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When Is Parenteral Nutrition Appropriate?

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Abstract

Parenteral nutrition (PN) represents one of the most notable achievements of modern medicine, serving as a therapeutic modality for all age groups across the healthcare continuum. PN offers a life-sustaining option when intestinal failure prevents adequate oral or enteral nutrition. However, providing nutrients by vein is an expensive form of nutrition support, and serious adverse events can occur. In an effort to provide clinical guidance regarding PN therapy, the Board of Directors of the American Society for Parenteral and Enteral Nutrition (ASPEN) convened a task force to develop consensus recommendations regarding appropriate PN use. The recommendations contained in this document aim to delineate appropriate PN use and promote clinical benefits while minimizing the risks associated with the therapy. These consensus recommendations build on previous ASPEN clinical guidelines and consensus recommendations for PN safety. They are intended to guide evidence-based decisions regarding appropriate PN use for organizations and individual professionals, including physicians, nurses, dietitians, pharmacists, and other clinicians involved in providing PN. They not only support decisions related to initiating and managing PN but also serve as a guide for developing quality monitoring tools for PN and for identifying areas for further research. Finally, the recommendations contained within the document are also designed to inform decisions made by additional stakeholders, such as policy makers and third-party payers, by providing current perspectives regarding the use of PN in a variety of healthcare settings.

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Key Terms and Definitions

Intestinal failure: The reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes such that intravenous supplementation is required to maintain health and/or growth.[1]

Intestinal insufficiency (or deficiency): The reduction of gut absorptive function that does not require intravenous supplementation but may require oral supplementation, enteral nutrition, or vitamin and trace element supplementation to maintain health and/or growth.[1]

Malnutrition, adult: An acute, subacute, or chronic state of nutrition in which a combination of varying degrees of overnutrition or undernutrition, with or without inflammatory activity, has led to a change in body composition and diminished function.[2]

The etiology-based nutrition diagnoses in adults in clinical practice settings are as follows:

Starvation-related malnutrition: Chronic starvation without inflammation (eg, anorexia nervosa).

Chronic disease-related malnutrition: Inflammation is chronic and of mild to moderate degree (eg, organ failure, pancreatic cancer, rheumatoid arthritis, sarcopenic obesity).

Acute disease or injury-related malnutrition: Inflammation is acute and of severe degree (eg, major infection burns, trauma, closed head injury).[2,3]

Malnutrition, pediatric: An imbalance between nutrient requirement and intake, resulting in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development, and other relevant outcomes. It is recommended that growth charts based on a standard deviation *z*-score system be used to track and assess nutrition status in children.[4,5]

Nutritionally-at-risk: Consider the individual nutritionally-at-risk if any of the following is present.

Nutritionally-At-Risk Adult

- Involuntary weight loss of 10% of usual body weight within 6 months or 5% within 1 month
- Involuntary loss of 10 lb within 6 months
- Body mass index (BMI) less than 18.5 kg/m^2
- Increased metabolic requirements
- Altered diets or diet schedules
- Inadequate nutrition intake, including not receiving food or nutrition products for more than 7 days[6]

Nutritionally-At-Risk Child

- Weight for length, weight for height, or sex less than 10th percentile (–1.28 *z*-score)
- BMI for age or sex less than 5th percentile (–1.64 *z*-score)
- Increased metabolic requirements
- Impaired ability to ingest or tolerate oral feeding
- Documented inadequate provision of or tolerance to nutrients
- Inadequate weight gain or a significant decrease in usual growth percentile[6]

Nutritionally-At-Risk Neonate

High Risk

- Preterm less than 28 weeks at birth
- Extremely low birth weight less than 1000 g
- Infant establishing feeds after episode of necrotizing enterocolitis or gastrointestinal perforation
- Infants with severe congenital gastrointestinal malformations (eg, gastroschisis)[6]

Moderate Risk

- Preterm 28th–31st weeks, otherwise well
- Intrauterine growth restriction (weight less than 9th percentile)
- Very low birth weight 1000–1500 g
- Illness or congenital anomaly that may compromise feeding[6]

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Summary of Recommendations

These consensus recommendations are designed to identify best practices, guide day-to-day clinical decisions, reduce variations in practice, and enhance patient safety. They are not intended to supersede the judgment of the healthcare professional based on the circumstances of the individual patient.

1: Parenteral Nutrition Use Based on Medical Diagnosis or Disease State

Adult

1A: Do not use parenteral nutrition (PN) based solely on medical diagnosis or disease state.

1B: Prior to initiating PN, conduct a full evaluation of the feasibility of using enteral nutrition (EN); reserve PN for clinical situations in which adequate EN is not an option.

Neonatal

1C: Consider PN for neonates in the critical care setting, regardless of diagnosis, when EN is unable to meet energy requirements for energy expenditure and growth.

Pediatric

1D: Use PN for children when the intestinal tract is not functional or cannot be accessed or when nutrient needs to provide for growth are greater than that which can be provided through oral intake or EN support alone.

2: Circumstances Where PN Is the Preferred Method of Nutrition Support

Adult

2A: Use PN in patients who are malnourished or at risk for malnutrition when a contraindication to EN exists or the patient does not tolerate adequate EN or lacks sufficient bowel function to maintain or restore nutrition status (Tables 1.1 and 1.2).

Neonatal and Pediatric

2B: Initiate PN for total or supplemental nutrient provision if EN is not feasible or not sufficient to meet total nutrient needs.

3: Determining When EN Is Not Feasible

Adult

3A: Evaluate clinical factors derived from history, physical examination, and diagnostic evaluations in determining if EN is contraindicated (Table 3.1).

Neonatal and Pediatric

3B: Initiate PN and withhold EN in neonatal and pediatric patients when a clear contraindication to EN exists, such as intestinal injury and perforation.

3C: Assess intestinal function and perfusion, as well as overall hemodynamic stability, when evaluating readiness for EN, rather than relying on strict adherence to a list of contraindications to EN, such as the presence of umbilical catheters or use of vasoactive medications.

4: Time Frame for Initiating PN

Adult

4A: Initiate PN after 7 days for well-nourished, stable adult patients who have been unable to receive significant (50% or more of estimated requirements) oral or enteral nutrients.

4B: Initiate PN within 3 to 5 days in those who are nutritionally-at-risk and unlikely to achieve desired oral intake or EN.

4C: Initiate PN as soon as is feasible for patients with baseline moderate or severe malnutrition in whom oral intake or EN is not possible or sufficient.

4D: Delay the initiation of PN in a patient with severe metabolic instability until the patient's condition has improved.

Neonatal

4E: Begin PN promptly after birth in the very low birth weight infant (birth weight less than 1500 g). Insufficient data exist to suggest a specific time frame in which PN is ideally initiated in more mature preterm infants or critically ill term neonates.

Pediatric

4F: For the infant, child, or adolescent with a self-limited illness, it is reasonable to delay starting PN for 1 week. However, initiate PN within 1–3 days in infants and within 4–5 days in older children and adolescents when it is evident that they will not tolerate full oral intake or EN for an extended period.

5: Selecting Appropriate Vascular Access for PN Administration

Global Recommendations

5A: Individualize the selection of vascular access device (VAD) for PN administration based on an evaluation of the risks and benefits of the device, clinical factors, and psychosocial considerations.

5B: Choose the smallest device with the fewest number of lumens necessary for the patient's needs.

5C: Dedicate 1 lumen of the VAD for PN administration when possible.

5D: Position the tip of the central venous access device (CVAD) in the lower third of the superior vena cava near the junction with the right atrium.

5E: Confirm optimal position of the CVAD tip prior to initiating PN.

6: Peripheral PN

Adult

6A: Use peripheral PN only for short-term purposes, no more than 10–14 days, as supplemental PN or as a bridge therapy during transition periods, where oral intake or EN is suboptimal or clinical circumstances do not justify placing a CVAD.

6B: Estimate the osmolarity of peripheral PN formulations.

6C: Maintain an upper limit of 900 mOsm/L for the peripheral PN formulations.

Neonatal and Pediatric

6D: In well-nourished neonatal and pediatric patients, use peripheral PN for short-term purposes until oral intake or EN can be established or to serve as a bridge to central PN.

7: Intradialytic PN

Global Recommendations

7A: Do not use intradialytic PN (IDPN) as the sole source of nutrition intervention in malnourished patients with chronic kidney disease (CKD).

7B: Consider IDPN for adult and pediatric patients with CKD who are malnourished and unable to tolerate adequate oral intake or EN.

8: Perioperative PN

Adult

8A: Consider preoperative PN in severely malnourished patients unable to tolerate sufficient oral intake or EN.

8B: Reserve postoperative PN for severely malnourished patients unable to tolerate EN for more than 7 days, unless initiated preoperatively.

Neonate and Pediatric

8C: Consider preoperative and postoperative PN in malnourished neonates and children who are unable to tolerate oral intake or EN.

9: PN Use in Palliative Care

Global Recommendations

9A: Do not use PN solely to treat poor oral intake and/or cachexia associated with advanced malignancy.

9B: Limit the use of PN in palliative care to carefully selected candidates, with an expected survival of 2–3 months, for whom oral intake or EN is not feasible.

9C: Evaluate clinical factors and performance status when selecting candidates for PN at the end of life.

9D: Involve patients and caregivers in a clear and complete dialogue regarding realistic goals of PN as well as the potential risks and burdens of therapy.

10: Home PN

Adult

10A: Consider home PN (HPN) for patients with intestinal failure who are clinically stable and able to receive therapy outside an acute care setting.

10B: Perform a thorough evaluation of medical and psychosocial factors that influence suitability for HPN.

10C: Address financial considerations/insurance coverage and patient responsibilities with patient and caregiver.

Pediatric

10D: Consider HPN for carefully selected, clinically stable pediatric patients who are expected to require PN for an extended period.

10E: Discharge all pediatric patients to the care of a pediatric home care team and infusion provider with pediatric experience.

11: Initiating PN in the Home Setting

Adult

11A: Establish organizational policies that delineate circumstances in which initiation of PN can take place outside the acute care setting.

11B: Delineate patient-centered eligibility criteria for initiating PN safely in the home setting.

11C: Develop strict protocols and procedures for initiating PN in the home setting, monitoring response to therapy, and documenting outcomes.

11D: Conduct a comprehensive medical, clinical, and psychosocial assessment of HPN candidates to assess risk factors for adverse events related to initiating PN.

11E: Consider initiating PN therapy at home only when assessment confirms that the benefits greatly outweigh the risks.

Pediatric

11F: In pediatric patients, do not initiate PN in the home setting; admit all patients to the hospital for initiating HPN.

12: Reducing the Risk of PN-Associated Complications

Global Recommendations

12A: Employ standardized processes for managing PN.

12B: Incorporate measures to reduce the risk of complications into organizational policies and procedures for administering PN.

12C: Utilize an interprofessional team of clinicians with expertise in nutrition support to manage PN.

12D: Educate PN prescribers, and demonstrate prescribing competencies for all clinicians writing PN orders.

13: PN Monitoring

Global Recommendations

13A: For patients of all ages and in all healthcare settings, provide interprofessional monitoring of clinical status and response to PN therapy by clinicians with expertise in managing PN.

13B: Modify the PN prescription as indicated per ongoing evaluation of gastrointestinal function, nutrition status, electrolyte balance, and (for pediatric patients) growth.

1: Wean PN when oral intake and/or EN achieves 50%–75% of requirements for energy, protein, and micronutrients, unless impaired gastrointestinal function precludes 100% absorption of nutrient needs.

2: Consider using a weaning protocol during the transition from PN to EN.

14: Tracking Appropriateness of PN Use

Adult

14A: Conduct a clinical review for each patient to assess PN appropriateness prior to compounding the PN admixture.

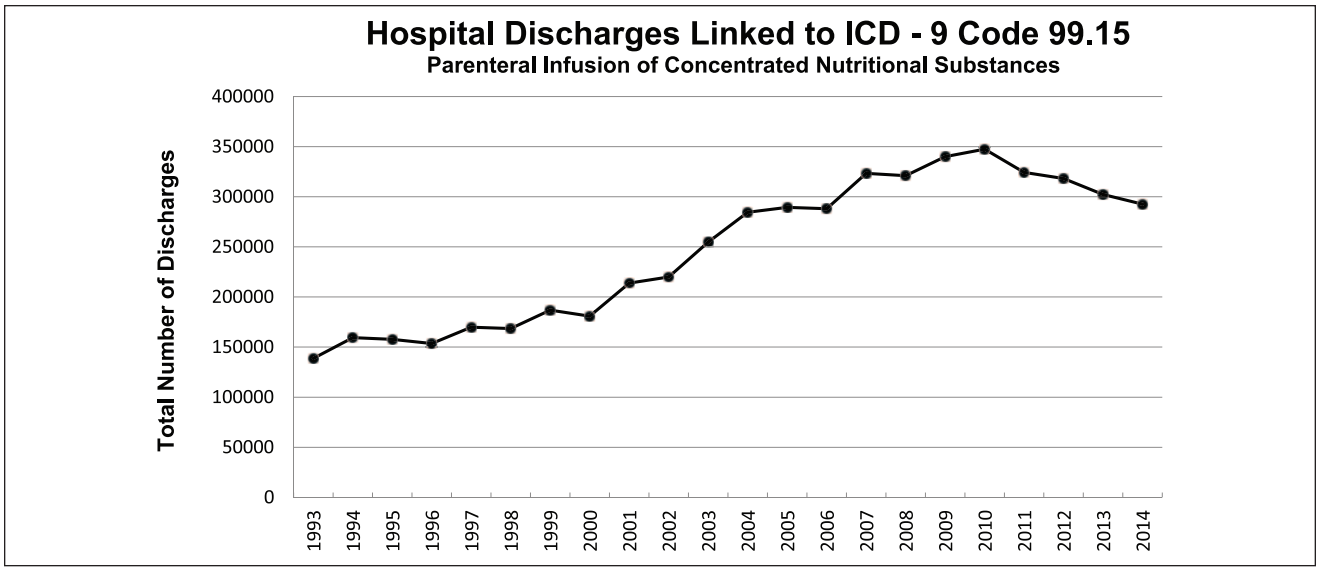

Figure 1. Total number of hospital discharges with the *ICD-9* code of 99.15, parenteral nutrition, 1993–2014. Data from National Inpatient Sample of the Healthcare Cost and Utilization Project from the Agency for Healthcare Research and Quality. http://hcupnet.ahrq.gov/. Accessed November 22, 2016.

14B: Implement a quality improvement process (eg, clinical audit, plan-do-study-act cycle, medication use evaluation) to ensure appropriate use of PN based on the best available evidence.

Pediatric

14C: Emphasize the measurement of PN appropriateness in neonates, children, and adolescents as a priority in institutional quality improvement efforts.

14D: Design metrics for monitoring PN appropriateness for each pediatric healthcare network or institution with available information technology and personnel resources to measure and adjust local practices.

15: Areas for Further Research

Introduction

Background

Since its inception nearly 50 years ago, PN has transformed clinical care while triggering an enduring debate about the role of intravenous nutrition in a variety of patient populations.[1] PN offers a life-sustaining option in situations where impaired gastrointestinal function prevents oral intake or EN. Yet, randomized controlled trials have not consistently demonstrated the effectiveness of PN administration, including studies comparing PN with EN or PN with the standard progression from intravenous fluids to an oral diet, with no nutrition intervention.[2] In fact, in some cases, PN administration appeared to contribute to unfavorable clinical outcomes.[2] It has been suggested that disparities in study design and the use of clinical practices now considered suboptimal may have contributed to the unfavorable results of these studies.[3,4] The use of PN in patients with sufficient gastrointestinal function to allow successful EN may also contribute in unfavorable outcomes in comparisons of PN with EN. In addition, a failure to consider metabolic and pathophysiologic patient characteristics when interpreting and designing nutrition studies may be a factor in the lack of evidence supporting the effectiveness of PN.[5]

Historical prescribing patterns for PN may also have influenced outcomes. Early enthusiasm for intravenous feeding led to extensive use of PN for a broad range of medical conditions, at times irrespective of nutrition status or gastrointestinal function.[3,4,6,7] More recent studies conducted with modern protocols for management of PN suggest that PN can be safely administered to critically ill patients without adversely affecting outcomes.[8,9] Although many questions about PN therapy remain unanswered, it is clear that judicious selection of candidates and adherence to evidence-based clinical practice guidelines form the foundation of appropriate PN therapy.

Trends in PN Use

Comprehensive data related to patterns of PN utilization are scarce. One large-scale description of PN use in U.S. hospitals revealed that PN was administered most frequently in non–critical care settings, followed by neonatal intensive care units and intensive care units.[10] In this study, duration of PN averaged 6.5 days and 6.1 days for noncritical care patients and critically ill patients, respectively, with a longer duration (8.9 days) in neonatal intensive care units. The average age of adults receiving PN was 66 years, older than the mean age of the entire study population.[10] Another recent report of PN use found that 12.8% of adults receiving PN were 80 years of age or older with outcomes similar to those of their younger counterparts.[11]

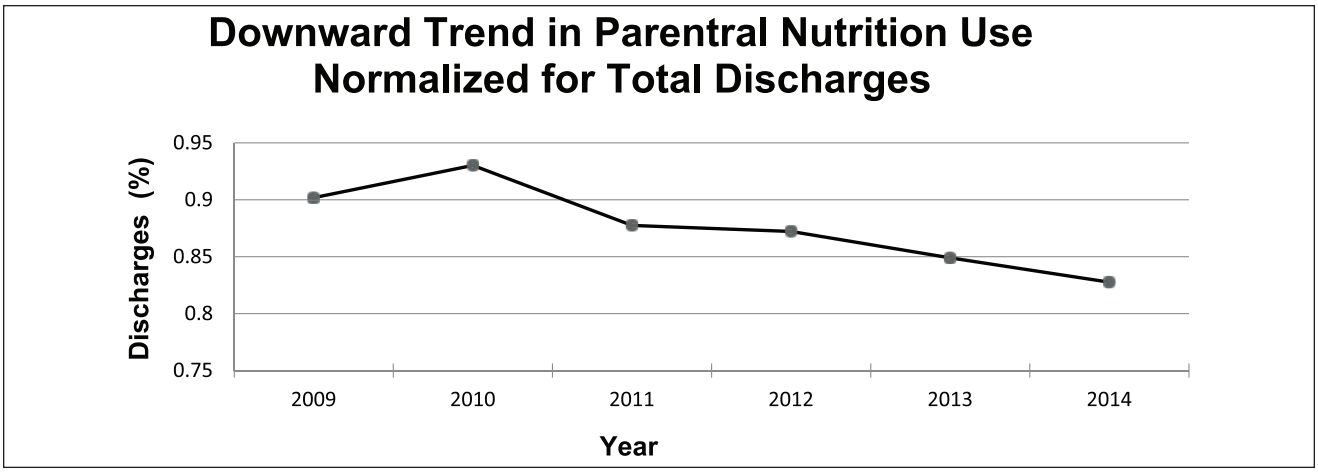

Figure 2. Parenteral nutrition utilization as a percentage of total hospital discharges. Data from National Inpatient Sample of the Healthcare Cost and Utilization Project from the Agency for Healthcare Research and Quality. http://hcupnet.ahrq.gov/. Accessed November 22, 2016.

Information derived from hospital discharges regarding trends in PN use indicates that after more than tripling in the years from 1993 to 2010, PN use has declined for 4 consecutive years.[12,13] Figure 1 depicts this trajectory. In 2014, the most recent year for which data are available, the *ICD-9* code for PN was linked to 292,655 hospital discharges, a statistically significant drop from levels reported in 2010 ($P < .01$). This downward trend persists when the data are normalized for total hospital discharges, which have also fallen in recent years.[13] As shown in Figure 2, PN use fell from 0.93% of hospital discharges in 2010 to 0.82% in 2014. When stratified by age, the data show that PN utilization has remained stable in patients less than 1 year of age, at approximately 0.3% of hospital stays. The steepest decline—from 0.24% to 0.19%—took place in adults aged 65 years or older. Additional data gathered in a large retrospective cohort study from 2001–2008 suggest that a decline in PN use occurred among critically ill adults in the years before the downward trend became evident in national database statistics.[14]

No studies have examined the reasons underlying these trends, but a number of factors in today's healthcare environment could play a role, including greater adherence to guidelines and practice recommendations, changing perceptions regarding the risks and benefits of PN administration, cost-containment efforts, drug shortages, and concern regarding the hazards of excess fluid administration in critically ill patients.[12,14] Although this information sheds some light on current trends in PN use, the available data address only PN administered in hospitals and do not include individuals who receive PN outside the acute care setting, which has expanded across the continuum of care to include long-term acute care, skilled nursing facilities, rehabilitation centers, and home care. However, no comprehensive data are available to suggest an increased use of PN outside of hospitals.

