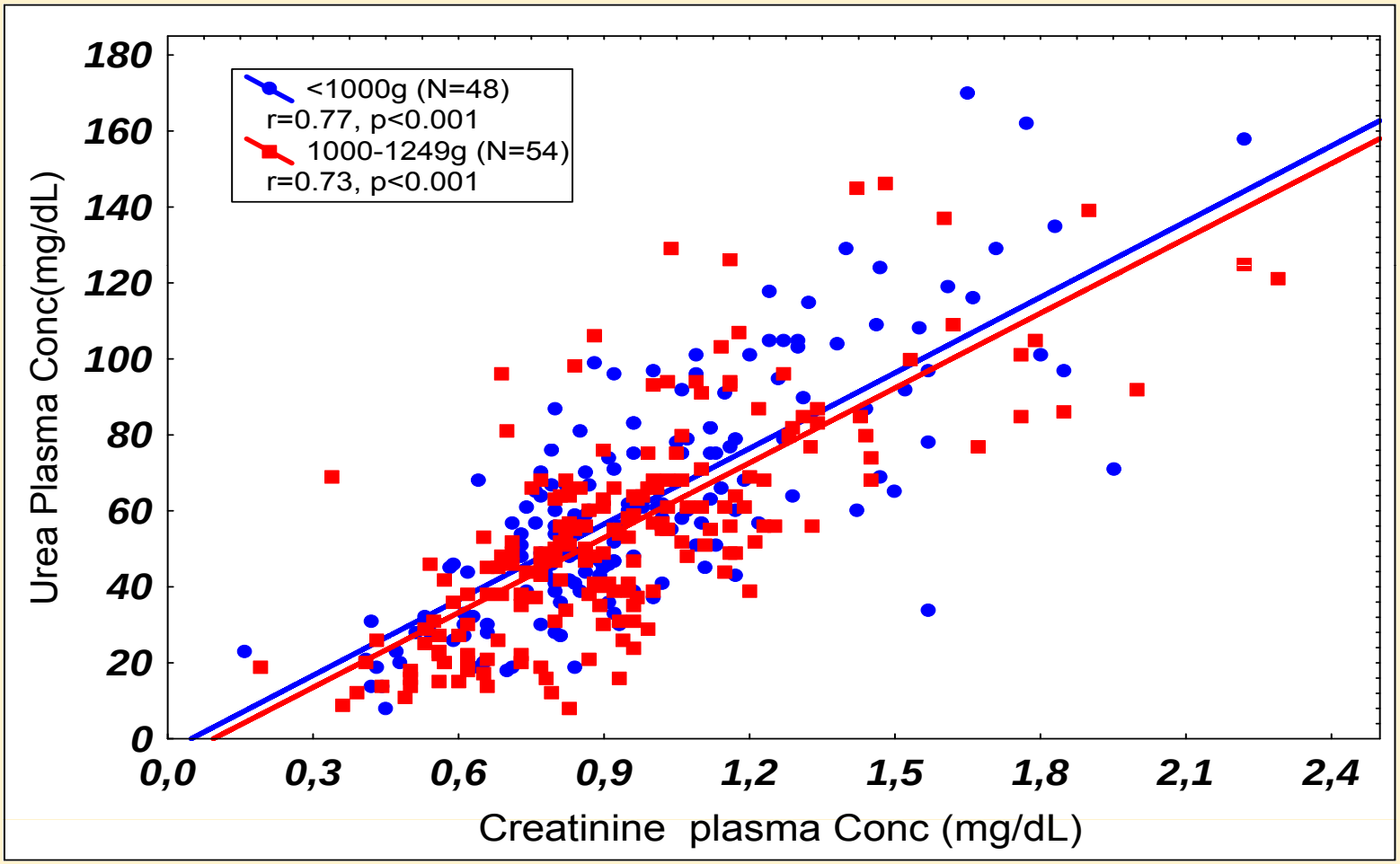
Consequences of aggressive nutitional approach in VLBW infants



