



ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Organisational aspects

JWL. Puntis^a, I. Hojsak^{b, *}, J. Ksiazyk^c, the ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition¹

^a The General Infirmary at Leeds, Leeds, UK

^b Children's Hospital Zagreb, Zagreb, Croatia

^c The Children's Memorial Health Institute, Warsaw, Poland



ARTICLE INFO

Article history:

Received 29 May 2018

Accepted 29 May 2018

1. Methods

Literature search

Timeframe: publications from 2004 until December 2017 were considered

Type of publications: randomized trials, observational studies (case-controls, prospective cohort studies, case series, retrospective data), meta-analyses, systematic reviews

Key words: nutrition support; nutrition assessment; nutrition team; nutrition and monitoring; nutritional rehabilitation; parenteral nutrition and filter; infusion pumps; anthropometry and parenteral nutrition; nutrition and ordering

* Corresponding author.

E-mail address: ivahojsak@gmail.com (I. Hojsak).

¹ ESPGHAN/ESPEN/ESPR/CSPEN working group on Pediatric Parenteral Nutrition: BRAEGGER Christian, University Children's Hospital, Zurich, Switzerland; BRONSKY Jiri, University Hospital Motol, Prague, Czech Republic; CAI Wei, Shanghai Jiao Tong University, Shanghai, China; CAMPOY Cristina, Department of Paediatrics, School of Medicine, University of Granada, Granada, Spain; CARNIELLI Virgilio, Polytechnic University of Marche, Ancona, Italy; DARMAUN Dominique, Université de Nantes, Nantes, France; DECSI Tamás, Department of Pediatrics, University of Pécs, Pécs, Hungary; DOMELLÓF Magnus, Department of Clinical Sciences, Pediatrics, Umeå University, Sweden; EMBLETON Nicholas, Newcastle University, Newcastle upon Tyne, The United Kingdom; FEWTRELL Mary, UCL Great Ormond Street Institute of Child Health, London, UK; FIDLER MIS Nataša, University Medical Centre Ljubljana, Ljubljana, Slovenia; FRANZ Axel, University Children's Hospital, Tuebingen, Germany; GOULET Olivier, University Sordonne-Paris-Cité; Paris-Descartes Medical School, Paris, France; HARTMAN Corina, Schneider Children's Medical Center of Israel, Petach Tikva, Israel and Carmel Medical Center, Haifa Israel; HILL Susan, Great Ormond Street Hospital for Children, NHS Foundation Trust and UCL Institute of Child Health, London, United Kingdom; HOJSAK Iva, Children's Hospital Zagreb, University of Zagreb School of Medicine, University of J. J. Strossmayer School of Medicine Osijek, Croatia; IACOBELLI Silvia, CHU La Réunion, Saint Pierre, France; JOCHUM Frank, Ev. Waldkrankenhaus Spandau, Berlin, Germany; JOOSTEN, Koen, Department of Pediatrics and Pediatric Surgery, Intensive Care, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands; KOLAČEK Sanja, Children's Hospital, University of Zagreb School of Medicine, Zagreb, Croatia; KOLETZKO Berthold, k LMU – Ludwig-Maximilians-Universität Munich, Dr. von Hauner Children's Hospital, Munich, Germany; KSIAZYK Janusz, Department of Pediatrics, Nutrition and Metabolic Diseases, The Children's Memorial Health Institute, Warsaw; LAPILLONNE Alexandre, Paris-Descartes University, Paris, France; LOHNER Szimonetta, Department of Pediatrics, University of Pécs, Pécs, Hungary; MESOTTEN Dieter, KU Leuven, Leuven, Belgium; MIHÁLYI Krisztina, Department of Pediatrics, University of Pécs, Pécs, Hungary; MIHATSCH Walter A., Ulm University, Ulm, and Helios Hospital, Pforzheim, Germany; MIMOUNI Francis, Department of Pediatrics, Division of Neonatology, The Wilf Children's Hospital, the Shaare Zedek Medical Center, Jerusalem, and the Tel Aviv University, Tel Aviv, Israel; MØLGAARD Christian, Department of Nutrition, Exercise and Sports, University of Copenhagen, and Paediatric Nutrition Unit, Rigshospitalet, Copenhagen, Denmark; MOLTU Sissel J., Oslo University Hospital, Oslo, Norway; NOMAYO Antonia, Ev. Waldkrankenhaus Spandau, Berlin, Germany; PICAUD Jean Charles, Laboratoire CarMEN, Claude Bernard University Lyon 1, Hôpital Croix Rousse, Lyon, France; PRELL Christine, LMU – Ludwig-Maximilians-Universität Munich, Dr. von Hauner Children's Hospital, Munich, Germany; PUNTIS John, The General Infirmary at Leeds, Leeds, UK; RISKIN Arie, Bnai Zion Medical Center, Rappaport Faculty of Medicine, Technion, Haifa, Israel; SAENZ DE PIPAON Miguel, Department of Neonatology, La Paz University Hospital, Red de Salud Materno Infantil y Desarrollo – SAMID, Universidad Autónoma de Madrid, Madrid, Spain; SENTERRE Thibault, CHU de Liège, CHR de la Citadelle, Université de Liège, Belgium; SHAMIR Raanan, Schneider Children's Medical Center of Israel, Petach Tikva, Israel; Tel Aviv University, Tel Aviv, Israel; SIMCHOWITZ Venetia, Great Ormond Street NHS Trust, London, The United Kingdom; SZITANYI Peter, General University Hospital, First Faculty of Medicine, Charles University in Prague, Czech Republic; TABBERS Merit M., Emma Children's Hospital, Amsterdam UMC, Amsterdam, The Netherlands; VAN DEN AKKER Chris H.B., Emma Children's Hospital, Amsterdam UMC, Amsterdam, The Netherlands; VAN GOUDOEVER Johannes B., Emma Children's Hospital, Amsterdam UMC, Amsterdam, The Netherlands; VAN KEMPEN Anne, OLVG, Amsterdam, The Netherlands; VERBRUGGEN Sascha, Department of Pediatrics and Pediatric Surgery, Intensive Care, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands; WU Jiang, Xin Hua Hospital, Shanghai, China; YAN Weihui, Department of Gastroenterology and Nutrition, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China.

<https://doi.org/10.1016/j.clnu.2018.06.953>

0261-5614/© 2018 European Society for Clinical Nutrition and Metabolism. Published by Elsevier Ltd. All rights reserved.

