ALIMENTACIÓN PARENTERAL EN EL RECIÉN NACIDO PREMATURO

DR MANUEL ALEJANDRO PAREDES MELLA

HOSPITAL PUERTO MONTT SEPTIEMBRE 2023


HAMBURGER
ingredients
Sesame Bun
Pickles
Tomato
Eggs
Green Pepper
Olives
Lettuce
Lettuce
Onion Rings
Olives
Yellow Pepper
Beef Patty
Cheese
Red Pepper

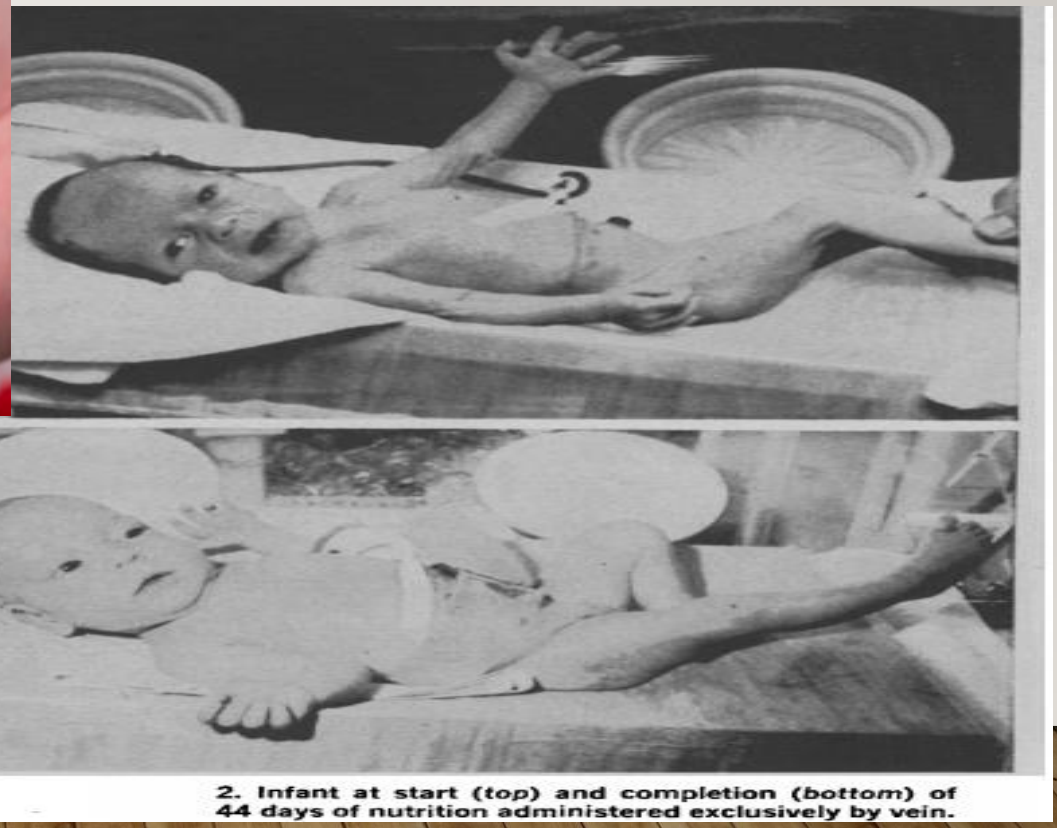
Table 10.1 Milestones in the development of Total Parenteral Nutrition. (Adapted from [1])

Year	Accomplishment	Investigators
1913	Intravenous infusion of hydrolyzed proteins in animals (dogs) with demonstration of use for nutrition	VanSlyke/Meyer
1915	Intravenous infusion of fat in animals with demonstration of use for nutrition	Murlin/Riche
1924	First continuous intravenous drip infusion of glucose in humans	Matas
1935	First intravenous infusion of cottonseed oil emulsions in humans	Holt
1938	Identification of the essential amino acids and their requirements in humans	Rose
1939	Demonstration of requirements of intravenous amino acids and protein hydrolysates in humans	Elman/Weiner
1940	Demonstration of utilization of crystalline amino acids infused intravenously in humans	Shohl/Blackfan/Dennis
1944	First complete intravenous feeding (water, saline, fat, carbohydrate, amino acids) for 5 days in a 5-month old infant with Hirschsprung's disease	Helfrick/Abelson
1945	Development of first polyethylene catheters for intravenous infusions in humans	Zimmermann
1949	Development of first continuous delivery technique for long-term intravenous infusion of nutrients in dogs	Rhoads/Parkins/Vars
1952	First description of percutaneous subclavian venipuncture to achieve rapid transfusion in severely injured war victims	Aubaniac
1956	Demonstration that intravenous infusion of plasma as the sole protein source in dogs fed a protein-free diet orally could support growth	Allen/Stemmer/Head
1961	Development of first, safe, standardized, and stable intravenous fat emulsion (soybean oil stabilized by egg phosphatides)	Schuberth/Wretlind
1966	Demonstration of long-term normal growth and development in Beagle puppies receiving total parenteral nutrition by central vein	Dudrick/Vars/Rhoads
1967	Infraclavicular, percutaneous subclavian catheterization for central venous pressure monitoring in humans	Mogil/DeLaurentis/Rosemond
1968	First documentation of normal growth and development in an infant nourished entirely by central venous total parenteral nutrition	Dudrick/Wilmore
1968	First comprehensive technique for long-term total parenteral nutrition in human adults and infants	Dudrick/Wilmore/Vars/Rhoads