Appropriate PN Therapy

The broad range of healthcare settings in which PN therapy currently takes place, combined with the decline in dedicated nutrition support teams, raises the potential for gaps to exist in the expertise of the clinicians initiating and managing PN therapy.[15] Within this context, efforts to delineate appropriate PN use aim to promote clinical benefits while minimizing the risks associated with the therapy.[16] This process begins with recognizing clinical indications for PN as well as situations in which PN is not likely to be of benefit. After the judicious selection of candidates, appropriate PN use continues with developing a PN prescription that meets individual requirements, monitoring the response to therapy, adjusting the therapeutic plan as indicated, and ensuring a prompt, seamless transition when PN is no longer required. A collaborative approach that crosses professional and departmental boundaries is an essential component of appropriate PN therapy. The recommendations found in this document build on previous ASPEN PN safety initiatives, including "A.S.P.E.N. Clinical Guidelines: Parenteral Nutrition Ordering, Order Review, Compounding, Labeling, and Dispensing" and "A.S.P.E.N. Parenteral Nutrition Safety Consensus Recommendations."[16,17]

Target Audience and Scope

In the spring of 2014, the ASPEN Board of Directors convened an interprofessional task force composed of physicians, nurses, dietitians, and pharmacists, charged with examining clinical questions surrounding PN use. In the initial phase of this project, the group decided against developing a paper narrowly focused on *indications* for PN based on medical diagnosis, in favor of a document that provides guidance on the *appropriate use* of PN therapy in a variety of clinical circumstances. Thus, the recommendations found in this paper extend beyond the selection of candidates to include additional factors that constitute appropriate PN therapy, such as those shown in Table 1.

This document addresses PN use in adult, pediatric, and neonatal populations—in all phases of the lifespan and across the healthcare continuum. Recommendations specific to geriatric patients are included as warranted by supporting literature. The consensus recommendations are intended to

Table 1. Elements of Appropriate PN Use.

• Identify clinical indications for PN, including manifestations of acute and chronic intestinal failure
• Recognize situations in which PN is not likely to be of benefit
• Initiate PN based on gastrointestinal function, nutrition status, and clinical status
• Select the vascular access device best suited to the therapy planned
• Implement measures to promote safety and reduce adverse outcomes
• Evaluate response to therapy
• Adjust in the therapeutic plan based on ongoing monitoring
• Assess continued need for PN
• Transition promptly to oral or enteral nutrition as feasible
• Collaborate across disciplines and departmental boundaries

PN, parenteral nutrition.

provide clinical guidance regarding PN therapy for organizations and individual professionals, including physicians, nurses, dietitians, and pharmacists. They not only support decisions related to initiating and managing PN but also serve as a guide for developing quality monitoring tools for PN and for identifying areas for further research. Finally, the recommendations contained within the document are designed to inform decisions made by additional stakeholders, such as policy makers and third-party payers, by providing current perspectives regarding the use of PN in a variety of healthcare settings.

Format of PN Consensus Recommendations

In contrast to clinical practice guidelines developed by ASPEN, this paper addresses questions regarding the appropriate use of PN for which the strength of the evidence in the literature does not support GRADE level recommendations, instead relying on weaker supporting literature, expert opinion, and consensus recommendations. In a departure from previous ASPEN standards, the consensus recommendations for each question appear as concrete action statements without qualifiers such as "shall," "should," or "may."

These recommendations are not clinical guidelines as defined by ASPEN; however, the need to deliver clinical practice information to clinicians, even when it is of a consensus nature from practice experts, remains an important role of ASPEN (www.nutritioncare.org). In the absence of high-quality evidence applicable to all clinical circumstances, the consensus recommendations are designed to identify best practices, guide day-to-day clinical decisions, reduce variations in practice, and enhance patient safety. These recommendations are not intended to supersede the judgment of the healthcare professional based on the circumstances of the individual patient.

Methodology

The interprofessional members of the task force identified key decision points and clinical management issues related to appropriate PN therapy. From this outline, the group developed questions that were revised through a series of meetings until agreement was reached regarding the scope and relevance of each question. Both adult and pediatric clinical experts contributed to the responses to each question.

Literature searches were then performed with keywords related to the topic *parenteral nutrition and intravenous nutrition*, both as individual terms and in combination with modifiers such as *indications*, *outcomes*, *adverse events, complications*, *standards*, *adult*, *neonate*, *pediatric*, *child*, and *geriatric.* Additional keyword searches were conducted to include the focus of each question, including *enteral nutrition contraindications, malnutrition, nutrition screening, perioperative, peripheral PN, intradialytic PN, home PN, palliative care, monitoring*, and *quality assurance*. The literature search included MEDLINE, PubMed, Cochrane Database of Systemic Reviews, the National Guidelines Clearinghouse, and an Internet search with the Google Scholar search engine for scholarly articles, as well as manual searches of bibliographies for full-text articles published in English through an end date of September 2016. Abstracts, theses, conference reports, and other forms of "gray literature" were not included.

Despite extensive clinical experience with PN across the healthcare continuum, relatively few high-level controlled studies address outcomes of PN administration in patients who are not critically ill. Overall, the available papers displayed considerable heterogeneity in quality and methodology. The panel gave preference to randomized controlled trials, but other sources of evidence were used to support the recommendations, including nonrandomized cohort trials, prospective observational studies, and retrospective case series. In addition to consulting ASPEN clinical practice guidelines and consensus recommendations,[16-18] the panel examined relevant guidelines from other professional societies to assess congruence and variations in practice among other countries.

The recommendations are presented in a question-and-answer format addressing clinical scenarios that nutrition support clinicians commonly encounter. Given the limitations of the available evidence, the recommendations are stated as consensus statements based on expert opinion.

Conflict of Interest

All authors completed an ASPEN conflict of interest form for copyright assignment and financial disclosure. No input or funding for this project came from industry, and no industry representatives participated in the task force meetings.

Review Process

The paper underwent a series of reviews throughout all phases of its development and was approved by the ASPEN Board of Directors.

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Question 1: Is PN ever routinely indicated for any specific medical diagnosis, clinical condition, or disease state?

Recommendations

Adult

1A: Do not use PN based solely on medical diagnosis or disease state.

1B: Prior to initiating PN, conduct a full evaluation of the feasibility of using EN; reserve PN for clinical situations in which adequate EN is not an option.

Neonatal

1C: Consider PN for neonates in the critical care setting, regardless of diagnosis, when EN is unable to meet energy requirements for energy expenditure and growth.

Pediatric

1D: Use PN for children when the intestinal tract is not functional or cannot be accessed or when nutrient needs to provide for growth are greater than that which can be provided through oral intake or EN support alone.

Rationale

Recommendation 1A: Determining the need for PN is not exclusively diagnosis dependent. As a medical therapy, PN has not been shown to heal or treat any specific disease or medical condition other than malnutrition. In cases where previously healthy patients have experienced an acute gastrointestinal catastrophe, such as extensive intestinal necrosis, PN is used to prevent the malnutrition that would inevitably develop without nutrition intervention. The primary intent of PN is to deliver nutrients that support physiologic needs while targeted medical interventions take place, in situations where oral intake or EN is not feasible.[1,2] (Refer to Question 4 for more information regarding timing.) The importance of providing adequate nutrition during times of illness and catabolism has been extensively researched. Surgeons in the early 20th century associated poor clinical outcomes in patients with low body weight, as compared with those with normal body weight or adequate baseline nutrition.[3] Despite the general acceptance of the interplay among illness, nutrition, and outcomes, determining which patients will likely benefit from PN remains a clinical dilemma.

In 2001, a landmark technical review of 82 randomized controlled trials (RCTs) evaluated the clinical efficacy of PN versus standard therapy both globally and by specific disease state.[2] The investigators examined data covering a range of medical conditions for which PN was commonly prescribed. Only a very limited set of PN recipients garnered any benefit in regard to complications and mortality.[2] Overall, the majority of RCTs failed to show a benefit attributable to PN, and in some cases, PN actually appeared to cause harm, most notably by contributing to higher rates of infectious complications.[2] A number of limitations plagued these RCTs, including small sample sizes, significant heterogeneity, failure to control for severity of illness, and the exclusion of those who would go more than 2 weeks without nutrition.[2] In addition, due to ethical concerns, most RCTs excluded severely malnourished patients, eliminating the group that would be most likely to benefit from nutrition intervention. In some studies, PN was also provided to well-nourished patients, thus potentially including individuals without a clear need for PN. As a result, the findings of many early PN studies cannot be extrapolated to severely malnourished patients.[4-6]

Early trials with PN commonly delivered 30–35 calories per kilogram of body weight, a practice that is no longer

routinely employed. "Hyperalimentation" was based on the premise that if adequate nutrition was good, more would prove better—once considered a standard for PN delivery.[4-6] The provision of nutrients in excess of requirements is associated with an array of physiologic problems that contribute to unfavorable outcomes, including hyperglycemia, hepatic dysfunction, infections, and respiratory compromise.[2,4-6] Many of these studies took place in an era where the accepted range for blood glucose levels was much higher than that set by today's standards.[5] For example, the increase in septic complications described in the Veterans Affairs PN Cooperative Study was originally attributed to the lipid component of the PN formula; however, it is now recognized that aggressive feeding protocols and poor glycemic control likely contributed to the unfavorable outcomes seen in this trial.[4,7] Finally, the results of older PN outcome studies reflect the impact of outdated standards of care for vascular access devices. Although PN is an independent risk factor for infection, the institution of "care bundles" for the insertion and maintenance of central venous access devices has reduced infection rates, curtailing one of the most common and serious adverse events associated with PN administration.[8]

In contrast, more recent trials of PN use in critically ill patients suggest that PN may not contribute to adverse events, particularly regarding infectious complications.[9,10] These studies challenge the perception of harm linked to PN administration. Both trials took place under conditions in which current standards for glycemic control and nutrient intake were employed, providing evidence that much of the harm previously associated with PN can largely be avoided. Further research that incorporates current standards of care is needed to more clearly define the role of PN and its associated risks in a variety of clinical circumstances and patient populations, as well as across the continuum of clinical settings from intensive care to home care.

Recommendation 1B: Although PN serves as a life-sustaining treatment in situations where impaired gastrointestinal function precludes adequate nutrition intake, clinical practice guidelines uniformly support the use of EN as the preferred route of nutrition delivery.[11-14] Therefore, the feasibility of such an approach should be fully evaluated before initiating PN. In recent years, therapeutic diet interventions, improvements in enteral access, protocols for EN administration, and specialized enteral formulas have led to a broader definition of "functional gut." These developments allow successful oral intake and EN in patients with medical conditions once thought to require bowel rest. For example, studies of EN in severe acute pancreatitis demonstrate an association between EN administration and favorable clinical outcomes, including decreased rates of mortality, infectious complications, organ failure, and surgical interventions.[15-21]

Numerous studies also suggest benefits of EN versus PN in critically ill patient populations.[14] Beneficial outcomes associated with EN include reductions in infections (pneumonia, central line infections, abdominal abscess), cost of (nutrition) therapy, and hospital length of stay.[22-24] Several meta-analyses comparing the 2 routes of nutrition support provide further support regarding benefits for those receiving EN during a critical illness.[23,25-29] Detailed recommendations for nutrition support in the intensive care unit can be found in the Society of Critical Care Medicine and ASPEN 2016 "Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient."[14]

Factors other than disease state should guide decisions regarding the initiation of PN, including ability to safely access the gut,[30] severity of disease (catabolic state or critical illness),[4,14,30] baseline nutrition status of the patient,[4,14,30] timing of starting PN and anticipated length of therapy,[2,4] medical interventions aimed at promoting EN (including prior attempts to gain enteral access),[30] metabolic stability,[30] and end-of-life considerations.[14,30] Table 1.1 provides more information about clinical scenarios in which PN may be required.

Medical diagnosis does not definitively determine the need for PN, even for disorders closely associated with intestinal failure (IF). Patients with IF lack sufficient gut function to maintain the minimal macronutrient, water, and/or electrolyte absorption to foster health and/or growth, a situation that often results in long-term dependence on PN.[31,32] Short bowel syndrome (SBS) accounts for the majority of cases of IF, but additional pathophysiologic causes include intestinal fistula, gastrointestinal motility disorders, mechanical obstruction, and extensive small bowel mucosal disease.[32] These aberrations can be the consequence of mesenteric ischemia, Crohn's disease, radiation enteritis, malignancy, trauma, surgical complications, volvulus, or congenital villus atrophy.[2,32-38] Not all patients with these conditions develop IF. Some exhibit symptoms better described as intestinal insufficiency, a disorder that shares similar characteristics to IF but with important differences. Patients with intestinal insufficiency do not require intravenous supplementation. Instead, goals for health and growth may be achieved through oral supplementation, EN, or vitamin and trace element supplementation, alone or in combination.[32]

With IF, the need for PN typically falls along some point on a continuum between complete PN dependence and nutrition autonomy. PN administration may provide the patient's total nutrition requirements, or for those with some degree of absorptive capacity, PN serves as a supplement to oral intake or EN. To better identify this situation, the European Society for Clinical Nutrition and Metabolism endorses a classification system to delineate IF based on the onset of the condition and parenteral support requirements.[32] See Table 1.2 for the 3 types of IF in detail. The need for PN is often dynamic. PN dependence may fluctuate over time with changes in clinical status or during exacerbations or remissions in the underlying gastrointestinal condition, underscoring the importance of ongoing

Table 1.1. Examples of Conditions Likely to Require Parenteral Nutrition Across the Life Cycle.[31,32,36,38]

Category	Example	Clinical Features
Impaired absorption or loss of nutrients	Short bowel syndrome, complications of bariatric surgery, intestinal atresia, gastroschisis, volvulus, meconium ileus, necrotizing enterocolitis, mesenteric thrombosis, trauma	Bowel length—adults: 60 cm with colon in continuity, 120 cm without colon in continuity Neonate and pediatric: Inability to meet nutrient, electrolyte, and fluid requirements regardless of intestinal length Weight loss, failure to thrive, fluid and electrolyte disturbances
	High output intestinal fistula (more than 500 mL/d)	Bypasses significant absorptive mucosal area; location precludes enteral access or high-volume output with enteral nutrition
	Neutropenic colitis	Typhlitis or opportunistic infection in an immune-compromised patient
	Small bowel mucosal disease • Radiation or chemotherapy related enteritis • Congenital diseases (microvillus inclusion disease, tufting enteropathy) • Autoimmune enteropathy • Intractable diarrhea of infancy	Intractable diarrhea, weight loss, failure to thrive, unresponsive to medical management
Mechanical bowel obstruction	Intrinsic or extrinsic blockage of intestinal lumen • Stenosis or strictures • Inflammatory disease • Peritoneal carcinomatosis • Severe adhesive disease • Severe superior mesenteric artery syndrome	Recurrent or intractable vomiting, limited oral intake Unamenable to medical, surgical, or interventional treatment (placement of stent or enteral access device)
Need to restrict oral or enteral intake: bowel rest	Ischemic bowel	Mesenteric artery stenosis, intestinal angina, abdominal compartment syndrome, or low flow states
	Severe pancreatitis	Increased pain or serum lipase levels with enteral nutrition, infected pancreatic phlegmon or pseudocyst, complex pancreatic fistula, abdominal compartment syndrome
	Chylous fistula	Increased output with low-fat diet or elemental formula
	Preoperative status	Severely malnourished adults with nonfunctional gastrointestinal tract for 7–10 d prior to surgery
Motility disorders	Prolonged ileus	Diffuse peritonitis or related to medical treatment or other disease state Time to intervention varies per nutrition and clinical status
	Pseudo-obstruction, scleroderma, visceral organ myopathy, very long segment Hirschsprung's disease	Failure to tolerate adequate oral intake or enteral nutrition
	Severe adhesive disease	"Frozen abdomen" with chronic obstructive symptoms and malnutrition
Inability to achieve or maintain enteral access	Varies with clinical circumstances	Hemodynamic instability, active gastrointestinal bleeding, severe neutropenic fever, or low birth weight infant

monitoring and reassessment of the feasibility of EN. In SBS, the degree of intestinal function varies depending on anatomic bowel length, specific location of the resection, integrity of the bowel mucosa, presence of underlying disease, and ability to adapt or compensate with diet and medication over time.[31-34] Initially, these patients may rely heavily on PN or treatment with intravenous fluid and electrolytes, but as adaptation occurs, some individuals will achieve various levels of nutrition autonomy with the help of diet modifications and medications.[31,34]

Table 1.2. Intestinal Failure Categories Based on Onset and Parenteral Support Requirements.[32]

Category	Intestinal Dysfunction	Nutrition Support Requirements
Type I	A common, acute, short-term, and self-limiting condition, which occurs following abdominal surgery or in association with certain critical illness. Condition typically lasts less than 14 d.	Generally requiring short courses of intravenous fluid and/or nutrition support.
Type II	A prolonged, acute condition; often in septic, metabolically unstable patients, requiring complex multidisciplinary care Often occurs in association with an intra-abdominal catastrophe. May also include an acute complication of Type III, resulting in an "acute on chronic" condition.	Requires intravenous supplementation over periods of weeks or months.
Type III	Chronic condition in metabolically stable patients; condition may be reversible or irreversible.	Requiring intravenous supplementation over months or years (including lifelong).

Neonatal Considerations

Recommendation 1C: Although a list of neonatal diagnoses warranting the use of PN may be compiled, perhaps a more appropriate context to consider is the neonate's lack of significant nutrient stores as well as the substantial energy requirement for growth in contrast to energy expenditure in adults, on a per-body-weight basis.[39,40] Suboptimal growth during hospitalization is well documented in the neonatal population, and insufficient parenteral energy is a major contributor to this morbidity.[41-45] For preterm infants or critically ill term infants, intestinal dysfunction or concerns of impaired intestinal perfusion may cause slow introduction and advancement of EN.[46,47] Therefore, constant attention must be paid to providing adequate energy for growth, regardless of the diagnosis; if sufficient intake cannot be provided via EN, then PN is warranted.

Justification for optimal energy delivery throughout hospitalization is the direct association between early growth and neurodevelopment.[48,49] Parenteral nutrients, specifically protein, even in the first days of life may have lasting effects on growth and neurodevelopment.[50-52] Although recommended doses are published, the precise dose of parenteral macronutrients in relation to total energy is not yet defined, and increasing parenteral protein delivery has not always been associated with benefits in growth and development.[53] Despite critical illness, PN promotes an anabolic state in the neonate.[43,54,55] Although a substantial portion of data exists for the very low birth weight population (birth weight less than 1500 g), limited data suggest benefit in short-term growth by providing PN soon after birth in more mature preterm infants.[56] Results from ongoing clinical trials will further understanding regarding influences of early PN exposure on infant development.[57]

Surgical neonates are at high risk for inadequate energy intake early in life and in the perioperative period without the use of PN. A congenital anomaly requiring surgery in the neonatal period is associated with poor growth throughout the first year of life, and inadequate nutrition is a contributing factor.[58,59] Infants with congenital gastrointestinal disorders requiring surgery, such as gastroschisis, may not receive EN before 2 weeks of age and may not reach full EN until after 2 months of age.[60,61] For neonates with congenital heart disease, the postoperative period requires fluid restriction and multiple intravenous medication continuous infusions, which limit the ability to provide sufficient parenteral energy to meet even resting energy expenditure requirements.[62] PN is a mitigating factor of poor growth in infants born with congenital heart disease.[63,64] Question 4 discusses relevant concerns regarding when to initiate PN in neonates.