Table: Recommendations on organizational aspects of parenteral nutrition

R 11.1	Supervision of nutritional support in intestinal failure may be provided by a multidisciplinary nutritional support team (LoE 2–, RG 0, strong recommendation for)
R 11.2	Accurate anthropometrics and thorough clinical evaluation of patients receiving PN may be undertaken by a skilled practitioner (GPP, strong recommendation for)
R 11.3	The frequency of laboratory assessment may be based on patient's clinical condition (from once daily to 2–3 times per week) (LoE 4, RG 0, strong recommendation for)
R 11.4	All PN solutions may be administered with accurate flow control; the infusion system should be under regular visual inspection; peripheral infusions should be checked frequently for signs of extravasation or sepsis; the pump should have free flow prevention if opened during use, and have lockable settings (GPP, strong recommendation for)
R 11.5	PN solutions may be administered through a terminal filter: lipid emulsions (or all-in-one mixes) can be passed through a membrane pore size of 1.2–1.5 µm; aqueous solutions can be passed through a 0.22 µm filter (GPP, strong recommendation for)
R 11.6	PN solutions for the premature newborns should be protected against light in order to prevent generation of oxidants (LoE 1–, RG B, strong recommendation for)
R 11.7	Cyclical PN may start once patients are in a stable clinical condition and can maintain normoglycaemia during a period without PN infusion (GPP, strong recommendation for)
R 11.8	In order to prevent hypo/hyperglycaemia infusion rate may be tapered up gradually during the first 1–2 h and tapered down during the last 1–2 h of infusion when cyclic PN is administered (GPP, strong recommendation for)
R 11.9	Complete enteral starvation (i.e. 'TPN') may be avoided by giving some enteral feed whenever possible, even if only a minimal amount is tolerated (GPP, strong recommendation for)
R 11.10	When increasing enteral feed, only one change at a time may be made, to assess tolerance (GPP, strong recommendation for)
R 11.11	In severe intestinal failure, feed volumes may be increased slowly, according to digestive tolerance (GPP, strong recommendation for)
R 11.12	Enteral feeding may be introduced as a liquid feed infused continuously by tube over 4–24 h periods, using a volumetric pump (GPP, conditional recommendation for)
R 11.13	Bolus liquid feed may be given via feeding tube, or by mouth as sip feed if tolerated (GPP, conditional recommendation for)
R 11.14	Children who rapidly recover intestinal function may be weaned straight onto normal food (GPP, conditional recommendation for)
R 11.15	In newborns and infants with intestinal failure breast milk may be the enteral feed of first choice (GPP, strong recommendation for)
R 11.16	If breast milk is not available, the choice of substitute can be based on clinical condition; in early infancy and severe illness it is reasonable to start with elemental formula, switching to extensively hydrolysed and then to polymeric feeds (GPP, strong recommendation for)
R 11.17	Enteral feed may be given at normal concentrations (i.e. not diluted) (GPP, conditional recommendation for)
R 11.18	PN should be reduced in proportion to, or slightly more than the increase in EN (GPP, conditional recommendation for)
R 11.19	If a chosen weaning strategy fails, try again more slowly (GPP; conditional recommendation for)

Language: English

Search: Searches were performed in three stages. First, all the titles with the relevant key words were retrieved by the Cochrane Collaboration Department from Budapest, who also performed the first reduction. Members of the Working Group subsequently read all the titles and abstracts, and selected potentially relevant ones. These were retrieved and full articles were assessed.

2. Ordering and monitoring parenteral nutrition in hospital

2.1. Introduction

The purpose of parenteral nutrition (PN) is to correct or prevent nutritional deficiencies when adequate enteral nutrition is precluded by impairment or immaturity of gastrointestinal function. Having identified a patient in need of PN, the process of ordering and monitoring is aimed at ensuring safe and effective nutritional support. Provision of PN should be part of an overall nutritional care plan that includes detailed nutritional assessment. Nutritional goals should be set, and an estimate made of the probable duration of PN. The whole process is dynamic: ongoing nutritional support should reflect changes in nutritional and clinical status and be overseen by a multidisciplinary nutrition team.

2.2. Nutrition support teams

R 11.1	Supervision of nutritional support in intestinal failure may be provided by a multidisciplinary nutritional support team (LoE 2–, RG 0, strong recommendation for, strong consensus)
---------------	---

A multidisciplinary nutrition support team (NST; e.g. doctor, nurse, dietitian/nutritionist, pharmacist, etc.) has an important role in promoting and coordinating optimum nutritional care, educating

staff, developing guidelines, promoting research [1] (LoE 2–) and reducing inappropriate use of PN [2] (LoE 2–). A team approach to nutritional support was associated with a reduction in catheter related blood stream infection rates in a number of different studies involving adult patients [3–8] (LoE 2–). Staff training by a nutrition nurse reduces the prevalence of catheter sepsis in infants [9] (LoE 2–). Other aspects of quality of care such as monitoring of nutritional status and assessment of requirements [8] are improved by a multidisciplinary approach [8,10] (LoE 2–). Savings made can more than justify the appointment of specialised staff such as nutrition nurse and dietitian [11] (LoE 2–). Experience in paediatric intensive care suggests introduction of a NST both decreases inappropriate use of PN in favour of enteral feeding and reduces mortality [12] (LoE 2–). In other settings it may be difficult to clearly document improvements in nutritional management, sometimes because of clinical factors that cannot be easily overcome [13]. Implementation of a NST has been recommended by the ESPGHAN Committee on Nutrition [14], and teams can play an important role in raising awareness of the importance of nutritional management throughout the paediatric department [15]. Outcome for patients with PN dependent intestinal failure (IF) appears to be improved by management under a multidisciplinary team [16] (LoE 2–) and such an approach is to be encouraged [17–21]. A NST is also essential for facilitating and supporting home parenteral nutrition [22,23].

2.3. Nutritional assessment

R 11.2	Accurate anthropometrics and thorough clinical evaluation of patients receiving PN may be undertaken by a skilled practitioner (GPP, strong recommendation for, strong consensus)
R 11.3	The frequency of laboratory assessment may be based on patient's clinical condition (from once daily to 2–3 times per week) (LoE 4, RG 0, strong recommendation for, strong consensus)

A multidisciplinary NST should oversee the process of PN [24] and patients be regularly nutritionally assessed. This provides a baseline of nutrition parameters, determines nutrition risk factors, identifies specific nutrition deficits, establishes nutrition needs for individual patients, and identifies factors that may influence the prescribing and administering of nutrition support therapy [25]. Nutritional assessment is divided into clinical examination, anthropometry, laboratory indices, and assessment of dietary intake [24].

2.3.1. Clinical examination

Clinical examination gives an important overall impression of health and includes the general appearance and activity level of the patient [24]. Monitoring parameters include vital signs and thorough physical assessment, together with clinical indicators of fluid and nutrient excess or deficiency [25].

2.3.2. Anthropometry

There should be accurate measurement of anthropometric variables such as weight, length/height and head circumference [24,26]. Anthropometric measures are reported with reference to population data, and plotted on appropriate growth charts. These charts include, in children <36 months of age: length-for-age, weight-for-age, head circumference-for-age, and weight-for-length, and in children ages 2–18 years: standing height-for-age, weight-for-age, and body mass index (BMI)-for-age and BMI centile (LoE 2+) [27]. Measures are usually expressed as percentiles or standard deviation scores (SDS). SDS allow changes over time to be detected more easily than with percentiles, which do not so readily reveal the precise degree of deviation from population norms [24].

Anthropometric measures have some limitations, for example, severe illness is often associated with fluid retention and oedema making weight measurements unreliable. Therefore, an assessment of fluid intake and output should accompany an evaluation of weight gain to determine whether the source of the weight is an increase in fluid or lean body mass [25]. Alternative anthropometric tools have been proposed for assessing malnutrition in patients affected by lower extremity oedema, ascites, steroid treatment or large solid tumour mass. Mid upper arm circumference (MUAC) may be a better indicator than weight for classification of acute malnutrition (LoE 2+) [26–29]. MUAC together with triceps skin fold thickness allows calculation of mid arm fat and muscle area, giving an insight into body composition [24]. Measurements should be undertaken by a trained and experienced individual such as dietician or nutrition support nurse, using standardized techniques. Serial measurements show changes over time and therefore provide a dynamic picture. The frequency of monitoring will depend on gestational age, postnatal age, underlying disease, severity of illness, degree of malnutrition, and level of metabolic stress [25].