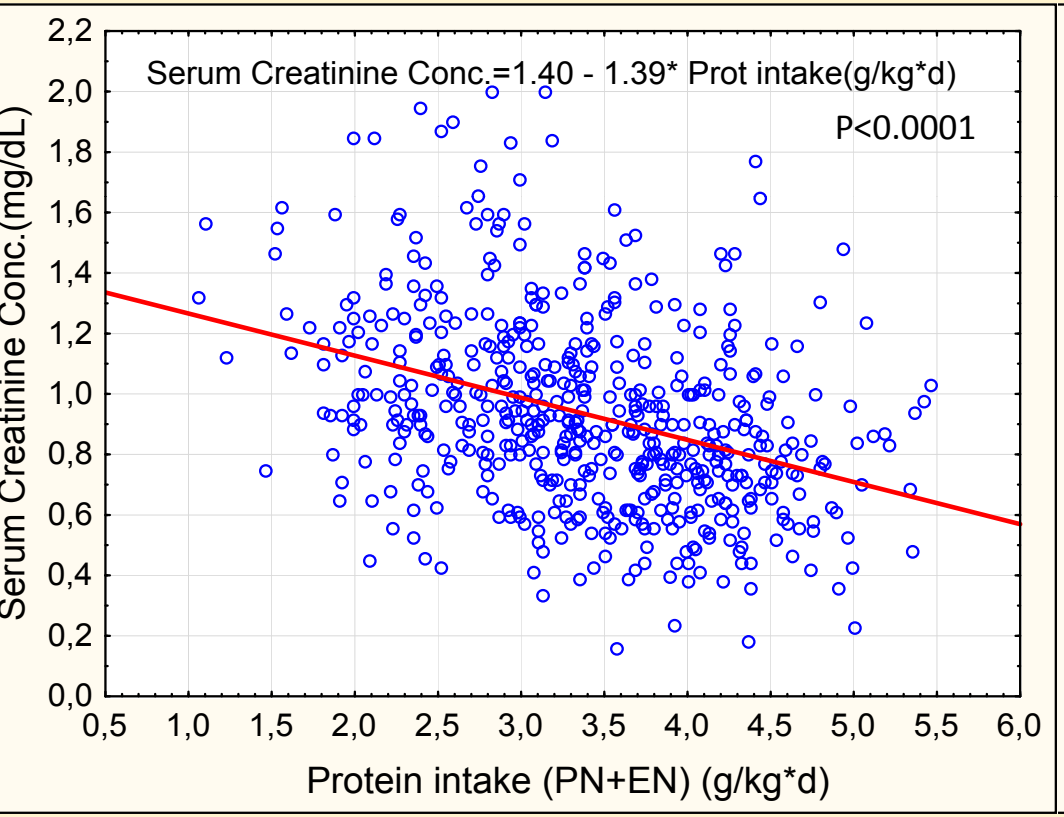


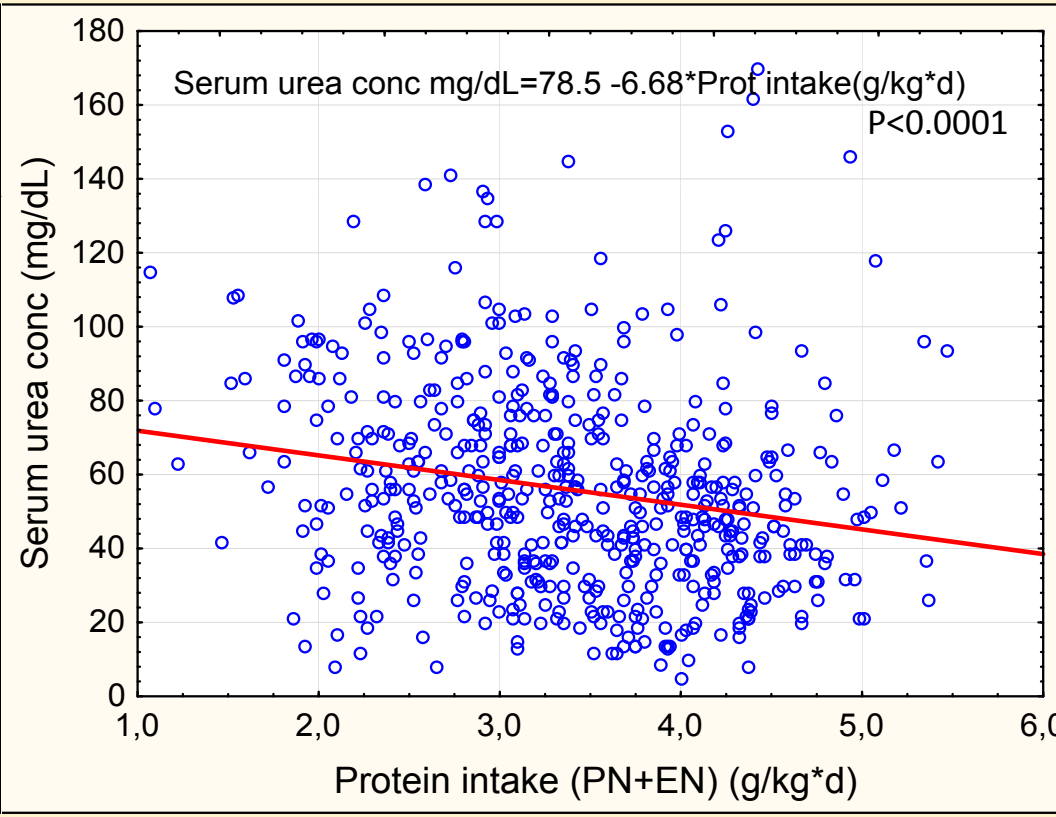
Consequences of aggressive nutitional approach in VLBW infants

BUN is not related to protein intake during the first weeks of age but is related to Renal immaturity.



