

ESPGHAN/ESPEN/ESPR guidelines on paediatric parenteral nutrition



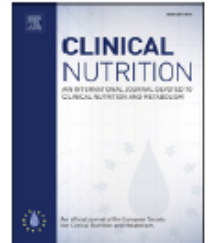
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ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Guideline development process for the updated guidelines

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Outline

- Evidence grading
- Energy
- Amino Acids
- Carbohydrates
- Lipids
- Vitamins and minerals
- Electrolytes and fluids

Guideline development

- The GRADE approach was used to assess the quality of evidence and to interpret findings
- Level of evidence (LOE)
- Grade of recommendation (GOR).
- The SIGN classification was used to assign both the evidence level and the recommendation grade.

General

- Preterm infant to 17 years
- Developed countries
- Indications
- Standard vs individualized



Energy requirements

Energy

Excess



Hyperglycaemia



Increase risk of infection, impaired liver functions (steatosis), abnormal metabolic programming

Inadequate



Impaired growth



Sub-optimal neurodevelopment



Increase risk of serious morbidity and mortality

Energy

- Presented as **total** energy (TE)
- **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.

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

	2005	2018	2018	2018
		Recovery Phase	Stable Phase	Acute Phase
Preterm	110-120	90-120		45-55
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

Preterm infants

- 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)
- 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)

Preterm infants

- 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 (LOE2++,RG B, strong recommendation)

Preterm infants

- Most clinicians aim for **120kcal/kg** (likelihood of nutritional deficits and need for catch-up)
- **30kcal/kg/day** lost when using enteral vs parenteral route
- Contribution of trophic feeds negligible

Practical application

Neonatal PN bags	10% (102/102/104)	6% (105)
75ml/kg	53kcal/kg	40kcal/kg
150ml/kg	106kcal/kg	81kcal/kg

Building feeds

	D1	D2	D3	D4
10% bag	50kcal/kg	75kcal/kg	101kcal/kg	106kcal/kg
6% bag	38kcal/kg	57kcal/kg	77kcal/kg	81kcal/kg

Amino Acids (AA)

Preterm Infants

In preterm infants the amino acid supply should start on the **first postnatal day with at least 1.5g/kg/d** to achieve an anabolic state. (LOE1++, RG A, strong recommendation)

In preterm infants the parenteral amino acid intake from postnatal **day 2** onwards should be between **2.5g/kg/d and 3.5g/kg/d** and should be accompanied by non-protein intakes $>65\text{kcal/kg/d}$ and adequate micronutrient intakes. (LOE 1+, RG A, strong recommendation)

Preterms Infants

- In preterm infants, parenteral amino acid intakes **above 3.5g/kg/d** should only be administered as part of **clinical trials** (LOE 2+, RG 0, conditional recommendation)

Stable term infants

- A minimum amino acid intake of **1.5g/kg/d** should be administered to **stable term** infants to avoid a negative nitrogen balance while the maximum amino acid intake should **not exceed 3.0g/kg/d** (LOE1+, RG B, strong recommendation)

Summary: protein requirements

Age group	Protein
Preterm	1.5-3.5 g AA/kg
Term	1.5-3g AA/kg
Infants and children	1g AA/kg
3-12 years	1-2 g AA/kg
Adolescents	1-2g AA/kg

Practical application

Neonatal PN bags	10% (102/103/104)	6% (105)
75ml/kg	1.5gAA/kg	1.5gAA/kg
150ml/kg	3.1gAA/kg	3.1gAA/kg

Building feeds

	D1	D2	D3	D4
All bags	1.5g AA/kg	2.3g AA/kg	3.1g AA/kg	3.1gAA/kg

Specific amino acids (AA)

- AA requirement lower in parenterally fed than enterally fed – supply passes intestine, AA utilized by the intestine at varying rates
- Leucine utilisation 24% in children and 50% in preterm infants
- Lysine: 20%
- Glutamine: 50%

Cysteine

- Semi-essential amino acid
- Antioxidant properties and calcium homeostasis
- Low levels impair protein synthesis
- 50-75 mg/kg/d should be administered to preterm neonates

Tyrosine

- Semi-essential AA in neonatal period
- Hypertyrosinemia = neurological impairment
- Safe levels: 74mg/kg/d – 94mg/kg/d
- Lower limit 18mg/kg/day in preterm infants

Glutamine

- “Glutamine should not be supplemented additionally in infants and children up to the age of two years” Strong recommendations
- No effect on tolerance of enteral feeds, NEC or growth

Taurine

- “Taurine should be part of AA solutions for infants and children, although no firm recommendation can be made upon advisable lower or upper limits”
- Deficiency may increase glyco-conjugates of bile acids and result in cholestasis
- Data indicating that adequate taurine may prevent cholestasis