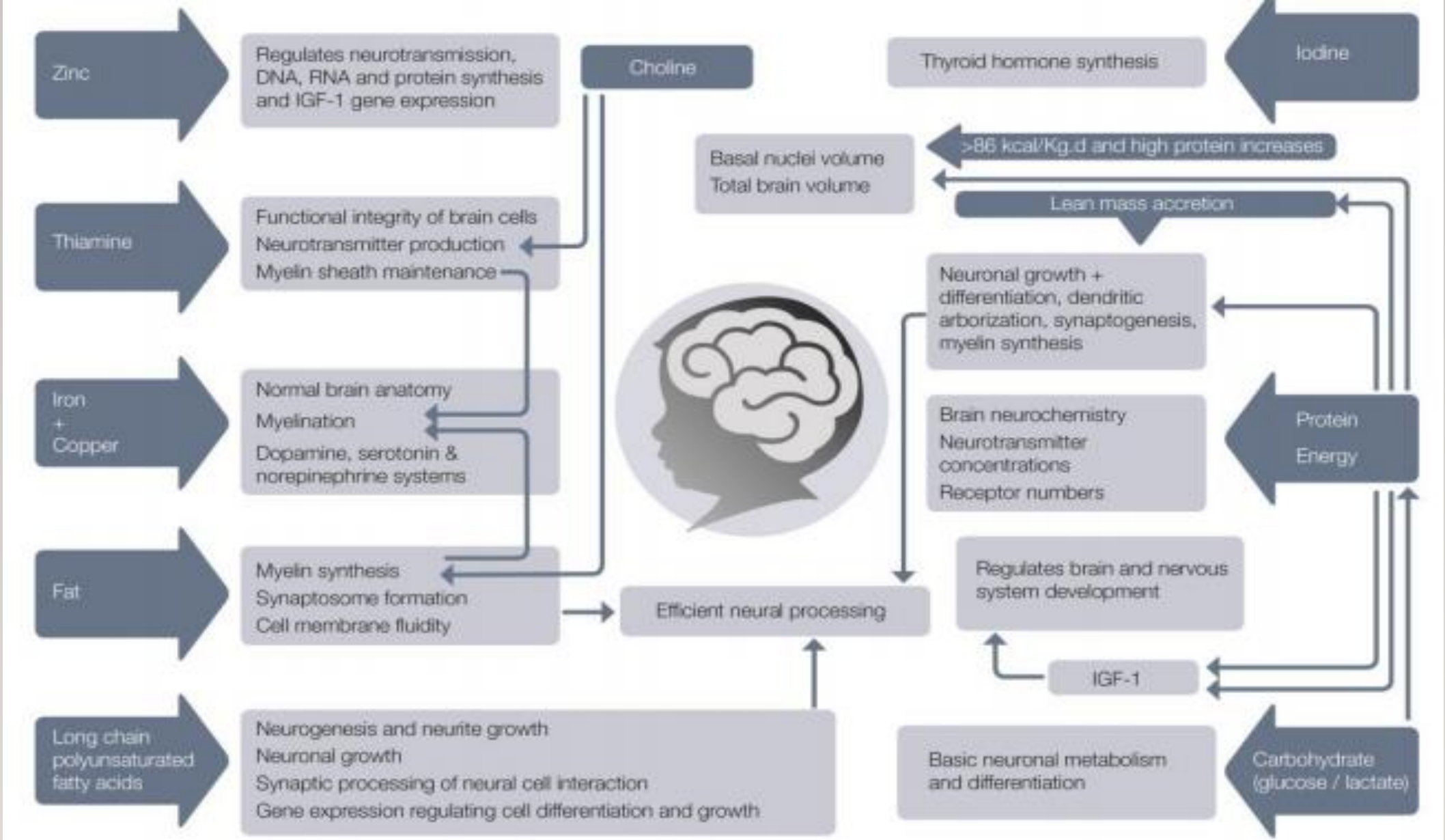
1913-1966

1967-1968

2. Infant at start (*top*) and completion (*bottom*) of 44 days of nutrition administered exclusively by vein.

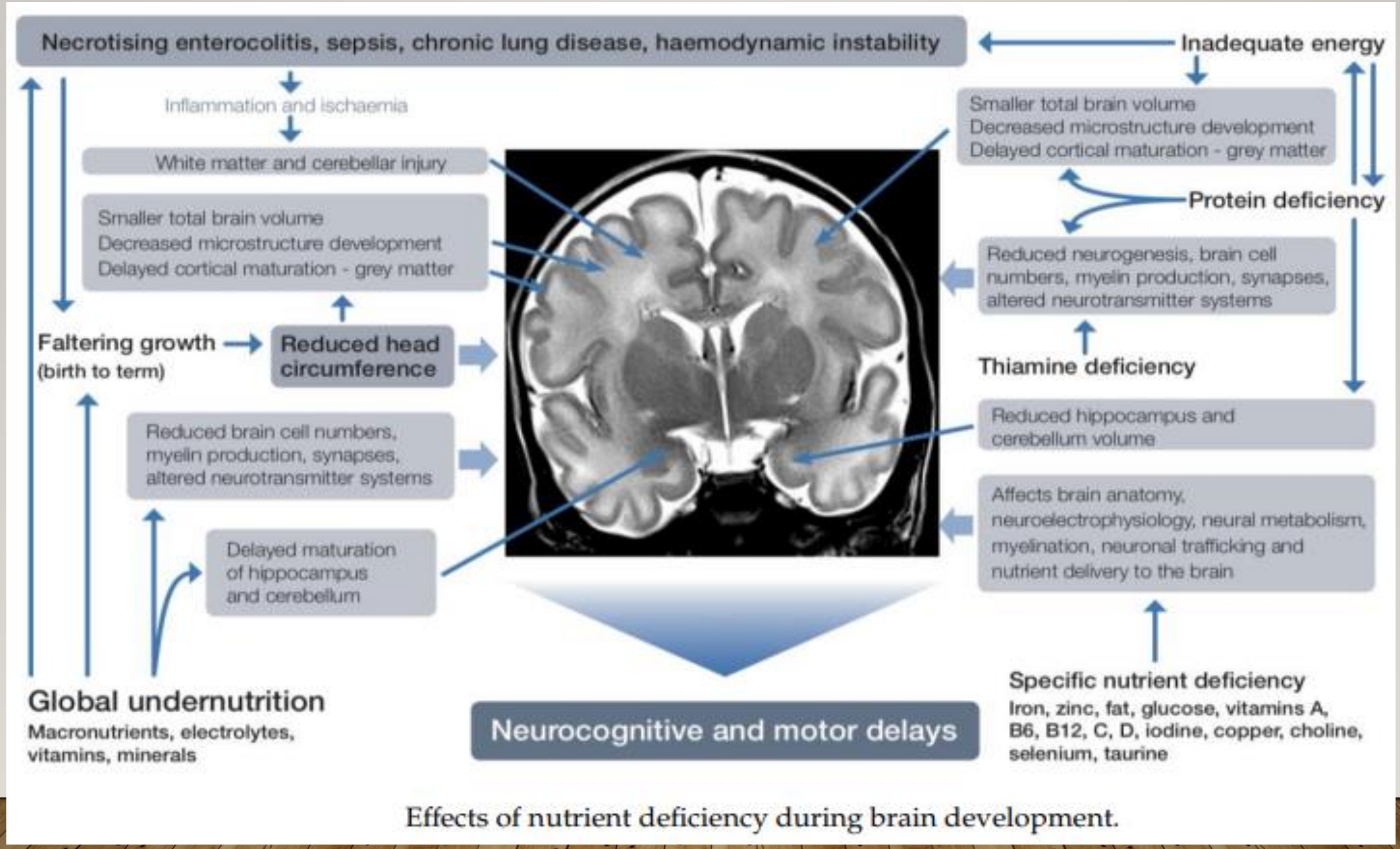


2. Infant at start (*top*) and completion (*bottom*) of 44 days of nutrition administered exclusively by vein.



Nutrients needed for normal brain development.

The Influence of Early Nutrition on Brain Growth and Neurodevelopment in Extremely Preterm Babies. Nutrients 2019, 11, 2029; doi:10.3390/nu11092029



Effects of nutrient deficiency during brain development.

Venous access

- Use a central venous catheter to give neonatal parenteral nutrition. Only consider using peripheral venous access to give neonatal parenteral nutrition if:
  - it would avoid a delay in starting parenteral nutrition
  - short-term use of peripheral venous access is anticipated, for example, less than 5 days
  - it would avoid interruptions in giving parenteral nutrition
  - central venous access is impractical.
- Only consider surgical insertion of a central venous catheter if:
  - non-surgical insertion is not possible
  - long-term parenteral nutrition is anticipated, for example, in short bowel syndrome.

ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Amino acids

EUROPEA 2018

Preterm infants

R 3.1	In preterm infants the amino acid supply should start on the first postnatal day with at least 1.5 g/kg/d to achieve an anabolic state. (LOE 1++, RG A, strong recommendation, strong consensus)
R 3.2	In preterm infants the parenteral amino acid intake from postnatal day 2 onwards should be between 2.5 g/kg/d to 3.5 g/kg/d and should be accompanied by non-protein intakes >65 kcal/kg/d and adequate micronutrient intakes. (LOE 1+, RG A, strong recommendation, strong consensus)
R 3.3	In preterm infants, parenteral amino acid intakes above 3.5 g/kg/d should only be administered as part of clinical trials (LOE 2+, RG 0, conditional recommendation, consensus)

Term infants

R 3.4	A minimum amino acid intake of 1.5 g/kg/d should be administered to stable term infants to avoid a negative nitrogen balance while the maximum amino acid intake should not exceed 3.0 g/kg/d (LOE 1+, RG B, strong recommendation, strong consensus)
R 3.5	Withholding parenteral nutrition, including amino acids, for 1 week in critically ill term infants while providing micronutrients can be considered (LOE 1+, RG B, conditional recommendation, consensus)

ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Energy

K. Joosten [a, *], N. Embleton [b], W. Yan [c], T. Senterre [d], the ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition[1]