2.3.3. Laboratory assessment

Besides laboratory investigation of baseline metabolic status before ordering PN, some laboratory data can be used as a marker of nutritional assessment. Routine electrolyte, mineral (calcium, phosphorus and magnesium), triglyceride and serum urea determination help to determine nutritional deficiencies (LoE 2+) [30]. Some laboratory tests which relate to visceral protein concentrations (e.g. haemoglobin, total lymphocyte count) help in the identification of malnutrition (LoE 2+) [31]. Proteins with the shorter half-life (i.e. pre-albumin or retinol-binding protein) when sequentially assessed reflect improving nutritional status better than albumin (LoE 2+) [32]. In hospitalised patients, albumin is most commonly low as part of an acute phase response to inflammation and redistribution of protein so that hypoalbuminaemia should not be attributed to malnutrition. No single

protein is ideal as an indicator of nutritional status since they are all affected by other non-nutritional physiological and pathologic states [24]. Other laboratory tests, such as the nitrogen excretion, nitrogen balance and plasma amino acid profile can help characterize protein deficit [33] but are not commonly used in clinical practice. Serum vitamin and trace element concentrations should be evaluated in long-term PN dependent patients (LoE 4) [25]. Daily monitoring may be required for newborns, infants, critically ill patients, those at risk of refeeding syndrome, patients transitioning between PN and enteral feeding, or those that have experienced complications associated with nutritional therapy (LoE 4) [25]. In clinically stable children, measurements may be repeated 2–3 times per week (LoE 4) [24].

2.3.4. Dietary intake

Nutritional assessment must include estimates of dietary and fluid intake (oral, enteral, and parenteral), output (urine, gastrointestinal losses), and a record of gastrointestinal symptoms. Information should be sought with respect to religious restrictions and food preferences or aversions [24,25].

2.4. PN ordering

Accepted goals for PN include prevention or correction of weight loss, and maintenance of normal growth. Any professionals ordering PN should be trained in its indications, complications and administration [34] and the whole process of PN (prescribing, compounding, delivering and monitoring) standardized as far as possible in order to decrease risk and promote effectiveness [35–37]. Protocol driven implementation of nutrition therapy may lead to better outcomes and has, for example, been shown to help preserve lean body mass in intensive care patients [38,39] (LoE 3). Electronic ordering systems can reduce the risk of prescription errors [40] and use of a standardised electronic PN ordering system or an order template as an editable electronic document is recommended [41]. The process of ordering requires very close collaboration between physician, clinical pharmacist and dietitian. In some centres, prescribing of PN has been passed from doctors to an experienced and trained pharmacist working with the NST [42]. Reference to established guidelines for ordering and managing PN encourages appropriate selection of patients and tailoring prescriptions to the particular needs of individuals [24]. Clinical practice guidance as an aide memoire can be included on PN ordering forms [43]. The whole process of PN requires audit and critical scrutiny since life threatening errors may occur during prescribing, transcription (conversion of prescription to volumes of additives in pharmacy), dispensing, delivery to wards, and during the administration process (incorrect infusion rates) [44].

2.5. Infusion equipment and in line filters

-
- | | |
|--------|--|
| R 11.4 | All PN solutions may be administered with accurate flow control; the infusion system should be under regular visual inspection; peripheral infusions should be checked frequently for signs of extravasation or sepsis; the pump should have free flow prevention if opened during use, and have lockable settings (GPP, strong recommendation for, strong consensus) |
| R 11.5 | PN solutions may be administered through a terminal filter: lipid emulsions (or all-in-one mixes) can be passed through a membrane pore size of 1.2–1.5 µm; aqueous solutions can be passed through a 0.22 µm filter (GPP, strong recommendation for, strong consensus) |
| R 11.6 | PN solutions for the premature newborn should be protected against light in order to prevent generation of oxidants (LoE 1–, RGB, strong recommendation for, strong consensus) |
-

One of the greatest hazards to patients during administration of intravenous nutrition arises from the risk of free flow or poor rate control of the infusion. To the potential risks of fluid overload and heart failure are added complications such as hyperglycaemia, hyperkalaemia and hyper-triglyceridaemia. A modern infusion pump with the capability to accurately deliver at low flow rates should be used whenever possible [45,46] (LoE 4). Alarm functions are essential, but sensitivity is often limited at low rates of flow. The ability of children to learn to manipulate devices and interfere with settings should not be underestimated. If pumps are not available, the use of portable, battery powered drop counting devices can provide effective warning of free flow conditions. New 'smart pumps' can be programmed so that starting and finishing infusion rates increase and decrease respectively when delivering cyclical PN in order to prevent hyper- and hypoglycaemia.

PN solutions contain particulate matter [47] (LoE 2–) and biochemical interactions can lead to chemical precipitates and emulsion instability; they also act as a media for microbiologic growth should contamination occur. Particulates in infusion fluid play a role in causing phlebitis with peripheral venous infusion [48] (LoE 2+). Particles can also harm the pulmonary endothelium and provoke a granulomatous pulmonary arteritis [47] (LoE 3). The routine use of in-line filtration has been advocated in children receiving large volume parenterals, and a randomised trial in a paediatric intensive care unit showed that filters were associated with a significant reduction in overall complication rate, a reduction in systemic inflammatory response syndrome, and a reduction in length of stay [48] (LoE 1++). In critically ill children therefore, it appears that infused particles may impair the microcirculation, induce systemic hypercoagulability and inflammation [49] (LoE 1++). A Cochrane review of inline filtration in the newborn found four studies (low quality evidence) that showed no benefits from use of filters [50] (LoE 2–). Some endotoxin retaining 0.22 µm filters allow cost saving, through extended use of the administration set. With the appropriate filters, giving sets can be used for 72–96 h. Many solutions are stable for extended hang-times but explicit stability advice should be sought from the manufacturer or a competent independent laboratory. Filter blockage is more likely to indicate a problem with the solution than the filter, and must be thoroughly investigated.

Intravenous PN solutions that are not photoprotected generate oxidants, which are harmful to cells. Premature infants in particular face an imbalance between high oxidant loads and immature antioxidant defences. A meta-analysis found that mortality in patients with light protected PN was half that in the light exposed group [51] (LoE 1+).

2.6. Cyclical PN

R 11.7	Cyclical PN may start once patients are in a stable clinical condition and can maintain normoglycaemia during a period without PN infusion (GPP, strong recommendation for, strong consensus)
R 11.8	In order to prevent hypo/hyperglycaemia infusion rate may be tapered up gradually during the first 1–2 h and tapered down during the last 1–2 h of infusion when cyclic PN is administered (GPP, strong recommendation for, strong consensus)

PN is always introduced as a continuous infusion over 24 h. Once patients are tolerating a full amount of PN and are stable both clinically and biochemically, the infusion time can be gradually reduced by hourly decrements over a period of days/weeks with frequent assessment of volume/rate tolerance and blood glucose [52,53]. This 'cycling' of PN (discontinuing nutrient infusion for a period time each day) should be established while in hospital so

that tolerance/safety can be confirmed prior to discharge home [53]. Cyclical PN has a protective effect against intestinal failure associated liver disease (IFALD) [54], and is generally a prerequisite for home PN since daytime freedom from infusion pumps improves quality of life. Several studies have shown metabolic differences between cyclical and continuous PN [24,55] while nitrogen balance is similar. In young children (<2 yr) abrupt discontinuation of PN infusion may cause hypoglycaemia; in older children the risk is much lower [55] (LoE 2++). Calcium loss increases during infusion of cyclical PN but not total daily loss of calcium, phosphorus, magnesium, or vitamin D compared with continuous infusion [55] (LoE 2++).

There is some evidence that cycling PN can prevent cholestasis [56–58] (LoE 2–), although the risk was not decreased in VLBW neonates when only the amino acid component of PN was cycled [59] (LoE 1–). Children almost always tolerate night time infusion over 10–14 h [24]. The optimal time to initiate cyclical PN is unknown, and cycling may not be tolerated in young infants due to immature gluconeogenesis, limited glycogen stores, and large glucose demands [56]. However, there is evidence that cycling of PN is safe even in clinically stable newborns [56,57] (LoE 2–).