Pediatric Considerations

Recommendation 1D: In older infants and children, just as in neonates, metabolic reserves are more limited, and energy requirements are higher than in adults. A key difference between the pediatric patient and the adult patient is the requirement for sufficient nutrients for growth.[65] Specifically, protein, lipid, and glycogen stores are lower in infants and children as compared with adults.[66-69] The energy and protein requirements based on weight are higher in infants and children than in adults.[70] Because of this, the importance of providing nutrition early in an infant's or child's course is more critical. If the gastrointestinal tract cannot be expected to support full nutrition, which includes providing adequate nutrition for growth, some supplemental PN support should be provided.[71,72]

Just as for adults, the specific indications for supplemental PN are based on intestinal function, disease severity, and the ability to gain enteral access. The benefits of providing even small amounts of trophic EN to the intestinal tract include promoting bowel adaptation and minimizing potential PN complications. In each indication discussed here, PN should be used when oral nutrient intake or EN is either impossible or inadequate by itself to meet the child's nutrition needs.

IF, which has been defined by the inability of the gastrointestinal tract to absorb and digest adequate nutrients and fluids to sustain life and allow for growth in children without some PN support, is the clearest indication for PN.[73-75] The etiology of IF has been divided in to 3 categories: anatomic, mucosal,

and neuromuscular. Anatomic disorders include congenital or acquired causes of a decrease in intestinal length (SBS), such as atresias, gastroschisis, volvulus, meconium ileus, necrotizing enterocolitis, thromboses, and trauma. Mucosal disorders include microvillus inclusion disease, tufting enteropathy, autoimmune enteropathies, and other intractable diarrheas. Neuromuscular disorders include chronic intestinal pseudo-obstruction, very long segment Hirschsprung's disease, and mitochondrial disorders.[73] In some cases, IF is irreversible and requires lifelong PN or intestinal transplantation. In other cases, PN is required until full enteral autonomy can be achieved over months to years, which is often the case in SBS.

Children with chronic liver disease (eg, biliary atresia) who are awaiting liver transplant frequently have malnutrition due to the impact of organomegaly and ascites on gastric capacity, malabsorption associated with cholestasis, and increased energy requirements. It may not be possible to overcome this with EN alone. Since malnutrition is associated with worse pretransplant and posttransplant outcomes, PN use is warranted.[76]

In children with single ventricle physiology, growth failure is common and can adversely affect surgical and long-term neurodevelopmental outcomes. Contributing to poor nutrition is the impact of the cardiac condition itself on the gastrointestinal tract, need for fluid restriction, and high metabolic demands. The Feeding Work Group of the National Pediatric Cardiology Quality Improvement Collaborative strongly recommends PN early in the preoperative period and continuing postoperatively until EN is tolerated.[77]

In other conditions, the use of PN is limited to those who are unable to tolerate adequate oral intake or EN (see Question 4) or have preexisting malnutrition. This includes the critically ill[78] and those who have cancer, inflammatory bowel disease, or renal failure. For patients who are undergoing treatment for cancer or have received a stem cell transplant, PN use is reserved for situations characterized by severe mucositis, typhlitis, intestinal obstruction, and intractable vomiting.[79] With inflammatory bowel disease, PN has little use except in the case of fistulae, obstruction, toxic megacolon, and bowel resection resulting in SBS. In pediatric patients with chronic kidney disease, PN is indicated only if the child is unable to take in enough enterally to prevent malnutrition, which can occur when there is accompanying gastrointestinal dysfunction.[80]

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Question 2: Are there any circumstances in which PN is the optimal/preferred route for nutrition support?

Recommendations

Adult

2A: Use PN in patients who are malnourished or at risk for malnutrition when a contraindication to EN exists or the patient cannot tolerate adequate EN or lacks sufficient bowel function to maintain or restore nutrition status due to gastrointestinal dysfunction.

Neonatal and Pediatric

2B: Initiate PN for total or supplemental nutrient provision if EN is not feasible or not sufficient to meet total nutrient needs.

Rationale

Recommendation 2A: Nutrition support is indicated in patients who are malnourished or at risk for developing malnutrition.[1,2] In these cases, EN support has been generally accepted as the first line of nutrition support.[3] This preference for EN encompasses more than just protein and energy supplementation. The use of EN support may offer physiologic and immunologic benefits to the gut.[4-6] Prolonged disuse of the gut results in downregulation of many digestive enzymes that may become evident upon reinitiation of EN.[7,8] Furthermore, PN, in the past, may have increased the risk of infection due to intravenous access, which prolonged hospital and ICU stays, but this type of infectious complication has become less prevalent as central venous access device care and blood glucose control have improved.[9-12] However, PN has a role in malnourished patients who cannot tolerate EN support or who have permanent IF related to severe short bowel syndrome or dysmotility.

PN becomes the preferred method for nutrition support in patients who need nutrition support and have contraindications to EN or who cannot meet their needs with EN alone. For example, in patients with severe hemodynamic instability, prolonged ileus, vomiting or diarrhea, or persistent gastrointestinal bleeding, EN may not be an option.[13] EN may also be contraindicated in patients with bowel obstruction, significant gastrointestinal ischemia, or high-output fistula.[13] For these malnourished patients, PN may be needed to avoid protein and energy deficits, especially for those who are critically ill.

Neonatal Considerations

Recommendation 2B: For the neonate, PN is never considered optimal as compared with EN, yet limitations to feeding may make it temporarily the best option for nutrient provision. Metabolic derangements attributable to suboptimal composition of available PN formulations can be reversed through enteral delivery.[14] Poor bone mineralization results from limited calcium solubility in solution resulting from volume restriction, an inability to balance calcium and phosphate, as well as recent cysteine shortages, a PN additive used to increase calcium solubility.[15,16] Increasing concern exists that the lipid injectable emulsion (ILE) formulation is a relevant factor in the development of cholestatic liver disease in infants receiving prolonged PN with little to no EN; however, no definitive evidence to show causation exists yet.[17,18] In addition to the concern of cholestasis, fatty acid compositions of some ILE available in the United States do not meet the needs of the neonatal population aside from preventing essential fatty acid deficiency.[19-21] Safety concerns, specifically risk of mortality, were reported in a meta-analysis evaluating effects of not light protecting PN used for preterm infants.[22] Currently, adequate light protection may not be feasible, depending on the circumstances of whether PN is compounded on-site or at a central location. PN admixtures support growth of neonates; however, shortcomings with current compositions and the morbidity related to venous access do not allow for PN being considered a preferred mechanism of nutrition outright.

Pediatric Considerations

Recommendation 2C: Just as with adults and neonates, PN is never the preferred route for nutrition support if the oral or enteral route is an option. While the ability to provide PN has been lifesaving and can provide nutrients for growth when the intestinal tract is inadequate to do so alone, there are many complications associated with its use, including vascular access device–related problems (infections, thromboses), metabolic bone disease, hepatobiliary disease, and micronutrient deficiencies.[23-27]

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Question 3: What clinical factors should be assessed to determine if EN is feasible, including contraindications to EN, the functional status of the gastrointestinal tract, and the ability to achieve and maintain safe enteral access?

Recommendations

Adult

3A: Evaluate clinical factors derived from history, physical examination, and diagnostic evaluations in determining if EN is contraindicated.

Neonatal and Pediatric

3B: Initiate PN and withhold EN in neonatal and pediatric patients when a clear contraindication to EN exists, including intestinal injury and perforation.

Table 3.1. Contraindications to Enteral Access (Absolute and Relative).[16-18]

All types of enteral access
• Mechanical obstruction of the gastrointestinal tract
• Uncontrolled peritonitis
• Uncorrected coagulopathy or thrombocytopenia
• Bowel ischemia
• Recent gastrointestinal bleeding with high risk of recurrent bleeding (peptic ulcer disease or esophageal varices)
Nasal placement
• Basilar skull fracture: temporal, occipital, sphenoid, or ethmoid fracture
• Recent transsphenoidal surgery
• Facial, nasal, or sinus trauma
• Significant esophageal pathology: stricture, tumor, severe esophagitis
• Esophageal varices with recent banding (delay placement 72 h)
Percutaneous and surgical abdominal placement
• Massive ascites
• Hemodynamic instability
• Morbid obesity with large panniculus
• Gastric outlet or duodenal obstruction (percutaneous endoscopic or surgical gastrostomy)
• Anticipated duration less than 4 wk

3C: Assess intestinal function and perfusion, as well as overall hemodynamic stability, when evaluating readiness for EN, rather than relying on strict adherence to a list of contraindications to EN, such as the presence of umbilical catheters or use of vasoactive medications.

Rationale

Recommendation 3A: Enteral support, including oral intake or EN, may be contraindicated in certain patients. In malnourished patients with nonfunctioning gastrointestinal tracts or conditions for which EN cannot be delivered effectively, such as an inability to achieve and maintain safe enteral access or a disease state not allowing for enteral supplementation, PN may be necessary. Contraindications to EN include severe hemodynamic instability, prolonged ileus, intractable vomiting or diarrhea, upper gastrointestinal bleeding, bowel obstruction, major gastrointestinal ischemia, and high-output fistula.[1] Many of these contraindications may be assessed by history. If history is suggestive of intractable vomiting or diarrhea or extensive hematemesis or hematochezia, EN may not be an option. Physical examination also has a significant role in determining the hemodynamic instability, such as hypotension (loosely defined as systolic blood pressure less than 90 mm Hg or mean arterial pressure less than 65 mm Hg) or orthostatic hypotension in patients with possible pending hypovolemic shock or gastrointestinal bleeding.[2,3] Furthermore, physical examination may assess fistula output, abdominal distension as it relates to bowel obstruction or ileus, bowel sounds suggestive of obstruction (high-pitched tinkling early and reduced bowel sounds later) or ileus (hypoactive to absent bowel sounds, though not very sensitive), or pain level (pain out of proportion to physical examination may be suggestive of acute mesenteric ischemia).[4,5] Note that the absence of bowel sounds does not, per se, constitute a reason to delay or interrupt EN. However, when evaluated in conjunction with other components of the physical examination, reduced or absent bowel sounds suggest an increased risk for EN intolerance and the need for heightened vigilance as EN is initiated.[1] Diagnostic tests (eg, abdominal x-rays, computed tomography, and angiography) may also be helpful in determining gastrointestinal function by assessing for potential disease states that lead to significant functional impairment, such as ileus (dilated loops of bowel with air-fluid levels on upright film), obstruction (dilated loops of bowel), mesenteric ischemia (pneumatosis intestinalis), and perforation (free air in the peritoneum).

Even if no disease state is present to impair function, questions remain regarding the use of EN on improving outcomes and the ability to achieve and maintain safe enteral access. Over the past decade, new and innovative techniques have been identified for placing and securing enteral access devices, assessing the small intestine, and visualizing enteral access device placement by less invasive means.[6-8] These approaches have helped to reduce delays in placing appropriate enteral access devices and to promote broader use of EN. However, if the enteral access is deemed unsafe, PN is an alternative for protein and energy delivery. Table 3.1 provides more detail regarding contraindications to placing enteral access devices.

Neonatal and Pediatric Considerations

Recommendations 3B and 3C: Clinical practice of defining intestinal readiness for oral intake or EN in infants varies.[9] EN in the neonate has been safely provided in circumstances involving mechanical ventilation, medications including indomethacin in the presence of a patent ductus arteriosus, and the presence of umbilical catheters.[10,11] Recent data suggest that safe feeding practices may not need to include routine measurement of prefeeding gastric residuals.[12,13] Decision making regarding feeding readiness must incorporate changes in clinical status, vital signs, and physical examination findings, as well consideration of the volume of feedings to be fed.[14] Basing feeding decisions on gastric residuals in the neonate is challenging, as there is considerable overlap in residual characteristics among those with and without pathology.[12-14] Regardless, feeding protocols that detail both evaluation of and suggested clinical response to gastric residuals can still allow for improved feeding outcomes in neonatal populations.[15]

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Question 4: In patients for whom EN is not feasible, what is a reasonable time frame for initiating PN? (For patients who are well nourished, malnourished, nutritionally-at-risk, or hemodynamically or metabolically unstable)

Recommendations

Adult

4A: Initiate PN after 7 days for well-nourished, stable adult patients who have been unable to receive significant (50% or more of estimated requirements) oral or enteral nutrients.

4B: Initiate PN within 3–5 days in those who are nutritionally-at-risk and unlikely to achieve desired oral intake or EN.

4C: Initiate PN as soon as is feasible for patients with baseline moderate or severe malnutrition in whom oral intake or EN is not possible or sufficient.

4D: Delay the initiation of PN in a patient with severe metabolic instability until the patient's condition has improved.

Neonatal

4E: Begin PN promptly after birth in the very low birth weight infant (birth weight less than 1500 g). Insufficient data exist to suggest a specific time frame in which PN is ideally initiated in more mature preterm infants or critically ill term neonates.

Pediatric

4F: For the infant, child, or adolescent with a self-limited illness, it is reasonable to delay consideration of starting PN for a week. However, initiate PN within 1–3 days in infants and within 4–5 days in older children and adolescents when it is evident that they will not tolerate full oral intake or EN for an extended period.

Rationale

Recommendations 4A and 4B: Inadequate intake of nutrients is a known risk factor for the developing malnutrition.[1] According to the Academy of Nutrition and Dietetics/A.S.P.E.N. consensus malnutrition characteristics, energy intake of 50% or less than estimated requirements for 5–7 days meets both the severe and nonsevere threshold for 1 malnutrition criterion. In the outcome-based validated nutrition risk scoring system (Nutrition Risk Score 2002) developed by the European Society for Clinical Nutrition and Metabolism, food intake of 0%–25% in the preceding week was identified as a significant variable and by itself meets the scoring requirements to begin nutrition support defined as a score greater than 3.[2] When the presence of

disease is included, this raises an individual score to greater than or equal to 4, thereby suggesting an increased risk of developing malnutrition if nutrition support intervention does not begin. Nutrition risk scores that incorporate an element related to disease severity hold promise in serving as a tool for patients who are most likely to benefit from nutrition intervention.[2,3]

The length of time that an individual can withstand an absence of nutrient intake before detrimental clinical effects occur is unknown. In a 2001 technical review of PN, Koretz et al recommended delaying the start of PN for 10–14 days.[4] However, due to uncertainty about the onset of starvation-related malnutrition, clinical guidelines generally recommend beginning PN (supplemental or full) in patients who have failed to achieve nutrition goals after 7 days.[5-8]

Historically, the limited data available regarding the use of PN in high-risk or malnourished patients has hampered efforts to delineate circumstances in which PN is likely to improve outcomes. The classic experiment by Ancel Keys in 1946 demonstrated that healthy young men lost an average of 24% of their body weight over a 6-month period when fed 50% of their estimated energy requirements.[9] Unfortunately, the classic starvation model described by Keys does not represent the typical hospitalized patient, who is likely experiencing disease-state metabolism, thereby affecting nutrient metabolism and utilization.[1]

Factors such as baseline nutrition status, severity of illness, the rate of catabolism, and the presence of fat stores influence tolerance of suboptimal nutrition intake.[2,4] In a 1993 study of postoperative patients, Sandstrom found that morbidity and mortality increased after 14 days with no nutrition intervention.[10] Whether this association between a delay in feeding and postoperative complications is related to nutrition deprivation, severity of illness or other factors cannot be determined by this retrospective analysis of prospectively gathered data. A more recent study by Garth and colleagues provides some support for beginning PN earlier than 7 days to those who are nutritionally-at-risk.[11] This prospective evaluation of 95 patients undergoing surgical treatment identified 53% who experienced significant weight loss prior to hospital admission, a factor that was associated with a significantly longer length of stay. In their analysis of postoperative nutrient intakes, the authors demonstrated that those patients who took less than 7 days to achieve adequate nutrition (via oral intake, EN, or PN) were much less likely to experience a postoperative complication when compared with those who took more than 7 days (52% vs 13%, $P < .01$). This association may or may not hold true if evaluated via a randomized controlled trial.

Recommendation 4C: An association exists between moderate and/or severe malnutrition and a range of significant negative clinical outcomes, including longer lengths of hospital stay as well as increased infectious complications, postoperative infections, hospital readmission, and mortality.[12-16] Agarwal and colleagues prospectively demonstrated that moderate or severe malnutrition was associated with increased hospital length of stay, 30-day readmission rate, and 90-day in-hospital mortality rate.[17] In a more recent retrospective observational study, Guerra et al determined that the association between length of stay and undernutrition persists after adjusting for confounding variables such as disease, severity of illness, and age.[18] Nutrition screening is required for all admitted hospitalized patients and identifies those who may be at risk for either being malnourished or developing malnutrition. Patients identified as malnourished or nutritionally-at-risk through nutrition screening will undergo a full nutrition assessment to determine if malnutrition is in fact present. Those individuals who are found to be moderately or severely malnourished should receive nutrition intervention at the earliest opportunity. For the nutritionally-at-risk patient who remains nil per os for 7 days or longer due to surgical intervention or who is unable to receive enteral nutrients for any reason, initiation of PN should begin as soon as it is feasible to do so.[5,8]

Studies demonstrating improved clinical outcomes in malnourished individuals who receive PN are overall supportive. In a 2001 meta-analysis comparing PN with EN, Braunschweig et al demonstrated a lower mortality (relative risk [RR]: 3.0, 95% CI: 1.09–8.56) and infection risk (RR: 1.17, 95% CI: 0.88–1.56) with PN use versus standard care in those trials with high percentages of malnourished patients.[19] Conversely, in a meta-analysis of PN in the surgical patient, Heyland et al noted a trend toward reduced complications ($P = .066$) with the use of PN only in malnourished patients. No mortality risk difference was seen (RR: 1.13, 95% CI: 0.75–1.7).[20] None of the more recent studies evaluating early versus late PN or combined EN and PN specifically studied malnourished patients; therefore, their results cannot be extrapolated to this population.[21-23] In light of studies suggesting clinical benefits of preoperative PN in malnourished patients[24-26] and the aforementioned meta-analysis data, the early use of PN in malnourished patients unable to receive oral intake or EN is reasonable.

Recommendation 4D: Hemodynamic and metabolic instability is common in the severely ill patient. During the first 24–48 hours following a significant insult (trauma event, aspiration episode, cardiopulmonary arrest, etc), patients enter the "ebb" phase of the metabolic response, associated with hypovolemia, shock, and tissue hypoxia. This phase is characterized by reduced tissue perfusion, reduced oxygen consumption, and a lower metabolic rate.[27] Table 4.1 highlights clinical conditions that increase the risk for metabolic complications when initiating PN. In each case, the course of action will vary according to the abnormality present. Severe electrolyte abnormalities should be corrected prior to starting PN. Additional strategies to prevent metabolic complications may include adjustment in the volume and nutrient content of the initial PN formulation (eg, lower dextrose dose for baseline hyperglycemia) and a more conservative approach in advancing to goals. Vigilant laboratory monitoring with prompt intervention as needed will minimize the risk of developing complications.

Table 4.1. Clinical Conditions Warranting Cautious Initiation of Parenteral Nutrition in Adults.[52,53]

Conditions	Suggested Criteria
Hyperglycemia	Glucose greater than 180 mg/dL
Azotemia	Blood urea nitrogen greater than 100 mg/dL
Hypertriglyceridemia	Serum triglycerides greater than 200 mg/dL
Hyponatremia	Serum sodium less than 130 mEq/L
Hypernatremia	Serum sodium greater than 150 mEq/L
Hypokalemia	Serum potassium less than 3 mEq/L
Hypomagnesemia	Serum magnesium less than 1.3 mEq/L
Hypocalcemia	Ionized calcium less than 4.5 mg/dL
Hypophosphatemia	Serum phosphorus less than 2 mg/dL

Neonatal Considerations

Recommendation 4E: In considering when to initiate PN in neonates, their susceptibility to rapid accrual of significant energy, protein, and micronutrient deficits must be taken into account.[28,29] Delaying PN causes an immediate negative nitrogen balance in preterm infants, contributing to postnatal growth failure, a condition commonly documented in the neonatal intensive care unit.[29-31] A wait-and-see approach—reevaluating on a daily basis whether EN can be advanced while postponing PN initiation—could be expected to aggravate growth failure.[32] Although concern exists regarding the safest maximum dose of parenteral amino acids, early administration of parenteral protein, within hours of birth, has been observed to be safe.[33-38] Concerns regarding lipid intolerance historically led to withholding ILE for days after birth in the preterm population, yet recent data suggest safety and improved nitrogen balance from increasing provisions of nonprotein energy within the first day.[39,40] Essential fatty acid deficiency develops in as few as 3 days in neonates fed fat-free diets.[41]

Reduced energy and protein intake in the first weeks of life in preterm infants have been associated with increased risk of morbidity.[42,43] No direct causal relationship between reduced nutrient provision and morbidity or mortality has been established, but the potential for prompt and adequate nutrition in the first days of life seems to be a mechanism for favorably mediating outcomes and should not be overlooked.[42]

Full-term neonates cared for in the pediatric intensive care unit exposed to PN within 24 hours of admission, as compared with that after 1 week, had an associated increased risk of infection and longer intensive care unit stay.[44] All participants had some portion of EN during admission and received parenteral micronutrients, minerals, and vitamins even if not receiving PN. More data are needed on the precise safest timing for initiating PN—specifically, whether starting earlier than 1 week may be safe. In addition, these findings do not answer questions of timing for neonates who are not being fed by the enteral route or who are preterm or low birth weight.