[a] Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands
[b] Newcastle Neonatal Service, Newcastle Hospitals NHS Trust & Newcastle University, Newcastle upon Tyne NE1 4LP, UK
[c] Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China
[d] Service Universitaire de Néonatologie, Centre Hospitalier Régional (CHR) de la Citadelle, Centre Hospitalier Universitaire (CHU) de Liège, Université de Liège, Belgium

Table: Recommendations for energy in parenteral nutrition (PN)

R 2.1	For calculation of resting energy expenditure (REE) the use of Schofield's equation for weight can be recommended (LOE 2+, GPP, conditional recommendation)
R 2.2	Total parenteral energy requirements of stable patients can be calculated from resting energy requirements with adding constants for physical activity, (catch-up) growth and adjusted for disease states that increase or decrease REE (LOE 2+ RG 0, conditional recommendation)
R 2.3	In a subgroup of patients with suspected metabolic alterations or malnutrition, accurate measurement of energy expenditure using indirect calorimetry is desirable (LOE 3, GPP, conditional recommendation)
R 2.4	On the first day of life of premature neonates, at least 45–55 kcal/kg/day should be provided to meet minimal energy requirements (LOE 2+, RG 0, strong recommendation)
R 2.5	After the initial postnatal nadir of weight loss, aiming for a weight gain of 17–20 g/kg per day in very low birth weight infants is recommended to prevent dropping across weight centiles i.e. growth failure (LOE 2+, RG 0, strong recommendation)
R 2.6	In very low birth weight infants, to approximate intra-uterine lean body mass accretion and growth, energy intakes of 90–120 kcal/kg/day should be provided (LOE 2++, RG B, strong recommendation)
R 2.7	Reasonable parenteral energy requirements after the acute phase of critical illness can be estimated from REE (LOE 2–, RG 0, conditional recommendation)
R 2.8	In the stable phase of critical illness energy requirements can be increased by ~1.3 times REE to enable growth and catch-up growth and further increased in the recovery phase (LOE2–, RG 0, conditional recommendation)
R 2.9	Withholding PN for 1 week in critically ill children while giving micronutrients can be considered (LOE1+, RG B, conditional recommendation)

Energy requirements (kcal/kg/day) for parenteral nutrition in different phases of disease.

	2005	2016 Recovery phase	2016 Stable phase	2016 Acute phase
Preterm	110–120	90–120		45–55[a]
0–1	90–100	75–85	60–65	45–50
1–7	75–90	65–75	55–60	40–45
7–12	60–75	55–65	40–55	30–40
12–18	30–60	30–55	25–40	20–30

[a] Recommended energy intake during the first day of life.

ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Fluid and electrolytes

F. Jochum [a,*], S.J. Moltu [b], T. Senterre [c], A. Nomayo [a], O. Goulet [d], S. Iacobelli [e], the ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition[1]

Recommended parenteral fluid and electrolyte intake during the first days of life in neonates (Phase I of adaptation).[e]

	Days after birth				
	Day 1	Day 2	Day 3	Day 4	Day 5
Fluid intake[a] (ml/kg/d)					
Term neonate	40–60	50–70	60–80	60–100	100–140
Preterm neonate >1500 g	60–80	80–100	100–120	120–140	140–160
Preterm neonate 1000–1500 g	70–90	90–110	110–130	130–150	160–180
Preterm neonate <1000 g	80–100	100–120	120–140	140–160	160–180
Na[b,d] (mmol/kg/d)					
Term neonate	0–2	0–2	0–2	1–3	1–3
Preterm neonate >1500 g	0–2 (3)	0–2 (3)	0–3	2–5	2–5
Preterm neonate <1500 g	0–2 (3)	0–2 (3)	0–5 (7)	2–5 (7)	2–5 (7)
K[c,d] (mmol/kg/d)	0–3	0–3	0–3	2–3	2–3
Cl (mmol/kg/d)	0–3	0–3	0–3	2–5	2–5

[a] Postnatal fluid requirements are highly dependent on treatment conditions and environmental factors. Certain clinical conditions may afford modifications of daily fluid intakes, e.g. phototherapy (add volume ca. 10–20%), infants with asphyxia/respiratory distress syndrome/mechanical ventilation with humidified respiratory gases (reduce volume by ca. 10–20%).

[b] Careful adjustment of water and electrolyte administration is needed in ELBW infants at onset of diuresis and in polyuric patients. In cases of high urinary Na losses the need for Na supply may exceed 5 mmol/kg/d, especially in neonates <1500 g at the end of phase I.

[c] K administration should regard initial phase of oliguria and the risk of non-oliguric hyperkaliemia in VLBW infants. A deferment of parenteral K supply might be required to avoid hyperkaliemia.

[d] Parenteral Na and K supply should start latest before serum concentrations drop below recommended values.

[e] The recommendations of Table 1 are based on clinical experience, expert opinion, and extrapolated data from different studies in animals and humans.

Table 2

Recommended parenteral fluid and electrolyte intake for neonates during the intermediate phase (phase II) – prior to the establishment of stable growth.[a]

	Fluid (ml/kg/d)	Na (mmol/kg/d)	K (mmol/kg/d)	Cl (mmol/kg/d)
Term neonate	140–170	2–3	1–3	2–3
Preterm neonate >1500 g	140–160	2–5	1–3	2–5
Preterm neonate <1500 g	140–160	2–5 (7)	1–3	2–5

[a] The recommendations of Table 2 are based on clinical experience, expert opinions, and extrapolated data from different studies on animal and men.

Table 3

Recommended parenteral fluid and electrolytes intake for neonates during the first month of life with stable growth (phase III).[a]

	Fluid (ml/kg/d)	Na (mmol/kg/d)	K (mmol/kg/d)	Cl (mmol/kg/d)
Term neonate	140–160	2–3	1.5–3	2–3
Preterm neonate >1500 g	140–160	3–5	1–3	3–5
Preterm neonate <1500 g	140–160	3–5 (7)	2–5	3–5

[a] The recommendations of Table 3 are based on clinical experience, expert opinions, and extrapolated data from different studies on animal and men.

Review

Macronutrients and Micronutrients in Parenteral Nutrition for Preterm Newborns: A Narrative Review

Valentina Rizzo [1,2,*], Manuela Capozza [1], Raffaella Panza [1,2,*], Nicola Laforgia [3] and Maria Elisabetta Baldassarre [1]

Citation: Rizzo, V.; Capozza, M.; Panza, R.; Laforgia, N.; Baldassarre, M.E. Macronutrients and Micronutrients in Parenteral Nutrition for Preterm Newborns: A Narrative Review. *Nutrients* **2022**, *14*, 1530. https://doi.org/10.3390/nu14071530

- Restringir líquidos disminuye el riesgo de DAP, NEC
- Evitar la Deficiencia de Sodio puede llevar a mejorar la ganancia de peso
- La suplementación de potasio debería comenzar al lograr diuresis adecuada
- Pero … → aumenta el riesgo de Deshidratación, Malnutrición, Hipotensión, Hipoperfusión, Daño Renal, Hipoglicemia, Hiperosmolaridad e Hiperbilirrubinemia

ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Carbohydrates

Table: Recommendations for carbohydrates

R 5.1	The amount of glucose to be provided by PN should be guided by [1] the balance between meeting energy needs and the risks of overfeeding/excess glucose load [2], phase of illness (acute, stable, recovery/growing) [3], macronutrient supply by enteral and parenteral nutrition, and [4] glucose administered outside enteral and parenteral nutrition, e.g. with medication (GPP, conditional recommendation)
R 5.2	Excessive glucose intake should be avoided because it may be responsible for hyperglycemia (LoE 1−, RG A, strong recommendation), causes increased lipogenesis and fat tissue deposition together with subsequent liver steatosis and enhanced production of VLDL triglycerides by the liver (LOE 2+, RG B, strong recommendation), and may cause increased CO_2 production and minute ventilation (LoE 2+, RG B, strong recommendation)
R 5.3	Glucose intake does not lower protein catabolism in the acute phase of critical illness (LoE 1−, RG A, strong recommendation)
R 5.4	Recommended parenteral glucose supply in (pre)term newborns in mg/kg per min (g/kg per day) (LoE 2+, RG B, conditional

