AA 52. Biochemical monitoring to monitor parenteral nutritional adequacy and tolerance. If, why and when should these be measured/monitored and for how long? What are the reference ranges for the neonatal population?

Sodium	Triglycerides	Ammonia
Calcium	Blood urea nitrogen	Alkaline phosphatase
Phosphate	Bicarbonate	Parathyroid hormone
Magnesium	Creatinine	Liver function tests
Potassium	Haemoglobin	Trace elements
Blood gases	Ferritin	Fat-soluble vitamins
Blood glucose	Full blood count (including reticulocytes)	Urinary sodium and phosphate
Blood pH	Albumin and protein	Urinary glucose

Source recommendation	Back to question list
Source guideline title and developer	**ESPGHAN 2018** Puntis J, Hojsak I, Ksiazyk J, ESPGHAN/ESPEN/ESPR/CSPEN Working Group on Pediatric Parenteral Nutrition. ESPGHAN/ESPEN/ESPR guidelines on pediatric parenteral nutrition: organisational aspects. Clin Nutr 2018;37:2392e400. https://doi.org/10.1016/j.clnu.2018.06.953 and Australasian Paediatric Nutrition guidelines https://link.springer.com/article/10.1186/s12887-020-1958-9

Existing guidelines recommendation	Laboratory monitoring of parenteral nutrition

Investigation	Sample	Before starting parenteral nutrition	During parenteral nutrition before clinical and metabolic stabilisation			During parenteral nutrition, during clinical and metabolic stabilisation		
			Once/ 1–2 days	At least once a week	as required	Once/1–2 weeks	Once a month	As required
Sodium	Serum	X	X			X		
Potassium	Serum	X	X			X		
Chloride	Serum	X	X					X
Calcium	Serum	X	X			X		
Phosphorus	Serum	X	X			X		
Magnesium	Serum	X			X	X		
Zinc	Serum				X			X
Blood gases	Capillary	X		X		X		
Glucose	Capillary, whole blood	X	X			X		
Total protein	Serum	X		X		X		
Albumins	Serum	X		X			X	
BUN	Serum	X		X			X	
Creatinine	Serum	X		X			X	
Triglycerides	Serum	X			X			X
Cholesterol	Serum	X			X			X
Bilirubin	Serum	X			X		X	
AST	Serum	X			X		X	
ALT	Serum	X			X		X	
GGTP	Serum	X			X			X
AP	Serum	X			X			X
CBC	WB	X		X		X		
INR	Serum	X			X		X	
CRP	Serum	X			X			X
Vit. B12	Serum				X			X
Fe	Serum				X			X
Ferritin	Serum				X			X
PTH	Serum							X
25OHD3	Serum				X			X
Trace elements: Se, Zn, Cu				X				X
Urine electrolytes	Urine				X			

Biochemical reference ranges and parameters

Parameter	Neonatal reference range
Sodium	135–145 mmol/L
Potassium	3.5–6.0 mmol/L
Calcium (total/ionised)	2.0–2.7 mmol/L / 1.1–1.3 mmol/L
Phosphate	1.8–3.0 mmol/L
Magnesium	0.65–1.0 mmol/L
Blood glucose	2.6–6.5 mmol/L
Blood gases	pH 7.35–7.45, $PaCO_2$ 4.7–6.0 kPa, HCO_3 22–26 mmol/L
Blood pH	7.35–7.45
Urinary glucose	Negative
Triglycerides	<2.8 mmol/L (cut-off for reducing lipid infusion)
Blood urea nitrogen (BUN)	1.4–5.0 mmol/L
Bicarbonate	20–26 mmol/L
Creatinine	20–70 µmol/L (varies with GA, higher at birth)
Haemoglobin	140–200 g/L (preterm)
Ferritin	25–200 µg/L
Full Blood Count (FBC)	WBC 5–25 $x10^9$/L, Hb 140–200 g/L, Plt >150 $x10^9$/L
Reticulocytes	2–6% (higher postnatally if recovering from anaemia)
Albumin / Prealbumin	Albumin: 25–40 g/L; Prealbumin: 100–300 mg/L
Ammonia	<100 µmol/L
Alkaline Phosphatase (ALP)	100–500 U/L (up to 1000 U/L in growth phase)
Parathyroid Hormone (PTH)	1.6–6.9 pmol/L
Liver function tests (LFTs)	ALT <45 U/L, AST <100 U/L, GGT <200 U/L
Conjugated bilirubin	<17 µmol/L
Fat-soluble vitamins (A, D, E, K)	A: 0.7–1.5 µmol/L; D: >50 nmol/L; E: 11–46 µmol/L; K: 0.2–3.2 nmol/L
Trace elements	(e.g. Cu, Zn, Se, Mn) – lab-dependent norms
Transaminases	ALT/AST as part of LFT
Urinary sodium/phosphate	Urinary Na >20 mmol/L suggests adequate intake