Arginine

- “Arginine supplementation may be used for prevention of NEC in preterm infants” – conditional recommendation, strong consensus
- Arginine substrate for the production of nitric oxide
- Depletion is related to innate immune suppression
- 2002 study, double blind RCT, n=152.
 - Significantly decreased NEC, 1.5mmol/kg

Carbohydrates

Amount of CHO provided by PN should be guided by

- **Balance** between **meeting energy needs** and the risk of **overfeeding/excess glucose** load
- **Phase** of illness (acute, stable, recovery/growing)
- **Macronutrient** supply from **enteral** and parenteral supply
- Glucose supply administered from outside (i.e. **medication**)

Critical illness

- Glucose metabolism **highly modified** during **critical illness**
- **Protein catabolism** not modified with increased CHO intake

Endogenous glucose production (RGP)

- **ELBW (24-29 weeks) RGP** and gluconeogenesis on day 3-4 not affected by **glucose infusion rate**
- In contrast, **moderately preterm neonates at 31 weeks**, RGP **supressed** completely by PN glucose intake

Preterm infants

- Carbohydrate intake determined by **energy requirements, blood glucose levels and growth**
- Individualized with specific problems
 - hypo- or hyperglycaemia
 - severe perinatal asphyxia
 - hyperinsulinemia
 - long term PN with lipid intolerance
 - insufficient growth

Carbohydrates

	Day 1 Start with	Day 2 onwards Increase gradually over 2-3 days
Preterm newborn	4-8mg/kg/hr (5.8-11.5g/kg)	Target 8-10 (11.5-14.4) Min 4 (5.8); Max 12 (17.3)
Term newborn	2.5-5mg/kg/hr (3.6-7.2g/kg)	Target 5-10 (7.2-14.4) Min 2.5(3.6); Max 12(17.3)

	Day 1 Start with	Day 2 onwards Increase gradually over 2-3 days
Preterm newborn	5.4mg/kg/hr (7.8g/kg)	11mg/kg/min (15.5g/kg)
Term newborn	4.3mg/kg/hr (6.2g/kg)	11mg/kg/min (15.5g/kg)

Hyperglycaemia: Preterms

- Preterms defined as blood glucose **>10mmol/L**
 - Associated with increased morbidity
- **Insulin therapy** is effective in treating and preventing hyperglycaemia
 - leads to increased incidence of hypoglycaemia
- No evidence for **tight blood glucose management in the NICU**
- Recommendation
 - when **reasonable adaption of the glucose infusion rate** is insufficient to control neonatal hyperglycaemia
 - Insulin therapy at a **low starting dose**

Blood glucose monitoring

- Blood glucose measurements should preferably be performed on **equipment validated for use**. Such as blood gas analysers (LOE2+, RG B, strong recommendation)
- Repetitive and/or prolonged **hypoglycaemia $\leq 2.5\text{mmol/L}$** (45mg/dL) should be avoided in all ICU patients (extrapolated LOE 2+, RG 0, and strong recommendation)

Blood glucose monitoring

- Hyperglycaemia **>8mmol/L (145mg/dL)** should be avoided in **neonatal ICU patients** because it is associated with increased morbidity and mortality (LOE 2-, RG B, strong recommendation)
- In **neonates in the NICU**, repetitive blood glucose levels **>10mmol/L (180mg/dL)** should be treated with insulin therapy, when reasonable adaptation of glucose infusion rate has been insufficient (LOE 2++, RG 0, conditional recommendation)

Lipids

Intravenous lipid emulsions (ILE)

Early lipid initiation

- 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)

Early lipid initiation

- Recent meta-analysis and RCT's: Early lipid **safe and well tolerated**
 - Improved **growth**
 - Observational studies: role in **neurodevelopment**
 - Improved **nitrogen** balance
- **Excess** may impair immune system

Type of lipid: preterm infants

- In preterm infants, newborns and older children on short term PN, pure soybean oil (SO) ILEs may provide less balanced nutrition than composite ILEs. For PN lasting longer than a few days, **pure SO ILEs should no longer be used and composite ILEs with or without fish oil (FO) should be the first choice treatment** (LOE 1-, RG A, conditional recommendation)

Type of lipid: preterm infants

- **Mixture** of vegetable oils, compared to pure SO ILE, result in more favourable metabolic parameters and a more desirable lower PUFA supply
- Smaller preterms receiving ILE that do not contain FO develop early and severe DHA deficit
- Provide n-6 and n-3 precursor fatty acids, as well as n-6 and n-3 LC-PUFA, in balanced amounts and ratios

Type of lipid: preterm infant

- Systemic review and meta-analysis showed association of **less sepsis** episodes in infants receiving **non-pure SO based ILEs** as compared to SO ILE
- Reduction of ILEs 1g/kg/day did **not prevent cholestasis** (risk of EFA deficiency)

ILE dose: preterm infants

- In preterm and term infants, parenteral lipid intake **should not exceed 4g/kg/day**. (LOE 4, GPP, conditional recommendation for)
- Minimum linoleic acid (LA) intake of **0.25g/kg/day** can be given