	Day 1	Day 2 onwards
	Start with	Increase gradually over 2–3 days to
Preterm newborn	4–8 (5.8–11.5)	Target 8–10 (11.5–14.4) Min 4 (5.8); max 12 (17.3)
Term newborn	2.5–5 (3.6–7.2)	Target 5–10 (7.2–14.4) Min 2.5 (3.6); max 12 (17.3)

R 5.5	Newborns < 28 days of age, who have an episode of acute illness such as infection or sepsis, should temporarily receive the carbohydrate supply of day 1 (R5.4), guided by the blood glucose levels (GPP, conditional recommendation)
R 5.6	Recommended parenteral glucose supply in infants and children according to body weight and phase of illness. The units are mg/kg/min (g/kg per day) (LoE 1+, RG A, strong recommendation)

	Acute phase	Stable phase	Recovery phase
28 d–10 kg	2–4 (2.9–5.8)	4–6 (5.8–8.6)	6–10 (8.6–14)
11–30 kg	1.5–2.5 (2.2–3.6)	2–4 (2.8–5.8)	3–6 (4.3–8.6)
31–45 kg	1–1.5 (1.4–2.2)	1.5–3 (2.2–4.3)	3–4 (4.3–5.8)
>45 kg	0.5–1 (0.7–1.4)	1–2(1.4–2.9)	2–3 (2.9–4.3)

Acute phase = resuscitation phase when the patient requires vital organ support (sedation, mechanical ventilation, vasopressors, fluid resuscitation).
Stable phase = patient is stable on, or can be weaned, from this vital support.
Recovery phase = patient who is mobilizing.

R 5.7	Blood glucose measurements should preferably be performed on equipment validated for use such as blood gas analysers (LoE 2+, RG B, strong recommendation)
R 5.8	Hyperglycaemia >8 mmol/L (145 mg/dL) should be avoided in paediatric ICU patients because of increased morbidity and mortality (LoE 1+, RG A, strong recommendation)
R 5.9	In children in the PICU, repetitive blood glucose levels >10 mmol/L (180 mg/dL) should be treated with continuous insulin infusion (LoE 1+, RG A, strong recommendation)
R 5.10	Hyperglycaemia >8 mmol/L (145 mg/dL) should be avoided in neonatal ICU patients because it is associated with increased morbidity and mortality (LoE 2−, RG B, strong recommendation)
R 5.11	In neonates in the NICU, repetitive blood glucose levels >10 mmol/L (180 mg/dL) should be treated with insulin therapy, when reasonable adaptation of glucose infusion rate has been insufficient (LoE 2++, RG 0, conditional recommendation)
R 5.12	Repetitive and/or prolonged hypoglycaemia ≤2.5 mmol/L (45 mg/dL) should be avoided in all ICU patients (extrapolated LoE 2+, RG 0, strong recommendation)

	Day 1	Day 2 onwards
	Start with	Increase gradually over 2–3 days to
Preterm newborn	4–8 (5.8–11.5)	Target 8–10 (11.5–14.4) Min 4 (5.8); max 12 (17.3)
Term newborn	2.5–5 (3.6–7.2)	Target 5–10 (7.2–14.4) Min 2.5 (3.6); max 12 (17.3)

Newborns < 28 days of age, who have an episode of acute illness such as infection or sepsis, should temporarily receive the carbohydrate supply of day 1 (R5.4), guided by the blood glucose levels (GPP, conditional recommendation)

Recommended parenteral glucose supply in infants and children according to body weight and phase of illness. The units are mg/kg/min (g/kg per day) (LoE 1+, RG A, strong recommendation)

	Acute phase	Stable phase	Recovery phase
28 d–10 kg	2–4 (2.9–5.8)	4–6 (5.8–8.6)	6–10 (8.6–14)
11–30 kg	1.5–2.5 (2.2–3.6)	2–4 (2.8–5.8)	3–6 (4.3–8.6)
31–45 kg	1–1.5 (1.4–2.2)	1.5–3 (2.2–4.3)	3–4 (4.3–5.8)
>45 kg	0.5–1 (0.7–1.4)	1–2(1.4–2.9)	2–3 (2.9–4.3)

Acute phase = resuscitation phase when the patient requires vital organ support (sedation, mechanical ventilation, vasopressors, fluid resuscitation).
Stable phase = patient is stable on, or can be weaned, from this vital support.

Recommended parenteral glucose supply in (pre)term newborns in mg/kg per min (g/kg per day) (LoE 2+, RG B, conditional

	Day 1	Day 2 onwards
	Start with	Increase gradually over 2–3 days to
Preterm newborn	4–8 (5.8–11.5)	Target 8–10 (11.5–14.4) Min 4 (5.8); max 12 (17.3)
Term newborn	2.5–5 (3.6–7.2)	Target 5–10 (7.2–14.4) Min 2.5 (3.6); max 12 (17.3)

Newborns < 28 days of age, who have an episode of acute illness such as infection or sepsis, should temporarily receive the carbohydrate supply of day 1 (R5.4), guided by the blood glucose levels (GPP, conditional recommendation)

ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids

Alexandre Lapillonne [a, b, *], Nataša Fidler Mis [c], Olivier Goulet [d], Chris H.P. van den Akker [e], Jennifer Wu [f], Berthold Koletzko [g], the ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition[1]

[a] Department of Neonatology, APHP Necker-Enfants Malades Hospital, Paris-Descartes University, Paris, France
[b] Department of Pediatrics, Children's Nutrition Research Center, Baylor College of Medicine, Houston, TX, USA
[c] Department of Gastroenterology, Hepatology and Nutrition, Division of Paediatrics, University Medical Centre Ljubljana, Ljubljana, Slovenia
[d] Department of Pediatric Gastroenterology, Hepatology and Nutrition, Intestinal Failure Rehabilitation Center, National Reference Centre for Rare Digestive Diseases, APHP Necker-Enfants Malades Hospital, Paris-Descartes University, Paris, France
[e] Department of Pediatrics — Neonatology, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands
[f] Department of Clinical Nutrition, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China
[g] Dr von Haunersches Kinderspital, Div. Metabolic and Nutritional Medicine, Ludwig Maximilian Universität, University of Munich Medical Center, Munich, Germany

R 4.1	**In paediatric patients, intravenous lipid emulsions (ILE) should be an integral part of parenteral nutrition (PN) either exclusive or complementary to enteral feeding. (LoE 1−, RG A, strong recommendation for, strong consensus)**
R 4.2	**In preterm infants, lipid emulsions can be started immediately after birth and no later than on day two of life and for those in whom enteral feeding has been withdrawn, they can be started at time of PN initiation. (LoE 1−, RG A, strong recommendation for, strong consensus)**
R 4.3	**In preterm and term infants, parenteral lipid intake should not exceed 4 g/kg/day. (LoE 4, GPP, conditional recommendation for, strong consensus)**
R 4.4	**In children, parenteral lipid intake should be limited to a maximum of 3 g/kg/day. (LoE 3–4, RG 0, conditional recommendation for, strong consensus)**