Pediatric Considerations

Recommendations 4F: There are limited data on which to base recommendations for when PN should be initiated in the pediatric patient when EN is not feasible. However, reasonable consensus has existed among experts in this field. The shorter timeline advocated for starting PN in younger patients, particularly infants, is based on their decreased metabolic reserves and relatively higher energy requirements.[45] In creating teaching materials on the topic of PN, the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition recommended starting PN within 1–3 days in infants and 4–5 days in older children when EN is not possible.[46] However, data supporting this recommendation are limited. This has been echoed by Baker et al and, at least for the infant recommendations, in the A.S.P.E.N. Pediatric Nutrition Support Core Curriculum.[47,48] Infants or children with poor nutrition status at the onset of illness are at increased risk of depleting their metabolic stores; therefore, it has been recommended that PN be started earlier in these patients than in their previously healthy counterparts.[49-51] This is reasonable when an extended period of inadequate oral intake or EN is anticipated; thus, delaying the start of PN increases nutrition risk, even in previously well-nourished children. However, a recent multicenter trial in critically ill children raises questions about this timeline in others.[44] Fivez et al compared early provision of PN (within 24 hours) with late (day 8) in a large group of children admitted to the intensive care unit, almost half of whom were less than 1 year of age and demonstrated decreased infection rate, fewer intensive care days, and shorter hospital stays in the late PN group.[44] It is unclear whether this can be generalized to non–critical care settings, but it is thought provoking. It remains important to continue to weigh the risks and benefits of therapies and adjust as evidence becomes available.

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Question 5: What factors play a role in selecting and placing the appropriate vascular access device for PN administration?

Global Recommendations: Adults and Pediatric

5A: Individualize the selection of vascular access device (VAD) for PN administration based on an evaluation of the risks and benefits of the device, clinical factors, and psychosocial considerations.

5B: Choose the smallest device with the fewest number of lumens necessary for the patient's needs.

5C: Dedicate 1 lumen of the VAD for PN administration when possible.

5D: Position the tip of the CVAD in the lower third of the superior vena cava near the junction with the right atrium.

5E: Confirm and document the optimal position of the CVAD tip prior to initiating central PN.

Rationale

Recommendation 5A: Because many of the adverse events associated with PN stem from the presence of the VAD, a fundamental element of appropriate PN centers on selecting and placing the vascular device that is best suited for the therapy. A variety of peripheral and central VADs are available to deliver PN, each with distinct advantages and disadvantages. A careful vascular access assessment that weighs the benefits of each VAD option against potential complications is essential to safe and effective therapy.[1-3]

Although peripheral intravenous catheters (PIVs) can be used to administer dilute nutrient admixtures, a high rate of technical failure stands out as the chief disadvantage of these devices.[4] Candidates for peripheral PN must have sufficient venous integrity to allow infusion of relatively hypertonic nutrient admixtures without disrupting the nutrition regimen or other drug therapies should the device fail.[4]

PIVs are intended for short-term use, and the need for frequent reinsertion is an important limitation of these devices. Policies governing dwell time for PIVs vary. Guidelines issued by the Centers for Disease Control and Prevention suggest rotating insertion sites every 72–96 hours, whereas the Infusion Nurses Society standards recommend replacing PIVs only when clinically indicated, on the basis of regular inspection of the site for evidence of phlebitis or extravastation.[1,2,5] However, a recent large multicenter prospective study found an increase in phlebitis in PIVs after 96 hours in situ, supporting recommendations for scheduled site rotation.[6] A study that examined data related to primary bloodstream infection in adult hospitalized patients suggested a link between bloodstream infection and PIVs left in place longer than 72 hours.[7] These findings call into question the safety of allowing PIVs to remain in place until warning signs of malfunction appear. Until further research delineates the optimal dwell time for PIVs, scheduled rotation of PIV sites for peripheral PN may be the most prudent policy, considering the elevated risk for infectious and thrombotic complications associated with PN. Focused surveillance for bloodstream infection related to PIVs is needed to guide organizational decisions regarding PIV dwell time.[7]

The dubious reliability of PIVs is frequently cited as a reason for avoiding peripheral PN.[4] Yet at the same time, strategies for reducing central line–associated bloodstream infection (CLABSI) uniformly recommend limiting the use of CVADs in acute care settings, thus increasing pressure to rely on PIVs whenever possible.[1,2,8-10] Improvements in the design of peripheral midline catheters, which can remain in place for 29 days, may offer an alternative to conventional PIVs, but these devices are still prone to phlebitis, and no research has studied the use of these devices for peripheral PN.[10,11] Moreover, the location of these devices in a deeper vein may mask signs and symptoms of phlebitis, such as redness or pain.

Central PN administration circumvents many of the technical problems inherent to peripheral PN. However, CVADs remain a leading source of adverse events related to PN administration. For both adult and pediatric patients, CLABSI and deep vein thrombosis (DVT) rank among the most common complications associated with the use of CVADs.[12,13] CLABSI and DVT may cause acute harm from sepsis or pulmonary embolism, respectively. But the cumulative impact of CVAD complications also jeopardizes long-term outcomes of PN therapy. Recurrent episodes of sepsis increase the risk for PN-associated liver disease, a potentially devastating complication of long-term PN, especially among infants.[14-17] Eventually, infectious and thrombotic events related to the CVAD can deplete central venous access sites. For long-term PN recipients, progression of hepatic failure, recurrent

Table 5.1. Factors Associated With Complications of CVADs.[1,8,20-23,26,51]

Central Line–Associated Bloodstream Infection	Deep Vein Thrombosis
Parenteral nutrition	Parenteral nutrition
Prolonged catheter dwell time	Prolonged catheter dwell time
Multilumen devices	Multilumen devices
Femoral insertion site in obese adults	Femoral insertion site
Lengthy hospitalization before CVAD insertion	Multiple insertion attempts
Heavy microbial colonization at insertion site (favors upper extremity sites over neck or groin)	Left-sided insertion
Microbial colonization at the catheter hub	Catheter tip proximal to the cavoatrial junction
Multiple concurrent CVADs	Prior catheterization at same puncture site
Excessive manipulation of the catheter	Peripherally inserted central catheters
Prematurity (early gestational age)	Central line–associated bloodstream infection
Transfusion of blood products in children	

CVAD, central venous access device.

episodes of CLABSI, and/or loss of central venous access may ultimately lead to referral for small intestine transplantation.[18-20] Risk factors for CLABSI and DVT appear in Table 5.1. Note that PN administration independently raises the risk for infectious and thrombotic complications, underscoring the importance of careful CVAD selection when initiating PN.[21-23] The factors underlying this increased risk of complications are not clear, but an interplay among patient-related issues (eg, presence of inflammation and hypercoagulability), characteristics of the CVAD, and properties of the PN formulation itself likely play a role.[1,8,10,21-23]

Other factors that influence the selection of CVAD for PN include the patient's medical condition, developmental stage, concurrent intravenous therapies, anticipated duration of therapy, the setting in which PN is administered, and the complexity of postinsertion care. When long-term PN is planned, the patient's views regarding the choice of VAD becomes another important consideration in the selection process.[17] Above all, when PN is initiated, attention to principles related to the size of the CVAD and the position of the catheter tip can minimize complications and prolong the functional duration of the device.

Technological advances have produced a variety of options for vascular access. As shown in Table 5.2, the complication profile varies with each type of CVAD, with some devices better suited for PN administration than others.[1-3,8-13,24-30] An individualized approach to selecting the CVAD for PN administration that incorporates pertinent clinical information with a careful assessment of the risk/benefit profile of the device is essential to promoting optimal outcomes in patients receiving PN therapy. After the CVAD for PN administration is selected and inserted, meticulous attention to maintenance strategies aimed at preventing complications is essential.[8-10]

Recommendation 5B: Although multilumen CVADs have facilitated complex infusion therapy, additional lumens add to the risk for CLABSI and DVT.[8,9,26,27] Multilumen devices receive more frequent manipulation than single-lumen catheters, which most likely accounts for the increased rates of CLABSI reported with multilumen CVADs.[1,8,9,28] Studies of adult and pediatric home PN patients have identified multilumen catheters as a risk for CLABSI, leading several researchers to recommend using single-lumen catheters for home PN when feasible.[29-32] One meta-analysis determined that for every 20 single-lumen catheters placed in lieu of multilumen versions, 1 CLABSI would be avoided, a difference that the authors deemed to be clinically relevant.[33] Similarly, a recent simulation study of peripherally inserted central catheters (PICCs) concluded that hospitals could improve outcomes and decrease costs by instituting policies that stipulate single-lumen PICCs as the default option.[34] This information takes on greater significance when considering the elevated risk for CVAD complications that accompanies PN administration and intestinal failure.[15,35]

Larger-caliber CVADs are also more likely than smaller devices to create conditions that lead to thrombus formation, such as endothelial trauma, inflammation, stasis, and turbulent blood flow.[22] The risk for DVT is especially pronounced with PICCs as compared with other types of CVADs, particularly for patients who are critically ill, who are pregnant, or who have cancer.[36,37] One analysis of 2014 PICCs revealed that triple-lumen devices carried a 20-fold increase in risk for DVT when compared with single-lumen PICCs.[38]

A well-recognized link exists between thrombosis and CLABSI.[39,40] Microbial colonization occurs readily in the presence of a thrombus, setting the stage for subsequent CLABSI. In deciding to insert a multilumen CVAD for PN administration, the risk for CLABSI and DVT must be weighed against the benefits provided by the device.

Recommendation 5C: When multilumen CVADs must be used for PN, 1 lumen of the device should be dedicated exclusively for the PN administration.[2,9,10,41,42] This recommendation stems from a single study that showed a strong association between violations of the CVAD used to administer PN and infectious complications.[43] Although the strength of the evidence supporting this recommendation is

Table 5.2. Selection of Vascular Access Devices for Parenteral Nutrition.[1-3,24-31]

Type	Insertion	Dwell Time	Therapeutic Applications	PN Considerations
PIVs	Bedside insertion; less than 3 inches long; usually inserted in veins of forearm or hand.	72–96 h. Site rotation based on clinical indication is not recommended.	Use is limited by osmolarity restrictions; not suitable for home care due to high failure rates; not suited for home PN.	May be used for PPN for short-term therapy; requires careful assessment of venous integrity. PPN may increase the incidence of phlebitis, particularly in pediatric patients.
Peripheral midline catheters	Requires ultrasound-guided placement; 3–8 inches in long; inserted via the antecubital fossa into proximal basilic or cephalic veins—does not reach the central veins.	For therapies lasting longer than 6 d; can remain in place up to 29 d.	Same restrictions for osmolarity as those for other PIVs; not suited for home PN.	As above, associated with lower rates of phlebitis than short peripheral devices, but safety with PPN is unknown.
Percutaneous nontunneled central catheters	Bedside insertion; subclavian, internal jugular sites; femoral approach is possible but suboptimal for PN due to high infection risk.	5 d to a few weeks	Appropriate for acute care settings; not suited for home care.	Not designed for self-care by patient, easily dislodged, especially in children; preferred over PICC for access up to 14 d.
PICCs	Bedside insertion into basilic, cephalic, or brachial veins; tip rests in superior vena cava; easily removed at bedside. In difficult cases, may require fluoroscopic placement by interventional radiologist.	Maximum dwell time is unknown	Suitable for acute care and short- and medium-term PN for adults and pediatric patients.	Associated with an increased risk for deep vein thrombosis, limiting use for indefinite PN therapy and situations where vessel preservation is a priority. Antecubital location of exit site hinders self-care and activity. Clothing may not always cover insertion site—potentially having a negative impact on body image; may be easily to removed when infected or PN is no longer needed.
Tunneled catheters (Hickman or Broviac type)	Surgical or fluoroscopic insertion; bedside or outpatient removal	3 mo to years	Suitable for long-term PN; the presence of a cuff within the tunnel inhibits microbial migration and decreases risk of dislodgement.	No restrictions on upper extremity activity; position on chest facilitates self-care; catheter can be easily hidden under clothing.
Implanted ports	Surgical or fluoroscopic insertion via subclavian, internal jugular, or peripheral veins; a port (single or double) is implanted in a subcutaneous pocket; requires surgical removal.	6 mo to years	Primarily intended for low-frequency, intermittent access. Associated with lowest risk for CLABSI, due to reduced manipulation. The presence of an indwelling needle for continuous or frequent access offsets the reduced infection benefit.	Suitable for PN in selected circumstances; motivated patients can learn access procedures; body image remains intact; requires no local site care when device is not accessed. PN may increase risk for CLABSI and occlusion in children with cancer.
Special purpose catheters (sheath introducers, pulmonary artery catheters, apheresis catheters)	Bedside or fluoroscopic insertion techniques.	Dwell time varies with the device and indication for use.	Generally, large-bore devices; subject to manipulation when hemodynamic monitoring is performed; associated high levels of microbial contamination.	Pose increased risks CLABSI and thrombosis. Use of these devices for PN should be decided on a case-by-case basis, weighing the potential for complications against the risk of placing an additional line. PN should never be administered through a pressure monitoring circuit.
Percutaneous femoral central venous catheters	Similar to upper extremity catheters but relatively simple bedside insertion.	Not appropriate for long-term use; should be removed as soon as feasible.	Tip position should rest in the inferior vena cava.	PN administration is discouraged to high rate of complications associated with femoral vein insertion site. No data specific to osmolarity limits or PN administration are available.
Umbilical catheters	Surgical bedside insertion in critically ill neonates.	Arterial catheters: 5 d; venous catheters: 14 d.	Provides reliable, short-term venous access in acute care.	PN has been identified as a risk factor for infection with umbilical vein catheters. Catheters should be removed and not replaced is signs of infection or thrombosis develop.

CLABSI, central line–associated bloodstream infection; PICC, peripherally inserted central catheter; PIV, peripheral intravenous catheters; PN, parenteral nutrition; PPN, peripheral parenteral nutrition.

modest, the dedicated lumen policy remains a reasonable precaution. By limiting the frequency of manipulation, the dedicated lumen reduces the potential for microbial contamination. In addition, policies that restrict the use of the PN lumen offer the added benefit of avoiding coinfusion of potentially incompatible medications with the complex PN admixture.

The question of whether it is acceptable to administer PN through a lumen that has been used for other infusions remains unanswered; no research has examined this issue. A decision to insert a new CVAD for PN administration must take into consideration the risks and costs associated with the procedure. The presence of multiple simultaneous CVADs also exerts a strong influence on CLABSI rates, which may offset any potential advantage of inserting a "clean" line in cases where existing CVADs must remain in place.[44,45]

Recommendation 5D: For administration of hyperosmolar PN admixtures, the tip of the catheter should be positioned in the distal third of the superior vena cava near the junction with the right atrium.[1,2,17,41] At one time, catheters for PN administration were routinely placed in the right atrium, where rapid blood flow could provide optimal dilution of the hyperosmolar admixtures. However, the U.S. Food and Drug Administration strongly advises against placing catheters in the heart due to the potential for cardiac dysrhythmia, perforation, and tamponade.[46] While there is general agreement on the hazards of positioning a catheter deep in the right atrium, the safety of placing CVADs in the upper right atrium remains a topic of some debate.[21,47-49]

Yet, CVADs positioned in the upper portions of the superior vena cava are known to elevate the risk for thrombotic complications.[16,50-53] In one study involving patients with cancer, DVT occurred in 46% of cases in which the catheter rested in the brachiocephalic vein or the confluence of the brachiocephalic and the superior vena cava.[54] In the upper superior vena cava, left-sided catheters carry an added risk for DVT because the tip often abuts the vessel wall, where motion of the catheter may cause repeated trauma to the endothelium.[55,56] The infusion of hyperosmolar PN admixtures in this location may further contribute to catheter-associated complications by causing inflammation within the lumen of the vessel.

Recommendation 5E: For all newly inserted CVADs, correct position of the CVAD should be confirmed radiographically or fluoroscopically before PN administration. In pediatrics, ultrasound and electrocardiogram techniques have been suggested as potential alternatives to chest x-ray for confirming correct placement of CVADs, but further research is needed to better define clinical feasibility of these methods.[57] In addition, the position of the catheter should be reassessed before starting PN for adult patients who are admitted to the hospital with a CVAD in place.[54] For children who have CVADs in place for extended periods, verification of the catheter position should be considered to assess whether the catheter tip has retracted proximally as the child has grown.[47,54]

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Question 6: In which patients is peripheral PN a reasonable choice in providing nutrition support?

Recommendations

Adult

6A: Use peripheral PN only for short-term purposes, no more than 10–14 days, as supplemental PN or as a bridge therapy during transition periods, where oral intake or EN is suboptimal or clinical circumstances do not justify placing a central venous catheter.

6B: Estimate the osmolarity of peripheral PN formulations.

6C: Maintain an upper limit of 900 mOsm/L for the peripheral PN formulations.

Neonate and Pediatric

6D: In well-nourished pediatric patients, use peripheral PN for short-term purposes until oral intake or EN can be established or to serve as a bridge to central PN.

Rationale

Recommendation 6A: In the United States, concerns about the reliability of peripheral venous access and the uncertain benefits of therapy have limited the use of peripheral PN, but this route for intravenous nutrition has a more established role in Europe.[1] In recent years, guidelines for preventing CLABSI have recommended reducing CVAD use by placing peripheral devices, including midline catheters when feasible.[2] Whether the trend to avoid or delay CVAD placement has had an impact on patterns of peripheral PN use is not known.

High-quality research evaluating the patient populations who would benefit the most from peripheral PN is limited. The majority of published studies have included small sample sizes with limited information on comorbidities. Therefore, it is unclear whether patients' underlying disease states, severity of malnutrition, the functional status of the gastrointestinal tract, and other concurrent medical and/or surgical conditions play a key role on the safety and efficacy of peripheral PN administration. Existing literature shows that the experience of using peripheral PN is more extensive in patients with gastrointestinal tract cancer undergoing surgery than other disease states.[3-5] One recent retrospective observational trial of peripheral PN in postoperative colorectal cancer patients showed no clinical advantage with peripheral PN administration.[6] However, the study excluded malnourished subjects and focused on supplementation with branched-chain amino acids, limiting any applicability of the findings. In a case-control study, elderly patients (median age, 80 years) receiving peripheral PN and central PN had a greater incidence of candidemia than similar patients with no peripheral PN.[7] However, the researchers provided no details regarding energy provided or glucose control. Overall, there are insufficient high-quality data from well-conducted observational trials or randomized controlled trials to support the routine use of peripheral PN. If peripheral PN is used, multivitamins and trace elements should be added.[4] Another theoretical concern is that a much higher proportion of the daily energy will be provided by ILE in recipients of peripheral PN to reduce the total amount of fluid used in the PN regimen. High lipid intake may contribute to adverse outcomes, such as infection and hepatic dysfunction. It is also unclear whether the macronutrient distribution for peripheral PN should be different from that in central PN due to safety concerns, especially from the perspective of osmolarity and, when using total nutrient admixtures, stability.

The recommendation for a maximum duration of 10–14 days for peripheral PN stems from a series of reports from the 1990s that recommended peripheral PN as the first choice for PN administration as a strategy for avoiding CVAD insertion.[8-12] In these studies, difficulty maintaining peripheral venous access increased with the duration of therapy, typically after 10 days. Although complications related to PIV access remain an important factor limiting the use of peripheral PN, additional considerations—such baseline nutrition status and requirements, severity of illness, and fluid tolerance—play a role in guiding decisions regarding peripheral PN use. Table 6.1 provides more information to guide decisions regarding the appropriate initiation and duration of peripheral PN.