Year published	2018
Strength of recommendation	Conditional recommendation
GRADE certainty of evidence	Low to moderate
Were EtD and SoF available?	No
Is the recommendation recent and credible	Yes AGREE II score: 79%
Assessment of suitability for adolopment	
Is the recommendation relevant to local setting (population/ intervention/comparator)?	Yes

Are the judgements in the source EtD acceptable without modification?	Yes - with some exceptions and adaptations to make the monitoring more preterm rather than paediatric focussed: **Phosphate – No** We recommend routine monitoring of serum phosphate in preterm infants to reduce the risk of severe hypophosphataemia and refeeding syndrome. Since the publication of the ESPGHAN 2018 Parenteral Nutrition guidelines, there is a growing body of evidence linking hypophosphataemia and refeeding syndrome with clinically important morbidity and increased mortality in preterm infants. Preterm infants—particularly those with birth weight <1500 g or <10th centile for gestational age—are at heightened risk due to limited phosphate stores and rapid anabolic demands during early nutritional rehabilitation. Hypophosphataemia, especially if severe (<0.9 mmol/L) may contribute to metabolic instability, impaired respiratory, cardiac function and adverse neurodevelopmental outcomes. In light of emerging evidence, we believe that explicit guidance on phosphate monitoring for high-risk groups should be added to the ESPGHAN 2018 monitoring recommendations to improve safety during early parenteral and enteral nutrition and to reduce preventable complications associated with refeeding. **Urea** In a Cochrane review comparing higher versus lower amino acid intake in parenteral nutrition, six studies reported urea concentrations. The criteria for abnormal urea differed between the studies and varied from >10 mmol/L to 21 mmol/L. Given the importance of early amino-acid administration in preterm infants, limiting amino acid intake based on serum urea alone is not warranted. Urea levels up to 14 mmol/L may be considered acceptable in infants on parenteral nutrition provided there are no other parameters to suggest protein intolerance (eg hyperammonaemia >122 µmol/L). **Triglycerides (link to Question AA 1.6c Are there any indications (e.g. high triglycerides, sepsis) to wean, reduce or restrict parenteral lipid administration?)** ESPGHAN 2018 guidelines recommend monitoring of triglycerides in preterm infants and suggest a triglyceride level of 2.8 mmol/L as the upper limit. The monitoring of plasma triglyceride concentrations is not routine in Aotearoa New Zealand neonatal units. A retrospective review from an Australian NICU in which routine triglyceride monitoring was in place showed a hypertriglyceridaemia incidence of 33% in 23–25 weeks and 16% in 26–28 weeks. Severe hypertriglyceridaemia (>4.5 mmol/L) was noted in 10% in 23–25 weeks and 5% in 26–28 weeks. Hypertriglyceridaemia was not associated with mortality or morbidity when adjusted for gestation and birthweight. (Sinclair R, Lui K, Bolisetty S. Hypertriglyceridaemia in extremely preterm infants receiving parenteral lipid emulsions. Presented at 21st Annual Congress of Perinatal Society of Australia and New Zealand; Canberra; 2017 April 2–5.)
Are any local contextual factors different (e.g. cost, equity, feasibility)?	Access to extended trace element and vitamin testing may be limited in regional centres and requires coordination with tertiary laboratories.

EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Biochemical derangements may go undetected without structured monitoring during parenteral nutrition.	Yes	
Desirable effects	Early identification and correction of abnormalities improves safety and outcomes.	Favourable	
Undesirable effects	Frequent sampling may cause iatrogenic anaemia and distress for infants and caregivers.	Manageable	Use micro-sampling and rational testing.
Certainty of evidence	Expert consensus and observational data support structured monitoring.	Moderate	
Values and preferences	Clinicians prioritise safety and proactive detection; families expect comprehensive monitoring balanced against invasiveness.	Possibly some variability	
Balance of effects	Favourable benefit–risk ratio for routine structured monitoring.	Favourable	
Resources required	Costs of laboratory tests, staffing, equipment, and access to specialist assays.	Moderate	
Certainty of resource evidence	Based on expert opinion and clinical practice guidelines; direct trial evidence is limited.	Cost evaluations are limited.	
Cost-effectiveness	No studies identified	Likely	
Equity	Rural/low-resource settings may face barriers to full implementation.	Concern	
Acceptability	Monitoring is routine and supported in most NICUs.	High	
Feasibility	Feasible with standard protocols and lab access.	Yes	

Judgement criteria for EtD	
Decision Type	☐ Adopted as is ☑ Adapted ☐ De novo recommendation required
Explanation of adaptation	The recommendation has been adapted from ESPGHAN 2018 guidance to reflect current evidence or lack thereof, local clinical practice access considerations and to make the monitoring more preterm rather than paediatric focussed. Serum phosphate monitoring recommendations have been added to the ESPGHAN 2018 monitoring recommendations, cholesterol monitoring was removed, urinary sodium increased from >20 to >30 mmol/L and some missing reference ranges were added (LabPlus). ESPGHAN 2018 biochemical reference ranges and parameters are included for reference, but the use of local hospital or LabPlus reference ranges is encouraged.