First Author	Type of Study	Sample Size (*n*)	Intervention	Outcomes
Calkins KL [39] 2017	RCT	41	high (3–3.5 g/kg/day) versus low (1 g/kg/day) target dose of lipids	no significant differences in terms of sepsis, cholestasis, mortality. Increased mean weight gain in the first 28 days
Levit OL [40] 2016	RCT	127	high (3–3.5 g/kg/day) versus low (1 g/kg/day) target dose of lipids	no significant differences were found in terms of sepsis, cholestasis, mortality and length of stay. Decreased rates of necrotizing enterocolitis and retinopathy or prematurity
Lapillonne A [43] 2018	LG ESPGHAN		target dosage of lipids of 3–4 g/kg/day at maximum	Safe and effective
NICE Guideline [42] 2020			target dosage of lipids of 3–4 g/kg/day at maximum	Safe and effective
Vlaardingerbroek [44] 2013	RCT	144	comparing preterm babies started early (i.e., soon after birth) versus late (i.e., on day 2 of life) on lipid emulsions	no significant differences in anthropometric measures at discharge, late onset sepsis, necrotizing enterocolitis, retinopathy of prematurity and mortality rates

ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Calcium, phosphorus and magnesium

Table: Recommendations for calcium, phosphorus and magnesium in PN

R 8.1	In infants, children and adolescents on PN appropriate amounts of Ca, P and Mg should be provided to ensure optimal growth and bone mineralization (GPP, strong recommendation)
R 8.2	The mineral accretion of the fetus, healthy infant, child, and adolescent may be used as a reference for Ca, P and Mg provision (GPP, conditional recommendation)
R 8.3	In the individual infant appropriate PN should provide a simultaneous slight surplus of Ca, P, and Mg to ensure optimal tissue and bone mineral accretion (GPP, conditional recommendation)
R 8.4	Ca infusion may be used for prevention and treatment of early neonatal hypocalcaemia that is common and generally not associated with obvious clinical problems such as tetany (GPP, conditional recommendation)
R 8.5	In preterm infants on PN who were exposed to maternal Mg therapy, Mg intakes need to be adapted to postnatal blood concentrations (LoE 2, RG B, conditional recommendation)
R 8.6	Acidic solutions packaged in glass vials, such as calcium gluconate, are contaminated with aluminum and should not be used in PN (LoE 3, RG 0, strong recommendation)
R 8.7	It is recommended to use organic Ca and P salts for compounding of PN solutions to prevent precipitation (GPP, strong recommendation)
R 8.8	The adequacy of Ca and P intakes in preterm infants can be adjusted until both start being excreted simultaneously with low urine concentrations (>1 mmol/L) indicative of a slight surplus (extrapolated evidence derived from enteral nutrition LoE 2+ studies, RG B, conditional recommendation)
R 8.9	The recommended parenteral intake for calcium, phosphorus, and magnesium intake in newborns and children on parenteral nutrition in mmol (mg)/kg/d is as follows (LoE 2, 3 and 4, RG 0, conditional recommendation)

Age	Ca mmol (mg)/kg/d	P mmol (mg)/kg/d	Mg mmol (mg)/kg/d
Preterm infants during the first days of life	0.8–2.0 (32–80)	1.0–2.0 (31–62)	0.1–0.2 (2.5–5.0)
Growing Premature	1.6–3.5 (64–140)	1.6–3.5 (50–108)	0.2–0.3 (5.0–7.5) infants
0–6 m*	0.8–1.5 (30–60)	0.7–1.3 (20–40)	0.1–0.2 (2.4–5)
7–12 m	0.5 (20)	0.5 (15)	0.15 (4)
1–18 y	0.25–0.4 (10–16)	0.2–0.7 (6–22)	0.1 (2.4)

*Includes term newborns.

R 8.10	In preterm infants with intrauterine growth restriction on PN careful monitoring of the plasma phosphate concentration within the first days of life is required to prevent severe hypophosphataemia that can result in muscle weakness, respiratory failure, cardiac dysfunction, and death (LoE 3, RG 0, strong recommendation)
R 8.11	In preterm infants on early PN during the first days of life lower Ca, P and Mg intakes are recommended than in growing stable preterm infants (Table 1) (LoE 2, RG B, conditional recommendation)
R 8.12	In early PN when calcium and phosphorus intakes are low (Table 1) and protein and energy are optimized it is recommended to use a molar Ca:P ratio below 1 (0.8–1.0) to reduce the incidence of early postnatal hypercalcaemia and hypophosphataemia (LoE 2, RG B, strong recommendation)
R 8.13	In infants and children on PN regular monitoring of the individual alkaline phosphatase, Ca, P and Mg serum concentrations and Ca and P urine concentrations is required (Extrapolated evidence from LoE 2 and 3 studies, RG 0, strong recommendation)
R 8.14	In infants and children on long term PN the risk of metabolic bone disease requires periodic monitoring of Ca, P, vitamin D and bone mineral status (LoE 2 + and 3, RG 0, strong recommendation)

TENER PRESENTE QUE 1 MMOL DE CALCIO CORRESPONDE A 40 MG Y 1 MMOL DE FÓSFORO CORRESPONDE A 31 MG
(OJO QUE LA RELACIÓN CA-P EN EL PROGRAMA PARENTERAL ES EN MMOL Y NO EN MILIGRAMOS)

The recommended parenteral intake for calcium, phosphorus, and magnesium intake in newborns and children on parenteral nutrition in mmol (mg)/kg/d is as follows (LoE 2, 3 and 4, RG 0, conditional recommendation)

Age	Ca mmol (mg)/kg/d	P mmol (mg)/kg/d	Mg mmol (mg)/kg/d
Preterm infants during the first days of life	0.8–2.0 (32–80)	1.0–2.0 (31–62)	0.1–0.2 (2.5–5.0)
Growing Premature	1.6–3.5 (64–140)	1.6–3.5 (50–108)	0.2–0.3 (5.0–7.5) infants
0–6 m*	0.8–1.5 (30–60)	0.7–1.3 (20–40)	0.1–0.2 (2.4–5)
7–12 m	0.5 (20)	0.5 (15)	0.15 (4)
1–18 y	0.25–0.4 (10–16)	0.2–0.7 (6–22)	0.1 (2.4)

*Includes term newborns.

In preterm infants with intrauterine growth restriction on PN careful monitoring of the plasma phosphate concentration within the first days of life is required to prevent severe hypophosphataemia that can result in muscle weakness, respiratory failure, cardiac dysfunction, and death (LoE 3, RG 0, strong recommendation)