Cycle time may be shortened by 1–2 h each or every other day until the desired/tolerated goal for duration of infusion is achieved (LoE 4) [53]. In infants with poor enteral tolerance, infusion time should be decreased in 1 h steps. The most common adverse events associated with cyclical PN are hyperglycemia, and respiratory distress due to the increase in the rate of dextrose and fluid infusion [53,55]; abrupt discontinuation of infusion may also precipitate hypoglycaemia [55]. In order to prevent these adverse events, use of an infusion pump that allows a gradual increase in infusion rate during the first 1–2 h, and a tapering down during the last 1–2 h, is recommended (LoE 2–). Infusion rate of glucose, lipids and potassium should also be taken into account when final infusion rate is calculated (see Guideline section on 'Carbohydrates and Lipids').

2.7. PN monitoring

PN monitoring involves frequent clinical assessment including nutritional status and laboratory results. Biochemical monitoring needs to be tailored to the underlying clinical condition and also the duration of PN [60]; a suggested protocol is given in the Table 1. Good catheter care and aseptic delivery of nutrients are mandatory for prevention of catheter related infection. Assessment of fluid and electrolyte balance, particularly when there are abnormal losses from the gastrointestinal tract should result in early intervention when necessary. In stable patients, sudden changes in biochemical status are uncommon [61] (LoE 3); patients with organ failure or unusual fluid losses clearly require closer monitoring. For patients who are PN dependent long term, body composition is often abnormal with significant deficit in limb lean mass [62]. Metabolic bone disease is related to aluminium contaminating fluids, low serum vitamin D and insulin-like growth factor, and inflammation [63]. Bone mineral density is reduced particularly in children with congenital enterocyte disorders or severe dysmotility [64]. Annual bone mineral density assessment should be considered in children who remain PN dependent and are old enough (usually >5 y) to cooperate with a DEXA scan procedure. Once weaned from PN to full enteral feeding, periodic monitoring is still required to identify complications [65]. Children with short bowel continue to have bile salt malabsorption [66] and may develop fat soluble vitamin and trace element deficiencies [67], gallstones and renal stones [68], and anaemia from peri-anastomotic ulceration [69]. Despite resolution of cholestasis and portal inflammation, significant liver fibrosis and steatosis persist [70].

Table 1

Laboratory monitoring of parenteral nutrition. (X – when to perform the test, S – serum, plasma, WB – whole blood, CB – capillary blood, US – urine sample).

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	S	X	X			X		
Potassium	S	X	X			X		
Chloride	S	X	X					X
Calcium	S	X	X			X		
Phosphorus	S	X		X		X		
Magnesium	S	X			X	X		
Zinc	S				X			X
Blood gasses	CB	X		X		X		
Glucose	WB, CB	X	X			X		
Total protein	S	X		X		X		
Albumins	S	X		X			X	
BUN	S	X		X			X	
Creatinine	S	X		X			X	
Triglycerides	S	X			X			X
Cholesterol	S	X			X			X
Bilirubin	S	X			X		X	
AST	S	X			X		X	
ALT	S	X			X		X	
GGTP	S	X			X			X
AP	S	X			X			X
CBC	WB	X		X		X		
INR	S	X			X		X	
CRP	S	X			X			X
Vit. B12	S				X			X
Fe	S				X			X
Ferritin	S				X			X
PTH	S							X
25OHD3	S				X			X
Trace elements: Se, Zn, Cu				X				X
Urine	US	X		X			X	
Electrolytes in urine	US				X			X

3. Weaning and establishment of enteral feeding

R 11.9	Complete enteral starvation (i.e. 'TPN') may be avoided by giving some enteral feed whenever possible, even if only a minimal amount is tolerated (GPP, strong recommendation for, strong consensus)
R 11.10	When increasing enteral feed, only one change at a time may be made, to assess tolerance (GPP, strong recommendation for, strong consensus)
R 11.11	In severe intestinal failure, feed volumes may be increased slowly, according to digestive tolerance (GPP, strong recommendation for, strong consensus)
R 11.12	Enteral feeding may be introduced as a liquid feed infused continuously by tube over 4–24 h periods, using a volumetric pump (GPP, conditional recommendation for, strong consensus)
R 11.13	Bolus liquid feed may be given via feeding tube, or by mouth as sip feed if tolerated (GPP, conditional recommendation for, strong consensus)
R 11.14	Children who rapidly recover intestinal function may be weaned straight onto normal food (GPP, conditional recommendation for, strong consensus)

As with many aspects of the management of IF, there is little evidence base for specific nutritional practices [71]. Children with an acute episode of severe IF (e.g. following surgery or chemotherapy) may tolerate rapid reintroduction of normal diet. Those with primary gut disease need reintroduction of enteral feed tailored according to the underlying disorder. Appropriate minimal enteral feed should be given whenever possible to maintain gut mucosal structure [72] (LoE 3), encourage adaptation [73–76] (LoE 4) and reduce the risk of PN-associated liver disease [54,77] (LoE 3). In the newborn infant with short bowel, expressed breast milk is thought to optimise adaptation [78,79]. Maternal expressed breast milk (MEBM) can be given either fresh (in case of small bolus feeds)

or pasteurised (in case of continuous feeding); donor milk may be available if there is no MEBM [80]. In order to assess tolerance, no more than one management change should be made at a time, for example, when enteral volume is increased, the osmolality of the feed should remain the same. With limited gastrointestinal function, feed volumes must be increased cautiously and according to tolerance (usually assessed by diarrhoeal stools/stoma output) [81].

Potential life threatening risks from PN mean that the overriding clinical priority is to try and establish enteral autonomy. Risk of cholestasis is directly related to duration of PN [82] (LoE 1–) [83] (LoE 3). Enteral nutrition can be introduced as liquid feed infused continuously over 4–24 h periods via a feeding tube, using a volumetric pump [84]. The advantage of continuous feed is that full use is made of the functional capacity of the intestinal tract, particularly if given over 24 h [85]. Liquid enteral nutrition can be given by bolus via a feeding tube, or orally as sip feeds once gastrointestinal function has sufficiently improved. Oral feeding provokes release of epidermal growth factor from salivary glands and increases gastrointestinal secretion of trophic factors [65]. If vomiting or poor gastric emptying is a limiting factor in advancing feed volumes, jejunal tube feeding can be considered; in short bowel this has the potential to worsen diarrhoea.

Children who rapidly recover intestinal function can be weaned straight onto normal food. However, if there is any possibility of persisting intestinal inflammation, diet may need to be adjusted. There may be an increased incidence of cow milk or soya protein intolerance in newborns with short gut and prognosis is improved with breast milk [77] (LoE 3) or amino acid based formula feed [86] (LoE 3).

Every possible attempt must be made to encourage children to eat normally. Even small bolus feeds by mouth can help to avoid the development of oral hypersensitivity and feed aversion. Spoon

feeding should be introduced at the normal time of 4–6 months of age, even if only small amounts of feed can be offered. Sometimes solids appear better tolerated than an increase in liquid feed. Occasionally, oral aversion is associated with underlying gastro-oesophageal reflux [87] that worsens with an increase in feed.

3.1. Type of feed

R 11.15	In newborns and infants with intestinal failure breast milk may be the enteral feed of first choice (GPP, strong recommendation for, consensus)
R 11.16	If breast milk is not available, the choice of substitute can be based on clinical condition; in early infancy and severe illness it is reasonable to start with elemental formula, switching to extensively hydrolyzed and then to polymeric feeds (GPP, strong recommendation for, strong consensus)

Enteral feeding may be limited in IF because of dilated small bowel, dysmotility, bacterial overgrowth and increased permeability [88]. In infancy, feeding options include breast milk, polymeric, extensively hydrolyzed or amino-acid based elemental formula [54]. There is evidence that breast milk is associated with shorter duration of PN (LoE 3) [77,89,90]. In some patients the use of polymeric feeds may be associated with the development of cow milk protein allergy [91,92]. Case reports and small case series have shown that amino-acid based formulae were more efficient in decreasing the requirements for PN than extensively hydrolyzed feeds (LoE 3) [77,86,93–95]. However, the only small randomized study (involving ten infants with SBS) compared hydrolyzed with non-hydrolyzed enteral formula, found no difference in terms of weight gain, tolerance and energy expenditure (LoE 1–) [96].