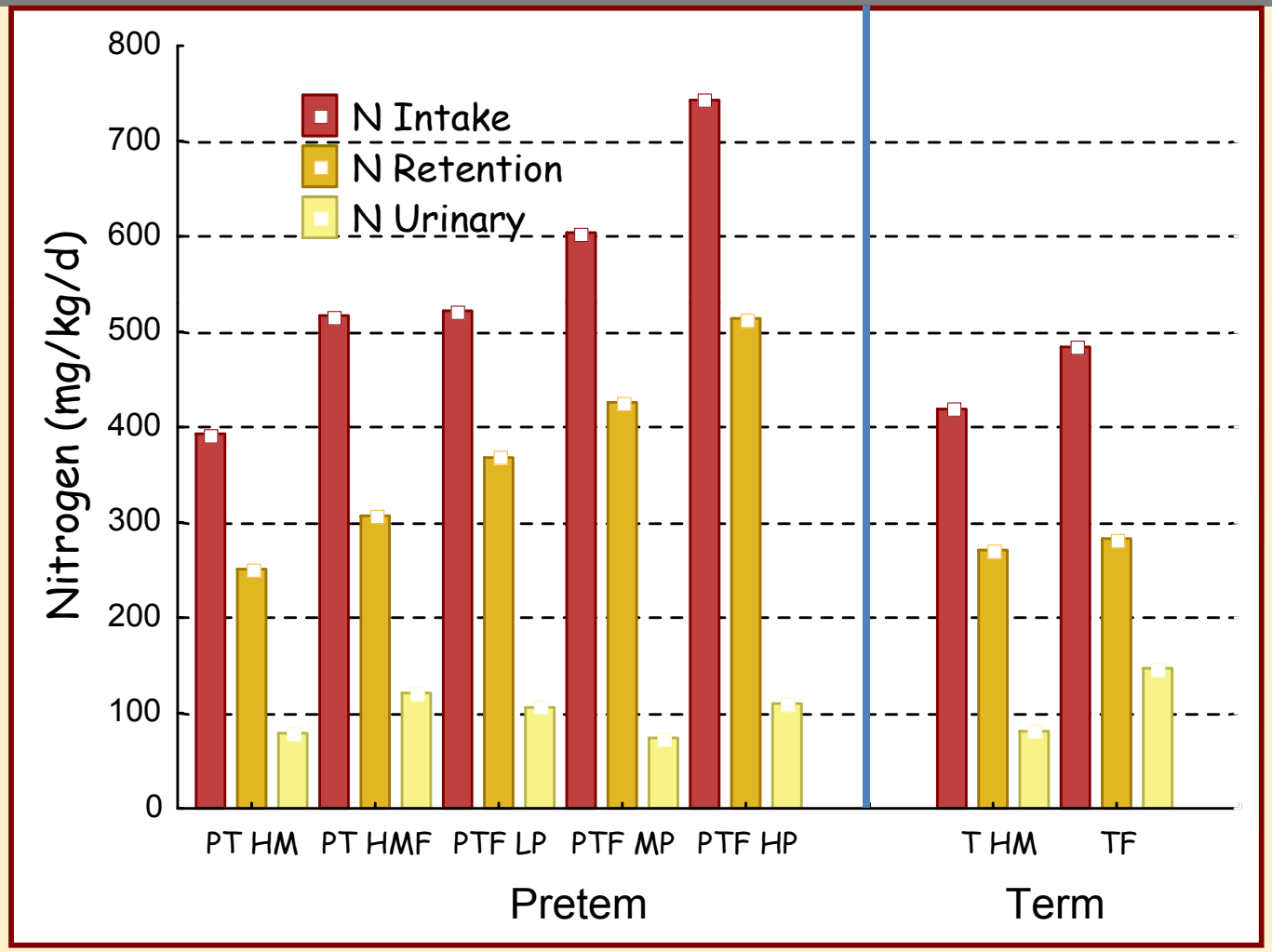
Consequences of aggressive nutitional approach in VLBW infants





Risk of Protein overload in preterm infants

Effect of nitrogen intake on nitrogen urinary excretion in VLBW infants



Putet & al 1984,1987

Rigo &al 1995, 1999

Cooke & al 2006

Conclusions

1. *Positive nitrogen balance from the first day of life, improves the matabolic use of potassium and phosphorus available for LBM gain.*
2. *Optimal nutrition from birth with high AA >2.5g/kg*d increasing to 4-4.5 g of protein during the first week of life could induce a new metabolic syndrome associating hypophosphatemia, hypercalcemia, and hypokaliemia .*
3. *Parenteral guidelines need to be revised to provide well balanced parenteral solution providing adequate minerals and electrolytes from the first day of life.*
4. *In enteral nutrition, the use of PTF with high P/E ratio increases the requirements for phosphorus and potassium.*
5. *PTF with a Ca/P ratio of 2 are at risk to induce hypophosphoremia in VLBW infants.*
6. *Ca/P ratio and K guidelines need to be revised*

What is the Divine feeding regimen for Preterm Infants?