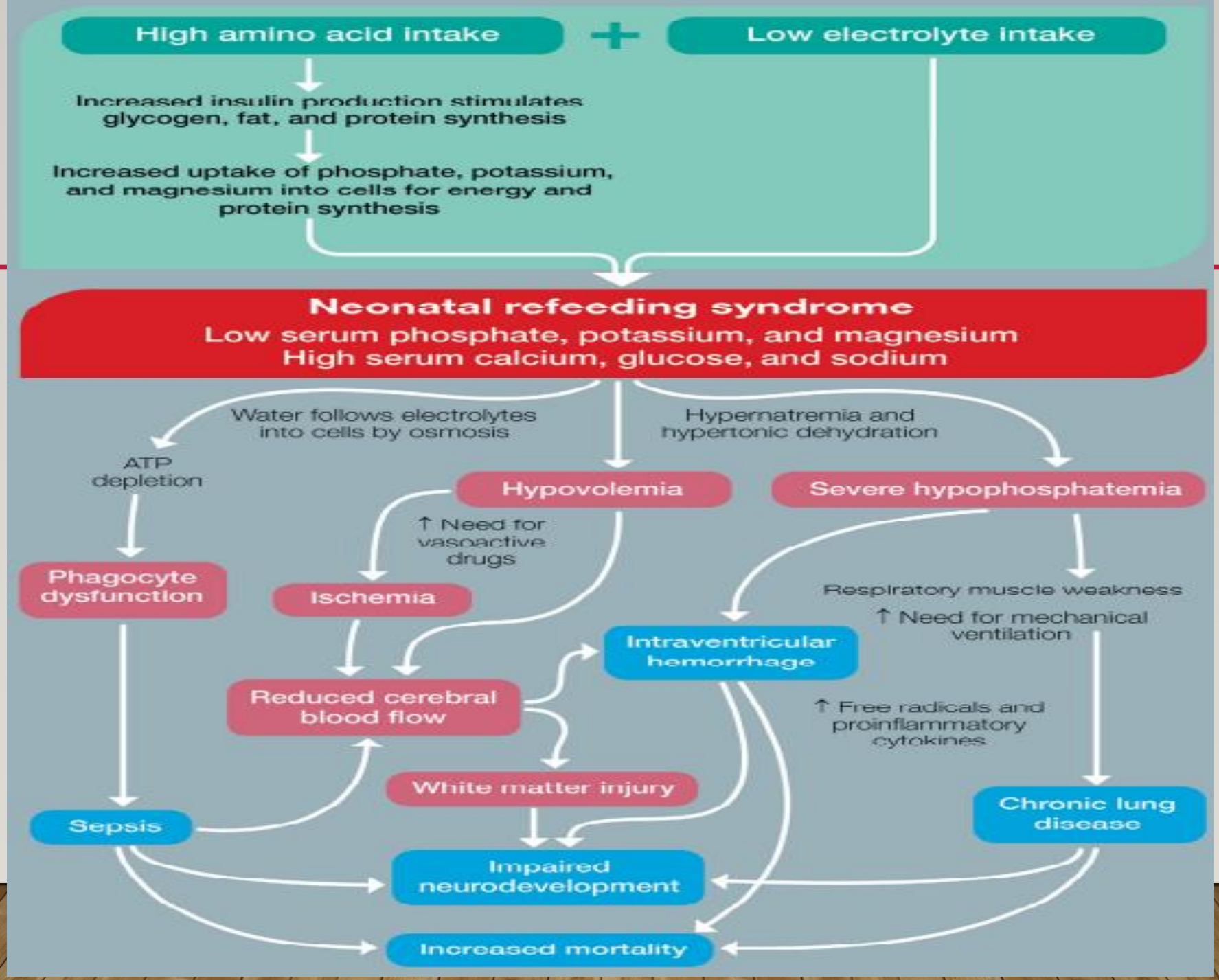
In preterm infants on early PN during the first days of life lower Ca, P and Mg intakes are recommended than in growing stable preterm infants (Table 1) (LoE 2, RG B, conditional recommendation)

In early PN when calcium and phosphorus intakes are low (Table 1) and protein and energy are optimized it is recommended to use a molar Ca:P ratio below 1 (0.8–1.0) to reduce the incidence of early postnatal hypercalcaemia and hypophosphataemia (LoE 2, RG B, strong recommendation)

ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Iron and trace minerals

Estimated parenteral requirements of iron and trace minerals (μg/kg/d).

Mineral	Preterm	0–3 mo	3–12 mo	1–18 y	Max dose
Iron	200–250	50–100	50–100	50–100	5 mg/d
Zinc	400–500	250	100	50	5 mg/d
Copper	40	20	20	20	0,5 mg/d
Iodine	1–10	1	1	1	
Selenium	7	2–3	2–3	2–3	100 μg/d
Manganese	≤1	≤1	≤1	≤1	50 μg/d
Molybdenum	1	0.25	0.25	0.25	5 μg/d
Chromium	–	–	–	–	5 μg/d


High amino acid intake
+
Low electrolyte intake
Increased insulin production stimulates glycogen, fat, and protein synthesis
Increased uptake of phosphate, potassium, and magnesium into cells for energy and protein synthesis
Neonatal refeeding syndrome
Low serum phosphate, potassium, and magnesium
High serum calcium, glucose, and sodium
Water follows electrolytes into cells by osmosis
Hypernatremia and hypertonic dehydration
ATP depletion
Hypovolemia
Severe hypophosphatemia
↑ Need for vasoactive drugs
Phagocyte dysfunction
Ischemia
Respiratory muscle weakness
↑ Need for mechanical ventilation
Intraventricular hemorrhage
Reduced cerebral blood flow
↑ Free radicals and proinflammatory cytokines
White matter injury
Sepsis
Chronic lung disease
Impaired neurodevelopment
Increased mortality

Citation: Guiducci, S.; Duci, M.; Moschino, L.; Meneghelli, M.; Fascetti Leon, F.; Bonadies, L.; Cavicchiolo, M.E.; Verlato, G. Providing the Best Parenteral Nutrition before and after Surgery for NEC: Macro and Micronutrients Intakes. *Nutrients* **2022**, *14*, 919. https://doi.org/10.3390/nu14050919

Review

Providing the Best Parenteral Nutrition before and after Surgery for NEC: Macro and Micronutrients Intakes

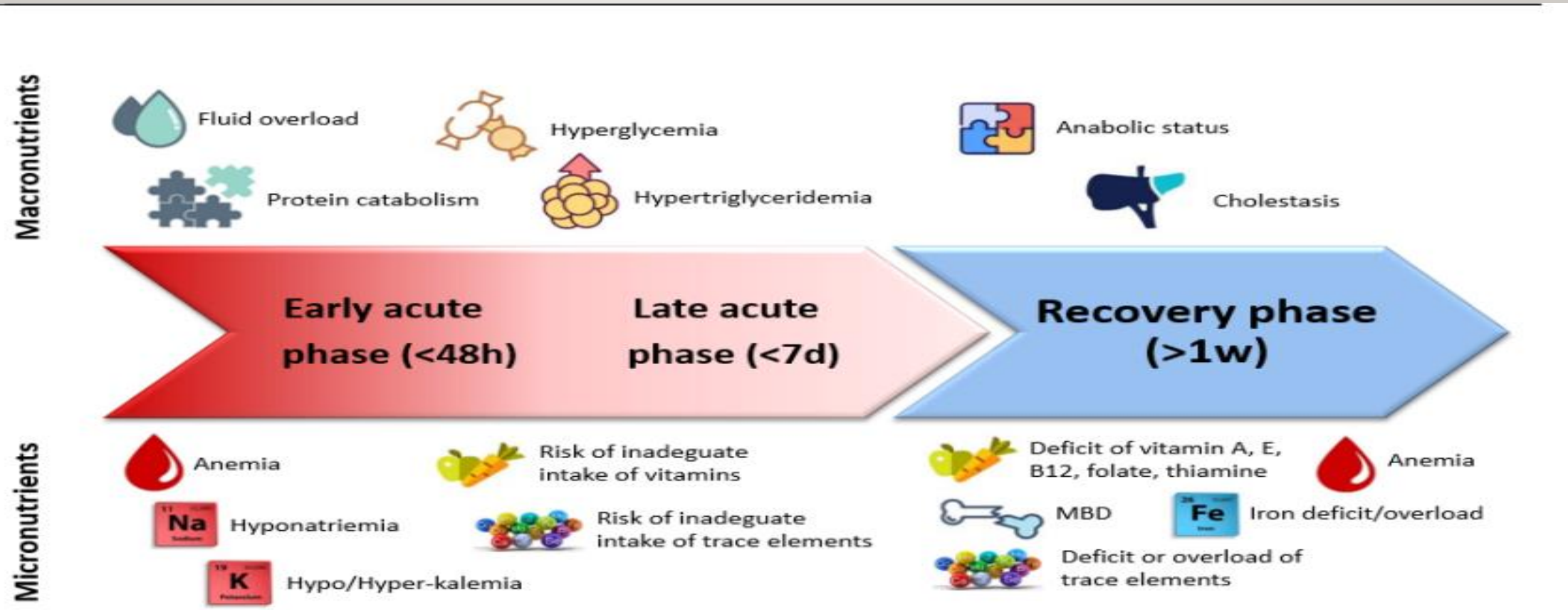


Figure 1. Timeline of metabolic response and main macro and micronutrient-related alterations in different phases of the disease (early acute, late acute, and recovery phase) [12–23].