In children with SBS, continuous enteral nutrition is often recommended [79,97–101]. It has been found that in children both with protracted diarrhoea and SBS continuous feeding improved enteral tolerance and weight gain (LoE 3) [102]. However, bolus feeding is more physiological, helps in development of oral motor skills, provides a cyclical hormonal surge and stimulates gall-bladder emptying [103]. Therefore, small oral bolus feeds during the day should be initiated as soon as possible (usually as an adjunct to continuous enteral feeding during the night) in order to avoid tube-feeding associated complications. In preterm infants guidelines for enteral nutrition should be followed [104].

3.2. Weaning from parenteral nutrition

R 11.17	Enteral feed may be given at normal concentrations (i.e. not diluted) (GPP, conditional recommendation for, strong consensus)
R 11.18	PN should be reduced in proportion to, or slightly more than the increase in EN (GPP, conditional recommendation for, consensus)
R 11.19	If a chosen weaning strategy fails, try again more slowly (GPP, conditional recommendation for, strong consensus)

A reduction in the amount of PN may be attempted as soon as the child is stabilised i.e. intestinal losses from vomiting and diarrhoea have been minimised and an optimal nutrition state reached. All children on PN should continue to have a minimum amount of enteral feed to maintain pancreatico-biliary secretion and promote gut mucosal integrity [105] (LE 3) whenever possible. As soon as a small amount of feed is tolerated, the volume should be increased [81,106–108] (LoE 4). Feed should be given at normal concentrations and not diluted, otherwise the child will achieve normal fluid volume intake without adequate nutrition. The aim should be to maintain a good nutritional intake by decreasing parenteral and

increasing enteral feed by similar amounts. Enteral tolerance is more likely to be achieved by avoiding excessive fluid intake. In children with more severe IF, enteral feeds may need to be increased as slowly as 1 mL/kg/24 h. If a chosen weaning strategy fails it is worth trying again, but at a slower pace (smaller increments). Overfeeding may promote bacterial overgrowth causing inflammation, increased permeability, sensitisation and allergy, translocation, sepsis and cholestasis [109].

In children who are stable and thriving at home, PN can be reduced by dropping one night/week of PN providing there is no risk of dehydration. If tolerated, further reductions are made by reducing one night at a time over several months. Alternatively, weaning can be facilitated by reducing/halving the PN given one night a week and seeing how well the child tolerates this approach. If fluid and electrolyte loss is the main issue, administration of glucose and electrolyte solution by enteral feeding tube may maintain hydration. In infants a night off PN would usually only be tried when at least 50% of nutrients are being tolerated enterally. Tolerance of a night without PN varies according to the underlying disease, the size of the child and their ability to maintain hydration. A night off is usually well tolerated by children with SBS who are stable and have improving intestinal function, but may be delayed in the presence of bacterial overgrowth and associated enteritis [110]. In children with chronic intestinal pseudo-obstruction, especially with ileostomy and major gastrointestinal fluid losses, increased enteral fluid intake during a night off PN may provoke diarrhoea. The child's ability to tolerate a reduction in PN is assessed by monitoring weight gain, growth and blood indices. Unabsorbed enteral feed in the colon may lead to D-lactic acidosis due to fermentation by the colonic bacterial flora. Although some studies have indicated that bacterial fermentation is more of a problem in the absence of ileocaecal valve [111] (LoE 3), this does not always seem to be the case [110] (LoE 3). This complication may be prevented/treated by a low fibre diet, bicarbonate, and sometimes antibiotics such as metronidazole or the non-absorbable rifaximin; probiotics may also be helpful [110] (LoE 3). Sometimes it is necessary to reduce intestinal nutrient load and increase PN whilst waiting for intestinal adaptation to progress allowing for recommencement or continuation of the weaning process.

3.3. Psycho-social and developmental aspects of feeding

Maintaining small volumes of feeds by mouth is important to prevent oral hypersensitivity and promote the development of oro-motor feeding skills. If continuous feeds are being given, an hours worth of feed can be taken by mouth every 4 h. Solids should be started at the usual recommended age for healthy infants where possible. It is best to limit these initially to a few foods that are least likely to have an allergenic effect (e.g. rice, chicken, carrot) especially if there is intestinal inflammation. Foods should also be suitable for the underlying intestinal disease e.g. low lactose, low in LCT fat or low fibre in short bowel and/or extensive colonic resection. When solids are introduced the aim is to encourage normal textures for age [87] (LoE 4). Maternal bonding can be supported by encouraging involvement with feeding and close contact between mother and child. In younger infants when bolus feeds are required, active involvement of parents may have beneficial psychological and social effects. Feeding by mouth should be a pleasurable experience for both infant and parent. Even if the amount and range of foods are limited, normal feeding behaviour will be promoted and the risk of longer term feeding problems reduced [112]. A proportion of children will remain feeding tube dependent [113,114] but are amenable to specific treatment programmes aimed at establishing full oral feeding [115].

Conflict of interest

None declared.