Final Recommendation	
Recommendation statement (adapted)	See table below
Final Recommendation	Adapted tables above. **Recommended monitoring for refeeding syndrome** For babies with a birthweight <1500 g or <10th centile, monitor serum phosphate and calcium on days 3, 5 and 7 and then alternate days until commenced on fortified breastmilk or preterm formula. **Urea** Limiting amino acid intake based on serum urea alone is not warranted. Urea levels up to 14 mmol/L may be considered acceptable in infants on parenteral nutrition provided there are no other parameters to suggest protein intolerance (eg hyperammonaemia >122 µmol/L). **Triglycerides** *(link to Question AA 1.6c Are there any indications (e.g. high triglycerides, sepsis) to wean, reduce or restrict parenteral lipid administration?)* The routine monitoring of plasma triglyceride concentrations is not recommended.
Strength	Conditional
Certainty of evidence	Low to moderate
Basis for decision	Monitoring supports early intervention and improves parenteral nutrition safety. Although largely based on expert consensus, it reflects established neonatal practice.
Subgroup Considerations	Extremely preterm or metabolically unstable infants require more intensive and frequent testing; stable or convalescing infants may require reduced frequency.
Implementation Considerations	Protocols should specify monitoring intervals and available tests. Regional centres may need referral pathways or courier services for specialist assays.
Monitoring and Evaluation	Audit testing compliance, turnaround time, complication rates and frequency of critical abnormal results to guide practice improvement.
Research Priorities	Define optimal monitoring frequency; validate predictive biochemical markers of nutrient adequacy and toxicity; evaluate less invasive testing strategies.

Biochemical monitoring for babies on parenteral nutrition

Investigation	Neonatal reference range	Before clinical and metabolic stabilisation		Once clinically and metabolically stable		
		Every 1–2 days	As required*	Every 1–2 weeks	After one month on PN, then monthly	As required*
Glucose	2.6–6.5 mmol/L	X		X		
Blood gases (capillary)	pH 7.35–7.45, PCO_2 4.7–6.0 kPa, HCO_3 22–26 mmol/L	X		X		
Sodium	134–148 mmol/L	X		X		
Potassium	4.5–6.0 mmol/L	X		X		
Chloride	90–114 mmol/L	X				X
Calcium	Total 1.8–2.1 mmol/L, Ionised 1.15–1.45 mmol/L	X			X	
Phosphorus	1.8–3.0 mmol/L (*see footnote for frequency*)	X			X	

Investigation	Neonatal reference range	Before clinical and metabolic stabilisation		Once clinically and metabolically stable		
		Every 1–2 days	As required*	Every 1–2 weeks	After one month on PN, then monthly	As required*
Magnesium	0.7–1.0 mmol/L		X			X
Zinc	9–17 µmol/L		X			X
Total protein	45–75 g/L		X			X
Albumin	25–40 g/L		X			X
Urea	1.0–4.0 mmol/L		X			X
Creatinine	<95 µmol/L		X			X
Triglycerides	<3 mmol/L		X			X
Bilirubin (conjugated)	<20 µmol/L		X		X	
AST	<80 U/L		X		X	
ALT	<45 U/L		X		X	
GGT	<150 U/L		X		X	
ALP	80–600 U/L (up to 1000 U/L in growth phase)		X		X	
PTH	1.7–7.3 pmol/L		X		X	
Vitamin A	0.7–1.5 µmol/L (200-800 µg/L)		X		X	
Vitamin B_{12}	170–800 pmol/L		X		X	
Vitamin D	>50 nmol/L		X		X	
Vitamin E	11–46 µmol/L Starship, 5 – 50 µmol/L Waikato 23-70 µmol/L Christchurch		X		X	
INR	Lab-dependent norm		X		X	
Trace elements: Se, Zn, Cu	Lab-dependent norms					X
C-reactive protein	0–5 mg/L		X			X
Iron	10-31 µmol/L		X			X
Ferritin	15–400 µg/L		X			X
Urine electrolytes	Urinary Na >30 mmol/L adequate for growth					X

*AST aspartate aminotransferase, ALT alanine aminotransferase, GGT gamma-glutamyl transferase, ALP alkaline phosphatase, INR International normalised ratio (an elevated INR may indicate vitamin K deficiency), PTH parathyroid hormone, PN parenteral nutrition *no routine monitoring is recommended. Individualised monitoring may be needed based on the clinical situation.*

Monitoring for refeeding syndrome: For babies with a birthweight <1,500 g or <10th centile, monitor serum phosphate and calcium on days 3, 5 and 7 and then on alternate days until commenced on fortified breastmilk or preterm formula.

Urea: Limiting amino acid intake based on serum urea alone is not warranted. Urea levels up to 14 mmol/L may be considered acceptable in infants on parenteral nutrition provided there are no other parameters to suggest protein intolerance (e.g. hyperammonaemia >122 µmol/L).

Triglycerides: The routine monitoring of plasma triglyceride concentrations is not recommended.