ILE delivery: preterm infants

- In preterm infants, ILEs should be protected by **validated light-protected tubing**. (LOE 1-, RG B, strong recommendation for





ILE: Monitoring




- In patients with **severe unexplained thrombocytopenia, serum triglyceride concentrations** should be monitored and a reduction of parenteral lipid dosage may be considered. (LOE 3-4, GPP, conditional recommendation)

ILE: Monitoring

- Markers **of liver integrity and function**, and **triglyceride concentrations** in serum or plasma should be monitored regularly (LOE 2-, RG B, strong recommendation for)

Vitamin and minerals

Mineral	Preterm	0-3 mo	Max dose	150ml/kg
Iron	200-500	50-100	5mg/d	None
Zinc	400-500	250	5mg/d	225ug 
Copper (ug)	40	20	0.5mg/d	18ug 
Iodine	1-10	1		0.9ug 
Selenium (ug)	7	2-3	100ug/d	1.8ug 
Manganese	≤1	≤1	50ug/d	0.9ug
Molybdenum	1	0.25	5ug//d	-
Chromium	-	-	5ug/d	-

	Preterm Infants	Infants-12 months	150ml/kg
Vitamin A	700-1500IU/kg/d (227-455ug/kg/d)	150-300ug/kg/d or 2300IU/kg/d (167ug/d)	138IU 
Vitamin D	200-1000IU/d or 80-400IU/kg/D	400IU /d or 40- 150IU/kg/d	23IU 
Vitamin E	2.8-3.5mg/kg/d or 2.8-3.5 IU/KG/d	2.3-3.5mg/kg/d or 2.8-3.5 IU/KG/D	0.42IU 
Vitamin K	10ug/kg/d (recommended, but currently not possible)	10ug/kg/d (recommended, but currently not possible)	12ug

	Requirements	150ml/kg	
Vitamin C	15-25mg/kg/d	10	↓
Thiamine	0.35-0.50mg/kg/d	0.32	↓
Riboflavin	0.15-0.2mg/kg/d	0.36	
Pyridoxine	0.15-0.2mg/kg/d	0.4	
Niacin	4-6.8mg/kg/d	4	
Vitamin B12	0.3ug/kg/d	0.5	
Pantothenic Acid	2.5mg/kg/d	1.5	↓
Biotin	5-8ug/kg/d	6	↓
Folic Acid	56ug/kg/d	40	↓

Calcium, Magnesium, Phosphorus

Age	Ca mmol/kg/d	P mmol/kg/d	Mg mmol/kg/d
Preterm infants during the first days of life	0.2-2.0	1.0-2.0	0.1-0.2
Growing Premature	1.6-3.5	1.6-3.5	0.2-0.3
0-6 months	0.8-1.5	0.7-1.3	0.1-0.2

Provision at 150ml/kg

Ca mmol/kg/d	P mmol/kg/d	Mg mmol/kg/d
3.2	2.5	0.25

Fluid recommendation

Days after Birth					
	Day 1	Day 2	Day 3	Day 4	Day 5
Fluid intake (ml/kg/d)					
Term neonate	40-60	50-70	60-80	60-100	100-140
Preterm neonate >1500g	60-80	80-100	100-120	120-140	140-160
Preterm neonate 1000-1500g	70-90	90-110	110-130	130-150	160-180
Preterm neonate <1000g	80-100	100-120	120-140	140-160	160-180

GSH protocol

Days after Birth					
	Day 1	Day 2	Day 3	Day 4	Day 5
Fluid intake (ml/kg/d)					
Term neonate	60	96	132	150	150
Preterm neonate >1500g	60	96	132	150 (160)	160
Preterm neonate 1000-1500g	70-80	106	142	150 (160)	160
Preterm neonate <1000g	90	126	150 (160)	150 (160)	160

Na, K, Cl: phase 1

Na (mmol/kg/d)					
	Day 1	Day 2	Day 3	Day 4	Day 5
Term neonate	0-2	0-2	0-2	1-3	1-3
Preterm neonate >1500g	0-2(3)	0-2(3)	0-3	2-5	2-5
Preterm neonate <1500g	0-2 (3)	0-2 (3)	0-5(7)	2-5(7)	2-5(7)
K (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

GSH Protocol

<1000g/ starting volume 90ml/kg TPN

	Day 1	Day 2	Day 3
Na	1.9	2.7	3.2
K	1.5	2.1	2.5
Cl	3.8	5.3	6.4

Na, K, Cl: phase 2

	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 >1500g	140-160	2-5	1-3	2-5
Preterm neonate <1500g	140-160	2-5 (7)	1-3	2-5

Na, K, Cl: phase 3

	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>1500g	140-160	3-5	1-3	3-5
Preterm neonate<1500g	140-160	3-5(7)	2-5	3-5