References

- [1] Jonkers CF, Prins F, Van Kempen A, Tepaske R, Sauerwein HP. Towards implementation of optimum nutrition and better clinical nutrition support. *Clin Nutr* 2001;20:361–6.
- [2] Puntis JWL, Booth IW. The place of a nutritional care team in paediatric practice. Intensive therapy and clinical monitoring. *Intensive Ther Clin Monit* 1990;11:132–6.
- [3] Faubion WC, Wesley JR, Khalidi N, Silva J. Total parenteral nutrition catheter sepsis: impact of the team approach. *J Parenter Enteral Nutr* 1986;10:642–5.
- [4] Jacobs DO, Melnik G, Forlaw L, Gebhardt C, Settle RG, DiSipio M, et al. Impact of a nutritional support service on VA surgical patients. *J Am Coll Nutr* 1984;3:311–5.
- [5] Keohane PP, Jones BJ, Attrill H, Cribb A, Northover J, Frost P, et al. Effect of catheter tunnelling and a nutrition nurse on catheter sepsis during parenteral nutrition. A controlled trial. *Lancet* 1983;2:1388–90.
- [6] Nehme AE. Nutritional support of the hospitalized patient. The team concept. *J Am Med Assoc* 1980;243:1906–8.
- [7] Sanders RA, Sheldon GF. Septic complications of total parenteral nutrition. A five year experience. *Am J Surg* 1976;132:214–20.
- [8] Traeger SM, Williams GB, Milliren G, Young DS, Fisher M, Haug 3rd MT. Total parenteral nutrition by a nutrition support team: improved quality of care. *J Parenter Enteral Nutr* 1986;10:408–12.
- [9] Puntis JW, Holden CE, Smallman S, Finkel Y, George RH, Booth IW. Staff training: a key factor in reducing intravascular catheter sepsis. *Arch Dis Child* 1991;66:335–7.
- [10] Dalton MJ, Schepers G, Gee JP, Alberts CC, Eckhauser FE, Kirking DM. Consultative total parenteral nutrition teams: the effect on the incidence of total parenteral nutrition-related complications. *J Parenter Enteral Nutr* 1984;8:146–52.
- [11] Kennedy JF, Nightingale JM. Cost savings of an adult hospital nutrition support team. *Nutrition* 2005;21:1127–33.
- [12] Gurgueira GL, Leite HP, Taddei JA, de Carvalho WB. Outcomes in a pediatric intensive care unit before and after the implementation of a nutrition support team. *J Parenter Enteral Nutr* 2005;29:176–85.
- [13] Lambe C, Hubert P, Jouvet P, Cosnes J, Colomb V. A nutritional support team in the pediatric intensive care unit: changes and factors impeding appropriate nutrition. *Clin Nutr* 2007;26:355–63.
- [14] Agostoni C, Axelson I, Colomb V, Goulet O, Koletzko B, Michaelsen KF, et al. The need for nutrition support teams in pediatric units: a commentary by the ESPGHAN committee on nutrition. *J Pediatr Gastroenterol Nutr* 2005;41:8–11.
- [15] Duclos A, Touzet S, Restier L, Ocellini P, Cour-Andlauer F, Denis A, et al. Implementation of a computerized system in pediatric wards to improve nutritional care: a cluster randomized trial. *Eur J Clin Nutr* 2015;69:769–75.
- [16] Wales PW, Allen N, Worthington P, George D, Compher C, the American Society for Parenteral and Enteral Nutrition, et al. A.S.P.E.N. clinical guidelines: support of pediatric patients with intestinal failure at risk of parenteral nutrition-associated liver disease. *J Parenter Enteral Nutr* 2014;38:538–57.
- [17] Torres C, Sudan D, Vanderhoof J, Grant W, Botha J, Raynor S, et al. Role of an intestinal rehabilitation program in the treatment of advanced intestinal failure. *J Pediatr Gastroenterol Nutr* 2007;45:204–12.
- [18] Beath S, Pironi L, Gabe S, Horslen S, Sudan D, Mazeriegos G, et al. Collaborative strategies to reduce mortality and morbidity in patients with chronic intestinal failure including those who are referred for small bowel transplantation. *Transplantation* 2008;85:1378–84.
- [19] Cowles RA, Ventura KA, Martinez M, Lobritto SJ, Harren PA, Brodrie S, et al. Reversal of intestinal failure-associated liver disease in infants and children on parenteral nutrition: experience with 93 patients at a referral center for intestinal rehabilitation. *J Pediatr Surg* 2010;45:84–7. discussion 87–88.
- [20] Ba'ath ME, Almond S, King B, Bianchi A, Khalil BA, Morabito A. Short bowel syndrome: a practical pathway leading to successful enteral autonomy. *World J Surg* 2012;36:1044–8.
- [21] Sigalet D, Boctor D, Brindle M, Lam V, Robertson M. Elements of successful intestinal rehabilitation. *J Pediatr Surg* 2011;46:150–6.
- [22] Johnson T, Sexton E. Managing children and adolescents on parenteral nutrition: challenges for the nutritional support team. *Proc Nutr Soc* 2006;65:217–21.
- [23] Murray JS, Mahoney JM. An integrative review of the literature about the transition of pediatric patients with intestinal failure from hospital to home. *J Spec Pediatr Nurs* 2012;17:264–74.
- [24] Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R, G. Parenteral Nutrition Guidelines Working, et al. 1. Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), supported by the European Society of Paediatric Research (ESPR). *J Pediatr Gastroenterol Nutr* 2005;41(Suppl. 2):S1–87.
- [25] Corkins MR, Griggs KC, Groh-Wargo S, Han-Markey TL, Helms RA, Muir LV, et al. Standards for nutrition support: pediatric hospitalized patients. *Nutr Clin Pract* 2013;28:263–76.
- [26] Mehta NM, Corkins MR, Lyman B, Malone A, Goday PS, Carney LN, et al. Defining pediatric malnutrition: a paradigm shift toward etiology-related definitions. *J Parenter Enteral Nutr* 2013;37:460–81.
- [27] Becker P, Carney LN, Corkins MR, Monczka J, Smith E, Smith SE, et al. Consensus statement of the academy of nutrition and dietetics/American society for parenteral and enteral nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition). *Nutr Clin Pract* 2015;30:147–61.
- [28] Myatt M, Khara T, Collins S. A review of methods to detect cases of severely malnourished children in the community for their admission into community-based therapeutic care programs. *Food Nutr Bull* 2006;27:S7–23.
- [29] Mwangome MK, Fegan G, Prentice AM, Berkley JA. Are diagnostic criteria for acute malnutrition affected by hydration status in hospitalized children? A repeated measures study. *Nutr J* 2011;10:92.
- [30] Hulst JM, van Goudoever JB, Zimmermann LJ, Tibboel D, Joosten KF. The role of initial monitoring of routine biochemical nutritional markers in critically ill children. *J Nutr Biochem* 2006;17:57–62.
- [31] Feferbaum R, Delgado AF, Zamberlan P, Leone C. Challenges of nutritional assessment in pediatric ICU. *Curr Opin Clin Nutr Metab Care* 2009;12:245–50.
- [32] Delgado AF, Kimura HM, Cardoso AL, Uehara D, Carrazza FR. Nutritional follow-up of critically ill infants receiving short term parenteral nutrition. *Rev Hosp Clin Fac Med Sao Paulo* 2000;55:3–8.
- [33] Hulst J, Joosten K, Zimmermann L, Hop W, van Buuren S, Buller H, et al. Malnutrition in critically ill children: from admission to 6 months after discharge. *Clin Nutr* 2004;23:223–32.
- [34] Boullata JI, Gilbert K, Sacks G, Labossiere RJ, Crill C, Goday P, et al. A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. *J Parenter Enteral Nutr* 2014;38:334–77.
- [35] Seres D, Sacks GS, Pedersen CA, Canada TW, Johnson D, Kumpf V, et al. Parenteral nutrition safe practices: results of the 2003 American Society for Parenteral and Enteral Nutrition survey. *J Parenter Enteral Nutr* 2006;30:259–65.
- [36] Stewart JAD, Mason DG, Smith N, Protosapa K, Mason M. A mixed bag: an enquiry into the care of hospital patients receiving parenteral nutrition. A report by the National Confidential Enquiry in Patient Outcome and Death. London: NCEPOD; 2010.
- [37] Mason DG, Puntis JW, McCormick K, Smith N. Parenteral nutrition for neonates and children: a mixed bag. *Arch Dis Child* 2011;96:209–10.
- [38] Zamberlan P, Delgado AF, Leone C, Feferbaum R, Okay TS. Nutrition therapy in a pediatric intensive care unit: indications, monitoring, and complications. *J Parenter Enteral Nutr* 2011;35:523–9.
- [39] Skillman HE. Monitoring the efficacy of a PICU nutrition therapy protocol. *J Parenter Enteral Nutr* 2011;35:445–6.
- [40] Potts AL, Barr FE, Gregory DF, Wright L, Patel NR. Computerized physician order entry and medication errors in a pediatric critical care unit. *Pediatrics* 2004;113:59–63.
- [41] Ayers P, Adams S, Boullata J, Gervasio J, Holcombe B, Kraft MD, et al. A.S.P.E.N. parenteral nutrition safety consensus recommendations. *J Parenter Enteral Nutr* 2014;38:296–333.
- [42] Powell M, Martin H, Puntis JWL, Goss I. A study of the impact and the cost-effectiveness of introducing hospital pharmacist prescribing into neonatal parenteral nutrition. *Proc Nutr Soc* 2001;60:P99A.
- [43] Porcelli PJ. Practice ordering guidance for neonatal parenteral nutrition. *J Perinatol* 2007;27:220–4.
- [44] Narula P, Hartigan D, Puntis JWL. The frequency and importance of reported errors related to parenteral nutrition in a regional paediatric centre. *e-SPEN* 2011;6:e131–4.
- [45] Auty B. Advances in infusion pump design. In: Rennie M, editor. *Intensive care Britain 1991*. London: Greycoat Publishing; 1992. p. 95–102.
- [46] Auty B. Infusion equipment. In: Rennie M, editor. *Intensive care Britain 1991*. London: Greycoat Publishing; 1992. p. 138–43.
- [47] Puntis JW, Wilkins KM, Ball PA, Rushton DI, Booth IW. Hazards of parenteral treatment: do particles count? *Arch Dis Child* 1992;67:1475–7.
- [48] Jack T, Boehne M, Brent BE, Hoy L, Koditz H, Wessel A, et al. In-line filtration reduces severe complications and length of stay on pediatric intensive care unit: a prospective, randomized, controlled trial. *Intensive Care Med* 2012;38:1008–16.
- [49] Boehne M, Jack T, Koditz H, Seidemann K, Schmidt F, Abura M, et al. In-line filtration minimizes organ dysfunction: new aspects from a prospective, randomized, controlled trial. *BMC Pediatr* 2013;13:21.
- [50] Foster JP, Richards R, Showell MG, Jones LJ. Intravenous in-line filters for preventing morbidity and mortality in neonates. *Cochrane Database Syst Rev* 2015;8. Art No: CD005248A.
- [51] Chessex P, Laborie S, Nasef N, Masse B, Lavoie JC. Shielding parenteral nutrition from light improves survival rate in premature infants: a meta-analysis. *J Parenter Enteral Nutr* 2017;41:378–83.
- [52] Slicker J, Vermilyea S. Pediatric parenteral nutrition: putting the microscope on macronutrients and micronutrients. *Nutr Clin Pract* 2009;24:481–6.
- [53] Suryadevara S, Celestin J, DeChicco R, Austhof S, Corrigan M, Speerhas R, et al. Type and prevalence of adverse events during the parenteral nutrition