Recommendations 6B and 6C: Peripheral veins cannot tolerate highly concentrated solutions. Therefore, peripheral PN admixtures are limited by their osmolarity. Admixtures with high osmolarity are associated with high risk of phlebitis. There is some debate regarding the maximum osmolarity for peripheral PN.[13,14] A retrospective cohort study in adult patients showed that peripheral PNs with a final osmolarity of 993 mOsm/L infused via a short (20- or 22-gauge) polyurethane catheter for less than 15 days were well tolerated.[15] Current ASPEN guidelines for adult and children recommend maintaining osmolarity less than 900 mOsm/L for peripheral vein infusions,[16,17] The Infusion Nurses Society has also recently raised its osmolarity limit for peripheral vein infusions from 600 mOsm/L to 900 mOsm/L.[18] The European Society for Clinical Nutrition and Metabolism guidelines set the limit at 850 mOsm/L.[1]

ASPEN PN safety consensus recommendations stipulate that osmolarity be calculated to ensure that the PN formulation is appropriate for the route of administration (peripheral vs central vein).[19] However, one study suggested that the commonly used estimation method may underestimate the true osmolality of compounded formulations. Although a new predictive method has been proposed, it requires additional research to validate its accuracy.[20] When peripheral PN use is necessary, the intravenous site must be monitored frequently for signs of phlebitis. (See Question 5 for more information regarding vascular access for peripheral PN.) A lower osmolarity limit should be considered in patients at risk for phlebitis or other vascular complications. Well-designed prospective randomized controlled trials are needed to determine the range of indications for peripheral PN in which its use would be beneficial.

Neonatal and Pediatric Considerations

Recommendation 6D: In pediatric patients, peripheral PN is intended for short-term use to supplement EN, when central venous access is not possible.[21] Due to the difficulty of meeting energy and protein needs within a tolerable osmolarity and volume, peripheral PN should be used only in previously well-nourished patients or those have only mild nutrition deficits. In addition, peripheral PN should be considered only when it is

Table 6.1. Characteristics of Peripheral PN.[27,29]

Aspect of Peripheral PN Therapy	Clinical Considerations
Vascular access	Avoids risks inherent to central venous access Maximum osmolarity = 900 mOsm/L Requires assessment of risk factors for difficult intravenous access • Obesity • Extremes in age (neonates and elderly) • History of multiple venous cannulations • History of intravenous drug use Associated with increased rates of phlebitis Extravasation of nutrient admixtures can lead to tissue injury and necrosis Care setting is appropriate for management of peripheral intravenous catheters
Therapeutic goals	Expected duration 10–14 d or less Aims to prevent, rather than correct, nutrition deficits Serves as a supplement to oral intake or enteral nutrition or a bridge until central venous access device placement
Peripheral PN nutrient delivery	Frequently hypocaloric PN due to osmolarity limits Provides adequate dose of nutrients in some cases Requires relatively large fluid volumes Formulation cannot be concentrated Typically relies on lipid as a greater proportion of energy Osmolarity constraints may restrict electrolyte content
Patient-centered considerations	No evidence of severe hypermetabolism or catabolic state Able to tolerate fluid volume of 2.5–3 L/d for adults, 120–125 mL/kg/d for neonates and 1.5 times maintenance needs for pediatric patients Stable electrolyte status, without elevated needs Sufficient renal function to tolerate fluid load required

PN, parenteral nutrition.

expected that the patient will successfully progress to full EN within 7–10 days.[21] If after 5–7 days of peripheral PN, a patient is not moving forward with oral intake or EN, placement of a CVAD and central PN should be considered.[22] Candidates for peripheral PN include children with short bowel syndrome who have temporarily had the CVAD removed for CLABSI and those with prolonged postoperative ileus.[23] Although peripheral PN reduces nutrient intake in neonates, any implications on growth and long-term outcomes are not reported.[24]

Phlebitis carries serious implications for the pediatric patient receiving peripheral PN. Infants and children have multiple risk factors for phlebitis and extravasation: small fragile veins, decreased peripheral circulation, capillary leakage, and flexible subcutaneous tissue. This makes short peripheral intravenous devices difficult to place and maintain, resulting in the need for repeated attempts at intravenous insertion, which can lead to complications, pain, and stress.[14,25,26]

As with adults, questions concerning the maximum tolerable osmolarity limit for peripheral PN in children remain a topic of debate.[14,23-26] To stay within the 900 mOsm/L limit, the final concentrations of typical peripheral PN admixtures must generally fall below 5% for amino acids and 10% for dextrose.[27] However, in pediatric patients, the use of peripheral PN admixtures with a final dextrose concentration of 12.5% is more prevalent than in adults due to higher carbohydrate needs.[14] Cies et al reported that the final osmolarity of peripheral PN admixtures did not have an effect on the rate of line-related events in neonatal and pediatric patients.[23] However, in a recent study of peripheral PN in children, Dugan et al found that admixtures with an osmolarity lower than 1000 mOsm/L resulted in less phlebitis than those that exceeded the 1000 mOsml/L limit.[28] Yet, regardless of osmolarity, the average time to phlebitis was 12 hours. The European Society for Paediatric Gastroenterology Hepatology and Nutrition guidelines state that phlebitis of peripheral veins can be expected when the osmolarity of the intravenous solution exceeds 600 mOsm/L.[26] Gura recommends that in pediatric patients, midline catheters be preferentially used for peripheral PN rather than short PIVs because of concerns regarding osmolarity and calcium limitation.[14] However, as with adults, midline catheters may reduce the incidence of dislodgement but still carry a risk for phlebitis, underscoring the need for close surveillance of the insertion site. Use of peripheral PN should be limited in pediatric patients and only when the benefits outweigh the risks. Table 6.1 provides a summary highlighting the clinical considerations involved in peripheral PN use.

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Question 7: In which patients is intradialytic PN a reasonable choice for nutrition support?

Global Recommendations

7A: Do not use intradialytic PN (IDPN) as the sole source of nutrition intervention in malnourished patients with chronic kidney disease (CKD).

7B: Consider IDPN for adult and pediatric patients with CKD who are malnourished and unable to tolerate adequate oral or enteral intake.

Rationale

Recommendations 7A and 7B: Malnutrition is common in patients with CKD. Protein-energy malnutrition is prevalent among patients undergoing hemodialysis and is strongly associated with cardiovascular mortality in patients with advanced CKD.[1-3] The cause of malnutrition in most CKD patients is multifactorial, which may include anorexia, increased nutrient loss from dialysis, impaired nutrient metabolism and utilization, metabolic acidosis, physical inactivity, chronic inflammatory response, and other changes to the neuroendocrine system. While the gastrointestinal tract is always the preferred route for nutrition interventions, the parenteral route is a viable option for individuals who cannot tolerate oral or enteral administration of nutrients.

IDPN refers to PN delivered during the hemodialysis procedure, typically by administering the nutrient admixture through the venous drip chamber of the dialysis circuit.[4-7] The majority of the published data include patients with CKD receiving intermittent hemodialysis, although limited data exist for patients on peritoneal dialysis receiving dialysates enriched with amino acids.[8-19] IDPN typically provides 500–1000 kcal and 50–100 g of amino acids in less than 1 L of volume per dialysis treatment. About 10% of the infused amino acids are lost in the dialysate.[20,21] Vitamins and trace elements are not routinely added to IDPN, because the additives can readily be removed in the dialysate. Instead, supplemented micronutrients should be added in the last 30 minutes of the IDPN cycle.[20]

Published data suggest that IDPN is generally safe and effective in improving nonfluid weight gain over time.[8-17] However, these studies generally suffer from a few common limitations: the sample sizes in most reports are small (less than 30 patients); the frequency and intensity of hemodialysis are not described or standardized; and oral nutrient intake is not controlled and often not monitored. These confounders have greatly limited the ability to extrapolate the efficacy of IDPN as a standard of care to all patients receiving hemodialysis.

From the clinical outcome standpoint, none of these studies address the impact of IDPN on long-term outcomes, such as the risk or progression of cardiovascular diseases, or overall survival. Two observational studies and 1 randomized controlled trial that attempted to evaluate whether IDPN offers a survival benefit showed widely different results. Note that among these studies, only 1 is an randomized controlled trial. Therefore, no strong evidence exists that IDPN improves survival, and no conflicting data of comparable stature are currently available.[22-24] It appears that in malnourished patients receiving hemodialysis, nutrition support via the enteral route is equally effective as IDPN when intake is tolerated.

The risks, complications, and cost-benefits associated with IDPN have not been thoroughly evaluated. Since most patients receive hemodialysis 2–3 times a week, IDPN can provide nutrition supplementation in only a limited capacity. The short but intense duration of glucose infusion (typically 2–3 hours) is nonphysiologic, and the risk of reactive hypoglycemia is high upon discontinuation of IDPN infusion, especially in patients with diabetes. With the cost of compounding intravenous admixtures, nursing care, and additional monitoring during and after IDPN infusion, the overall cost of IDPN is substantially higher than oral nutrition supplements. In general, third-party payers will provide coverage for IDPN only in cases of documented gastrointestinal dysfunction.

It is inappropriate to use IDPN alone as the sole nutrition intervention for patients with CKD who are malnourished. IDPN can be considered a supplemental nutrition intervention in patients when oral intake and/or EN interventions have failed or are insufficient to reach nutrition goals. Existing data suggest that IDPN is safe in selected patients and can increase weight, appetite, serum albumin levels, and survival in malnourished patients requiring hemodialysis. Additional research is needed to determine the best patient populations who would benefit from this intervention.

Pediatric Considerations

Pediatric patients with renal failure frequently suffer from malnutrition, growth failure, and short stature as adults.[25] A number of strategies are used to promote catch-up growth, including aggressive daily dialysis, treatment of metabolic bone disease, the use of recombinant human growth hormone, and improved nutrition status.[26] Oral intake and/or EN is always the first line of treatment to reverse malnutrition.[27] In patients where this is not successful due to feeding intolerance, volume restriction, or refusal to do EN and/or oral supplements, IDPN offers a noninvasive way to provide additional energy and protein intake to malnourished patients on hemodialysis. Administered during hemodialysis via venous access distal to the hemodialyzer, IDPN is not meant to be the sole source of nutrition but an adjuvant to oral intake and EN. When IDPN is provided in addition to oral intake and EN, weight[28] and BMI increase in children with organic and nonpsychosocial causes of malnutrition.[15,29,30] In addition, some research suggests that protein-energy wasting can be reversed.[31] IDPN has a good safety profile.[30] Indications for IDPN include 2 of the following criteria: serum albumin concentration less than 3.5 g/dL, evidence of protein malnutrition based on a normalized protein catabolic rate (less than 0.8 g/kg/d, energy intake less than 25 kcal/kg/d), weight loss equal to or greater than 10% ideal body weight over 3 months, dysfunctional gastrointestinal tract, inability to administer adequate EN especially if fluid limited, and inadequate weight gain over 1 month.[16,32]

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Question 8: What is the role of perioperative PN in patients undergoing elective/nonurgent surgery?

Recommendations

Adults

8A: Consider preoperative PN in severely malnourished patients unable to tolerate oral intake or EN.

8B: Reserve postoperative PN for severely malnourished patients unable to tolerate EN for more than 7 days unless initiated preoperatively.

Neonate and Pediatric

8C: Consider preoperative and postoperative PN in malnourished neonates and children unable to tolerate oral intake or EN.

Rationale

Recommendations 8A and 8B: Surgery is a stressful event on the physiology of the body. In patients with malnutrition, this added stress is associated with a negative impact, including increased mortality and complication rate.[1,2] In those patients undergoing surgery, more than one-third may be malnourished to some extent.[3] Malnourished surgical patients have an increased risk for a variety of negative outcomes, including infection, bacterial overgrowth in gastrointestinal tract, and poor wound healing.[4-7]

Malnutrition in perioperative surgical patients is evaluated through a combination of history, physical examination, and laboratory studies. This process should include nutrition screening, followed by formal nutrition assessment for those identified as nutritionally-at-risk through initial screening.[8] Multiple tools have been validated for nutrition screening and nutrition assessment to aid in accurately identifying patients with malnutrition.[9-13] Once the preoperative patient is identified as being malnourished, nutrition therapy may be required to prevent poorer outcomes, especially during major surgery or gastrointestinal surgery.[14] Although EN support is more common, PN support may have a role.

PN may have some impact in both the preoperative and postoperative periods. However, the exact timing and duration of perioperative PN is not fully defined. Preoperatively, PN is less preferred than EN.[15] Preoperative nutrition support is generally reserved for those patients who suffer from more severe malnutrition.[14,16] In these patients, preoperative PN may decrease overall complications but does not seem to affect mortality.[15,17] Furthermore, in patients undergoing gastrointestinal surgery who are malnourished and unable to tolerate EN, studies suggest that preoperative PN may decrease overall major complications.[18,19] Studies show that PN must be provided for 7–10 days to improve outcomes.[20] In the postoperative period, adequate nutrition is an important aspect of recovery. Although rapid initiation of EN is ideal and preferred, PN may have a role in those patients who are malnourished and unable to receive EN for more than 7 days.[14,21,22]

Neonates and Pediatric Considerations

Recommendation 8C: Surgery has been shown to cause metabolic changes resulting in hypermetabolism and catabolism. Providing adequate protein, energy, and micronutrients is key to prevent wound failure, infection, and mortality.[23] In pediatric patients, this is especially important given that children are growing and energy and protein needs are high. Individualized nutrition assessment, appropriate timing of postoperative nutrition support with a suitable and safe PN regimen when the gastrointestinal tract cannot be used, elimination of complications, optimal reintroduction of EN, and ongoing assessment of the PN regimen are important.[23] Whenever possible, oral intake and/or EN should be reintroduced postoperatively.[24] Malnutrition has been linked with postoperative wound infections and complications. This has been seen in children undergoing postoperative spinal fusion[25] and myelomeningocele repair.[26] Not only is energy intake important, but protein intake also influences outcomes. In infants undergoing gastroschisis surgery within 24 hours of birth, providing 2.5 g/kg/d of protein resulted in net positive nitrogen balance.[27]

Neonates and children with congenital heart disease often need palliative or corrective heart surgery and are at risk for poor growth and failure to thrive.[28] Infants with congenital heart disease are predisposed to energy and protein malnutrition as a consequence of metabolic dysregulation stemming from ischemia and reperfusion injury and postoperative hypermetabolism and hypercatabolism.[29] The metabolic response to surgery may be more severe than in older children and adults due to poor reserves.[28] Poor preoperative nutrition status is often made worse in the postoperative period due to the metabolic demands of surgery placing these infants and children at greater risk for developing infection and poor wound healing.[28] Often these children are critically ill in the perioperative period, with hemodynamic instability, hyperglycemia, hypotension, electrolyte disturbances, renal insufficiency, and fluid limitation due to the large number of required medication infusions (including inotropes). This results in less fluid being available for PN and the delivery of suboptimal nutrition with delayed sternal closure, wound infection, weight loss, and poor growth.[28] Larsen et al showed, in a group of 32 term infants who were receiving PN 1–4 days before and 10 days after open heart surgery, that lower energy intakes (less than 63 kcal/kg/d) were associated with increased duration of artificial ventilation, time to chest closure, time in intensive care unit and duration of hospital stay, increased duration of PN, and longer time to initiation and achieving goal EN. Infants with lower energy intake had greater morbidity over a 10-day postoperative period, and their cumulative energy deficit was a consequence of postoperative fluid restriction.[30] In children less than 24 months of age who had undergone cardiac surgery, acute and chronic protein-energy malnutrition was noted in almost 50% of children. The malnourished children had longer hospital stays and received only two-thirds of recommended energy and protein requirements on postoperative day 7. The study highlights the inadequacy of nutrition delivery.[29] Perioperative nutrition has important outcomes, not just on healing, but also on length of stay.

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Question 9: Is PN appropriate for patients in palliative care?

Global Recommendations

9A: Do not use PN solely to treat poor oral intake and/or cachexia associated with advanced malignancy.

9B: Limit the use of PN in palliative care to carefully selected candidates, with an expected survival of 2–3 months, for whom oral intake or EN is not feasible.

9C: Evaluate clinical factors and performance status when selecting candidates for PN at the end of life.

9D: Involve patients and caregivers in a clear and complete dialogue regarding realistic goals of PN, as well as the potential risks and burdens of therapy.

9E: Define criteria for discontinuing PN at the outset; consider stopping PN when the burdens and risks of PN outweigh potential benefits.

Rationale

Recommendation 9A: The question of whether to use PN at the end of life is controversial, raising clinical, ethical, and psychosocial challenges for patients, caregivers, and healthcare providers.[1-3] In the final weeks of life, loss of appetite and weight loss are common. The syndrome of anorexia and cachexia serves as a marker of advanced disease that is refractory to antineoplastic and nutrition intervention.[4-6] PN administration in patients with advanced cancer does not improve nutrition status, reverse cachexia, or improve survival.[3,4,6,7] Within the context of palliative care, the aim of nutrition care shifts away from maintaining or restoring nutrition status to maintaining or increasing comfort, by alleviating gastrointestinal symptoms, for example.[6,8] In addition to concerns regarding the lack of benefit, PN may also contribute to complications and other adverse events, such as central venous access device infection and hepatic dysfunction.[7,9]

At the end of life, weight loss and deteriorating nutrition status stand out as prominent stressors for patients and family members and, at times, acting as a source of conflict.[1,10,11] For terminally ill patients struggling with anorexia and cachexia, a conservative approach that aims to alleviate eating-related distress is most appropriate.[6] Open, empathetic communication with patients and caregivers is paramount in this process.[1,2] Other measures, such as optimizing symptom management and removing dietary restrictions, may also play a role in improving oral intake.[6] Requests by patients or family members for more aggressive nutrition intervention suggests a need for renewed efforts by the healthcare team to help patients deal with these difficult issues. At this point, prescribing PN to alleviate emotional distress would not serve the best interest of the patient.[7]

In exceptional cases where prognosis is not clear or when a potentially treatable cause of decline in nutrition status is present, a limited trial of PN may be in order. The plan to initiate PN should stipulate that PN will be withdrawn if no defined functional or clinical improvement in occurs within a specified period.[12]

Recommendation 9B: In each case, individualized interprofessional evaluation is needed to determine whether PN should be initiated in terminally ill patients. Numerous clinical factors influence this decision, including functional status, prognosis, the presence of significant comorbidities, and whether surgery or stenting is feasible.[2,13] At times, less tangible considerations support initiating PN. The presence of significant short-term goals, such as the desire to attend a wedding or survive for the upcoming birth of a grandchild, can justify

Table 9.1. Suitability Criteria for Parenteral Nutrition Use at End of Life.