Table 1. Energy requirements in parenteral nutrition (kcal/kg/day) during the different phases of disease in newborns, according to different authors.

Studies	Early Acute	Late Acute	Recovery
Moltu et al., 2021 [12]	40–55	60–80	90–120
Joosten et al., 2018 [16]	45–55	60–65	90–120
Feferbaum et al., 2010 [33]	49.4 +/− 13.1	/	68.3 +/− 10.9
Bauer et al., 2002 [34]	58 +/− 3	55 +/− 2	50 +/− 2
Jones et al., 1993 [35]	40.1–60.5 for 4–7 days post-surgery		

	What happens	What to do
	Fluid overload	Strict fluid monitoring (not exceed 160–170 ml/kg/day)
	Hyponatriemia, Hypo-Hyperkalemia	Adequate parenteral supplementation
	Hyperglycemia (>10mmol/L)	Adjust glucose infusion (6–4 g/kg/day in preterm-term respectively) and if necessary start insulin
	Early catabolism and late anabolism	Start protein intake with 1–2 g/kg/day and quikly reach 3.5 g/kg/day with adequate essential/conditionally essential (cysteine, taurine) amino acid integration
	Hypertriglyceridemia	Tailored intakes of lipids, starting with 1–2 g/kg/day and advancing to 3–4 g/kg/day monitoring triglycerides levels (keep < 3 mmol/L)
	Cholestasis	Use composite lipid emulsion Provide early enteral nutrition Avoid excessive caloric intakes Avoid sepsis Cycling parenteral nutrition when possible Monitor plasma copper and caeruloplasmin (risk overload) Monitor whole blood manganese (if > 220 nmol/l interrupt PN supplementation)

JPGN • Volume 73, Number 2, August 2021

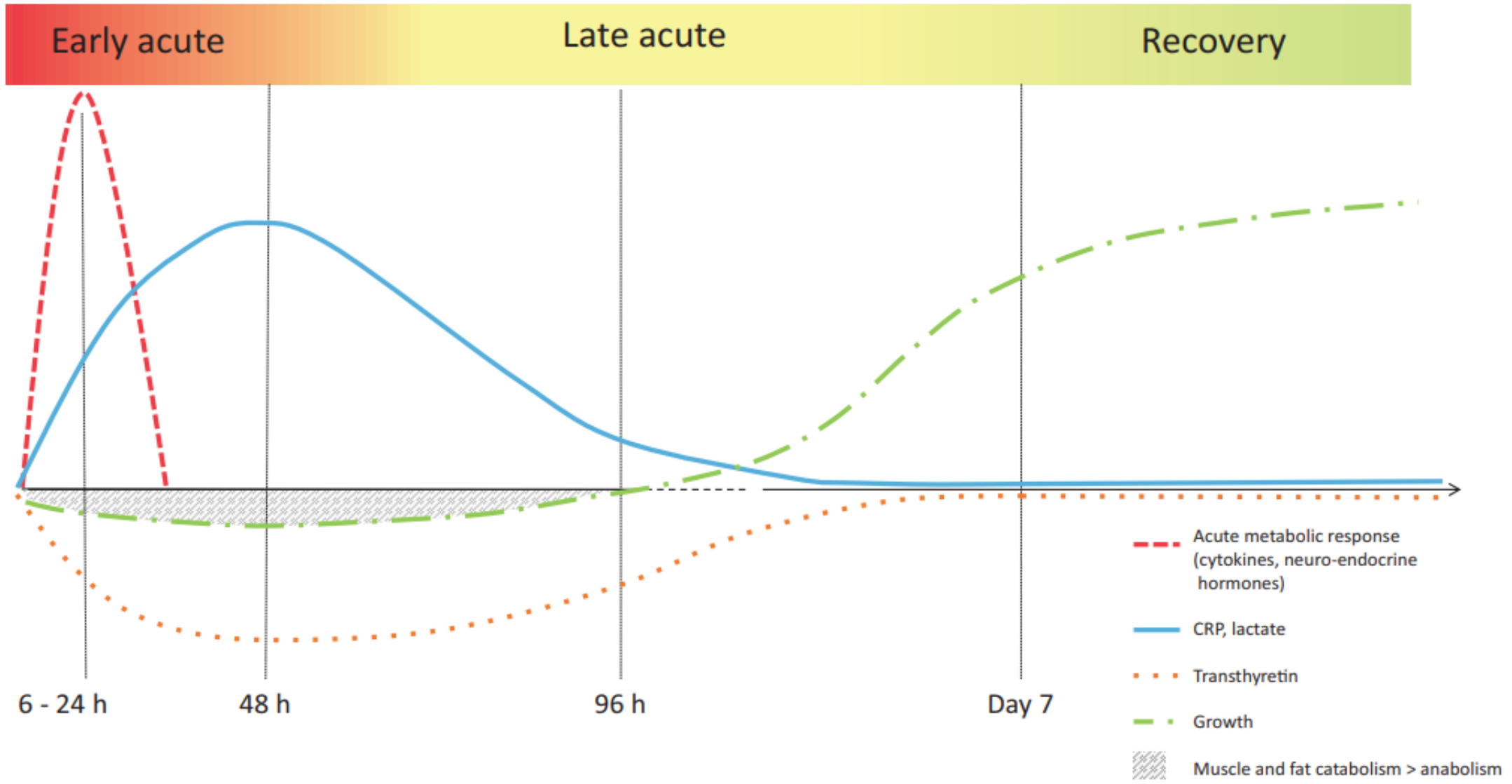


FIGURE 1. Simplified overview of different phases of critical illness. Note that the timing durations may be extremely variable.