- cycling process in patients being prepared for discharge. *Nutr Clin Pract* 2012;27:268–73.
- [54] Lacaille F, Gupte G, Colomb V, D'Antiga L, Hartman C, Hojsak I, et al. Intestinal failure-associated liver disease: a position paper of the ESPGHAN working group of intestinal failure and intestinal transplantation. *J Pediatr Gastroenterol Nutr* 2015;60:272–83.
- [55] Stout SM, Cober MP. Metabolic effects of cyclic parenteral nutrition infusion in adults and children. *Nutr Clin Pract* 2010;25:277–81.
- [56] Nghiem-Rao TH, Cassidy LD, Polzin EM, Calkins CM, Arca MJ, Goday PS. Risks and benefits of prophylactic cyclic parenteral nutrition in surgical neonates. *Nutr Clin Pract* 2013;28:745–52.
- [57] Jensen AR, Goldin AB, Koopmeiners JS, Stevens J, Waldhausen JH, Kim SS. The association of cyclic parenteral nutrition and decreased incidence of cholestatic liver disease in patients with gastroschisis. *J Pediatr Surg* 2009;44:183–9.
- [58] Collier S, Crough J, Hendricks K, Caballero B. Use of cyclic parenteral nutrition in infants less than 6 months of age. *Nutr Clin Pract* 1994;9:65–8.
- [59] Salvador A, Janeczko M, Porat R, Sekhon R, Moewes A, Schutzman D. Randomized controlled trial of early parenteral nutrition cycling to prevent cholestasis in very low birth weight infants. *J Pediatr* 2012;161:229–233 e1.
- [60] Hartl WH, Jauch KW, Parhofer K, Rittler P, M. Working group for developing the guidelines for parenteral nutrition of the German Association for parenteral nutrition, chapter 11. *Ger Med Sci* 2009;7. Doc17.
- [61] Puntis JW, Hall SK, Green A, Smith DE, Ball PA, Booth IW. Biochemical stability during parenteral nutrition in children. *Clin Nutr* 1993;12:153–9.
- [62] Pichler J, Chomtho S, Fewtrell M, Macdonald S, Hill S. Body composition in paediatric intestinal failure patients receiving long-term parenteral nutrition. *Arch Dis Child* 2014;99:147–53.
- [63] Appleman SS, Kalkwarf HJ, Dwivedi A, Heubi JE. Bone deficits in parenteral nutrition-dependent infants and children with intestinal failure are attenuated when accounting for slower growth. *J Pediatr Gastroenterol Nutr* 2013;57:124–30.
- [64] Diamanti A, Bizzarri C, Basso MS, Gambarara M, Cappa M, Daniele A, et al. How does long-term parenteral nutrition impact the bone mineral status of children with intestinal failure? *J Bone Miner Metab* 2010;28:351–8.
- [65] D'Antiga L, Goulet O. Intestinal failure in children: the European view. *J Pediatr Gastroenterol Nutr* 2013;56:118–26.
- [66] Pakarinen MP, Kurvinen A, Gylling H, Miettinen TA, Pesonen M, Kallio M, et al. Cholesterol metabolism in pediatric short bowel syndrome after weaning off parenteral nutrition. *Dig Liver Dis* 2010;42:554–9.
- [67] Wu J, Tang Q, Feng Y, Huang J, Tao Y, Wang Y, et al. Nutrition assessment in children with short bowel syndrome weaned off parenteral nutrition: a long-term follow-up study. *J Pediatr Surg* 2007;42:1372–6.
- [68] Nightingale JM, Lennard-Jones JE, Gertner DJ, Wood SR, Bartram CI. Colonic preservation reduces need for parenteral therapy, increases incidence of renal stones, but does not change high prevalence of gall stones in patients with a short bowel. *Gut* 1992;33:1493–7.
- [69] Charbit-Henrion F, Chardot C, Ruemmele F, Talbotec C, Morali A, Goulet O, et al. Anastomotic ulcerations after intestinal resection in infancy. *J Pediatr Gastroenterol Nutr* 2014;59:531–6.
- [70] Mutanen A, Lohi J, Heikkilä P, Koivusalo AI, Rintala RJ, Pakarinen MP. Persistent abnormal liver fibrosis after weaning off parenteral nutrition in pediatric intestinal failure. *Hepatology* 2013;58:729–38.
- [71] Barclay AR, Beattie LM, Weaver LT, Wilson DC. Systematic review: medical and nutritional interventions for the management of intestinal failure and its resultant complications in children. *Aliment Pharmacol Ther* 2011;33:175–84.
- [72] Williamson RC. Intestinal adaptation (first of two parts). Structural, functional and cytokinetic changes. *N Engl J Med* 1978;298:1393–402.
- [73] Levine GM, Deren JJ, Steiger E, Zinno R. Role of oral intake in maintenance of gut mass and disaccharide activity. *Gastroenterology* 1974;67:975–82.
- [74] Greene HL, McCabe DR, Merenstein GB. Protracted diarrhea and malnutrition in infancy: changes in intestinal morphology and disaccharidase activities during treatment with total intravenous nutrition or oral elemental diets. *J Pediatr* 1975;87:695–704.
- [75] Johnson LR, Copeland EM, Dudrick SJ, Lichtenberger LM, Castro GA. Structural and hormonal alterations in the gastrointestinal tract of parenterally fed rats. *Gastroenterology* 1975;68:1177–83.
- [76] Feldman EJ, Dowling RH, McNaughton J, Peters TJ. Effects of oral versus intravenous nutrition on intestinal adaptation after small bowel resection in the dog. *Gastroenterology* 1976;70:712–9.
- [77] Andorsky DJ, Lund DP, Lillehei CW, Jaksic T, Dicanzio J, Richardson DS, et al. Nutritional and other postoperative management of neonates with short bowel syndrome correlates with clinical outcomes. *J Pediatr* 2001;139:27–33.
- [78] C.o. Nutrition E, Agostoni C, Braegger C, Decsi T, Kolacek S, Koletzko B, et al. Breast-feeding: a commentary by the ESPGHAN committee on nutrition. *J Pediatr Gastroenterol Nutr* 2009;49:112–25.
- [79] Olieman JF, Penning C, Ijsselstijn H, Escher JC, Joosten KF, Hulst JM, et al. Enteral nutrition in children with short-bowel syndrome: current evidence and recommendations for the clinician. *J Am Diet Assoc* 2010;110:420–6.
- [80] Leaf A, Winterson R. Breast-milk banking: evidence of benefit. *Paediatr Child Health* 2009;19:395–9.
- [81] Gosselin KB, Duggan C. Enteral nutrition in the management of pediatric intestinal failure. *J Pediatr* 2014;165:1085–90.