Presence of a gastrointestinal condition precluding oral or enteral nutrition
Clinically and medically stable
Performance status sufficient to allow some participation in care • Karnofsky score greater than or equal to 50 for adults • No recommendation for specific cutoff on Lansky scale for pediatric patients
Expected survival of 2–3 mo
Availability of medical support for monitoring and follow-up for nutrition and nonnutrition healthcare issues, including symptom management
Willingness to adhere to scheduled laboratory monitoring
Availability of caregivers to assist with infusion procedures
Realistic expectations regarding benefits, understanding of risks and burdens of parenteral nutrition therapy

Adapted from Fuhrman MP, Herrmann VM. Bridging the continuum: nutrition support in palliative and hospice care. *Nutr Clin Pract*. 2006;21(2):134-141.

providing PN in a terminally ill patient.[14] Advanced age alone is not a valid reason for avoiding PN.[15,16] Table 9.1 provides more information regarding selection criteria when considering PN for individuals at the end of life. Despite the overall lack of benefit from PN in patients with advanced cancer, several case series in the literature suggest a supportive role for PN administration in a subset of patients with malignant bowel obstruction (MBO).[12-22]

PN has been shown to improve quality of life and confer a survival benefit in patients with MBO who are expected to survive 2–3 months, a point at which death is more likely to result from starvation than from disease progression.[2,15,17,23] In a retrospective study of 115 patients with MBO, median survival during PN was 6.5 months. Eleven patients survived 12 months or longer, and 2 patients were alive 4 years after initiating PN.[24] Patients and caregivers frequently associate PN administration with a sense of well-being and improved or stable quality of life.[3,11,25-28]

Most reports describing PN use in this population involve single centers with a small cohort of patients. One study, conducted in an inpatient palliative care unit, revealed that 1.8% of patients received PN during their stay in the unit.[29] However, some data suggest that PN use in palliative care may be more common than previously thought, with some variation across counties.[20,30] One systematic review with meta-analysis of home PN in patients with inoperable MBO involved 437 patients, one of the largest cohorts to date.[20] An additional multicenter observational study of home patients with incurable cancer included 414 subjects, with bowel obstruction listed as the indication in two-thirds of the cases.[28]

Information regarding the incidence of PN-related complications is not uniformly reported, but problems related to the vascular access device—most notably, infectious and mechanical complications—have been reported.[7] A recent study reported a low incidence of PN-related complications, including zero cases of line-related sepsis, but whether this outcome reflects current standards for PN management and care of the vascular access device or other factors is not known.[31] The presence of a venting gastrostomy tube, which is often used in tandem with PN to manage obstructive symptom, has been linked to a relatively high rate of complications.[16] Unplanned hospitalizations for managing treatment-related complications constitute an obvious setback at end of life, but no studies have examined the impact of these problems on quality of life.[16]

Recommendation 9C: Judicious clinical judgment is essential in selecting individuals who are most likely to benefit from PN. Before initiating PN for patients with MBO, all surgical, pharmacologic, or endoscopic treatment options to relieve obstructive symptoms should be considered.[9,19,32] No clear indicators are available to predict which patients will benefit from PN. Expected length of survival, which is a critical component of the selection process, should be 2–3 months in the absence of nutrition support.[2,6,15]

Prognostic models for estimating survival are often imprecise and error prone, but a recent study suggests that simple tools based on performance status may serve as reliable indicators of survival.[33] Most reports pertaining to PN administration in palliative care use a Karnofsky performance status index of 50 or higher as a guide for determining eligibility for PN therapy.[2,15,23,34,35] Table 9.2 provides detail regarding the use of the Karnofsky Performance Scale, which is designed for use with patients aged 16 years and older.[36] A similar scale has been developed for pediatric use (Lansky Performance Scale), but its applicability regarding PN use in palliative care requires further study.[37]

Recommendations 9D and 9E: Patients and family members must be fully involved in the decision-making process when PN is being considered. These discussions not only allow clarification of expectations and goals of care but also provide an opportunity for healthcare providers to review the risks and burdens of therapy, including the financial ramifications of PN therapy.[2,9,20,34]

Early conversations about initiating PN should also cover the circumstances that might lead to discontinuing therapy.[14,27] Like any medical intervention, PN should be continued only if it provides a benefit consistent with the goals of palliative care to reduce suffering and improve quality of life.[14] Withdrawing PN is a reasonable course of action when the burdens of care outweigh the benefits, the patient has experienced functional decline, or PN exacerbates symptoms, such as shortness of breath, ascites, or edema.[2,14] Ongoing evaluation of the burdens and response to therapy is critical to preventing PN from becoming a source of patient discomfort. From an ethical and legal standpoint, there is no differentiation between withholding and withdrawing therapy.[1] However, once started, PN may be difficult to stop, as withdrawing an element of care carries greater emotional weight than withholding therapy.[1,29] Sensitivity to the cultural values and religious beliefs of patients and families is crucial in this situation.

Table 9.2. Performance Assessment: Karnofsky and Lansky Scales.

Karnofsky Scale (Patients 16 Years and Older)		Lansky Scale (Patients Less Than 16 Years)	
Able to carry out normal activity; no special care needed		**Able to carry out normal activity; no special care needed**	
100	Normal, no complaints, no evidence of disease	100	Fully active
90	Able to carry on normal activity	90	Minor restriction in physically strenuous play
80	Normal activity with effort	80	Restricted in strenuous play, tires more easily, otherwise active
Unable to work, able to live at home, cares for most personal needs, a varying amount of assistance is needed		**Mild to moderate restriction**	
70	Cares for self, unable to carry on normal activity or to do active work	70	Both greater restriction of, and less time spent in play
60	Requires occasional assistance but able to care for most needs	60	Ambulatory up to 50% of the time, limited active play with assistance/supervision
50	Requires considerable assistance and frequent medical care	50	Considerable assistance required for any active play, fully able to engage in quiet play
Unable to care for self, requires the equivalent of institutional or hospital care, disease may be progressing rapidly		**Moderate to severe restriction**	
40	Disabled, requires special care and assistance	40	Able to initiate quiet activities
30	Severely disabled, hospitalization indicated although death not imminent	30	Needs considerable assistance for quiet activities
20	Very sick, hospitalization necessary	20	Limited to very passive activity initiated by others (watching TV)
10	Moribund, fatal process progressing rapidly	10	Completely disabled, not even passive play

Center for International Blood and Marrow Transplant Research, National Marrow Donor Program, and The Medical College of Wisconsin. Appendix L: Karnofsky/Lansky performance status. https://www.cibmtr.org/DataManagement/TrainingReference/Manuals/DataManagement/Documents/appendix-l.pdf. Published 2009. Accessed September 8, 2016. Used with permission.

Neonatal and Pediatric Considerations

Recommendations 9D and 9E: Stopping medical hydration or nutrition—PN in this context—is a morally and ethically permissible decision in some specific instances for neonatal patients after thorough and individual evaluations of the goals and expectations of care.[38,39] The evaluation should account for the child's interests, any potential net benefit of continuing PN, as well as burdens of the intervention. The process should include the parent or guardian in discussions and decision making.[39]

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Question 10: Which patients are appropriate for home PN therapy?

Global Recommendations

10A: Consider home PN (HPN) for patients with intestinal dysfunction who are clinically stable and able to receive therapy outside an acute care setting.

10B: Perform a thorough evaluation of medical and psychosocial factors that influence suitability for HPN.

10C: Address financial considerations/insurance coverage and patient responsibilities with the patient and caregiver.

Pediatric Recommendations

10D: Consider HPN for carefully selected, clinically stable pediatric patients who are expected to require PN for an extended period.

10E. Discharge all pediatric HPN patients to the care of a pediatric home care team and infusion provider with pediatric experience.

Rationale

Recommendation 10A: HPN plays a well-established role in the treatment of adults and children with intestinal failure.[1,2] HPN is indicated for clinically stable patients who cannot completely meet their nutrition requirements through oral intake or EN due to compromised digestion or absorption of nutrients.[3,4] Many HPN recipients depend on daily PN infusions, but for those with less severe gastrointestinal impairment, PN takes on a more supplemental role that allows some PN-free days. Common indications for HPN appear in Table 10.1. Wide variation exists in the data reported regarding the primary medical condition of patients requiring HPN. In many countries, the largest diagnostic category of HPN recipients consists of patients with active cancer, whereas Crohn's disease, short bowel syndrome, and surgical complications are more common reasons for HPN in others.[5-8] A downward trend in the use of HPN for Crohn's disease may reflect advances in the treatment of the disease, but more research is needed to confirm this premise.[5]

Irreversible gastrointestinal dysfunction can lead to long-term—even lifelong—dependence on HPN, but briefer courses of HPN are often appropriate.[3] Patients with complex surgical problems, such as an enterocutaneous fistula, may benefit from a more limited course of HPN.[8,9] For instance, on average, spontaneous closure of an enterocutaneous fistula takes place in 25 days for patients receiving PN.[9] In palliative care, a 2- to 3-month expected survival is commonly used to identify candidates who are likely to benefit from HPN.[10-12] In the current healthcare environment where PN administration is not considered a reason for extending an acute hospital stay, HPN is a

Table 10.1. Common Indications for Home Parenteral Nutrition.[2,3,36]

• Short bowel syndrome
• Crohn's disease
• Intestinal motility disorders
• Chronic bowel obstruction due to benign adhesions or strictures
• Radiation enteritis
• Malabsorptive disorders
• Intestinal and pancreatic fistula
• Gastrointestinal malignancy
• Malignant bowel obstruction, carcinomatosis
• Complications of bariatric surgery
• Gastroschisis
• Long-segment Hirschsprung's disease

cost-effective option versus treatment in the hospital, even for short courses of therapy.[2,13]

Recommendation 10B: Appropriate HPN demands the expertise of an interprofessional team, skilled in the management of all aspects of PN therapy, such as selecting a suitable vascular access, developing a PN prescription, monitoring response to therapy, detecting and treating complications, and weaning therapy as indicated.[2,4,13,14] Successful HPN management relies on collaboration among the referring physician, home infusion company (with expertise in HPN management), nutrition support clinicians, and home infusion nurses.[2] In addition to effective oversight by the clinical team, successful HPN hinges on the willing participation of thoroughly informed and educated patients and caregivers.[2,4,14]

As with all PN therapy, the primary factor for identifying appropriate candidates for HPN is the presence of medical conditions resulting in dependence on intravenous nutrition. In addition, the selection process requires a broader assessment of potential barriers to successful therapy.[3] Unstable clinical status, comorbidities such as uncontrolled diabetes mellitus or organ failure, and the complexity of the patient's home care needs may negatively alter the ability to develop a safe plan of care, making placement in an subacute or long-term acute care facility a better option.[2,12] Other factors that come into play when selecting candidates for HPN include an evaluation of the patient's understanding of the goals of care and the responsibilities for carrying out PN procedures, performance status, environmental cleanliness and safety, and cognitive ability.[2,3]

The active participation of patients and caregivers in the decision-making process is essential.[2-4] These discussions provide an opportunity to review the indication for HPN, the expected duration of therapy, and goals of care.[4] The benefits, risks, and burdens of therapy should be clear to patients and caregivers.[15] This discussion should describe the role of the patient and caregivers in carrying out HPN procedures and emphasize the importance of adhering to the proposed monitoring regimen, including follow-up appointments and scheduled laboratory tests.[2,16] Table 10.2 provides detail about the essential elements of a thorough assessment and teaching program for HPN candidates. Thorough education is critical for HPN candidates to achieve independence and successfully transition to home from an acute care setting.[17]

Table 10.2. HPN Checklist.

Assessment for HPN candidates
- ☐ Appropriateness of HPN: documentation of gastrointestinal failure
- ☐ Expected duration of HPN
- ☐ Short-term and long-term goals
- ☐ Appropriate vascular access for HPN
- ☐ Cognitive barriers to learning
  - ○ Need for interpreter
  - ○ Low literacy skills
  - ○ Memory deficits
- ☐ Physical barriers to learning
  - ○ Poor vision, hearing
  - ○ Low functional status
- ☐ Comorbidities, complexity of care (stomas, drains, wounds, etc)
- ☐ Evaluation of living arrangements
  - ○ Electricity, water, telephone, safety, working refrigerator, clean work area

Preparation and training for HPN
- ☐ Identification of home caregivers
- ☐ Identification of primary medical clinician
- ☐ Communication with home care company
- ☐ Distribution of contact information for patient and all care providers

Patient/caregiver education
- ☐ Hand hygiene
- ☐ Proper storage and handling of supplies
- ☐ Operation of infusion pump
- ☐ HPN preparation: sterile technique, additives
- ☐ Importance of adhering to oral or intravenous vitamin regimen
- ☐ Vascular access device care
  - ○ Dressing change (if applicable)
  - ○ Flushing
  - ○ Aseptic hub care ("scrub the hub")
  - ○ Antimicrobial lock (antibiotic or ethanol, if applicable)
- ☐ Monitoring
  - ○ Frequency of laboratory tests
  - ○ Daily weight
  - ○ Glucose monitoring
  - ○ Hydration status
  - ○ Checking temperature
  - ○ Recognizing complications (when to call healthcare provider)
- ☐ Emergency preparedness
  - ○ Establish plans for what to do during storms, extended power outages, evacuations, etc

At discharge
- ☐ Communication with home care company
- ☐ Verification of complete parenteral nutrition prescription to home care company with copy to patient
- ☐ Nursing visits
- ☐ Follow-up appointment

HPN, home parenteral nutrition. Adapted from Norman JL, Crill CM, Optimizing the transition to home PN in pediatric patients, *Nutr Clin Pract*. 2011;26(1):273-285; and Kumpf V, Tillman E, Home parenteral nutrition: safe transition from hospital to home, *Nutr Clin Pract*. 2012;27(6):749-757.

For HPN, the PN infusion is usually compressed to allow for time off each day.[18] For adult patients, HPN is typically cycled over 10–14 hours, (usually nocturnally) based on patient tolerance. Although cycled PN can contribute to metabolic disturbances (eg, glycemic control issues), this administration method offers physiologic and psychosocial benefits for long-term PN recipients. Nocturnal infusion of PN allows fuller participation in activities of daily living and can have a positive impact on QOL. The transition to cycled PN requires that patients be monitored closely for evidence of complications such as hyperglycemia or fluid intolerance, which warrants a more cautious approach to cycling the infusion. Adult patients generally tolerate abrupt discontinuation of PN without experiencing hypoglycemia.[18]

Although HPN undoubtedly provides a survival benefit to individuals with intestinal failure, the impact of this therapy on quality of life (QOL) outcomes serves as another key element in judging the success of treatment.[3] Historically, the literature has reported poor QOL among HPN recipients, similar to that of patients receiving chronic dialysis.[9,19] In particular, the complex nature of short bowel syndrome and its associated symptoms and complications constitutes a significant burden that is detrimental to QOL.[20] One study that explored the various components of QOL in depth noted that patients often expressed more positive opinions of the impact of HPN, seeing the therapy as a "lifeline" or "safety net."[19] A small qualitative study of HPN recipients reported that PN improved QOL despite the burdens associated with treatment.[21] These findings are comparable to studies of HPN use in oncology patients, who generally have a favorable perception of the impact of HPN on QOL.[22,23] In some cases, QOL may be related to the inability to eat, rather than dependence on the therapy itself. The wider use of a validated QOL questionnaire designed specifically for HPN recipients could shed more light on this issue and enable clinicians to better meet the humanistic needs stemming from long-term dependence on PN.[24]

Recommendation 10C: Unfortunately, insurance coverage figures prominently in decisions regarding HPN. Considerable variation exists in HPN reimbursement practices for commercial payers and federal insurance programs.[25] Although insurers recognize home care as a cost-effective alternative to a prolonged hospital stay, the costs associated with PN have led many third-party payers to develop eligibility criteria aimed at confirming medical necessity for HPN. For example, the Centers for Medicare and Medicaid Services (CMS) have established strict conditions that must be met to qualify for HPN reimbursement.[25] The approval process for HPN frequently requires documentation of the diagnostic and clinical factors that preclude oral intake or EN, which may include evidence of failed EN trials, operative reports, results of laboratory tests, and imaging studies.[2,4,25,26] Even after receiving confirmation of coverage, patients sometimes bear responsibility for substantial out-of-pocket costs.[25] More detail regarding CMS HPN eligibility criteria is publicly available through the CMS website, https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=242&ncdver=1&bc=AAAAQAAAAAAA.[27]

Pediatric Considerations

Recommendations 10D and 10E: In pediatric patients who require PN for an extended period, HPN is recognized as the best option for improving the QOL of these children and their families.[28] It is indicated for children who cannot digest and absorb food and who are able to receive therapy safely outside a hospital.[2] These patients have conditions of impaired digestion and absorption (short bowel syndrome, intractable diarrhea of infancy, immune dysregulation, Crohn's disease) and dysmotility (chronic intestinal pseudo-obstruction, intestinal failure) unresponsive to EN.[29,30]

Pediatric candidates for HPN must have appropriate CVADs and stable fluid, electrolyte, and glucose needs, as well as trained parents/guardians and appropriate home situations (as outlined in Table 10.2). In addition, HPN candidates must be cared for by a qualified and capable home infusion provider with pediatric experience. All patients should be discharged to the care of a HPN team. Some authors suggest that, for pediatric patients needing PN, the minimum duration of HPN be at least 30 days; however, a definitive time frame for the minimum duration of HPN has not been established.[30,31] Current trends toward briefer hospital admissions may make shorter courses of HPN a cost-effective option.[32] Outcome and survival are mainly determined by underlying diagnosis and management by a center experienced in HPN.[28] A large European benchmarking survey of adults and children showed that the risk of death is increased when the patient is not followed by an experienced HPN team; is less than 2 or more than 40 years of age; has a very short bowel remnant or stoma; or has myopathic chronic intestinal pseudo-obstruction, systemic sclerosis, radiation enteritis, intra-abdominal desmoid tumors, necrotizing enterocolitis, or congenital intestinal disorder.[33]

Successful home care depends greatly on the patient's support system and the ability of the parents/guardians to learn and independently perform medically complex procedures after appropriate training.[2] A primary caregiver (usually a parent) is trained with a backup caregiver. Prior to discharge, all patients need to have long-term and short-term goals determined and a primary pediatrician identified.[34] Candidates for HPN should have the primary disease and clinical condition stabilized, including fluid balance, glycemic control, and acute electrolyte and acid-base abnormalities. Since the PN prescription can generally be changed only once a week, clinical stability is essential. Pediatric patients require that the macronutrient, micronutrient, and energy intake be adjusted frequently to maintain normal growth.

As with adults, cycled PN for pediatric patients promotes greater mobility and participation in school and social events. The duration of the cycle depends on the age and weight of the

patient, with younger patients often requiring longer cycles. Infants may require 18-hour to 20-hour infusions, while adolescents may tolerate 10-hour to 12-hour nocturnal regimens. In children less than 3 years of age, PN must be tapered down at the end of the infusion to avoid rebound hypoglycemia.[18] In pediatric patients, the need for repeated phlebotomy for laboratory tests and acute clinical monitoring at home may pose difficulties and should be considered before discharge. Factors that should be assessed as part of the discharge-planning process include insurance coverage, a home safety evaluation, and a physical, nutrition, and psychological needs assessment.[2] The facility in which the patient is hospitalized plays a critical role in planning a safe transition to home.[34] An evaluation of the home infusion company and the team delivering care should take place prior to discharge, to verify they have experience with pediatric HPN recipients.[30] In addition to outlining a teaching plan for HPN, the checklist shown in Table 10.2 is useful in assessing readiness for discharge.[34] Children and their families who demonstrate resilience and positive attitudes are generally the most successful in transitioning to HPN.[35]

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Question 11: Under what circumstances can PN be safely initiated in the home setting?

Recommendations

Adult

11A: Establish organizational policies that delineate circumstances in which initiation of home PN (HPN) can take place outside the acute care setting.

11B: Delineate patient-centered eligibility criteria for initiating PN safely in the home setting.

11C: Develop strict protocols and procedures for initiating PN in the home setting, monitoring response to therapy, and documenting outcomes.

11D: Conduct a comprehensive medical, clinical, and psychosocial assessment of HPN candidates to assess risk factors for adverse events related to initiating PN.

11E: Consider initiating PN therapy at home only when assessment confirms that the benefits greatly outweigh the risks.

Pediatric

11F: In pediatric patients, do not initiate PN in the home setting; admit all patients to the hospital for initiating HPN.

Rationale

Recommendations 11A–11C: Although most HPN recipients continue a nutrition regimen that began in an acute care hospital, an inpatient admission is no longer considered a prerequisite for initiating HPN.[1] Once a topic of some debate, clinical experience suggests that HPN can be safely initiated in carefully selected patients.[2,3] However, no research data exist regarding outcomes for PN that is started in the home setting.

As with other aspects of nutrition support, safe HPN initiation requires the expertise of a well-functioning interprofessional team.[4,5] Providers of home infusion services must develop and adhere to policies and procedures for initiating PN at home that address patient selection, components of the initial and ongoing PN formulation, progression toward therapeutic goals, and the roles and responsibilities of each member of the team.[5] Effective management of HPN requires knowledge of underlying disease states and comorbidities, the impact of concomitant medical and pharmacologic treatments, management of fluid and electrolyte disturbances, and interpretation of laboratory values.[1,4,5]

Recommendation 11D: The first step in identifying appropriate candidates for initiating PN at home is to verify that the patient has a valid indication for long-term PN therapy. Then, each patient must undergo a thorough evaluation of the home environment, medical suitability, learning ability, the need for additional caregivers, and reimbursement sources.[1]

Not all HPN candidates are suitable for starting HPN outside the hospital environment. Each case must be determined on an individual basis. The presence of risk factors such as those found in Table 11.1 often require a level of clinical monitoring and intervention that can best be provided in an acute care setting. Additional nonclinical factors may influence the decision against initiating PN at home. For instance, patients who live in remote areas often present logistical challenges to adequate patient education, nursing follow-up, and response to urgent situations that might develop. In some cases, the logistical difficulties presented by the need for frequent laboratory monitoring in the initial phase of PN constitutes a significant barrier to safe HPN initiation outside the acute care environment.