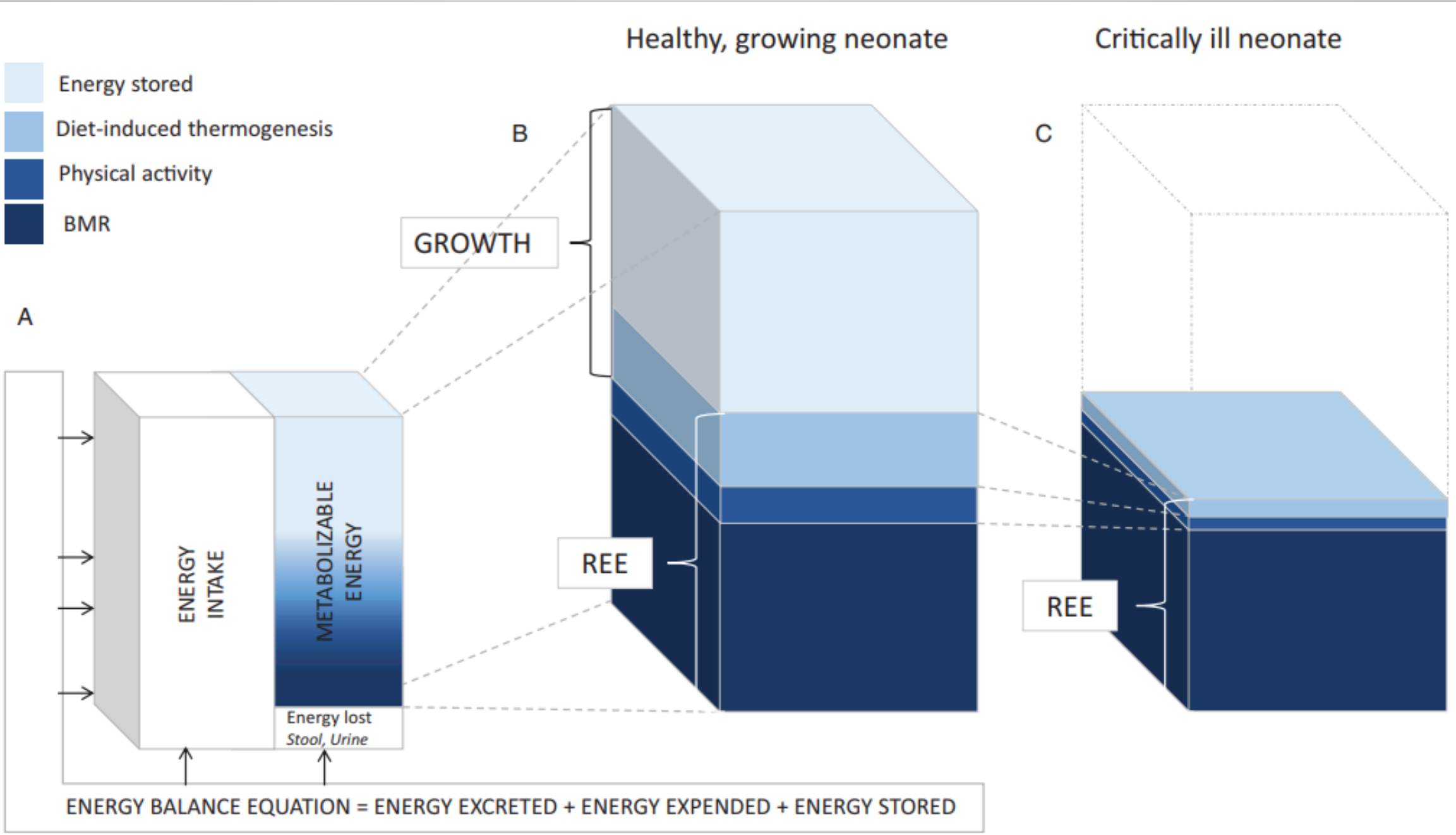


FIGURE 2. Energy balance in healthy and critically ill neonates. BMR = basal metabolic rate; REE = resting energy expenditure.

Hyperglycemia and prematurity: a narrative review

Pediatric Research (2023) 94:892–903

Table 1. Mechanisms that contribute to hyperglycemia in preterm newborns.

Factor	Decreased insulin	Effect (from general lack of insulin)
(a) Decreased production of insulin in preterm infants (e.g., defective processing of insulin in pancreatic β cells)	Yes	• Insulin levels increase with increasing GA • Reduced insulin-like growth factor-1 (IGF-I) • Preterm infants (especially those that are growth restricted) have low β cell mass
(b) High proinsulin/insulin ratio	Yes	• Processing of proinsulin in β-cells is partially defective • Proinsulin has insulin-like actions, but is 10 times less potent
(c) Paradoxical response to increasing glucose levels or increasing GIR	No	• Increase in GIRs may not result in decreased glucose production rate (do not result in anticipated decreased gluconeogenesis and vice versa)
(d) immaturity of GLUT receptors and associated poor sensitivity of peripheral tissues to insulin	No	• Decreased GLUT2 (pancreatic): decreased glucose-stimulated insulin secretion • Decreased GLUT2 (hepatic): low glucose sensitivity resulting in continued hepatic glucose production • Decreased GLUT4 (adipose, muscle): low glucose uptake
(e) Blunted hepatic insulin signaling	No	• Lack or decreased insulin effect specific to the liver (e.g., increased glycogenolysis and gluconeogenesis)

(f) Insulin resistance (e.g., counter-hormone production, glucagon, glucagon-like peptide 1, epinephrine, etc.)	No	• Common in septicemia, and with use of inotropes, steroids, etc. • Associated pro-inflammatory substances (IL1, 6 and TNFα), cause insulin resistance directly	36
(g) Zinc deficiency	Yes/no	• Zinc increases insulin secretion, posttranslational maturation (formation of the mature hexamers) and crystallization (storage in insulin granules) • Zinc increases intracellular signaling (PI3K and Akt) and by this action, decreased translocation of GLUT4 to the plasma membrane and hence decreased uptake of glucose • Zinc exhibits "insulin-like effect" by inhibiting the GSK-3β and increases glycogen synthesis. Zinc deficiency could result in decreased glycogen synthesis • Zinc inhibits the activity of FoxO1 which regulates gluconeogenesis and by this action zinc inhibits gluconeogenesis. Deficiency of zinc could result in increased gluconeogenesis	37–39

Akt protein Kinase B, *FoxO1* Forkhead box protein O1, *GA* gestational age, *GIR* glucose infusion rate, *GLUT* glucose transporter, *GSK-3β* glycogen synthase kinase-3 beta, *IGF-I* insulin-like growth factor-1, *IL* interleukin, *PI3K* phosphatidylinositol 3-kinase, *TNF* tumor necrosis factor.

TABLE 2. Theoretical energy and macronutrient needs during different phases of critical illness in the neonate

	Preterm infants			Term neonates <28 days		
	Early acute	Late acute	Recovery	Early acute	Late acute	Recovery
Energy ($kcal \cdot kg^{-1} \cdot day^{-1}$)						
Enteral	40–55	70–95	110–160	35–50	55–80	90–120
Parenteral*	40–55	60–80	90–120	15–40	45–70	75–85
Glucose ($g \cdot kg^{-1} \cdot day^{-1}$)†						
Enteral	5–8	7–11	11–15 (18)	4–6	6–10	9–15
Parenteral*	5–8 (10)	7–10 (12)	11–14 (17)	4–7 (10)	6–10	8–14
Glucose ($\sim mg \cdot kg^{-1} \cdot min^{-1}$)						
Enteral	3.5–5.5	5–7.5	7.5–10.5 (12.5)	3–5	4–7	6–10.5
Parenteral*	3.5–5.5 (7.0)	5–7 (8.5)	7.5–10 (12)	3–5 (10)	4–7	5.5–10
Protein ($g \cdot kg^{-1} \cdot day^{-1}$)						
Enteral	1.0–2.0	2.0–3.0	3.5–4.5	<1.5	1.5–2.5	2.0–3.5
Parenteral*	1.0–2.0	2.0–3.0	2.5–3.5	0 (−1.0)	1.5–2.5	2.0–3.0
Lipids ($g \cdot kg^{-1} \cdot day^{-1}$)						
Enteral	2.0–3.0	3.0–6.0	5.0–8.0	< 3.0	3.0–4.5	4.0–6.0
Parenteral*,‡	1.0–2.0	2.0–3.0	3.0–4.0	0 (−1.5)	1.5–2.5	3.0–4.0

*When supplementing parenteral nutrition, enteral intakes need to be considered (subtracted from estimated total needs) to optimize nutrient supply and reduce the risk of overfeeding. Note that parenteral energy needs are lower than enteral requirements, and that the maximum ranges of protein (amino acids) and lipids are lower than when given enterally.

†The glucose supply should be guided by plasma glucose measurements to avoid hypo- and hyperglycemia.

‡Lipids should be an integral part of PN (30–50% of nonprotein calories) and the nonprotein energy to protein ratio >25 kcal/g protein to facilitate protein utilization.

Complications Associated with Parenteral Nutrition in the Neonate

Complications of PN
• Metabolic disturbances
• Mechanical issues with the line
• Phlebitis and cellulitis
• Thrombosis
• IFALD
• CLASBIs
• Kidney stones and gallstones
• Metabolic bone disease

Benefits of PN
• Improved nutrition and growth
• Improved neurodevelopment
• LIFE-SAVING

Figure 1.
Common complications and benefits associated with parenteral nutrition (PN). PNALD, parenteral nutrition-associated liver disease (PNALD). CLASBIs, central line-associated bloodstream infections.