- [82] Lauriti G, Zani A, Aufferi R, Cananzi M, Chiesa PL, Eaton S, et al. Incidence, prevention, and treatment of parenteral nutrition-associated cholestasis and intestinal failure-associated liver disease in infants and children: a systematic review. *J Parenter Enteral Nutr* 2014;38:70–85.
- [83] Shores RD, Bullard JE, Aucott SW, Stewart FD, Haney C, Nonyane BA, et al. Analysis of nutrition practices and intestinal-failure associated liver disease in infants with intestinal failure. *Infant Child Adolesc Nutr* 2014;7:29–37.
- [84] Braegger C, Decsi T, Dias JA, Hartman C, Kolacek S, Koletzko B, et al. Practical approach to paediatric enteral nutrition: a comment by the ESPGHAN committee on nutrition. *J Pediatr Gastroenterol Nutr* 2010;51:110–22.
- [85] Goulet O, Ruemmele F, Lacaille F, Colomb V. Irreversible intestinal failure. *J Pediatr Gastroenterol Nutr* 2004;38:250–69.
- [86] Bines J, Francis D, Hill D. Reducing parenteral requirement in children with short bowel syndrome: impact of an amino acid-based complete infant formula. *J Pediatr Gastroenterol Nutr* 1998;26:123–8.
- [87] Strudwick S. Gastro-oesophageal reflux and feeding: the speech and language therapist's perspective. *Int J Pediatr Otorhinolaryngol* 2003;67(Suppl. 1):S101–2.
- [88] Vanderhoof JA, Young RJ. Hydrolyzed versus nonhydrolyzed protein diet in short bowel syndrome in children. *J Pediatr Gastroenterol Nutr* 2004;38:107.
- [89] Shiao SL, Su BH, Lin KJ, Lin HC, Lin JN. Possible effect of probiotics and breast milk in short bowel syndrome: report of one case. *Acta Paediatr Taiwan* 2007;48:89–92.
- [90] Heemskerk J, Sie GH, Van den Neucker AM, Forget PP, Heineman E, van Heurn LW. Extreme short bowel syndrome in a full-term neonate—a case report. *J Pediatr Surg* 2003;38:1665–6.
- [91] Mazon A, Solera E, Alentado N, Oliver F, Pamies R, Caballero L, et al. Frequent IgE sensitization to latex, cow's milk, and egg in children with short bowel syndrome. *Pediatr Allergy Immunol* 2008;19:180–3.
- [92] Ventura A, Pineschi A, Tasso M. Cow's milk intolerance and abdominal surgery: a puzzling connection. *Helv Paediatr Acta* 1986;41:487–94.
- [93] Christie DL, Ament ME. Dilute elemental diet and continuous infusion technique for management of short bowel syndrome. *J Pediatr* 1975;87:705–8.
- [94] Brewster D, Kukuruzovic R, Haase A. Short bowel syndrome, intestinal permeability and glutamine. *J Pediatr Gastroenterol Nutr* 1998;27:614–6.
- [95] De Greef E, Mahler T, Janssen A, Cuyppers H, Veereman-Wauters G. The influence of neocate in paediatric short bowel syndrome on PN weaning. *J Nutr Metab* 2010;2010.
- [96] Ksiazyk J, Piena M, Kierkus J, Lyszkowska M. Hydrolyzed versus non-hydrolyzed protein diet in short bowel syndrome in children. *J Pediatr Gastroenterol Nutr* 2002;35:615–8.
- [97] Vanderhoof JA, Young RJ. Enteral and parenteral nutrition in the care of patients with short-bowel syndrome. *Best Pract Res Clin Gastroenterol* 2003;17:997–1015.
- [98] Uko V, Radhakrishnan K, Alkhouri N. Short bowel syndrome in children: current and potential therapies. *Paediatr Drugs* 2012;14:179–88.
- [99] Dehmer JJ, Fuller MK, Helmrath MA. Management of pediatric intestinal failure. *Adv Pediatr* 2011;58:181–94.
- [100] Serrano MS, Schmidt-Sommerfeld E. Nutrition support of infants with short bowel syndrome. *Nutrition* 2002;18:966–70.
- [101] Vanderhoof JA, Young RJ, Thompson JS. New and emerging therapies for short bowel syndrome in children. *Paediatr Drugs* 2003;5:525–31.
- [102] Parker P, Stroop S, Greene H. A controlled comparison of continuous versus intermittent feeding in the treatment of infants with intestinal disease. *J Pediatr* 1981;99:360–4.
- [103] Jawaheer G, Shaw NJ, Pierro A. Continuous enteral feeding impairs gall-bladder emptying in infants. *J Pediatr* 2001;138:822–5.
- [104] Agostoni C, Buonocore G, Carnielli VP, De Curtis M, Darmaun D, Decsi T, et al. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2010;50:85–91.
- [105] Fisher RL. Hepatobiliary abnormalities associated with total parenteral nutrition. *Gastroenterol Clin North Am* 1989;18:645–66.
- [106] Wessel JJ, Kocoshis SA. Nutritional management of infants with short bowel syndrome. *Semin Perinatol* 2007;31:104–11.
- [107] Sigalel D, Lam V, Boctor D, Brindle M. Nutritional support of infants with intestinal failure: something more than fishy is going on here! *Pediatr Surg Int* 2013;29:975–81.
- [108] Cole CR, Kocoshis SA. Nutrition management of infants with surgical short bowel syndrome and intestinal failure. *Nutr Clin Pract* 2013;28:421–8.
- [109] Goulet O, Olieman J, Ksiazyk J, Spolidoro J, Tibboe D, Kohler H, et al. Neonatal short bowel syndrome as a model of intestinal failure: physiological background for enteral feeding. *Clin Nutr* 2013;32:162–71.
- [110] Kaufman SS, Loseke CA, Lupo JV, Young RJ, Murray ND, Pinch LW, et al. Influence of bacterial overgrowth and intestinal inflammation on duration of parenteral nutrition in children with short bowel syndrome. *J Pediatr* 1997;131:356–61.
- [111] Goulet OJ, Revillon Y, Jan D, De Potter S, Maurice C, Lortat-Jacob S, et al. Neonatal short bowel syndrome. *J Pediatr* 1991;119:18–23.

- [112] Cerezo CS, Lobato D, Pinkos B, LeLeiko N. Diagnosis and treatment of pediatric feeding and swallowing disorders. *Infant Child Adolesc Nutr* 2011;3:321–3.
- [113] Wright CM, Smith KH, Morrison J. Withdrawing feeds from children on long term enteral feeding: factors associated with success and failure. *Arch Dis Child* 2011;96:433–9.
- [114] Edwards S, Davis AM, Bruce A, Mousa H, Lyman B, Cocjin J, et al. Caring for tube-fed children: a review of management, tube weaning, and emotional considerations. *J Parenter Enteral Nutr* 2016;40:616–22.
- [115] Wilken M, Cremer V, Berry J, Bartmann P. Rapid home-based weaning of small children with feeding tube dependency: positive effects on feeding behaviour without deceleration of growth. *Arch Dis Child* 2013;98:856–61.