To reduce the risk of PN-related complications, home infusion companies develop protocols that stipulate a conservative approach to the initiation of PN.[1] These protocols typically stipulate that fluid and electrolyte disturbances be corrected prior to initiating PN. An infusion of conventional intravenous fluids may be warranted for patients with dehydration or electrolyte deficits. The initial PN prescription should contain a relatively low-dextrose dose to reduce the risk of refeeding syndrome or other metabolic disturbances. Progress toward the goal PN formulation and cycled administration can take place in a stepwise fashion, based on fluid tolerance and glycemic control.[1]

Recommendation 11E: Although factors related to the healthcare economy have created incentives to initiate PN at home, this option does offer patient-centered benefits beyond cost savings. For instance, education and monitoring take place in familiar environment with less disruption of daily activities. Avoiding a hospital admission also reduces exposure to hospital-borne pathogens and the risk of contamination of the vascular access device. In all cases, PN should be initiated outside an acute care environment only when the interprofessional assessment process determines that the benefits of initiating PN at home outweigh the risks.[1,5] Patient safety always takes priority over attaining nutrition goals.

Pediatric Considerations

Recommendation 11F: Pediatric patients should not have PN initiated at home because of the difficulty in making the day-to-day changes needed to get to a goal regimen. Central venous access is critical for infusing an HPN admixture and often requires sedation/general anesthesia for central venous access device placement. Depending on nutrition status, it can take up to 3–5 days to reach a goal PN regimen, and regimens will need to be changed daily. Cycling the PN regimen must be closely monitored to avoid hypoglycemia.[6] Parents need to be taught PN administration techniques and central venous access

Table 11.1. Situations in Which Initiating PN at Home Is Not Recommended.

Unstable medical status
Inability to obtain required laboratory monitoring
Significant risk for refeeding syndrome • Severe malnutrition • Severe involuntary weight loss: 10% or more of usual body weight in 6 mo or 5% or more of usual body weight in 1 mo
Presence of comorbidities associated with potential PN complications • Poorly controlled hyperglycemia • Major organ dysfunction • History of allergy/sensitivity to PN components (eg, eggs, soy)
Risk for Wernicke's encephalopathy • Alcohol abuse • Hyperemesis gravidarum • Intractable vomiting
Severe fluid, electrolyte, and/or acid-base disturbances • High-volume diarrhea or ostomy output • Fistula output greater than 1000 mL/d
Poor performance status • Low visual acuity • Poor manual dexterity
Lack of a supportive care partner
Inadequate vascular access

PN, parenteral nutrition.
Adapted from Newton A, DeLegge M, Home initiation of parenteral nutrition, *Nutr Clin Pract*. 2007;22(1):57-64; and Durfee SM, Adams SC, Arthur E, et al, ASPEN standards for nutrition support: home and alternate site care, *Nutr Clin Pract*. 2014;26(4):542-555.

device care, and they need to demonstrate competence in these areas. Patients need to be discharged to the care of home care companies and home nursing agencies that have staff trained in caring for pediatric patients.[7] Most home care companies do not have experience with pediatric patients and would therefore lack resources needed to safely start PN at home.

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Question 12: What strategies should healthcare organizations implement to reduce the risk of clinical complications associated with PN?

Global Recommendations

12A: Employ standardized processes for managing PN.
12B: Incorporate measures to reduce the risk of complications into organizational policies and procedures for administering PN.
12C: Use an interprofessional team of clinicians with expertise in nutrition support to manage PN.
12D: Educate PN prescribers and demonstrate prescribing competencies for all clinicians writing PN orders.

Rationale

Recommendation 12A: Adverse events associated with PN may stem from errors in the PN use process or as a result of factors related to therapy itself.[1,2] The therapy-related clinical complications associated with PN have been categorized as mechanical (eg, air embolus), infectious (eg, sepsis), metabolic (eg, electrolyte imbalance), and nutritional (eg, imbalance of macronutrients).[3] When considering the PN complications described in the literature, it is important to recognize that reported complication rates do not always reflect currently accepted best practices. In some cases, reported PN complications may be due to practices that are now considered to be unsafe or associated with complications.

Even when no overt errors have taken place, therapy-related complications may result from patient-related clinical factors (eg, underlying disease, severity of illness), variations in prescribing and monitoring patterns, and suboptimal standards for care of the vascular access device. As with PN-related errors, a key component of appropriate PN management involves recognizing potential clinical complications and implementing risk reduction strategies.[4] By using a standardized process for PN management, healthcare organizations may reduce complications related to the PN process.[5] The ASPEN parenteral nutrition clinical guidelines and PN safety consensus recommendations detail standardized procedures for all phases of the PN use process to avoid errors.[1,2] A similar approach is required to avoid therapy-related complications.

As early as 1974, Kaminski and Stolar published survey results showing that PN practices in hospitals deviated from standards of care.[6] Unacceptable practices occurred in several areas, such as skin preparation for catheter insertion, catheter care, and sterility of the infusion system. The survey results indicated the presence of several complications: catheter placement complications (12%), glucosuria (42%), dehydration (5%), fluid and electrolyte abnormalities (28%), and fevers not traced to a source other than PN (42%). Skoutakis and colleagues implemented a detailed protocol and PN team.

Standardization resulted in significant reductions in complications as compared with the data reported by Kaminski and Stolar: sepsis (less than 1%), electrolyte abnormalities (2.7%), and glucosuria (5%).[7]

The literature continues to highlight the need for standardizing PN management. A survey conducted by ASPEN in 2003 showed lack of consistency in ordering and labeling of PN.[8] Forty-six percent of responders reported adverse events directly related to PN that required intervention.[8] The most recent survey of PN use demonstrated that poor compliance with available guidelines remains a problem.[9]

Recommendation 12B: Regardless of care setting (acute care to home care), policies and procedures for the PN process should include measures to reduce the risk of complications (eg, promote glycemic control, avoid overfeeding, provide meticulous management of vascular access devices). These policies and procedures should incorporate the best available evidence regarding minimizing the risk of PN complications and improving outcomes, including scientific literature, clinical guidelines, standards, and the requirements of regulatory bodies.

Protocols that proactively seek to avoid adverse events associated with PN and strive to eliminate outdated practices have been associated with favorable PN outcomes. In an early report, Brown and Grenkoski showed a reduction in the incidence of sepsis from 12.5% to 5.1% in a community hospital after implementing PN procedures for catheter insertion and care, a nursing care plan, and a metabolic flow sheet.[10] More recent studies have demonstrated that PN does not contribute to complications when current standards for glycemic control and nutrient intake are used.[11,12]

Recommendation 12C: Literature supports PN management by an interprofessional team of clinicians with expertise in nutrition support. To improve quality of patient care and clinical outcomes, it has been suggested that nutrition support teams composed of a physician, a dietitian, a nurse, and a pharmacist, at a minimum, can create an institutional culture where all stakeholders value optimizing clinical nutrition care.[13] Given the complex nature of the PN process that crosses disciplines, collaboration is key to reduce the risk of complications.

Trujillo and colleagues found that PN prescribed by a nutrition support team versus an individual clinician resulted in fewer complications (34% vs 66% of PN days).[14] Nehme compared outcomes in patients receiving PN at a hospital managed by an interprofessional nutrition support team versus patients receiving PN at a hospital managed by physicians.[15] In patients managed by the interprofessional nutrition support team, 3% developed sepsis and 3% had an electrolyte imbalance, but there were no patients with glucosuria or death associated with nutrition support therapy.[15] In the patients without team management, 36% had electrolyte abnormalities, and 10 patients died from complications resulting from glucose imbalance that led to hyperosmolar hyperglycemic nonketotic syndrome.[15] In a systematic review, Naylor and colleagues showed that PN patients managed by an interprofessional nutrition support team had fewer total mechanical complications.[3] The 6 studies reporting mechanical complications included in the systematic review showed reductions in total mechanical complications ranging from 3.6% to 24% in PN patients managed by an interprofessional nutrition support team.[3]

Recommendation 12D: Prescribers should receive education and demonstrate competency to manage PN, a complex and high-risk medication, to reduce the risk of errors and therapy-related complications.[1,2,16,17] While there is limited literature, education in PN prescribing has been associated with decreases in overall PN prescription errors and overfeeding.[18-21] Consequently, prescribers from all disciplines should receive education on PN prescribing and monitoring led by clinicians with expertise in nutrition support.[13]

Competency in PN management may be demonstrated through certification as a nutrition support clinician or board certification.[16,17] The ASPEN model for competency demonstration for prescribers not certified in nutrition support includes the following: completion of a didactic/interactive PN order-writing course with a pretest and posttest, completing PN orders and modifying PN orders for competency evaluation by an experienced preceptor, and completing ongoing continuing education on nutrition support and PN order-writing assessment.[16,17]

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Question 13: For patients receiving PN, which parameters should be monitored to assess progress toward therapeutic goals, the need to adjust the PN prescription, and when to wean or discontinue this therapy?

Recommendations

Global Recommendations

13A: For patients of all ages and in all healthcare settings, provide interprofessional monitoring of clinical status and response to PN therapy by clinicians with expertise in managing PN.

13B: Modify the PN prescription as indicated per ongoing evaluation of gastrointestinal function, nutrition status, and, for pediatric patients, growth.

1: Wean PN when oral intake and/or EN achieves 50%–75% of requirements for energy, protein, and micronutrients, unless impaired gastrointestinal function precludes 100% absorption of nutrient needs.

2: Consider using a weaning protocol during the transition from PN to EN.

Rationale

Adult Considerations. **Recommendation 13A:** The PN monitoring process aims to determine appropriateness of the therapy, ensure attainment of nutrition goals, and reduce the risk of complications. This includes regular evaluation and documentation of the patient's nutrition status and an ongoing evaluation of gastrointestinal function.[1,2]

PN is a complex formulation consisting of limitless combinations of nutrient-based components that is not without significant risk.[3] This complexity—and the inherent potential for harm to the patient—requires formal processes that promote safety, prevent iatrogenic complications, and meet the patient's established nutrition needs. Safe PN administration starts with an understanding of macronutrients, micronutrients, fluid balance, and acid-base equilibrium.[3] Approaches for PN monitoring build on this foundational knowledge to help identify potential adverse events and prevent complications related to PN therapy.

A comprehensive evaluation of nutrient needs should be undertaken, and therapeutic nutrition goals should be established for patients requiring PN. The contribution of clinicians from an interprofessional team, who are well versed in this therapy, has been shown to minimize PN-related errors and improve patient outcomes.[3-5] Pharmacists play a role in ensuring that the PN formulation is compatible and stable, safeguarding against medication incompatibilities and recommending specific components during times of shortages. (For more information regarding product shortage management, visit the ASPEN website.[6]) To date, no strong research evidence is available to support the specific parameters or timing of such monitoring techniques, and the recommendations discussed here rely heavily on expert opinion.

Patients who are deemed appropriate for PN therapy and are metabolically stable, with normal serum electrolytes and blood glucose concentrations, make the most ideal candidates for initiating PN. Unfortunately, this is seldom the case, especially for the critically ill, metabolically stressed patient. Of further concern is the patient with severe malnutrition who is at risk for refeeding syndrome.[7] In this situation, the primary focus of care moves away from immediate provision of adequate energy and protein to preventing a nutrient-related imbalance or exacerbating an existing disturbance. Prior to starting PN, allergy information (egg allergy and reactions to any component of PN) and a history of infusion-related events must be determined. Monitoring parameters, such as those listed in Table 13.1, can limit adverse events related to PN therapy. In addition, this information can guide decisions about the macronutrient content of PN formulations in a way that optimizes fluid, electrolyte, and acid-base stability. Further discussion regarding appropriate indications and route of infusion are detailed in other sections of this paper.

The ingredients of the initial PN formulation should be based on assessment and review of the patient's clinical condition, active medical issues, nutrition status, nutrient requirements, fluid status, vital signs, medications, and biochemical data. Among the problems that occur with PN administration, hyperglycemia and electrolyte derangements are most common.[8] Therefore, monitoring the major electrolytes involved in nutrient metabolism and fluid homeostasis, blood glucose concentrations, and acid-base balance is important.[9] See Table 13.1 for a list of clinical monitoring parameters and Table 13.2 for detail

Table 13.1. Clinical Monitoring During PN: Hospitalized Patients (Adult and Pediatric).[1,10,17,19,30]

Parameter	Approach	Frequency
Physical examination	Including a nutrition-focused approach: • Micronutrient abnormalities • Muscle and fat stores • Fluid accumulation • Functional/developmental status	On initial examination[a]
Adults: evaluate weight and height	Use of stadiometer, knee height calculations, or arm span measures Weight scales used in a consistent manner; patients should not wear shoes or heavy garments	On initial examination, then weights daily until stable 2–3×/wk for stable patient
Neonates/pediatrics: growth parameters measured and documented on *z*-score charts	Children less than 36 mo old: • Weight for age • Head circumference for age • Weight for length • Length for age Children 2–20 y old: • Standing height for age • Weight for age • Body mass index for age • Length/height for age	Neonates: weight daily, length and head circumference weekly Infants daily weight, monthly head circumference and length Children: weight daily to twice weekly, height monthly
Determine energy and macronutrient needs	Use of appropriate predictive equations, indirect calorimetry, or nitrogen balance	On initial examination, then when changes in medical condition or activity level occur
Evaluate intake and output records	Oral or enteral intake, intravenous fluids and medications, blood products, urine, stool/ostomy/fistula output, other relevant wound/drain output	On initial examination, then daily until stable
Review vital signs	Blood pressure, respiratory rate, heart rate, temperature	On initial examination, then daily until stable
Blood glucose monitoring	Capillary glucose levels, in addition to correctional dose insulin program and ancillary orders for appropriate intervention for hypoglycemia	Every 1–24 h, as warranted by clinical status, discontinue once blood glucose values normalize and PN reaches target dextrose dose
Evaluation of micronutrient status	Serum levels vitamins, minerals, trace elements	When history, physical, and/or clinical evidence suggests an abnormality
Examination of VAD	Inspection and palpation to assess for redness, tenderness, or rash under dressing or along subcutaneous tunnel Observe for upper extremity edema Review position on chest x-ray	Daily assessment; x-ray confirmation at VAD placement, when admitted with a VAD in place, whenever concern for catheter displacement exists
Reassess continued need for PN therapy	Intake and output records, nutrition adequacy assessment, physical examination, radiologic evaluation	Daily; or with signs indicating return of or improvement in bowel function or with change in pertinent clinical condition
General response to therapy	Wound healing, stamina, functional status, progress toward weight or growth goals	Ongoing throughout the course of therapy

PN, parenteral nutrition; VAD, vascular access device.
[a]Physical examination should be done initially, then according to individual hospital nutrition reassessment policy.

regarding laboratory monitoring. Close review of intake and output records (medications, oral intake, blood transfusions, stool output, fistula drainage, etc) along with vital signs, blood urea nitrogen, and serum creatinine levels helps to determine the volume required for the PN prescription. These parameters should be evaluated daily until the patient's medical condition has stabilized and the PN formulation is revised to meet the goal for nutrient delivery.

Visceral protein concentrations, such as prealbumin, albumin, and transferrin, are unreliable markers of nutrition status.

Table 13.2. Laboratory Monitoring During PN (Adult and Pediatric).[1,10,17,19]

	Acute Care PN			Long-Term PN			
Parameter	Baseline	Days 1–7	Ongoing, Stable	Initial, Postdischarge	Weeks 1–4 (or Until Stable)	At 3 mo	Ongoing, Stable
Glucose, BUN, creatinine, electrolytes, calcium, magnesium, phosphorus	√	Daily × 3 or until stable	1–2×/wk or as clinically indicated	√	√		Monthly
CBC with differential	√	Daily × 3 or until stable	1–2×/wk	√	√		Monthly
Total bilirubin, direct bilirubin, AP, AST, ALT,	√		Weekly	√			Monthly
PTT, PT, INR	√		Weekly				Monthly
Triglyceride level	√	Pediatric: daily until stable then weekly	Weekly	√			Monthly
Serum proteins (to monitor inflammation)	√		Weekly	√			Monthly
Iron indices			As clinically indicated			√	Every 3–6 mo
Zinc, selenium, manganese, copper, chromium			As clinically indicated			√	Every 3–6 mo
Vitamin A, OH-25 vitamin D, vitamin E			As clinically indicated			√	Every 12 mo
Vitamin B_{12} and folate			As clinically indicated			√	Every 6–12 mo
TSH				As indicated			Every 12 mo
Carnitine			No guideline for adults			√ Pediatric patients	Every 3–12 mo

ALT, alanine aminotransferase; AP, alkaline phosphatase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CBC, complete blood count; INR, international normalized ratio; PN, parenteral nutrition; PT, prothrombin time; PTT, partial thromboplastin time; TSH, thyroid-stimulating hormone.

Yet obtaining a measure of these serum protein concentrations at baseline, then again at routine intervals, may provide some insight into a patient's medical condition, fluid status, and inflammatory process.[1,10] Nitrogen balance studies serve a useful function in assessing protein requirements and adequacy, especially in high-risk populations such as those with a protracted hospital course. Procedural limitations can influence the accuracy of nitrogen balance studies, especially in situations where insensible protein losses are high, such as those that occur in patients with significant wounds.

Prior to administering ILE, serum triglyceride concentrations should be determined, in particular for patients with a known history of elevated triglyceride concentrations and for those with risk factors for hypertriglyceridemia.[11] Hypertriglyceridemia—which could increase the risk of developing pancreatitis—has occurred in response to rapid infusion of ILE, propofol use, overfeeding, suboptimal glucose control, and inflammation.[11] Triglyceride levels less than 400 mg/dL are acceptable, and the contribution of energy from lipids should not account for more than 30% of total energy intake.[11,12] Optimal triglyceride monitoring should occur weekly, when ILE intake increases, and during sepsis (when ILE is being administered only as a means to prevent essential fatty acid deficiency). Frequency of monitoring should be adjusted per the acuity of illness and the clinical stability of the patient.[1]

Obtaining a liver function panel at baseline and weekly is recommended due to concerns for PN-associated hepatobiliary disorders, which can occur shortly after starting PN and pose an increasing risk to the patient the longer he or she receives PN.[1] Historically, the PN admixture itself has been considered the sole cause of these hepatobiliary disorders.[11,13] Yet more recent evidence suggests that this phenomenon results from a complex array of factors shared by many patients who require PN.[11,13] Adult patients reliant on PN can be affected by steatosis, gallbladder stasis with accompanying sludge/stones, and/or cholestasis.[13] Steatosis, thought to be a complication of overfeeding, is identifiable by elevations of serum aminotransferase and can occur in adults within 2 weeks of initiating PN, even if the patient is clinically asymptomatic.[11] Gallbladder stasis with subsequent development of sludge or stones and consequent cholecystitis appears to correlate more with lack of enteral stimulation than the actual PN components and is more prevalent the longer an individual requires PN.[9] PN-associated cholestasis is less prevalent in adults than children and affects those receiving long-term PN.[11,13,14] Monitoring pertinent laboratory tests, providing a balanced nutrient profile that does not promote overfeeding, allowing for the ingestion of oral intake or EN (as appropriate), and instituting measures to prevent infection are strategies for preventing hepatobiliary complications.[11,13-15]

Further potential complications that should not be overlooked include those related to the VAD, as discussed in Question 5. For this reason, the clinician should routinely evaluate the CVAD for external evidence of potential problems, although fever is often the only sign of CLABSI. In patients receiving cycled PN, a temperature elevation that occurs as the infusion begins may be an indication of microbial colonization of the CVAD. In this case, blood cultures are warranted to evaluate the source of the fever. For HPN, patients should receive a thermometer and instructions for correct use, so they can assume responsibility for this aspect of monitoring after discharge.

Ongoing dialogue with nurses can also ensure that PN is being completely infused and nutrient needs are being met as prescribed. It is not uncommon for PN to be interrupted due to inadequate venous access, medication incompatibilities, or other concurrent medical interventions. This situation may be improved by adjusting the PN administration routine (eg, cycling) or the medication administration schedule to help meet the patient's needs.

For patients receiving PN in long-term care or home settings, therapeutic monitoring should continue but not as frequently, based on the metabolic stability of the patient and the frequency of changes that are required in the PN formulation. Home care visits are used to obtain the patient's vital signs, measure and record weight, assess hydration status, review pertinent physical examination findings, assess the CVAD, review medication use (including compliance with oral or intravenous vitamin regimens), and evaluate readiness to transition to oral nutrition. All laboratory results should be documented at baseline, upon hospital discharge, or at the beginning of HPN and then regularly throughout the course of therapy.[16] Table 13.3 provides more information about monitoring for HPN recipients.

Pediatric Considerations. **Recommendation 13A:** As with adults, PN in pediatric patients is considered a high-alert medication and should be used only by trained professionals under the supervision of a nutrition support team. It is important to have PN protocols in place to allow for safe and standardized administration of PN. In neonatal and pediatric patients, the regimen must be tailored to the age of the patient and diagnosis since nutrition needs vary greatly from birth through adolescence. An individualized nutrition care plan must be developed for each patient and should be assessed daily as PN is initiated and less frequently once the patient is on a stable regimen.[17] ASPEN standards state that nutrition goals should include short-term and long-term objectives. In addition, a plan for monitoring the effect of interventions should be clearly stated in the nutrition care plan.[18] Not only should adherence to the plan and tolerance of the regimen be monitored, but weight gain and growth should also be assessed by *z*-scores or percentiles for weight and length/height.[19] Close monitoring and timely adjustment of the regimen are essential in providing safe PN. The opportunity for changing to EN should be periodically assessed, and when possible, efforts to transition from PN to EN should take place. Nutrition assessment, recommendation, activation, and evaluation of the plan form a continuous cycle that needs to be followed by the practitioner.[17,18]

Table 13.3. Monitoring PN in the Home and at Alternate Sites.[1,2,17,29,30]

Assessment Parameters	Frequency of Monitoring
Signs and symptoms of intolerance to therapy	Weekly or at each home visit and patient encounter
Home environment assessment (running water, electricity, telephone, safe and sanitary conditions, etc)	Prior to discharge to that environment, then regularly throughout the course of therapy
Vital signs	At each home visit and patient encounter
Weight changes and/or growth as appropriate; maintain weight/growth charts	Weekly and at each home visit and patient encounter
Children less than 36 mo old: • Length for age • Weight for age • Head circumference for age • Weight for length Children 2–20 y old: • Standing height for age • Weight for age • Body mass index for age • Length/height for age	Monthly and at all patient encounters with healthcare providers Documented on *z*-score growth charts
Hydration status	Baseline and regularly throughout the course of therapy
Review of systems and/or physical examination	Weekly or at each home visit and patient encounter with healthcare provider
Clinical signs of nutrient deficiencies or excesses	Baseline, weekly until stable, then monthly
Other disease states or conditions that may affect the nutrition therapy	Baseline and regularly throughout the course of therapy
Dual-energy x-ray absorptiometry scan	Baseline when expected duration of PN exceeds 6 mo, then annually
Liver and biliary tract ultrasonography	As clinically indicated
Assess readiness to begin or advance oral and/or enteral intake; provide dietary guidance as indicated	Baseline and at every patient encounter
Interaction between nutrition therapy and medications	Baseline, when medication changes occur, then monthly
Functional status and performance	Weekly
Psychosocial status, quality of life, sleep disturbances, etc	Weekly
Vascular access device and insertion/exit site	Baseline and weekly
Evaluate patient compliance with techniques and procedures of nutrition therapy, storage of formulations, and supply inventory	Weekly or at each home visit

PN, parenteral nutrition.

As discussed in Question 5, the choice of VAD should be based on the nutrition care plan: duration of therapy and osmolarity of the admixture. If PN is to be administered for more than 5 days or when the osmolarity of the PN formulation is greater than 900 mOsm/L, then central venous access should be obtained.[20] In patients receiving peripheral PN, frequent monitoring of the intravenous site for early signs of infiltration per hospital policy is important. Adherence to standard venous access care policies to prevent PN complications, including central line–associated bloodstream infection, should be part of the monitoring process.

Monitoring parameters are chosen relative to the goals and timing of the specific interventions and will depend on the clinical condition, degree of malnutrition, existing deficiencies, and needs and age of the child. Monitoring the PN regimen includes weight gain, growth, fluid status, clinical status, tolerance to PN and EN, medication changes, laboratory values, and PN complications. Frequency depends on age of the patient, severity of illness, response to the nutrition regimen, comorbid illness, and degree of malnutrition[17] (see Table 13.1). In malnourished children where refeeding syndrome is a possibility, more frequent monitoring is appropriate. Tolerance to the PN volume and macronutrients can be determined by weight changes, monitoring input and/or output volumes and vital signs, laboratory testing, use of diuretics and

steroids, and physical examination. Bedside monitoring of capillary glucose concentrations is critical in at-risk patients, especially during cycling of PN. If the evaluation shows that the goals are not being met or that new problems/risks have arisen, reassessment of the nutrition care plan should occur.[18] Appropriate growth charts that incorporate *z*-scores should be used to monitor growth.[19] Assessment of actual versus projected energy and protein intake should routinely take place, especially when response to therapy does not match goals.[21]

Changes in PN ingredients may affect the stability or compatibility of the PN admixture.[17] Therefore, the PN order review and preparation require supervision by an experienced PN pharmacist.[3] This is especially critical in neonates who have high calcium and phosphorus requirements. ASPEN guidelines state that each PN admixture should be inspected for signs of gross particulate contamination, discoloration, particulate formation, and phase separation at the time of compounding and before administration. Additionally, an experienced pharmacist can be helpful in navigating PN micronutrient shortages. Drug-nutrient interactions and incompatibilities must be monitored since this may affect the delivery of the PN, especially if the patient has a single-lumen CVAD.[1,18]

Laboratory monitoring is essential for assessing PN tolerance, detecting nutrient deficiencies, and preventing metabolic complications. The parameters monitored and the schedule for performing laboratory tests must be customized according to the clinical and metabolic stability of the patient. Excessive phlebotomy can result in anemia, requiring blood transfusion, a critical event for a small neonatal or pediatric patient. Laboratory testing includes measurement of serum electrolytes, minerals, glucose, and triglycerides, as well as renal function and acid-base balance. Baseline laboratory tests should be obtained by following daily serum electrolytes, glucose, blood urea nitrogen, creatinine, magnesium, phosphorus, and triglyceride concentrations until the goal regimen has been reached, at which point the frequency of laboratory testing can be decreased. See Table 13.2 for more information about the frequency of laboratory monitoring in pediatric patients receiving PN. Abnormalities in laboratory tests signal a need for repeat testing, which should be performed after appropriate dose adjustments are made to the PN formulation.[17]

In the pediatric intensive care unit (PICU), adequate nutrition is often not achieved because of fluid restriction, limited access to enteral and parenteral routes, interruptions and restriction of delivery of nutrition due to procedures, and medication incompatibilities. Achieving nutrition goals (especially in the early phase of critical illness), determining actual energy intake, ensuring adequate protein intake, and initiating PN early when EN is not possible are important strategies aimed at preventing accumulation of protein and energy deficits.[22] The value of ongoing education cannot be underestimated. Lambe et al showed that education provided by a nutrition support service/team throughout a residency training program partially corrected the deficiencies in nutrition monitoring in the PICU.[23] Algorithms with ongoing monitoring education and appropriate feedback are also helpful. The first 5 days after admission to the PICU are critical to prevent energy deficit accumulation and achieve the energy goal early in the course of illness. Younger patients and increased length of stay negatively influenced cumulative energy balance. Fluid restriction, a high Pediatric Risk of Mortality score, an inflammatory state, and more serious illness are important factors influencing the energy deficit.[23] Perioperative PN management also plays an important role in infants and children, especially those who are chronically ill, because the high metabolic demands and limited energy stores of these patients make them less tolerant of perioperative fasting than adults. Fasting often leads to hypoglycemia and the stress response to surgery results in hyperglycemia. Patients receiving PN are at increased risk for developing intraoperative hypoglycemia and hyperglycemia; thus, optimal monitoring is critical.[24]

Adult Recommendations. **Recommendation 13B:** To successfully wean or transition from PN therapy, return of or improvement in bowel function must occur (eg, as seen with adaptation in short bowel syndrome).[1] For the hospitalized patient, tolerance of oral intake or EN should be confirmed. Generally, PN is not fully discontinued until the patient consistently consumes at least 50%–75% of energy and protein needs orally or through EN, with signs of continuing improvement.[1] At times, this process is quite rapid, and PN can be withdrawn in a very short period without significant modification. However, patients with a complicated hospital course and/or malnutrition may require longer weaning periods and should demonstrate higher oral intakes than those not malnourished. Patients with severe gastrointestinal disease may require an extended weaning period or, in some cases, may never successfully transition off PN. Table 13.4 provides additional recommendations for weaning long-term PN.

Oral intake is often substantially reduced following complicated care—for example, in the intensive care unit[25] or in the older adult.[26] In those receiving EN, transition from PN should be achieved via a weaning protocol to prevent overfeeding and fluid overload.[26] Dervan and colleagues used a PN weaning protocol in which PN was decreased by 30 mL/h once EN achieved the same rate and was discontinued when EN reached goal infusion rate. They demonstrated less overfeeding with the protocol than prior to the protocol.[27] During times of prolonged weaning, the PN prescription may require daily adjustments with dextrose, amino acids, ILE, and even electrolytes and fluid. The goal of this tactic is to balance the patient's EN intake with the PN yet provide enough nutrition to continue to support needs.[1] Alternatively, in metabolically stable adults, PN can be weaned by reducing the number of days that PN is infused each week. This strategy offers benefits in terms of quality of life while reducing manipulation of the CVAD. However, patients must be closely monitored for fluid and electrolyte abnormalities, weight loss, and other evidence of nutrition decline.[28]

Table 13.4. Recommendations for Weaning Long-Term PN for Adult and Pediatric Patients.[17,28]

• Routinely assess gastrointestinal function for readiness to begin or advance oral or enteral intake.
• Verify metabolic and clinical stability on current PN regimen.
• Establish clear goals with patient to reduce or eliminate dependence on PN.
• Optimize pharmacologic management of gastrointestinal symptoms, such as anorexia, nausea, and diarrhea.
• Provide nutrition counseling and dietary guidance as indicated.
• Monitor weight and hydration status closely.
• Consider increasing the frequency of weight and laboratory monitoring during the transition.
• Assess the need to provide oral vitamin and mineral supplementation.
• Eliminate 1 or 2 nonconsecutive infusions per week; in children, consider weaning by a small percentage every week.
• Adjust PN during the transition to avoid overfeeding.
• Consider further reductions if nutrition and hydration remains stable.
• Evaluate the need for oral or intravenous fluid and/or electrolyte supplementation.
• Make a nutrition monitoring plan after PN is stopped to ensure safe transition to full oral or enteral nutrition.

PN, parenteral nutrition.

Pediatric Considerations. **Recommendation 13B:** Once goal PN regimen is achieved, growth and development needs should be periodically assessed, especially in the home care setting, where PN can continue for extended periods. Goals must be adjusted as the patient grows, and changes must be communicated to all healthcare providers involved in the care of the patient.[29] European Society of Paediatric Gastroenterology, Hepatology and Nutrition guidelines recommend monitoring by a specialized team (physician, nurse, dietitian, pharmacist, social worker, and psychologist) that has experience and sufficient resources to maintain standards of care. Regular outpatient follow-up is essential, especially in infants. Patients must have 24-hour access by phone to a local team for optimal care.[30] ASPEN clinical guidelines suggest that growth, biochemical parameters, energy intake, macronutrient and micronutrient intake, intercurrent illnesses, and gastrointestinal function be monitored to prevent complications.[17,18] Caregivers should initially monitor weight, fluid status, intake, and output daily, with temperature and urinary glucose reading daily to weekly as indicated by the patient's clinical status. Physical examination and anthropometrics should be performed at regular intervals. Initially, laboratory testing should occur weekly and gradually decreased in frequency over time in stable patients. Serum vitamin concentrations, trace elements and carnitine levels, iron status, and platelet levels should also be monitored. Table 13.2 provides more information regarding the recommended frequency of laboratory testing in pediatric patients receiving PN. In addition to surveillance for micronutrient deficiencies, pediatric HPN recipients should be screened for aluminum toxicity, which can contribute to metabolic bone disease. Because chronic PN is associated with an increased risk for metabolic bone disease, bone health should be monitored in patients receiving PN for >6 months.[2]

Comprehensive monitoring is a key component of the care of the pediatric patient receiving PN, both in the acute care setting and in the home, as outlined in Table 13.3 and Table 13.4.

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Question 14: How should healthcare organizations track/monitor PN use for appropriateness?

Recommendations

Adult

14A: Conduct a clinical review for each patient to assess PN appropriateness prior to compounding the PN admixture.

14B: Implement a quality improvement process (eg, clinical audit, plan-do-study-act cycle, medication use evaluation) to ensure appropriate use of PN based on the best available evidence.

Neonatal and Pediatric Considerations

14C: Emphasize the measurement of PN appropriateness in neonates, children, and adolescents as a priority in institutional quality improvement efforts.

14D: Design metrics for monitoring PN appropriateness for each pediatric healthcare network or institution with available information technology and personnel resources to measure and adjust local practices.

Recommendation 14A: As described in the A.S.P.E.N. Parenteral Nutrition Safety Consensus Recommendations, the PN verification process includes a clinical review to assess PN appropriateness prior to compounding the PN formulation.[1] In a prospective clinical review, clinicians should ensure that the prescribed indication is consistent with guidelines; that the osmolarity of the formulation falls within accepted limits for the route of administration; that the dose of each macronutrient, micronutrient, and nonnutrient medication is appropriate for patient-specific needs; that the formulation is compared with the previous day's PN formulation to assess changes; and that additive dosing is evaluated for appropriateness based on current laboratory data.[1] Open interprofessional communication is essential for resolving concerns related to the appropriateness of the PN order.

Recommendation 14B: Clinical audit serves a strategy to assess the provision of PN against the best available evidence, including scientific literature, clinical guidelines, standards, and state and federal rules and regulations.[2,3] The National Institute for Health and Clinical Excellence defined clinical audit as "a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria and the implementation of change."[2] An institution's clinical audit should involve identification of current practice standards, collection of data to measure current practice against standards, implementation of required changes to meet standards, and remeasurement of practice to determine if improvement has occurred.[2] Table 14.1 provides a clinical audit checklist.

The plan-do-study-act cycle is another quality improvement strategy commonly used in healthcare to test change. In monitoring PN use for appropriateness after a change, such as implementation of a new institutional policy or procedure, the plan-do-study-act cycle could be accomplished by developing a plan to test the change (plan), completing the test (do), analyzing the data to determine if the change addressed the quality issue (study), and then more broadly implementing the change or revising it based on results from the test (act).[4]

As another strategy to monitor PN for appropriateness, the American Society of Health-System Pharmacists provides guidance regarding medication use evaluations.[5] A medication use evaluation is "a performance improvement method that focuses on evaluating and improving medication-use processes with the goal of optimal patient outcomes."[5]

Previous studies evaluating appropriateness of PN have defined inappropriate use based on ASPEN clinical guidelines. Inappropriate use of PN has been variable; therefore,

Table 14.1. Clinical Audit Checklist.

Stage 1: Plan for audit	**Checklist (√)**
Step 1: Involve stakeholders	□
Step 2: Determine the audit topic	□
Step 3: Plan the delivery of audit fieldwork	□
Stage 2: Select standard/criteria	
Step 1: Identify standard (evidence based)	□
Step 2: Identify audit criteria—measurable statements of what should be happening	□
Step 3: Set targets/expected performance levels	□
Step 4: Agree acceptable exceptions (if appropriate)	□
Stage 3: Measure performance	
Step 1: Collect data	□
Step 2: Analyze data	□
Step 3: Draw conclusions	□
Step 4: Present results	□
Stage 4: Make improvements	
Step 1: Share audit report	□
Step 2: Review areas for improvement and agree priorities for action	□
Step 3: Identify appropriate interventions	□
Step 4: Develop quality improvement plan (if required)	□
Step 5: Identify • Persons responsible for each task/action • Reasonable timescale for completion • How and when progress will be measured	□
Step 6: Ensure that change is supported by those with the necessary authority to effect such change	□
Stage 5: Sustain improvements	
Step 1: Monitor implementation of changes	□
Step 2: Report on progress of implementation as required	□
Step 3: Reaudit to ensure that changes have improved practice, and decide if further audit procedures are required	□

Checklist from Health Service Executive Quality Improvement Division. *Clinical Audit Support Documents*. http://www.hse.ie/eng/about/Who/qualityandpatientsafety/Clinical_Audit/clinicalauditdocuments.html. Accessed January 17, 2017. Used with permission.

healthcare organizations should use strategies such as clinical audits or evaluations to ensure appropriate use based on the best available evidence. In single-center studies evaluating the appropriateness of PN, rates of inappropriate use have ranged from 5% to 45%.[6-11] At four tertiary care hospitals in South Carolina, the rate of inappropriate PN use in hospitalized adult patients was 32%.[12]

Table 14.2 provides examples of monitoring indicators for PN appropriateness to potentially include in quality improvement processes.

Neonatal and Pediatric Considerations

Recommendations 14C and 14D: Within a pediatric hospital, the neonatal, pediatric, and cardiac intensive care units, as well as the oncology/bone marrow transplantation unit and the gastrointestinal/surgery areas, likely have the highest rate of PN administration. Tracking PN use in these populations would be facilitated by consensus regarding appropriate circumstances for providing and monitoring of PN.[13] The indications, timing of PN initiation, initial and maximum macronutrient doses, as well as the characteristics of PN recipients all show marked variability across neonatal and PICUs.[14-19] In an international survey of PICUs, nutrition delivery was inadequate in mechanically ventilated patients.[17] This study also revealed a high prevalence of malnutrition on admission and striking inability to deliver the prescribed energy and protein to patients in the PICU. PN exposure was associated with higher mortality, and PICUs that used protocols for initiating and advancing nutrient intake had lower prevalence of acquired infection.[17] Healthcare organizations may improve clinical outcomes in critically ill children by systematically collecting outcome data associated with nutrition therapy.

Investigating the causes of inadequate delivery of nutrition may also affect outcomes. In measuring the duration and causes of interruptions to nutrition support in the PICU, patients were documented as receiving no nutrition for more than 40% of the hospital stay and receiving just above 50% of their energy needs.[20] The study identified prolonged time to initiation and interruptions in

Table 14.2. Examples of Monitoring Indicators for PN Appropriateness.[1,6,8,12,21]

Indicator	Evidence of Appropriate PN Utilization
Gastrointestinal function	Clinical documentation • Evidence of nonfunctioning gastrointestinal tract from history, physical, diagnostic studies • Evidence of failed EN trials • Inability to achieve or maintain safe enteral access • For neonatal and pediatric patients, inability to sustain growth through oral or enteral nutrition
Patient selection	Congruence with therapeutic plan • Aggressive nutrition intervention warranted • Consideration of risks vs potential benefits • Patient/family agreement with plan
Utilization trends	Statistical monitoring • Number of PN recipients • PN patient days and average daily PN census • PN utilization compared with published benchmarks • Number of appropriate and inappropriate PN days • Percent of inappropriate PN orders • Wastage
Timing	Initiation • No PN for first 7 d of a critical illness in adults • No PN for first 7 d postoperatively for well-nourished adults • Initiate central PN in adults and children when the anticipated duration of therapy is 5–7 d to justify insertion of a CVAD • Begin PN in well-nourished adults for inability to reach nutrition goals with EN in 7 d • Begin PN in nutritionally-at-risk adults for inability to reach nutrition goals with EN within 3–5 d • Very low birth weight neonates (less than 1500 g), begin PN promptly after birth • Pediatrics: begin PN in 1–3 d when EN is not feasible • Older children: begin PN in 4–5 d
Duration	Course of therapy • Return of gastrointestinal function is expected to exceed 5–7 d • Weaning of PN when oral and/or EN intake reaches 50%–75% of goal without evidence of feeding intolerance
Vascular access	Type and location of device • Intravenous access is suited to type of therapy and duration of therapy • Verification and documentation of optimal tip position • PN-associated CLABSI and DVT rates
Adequacy/efficacy	PN formulations • Consistent with ASPEN clinical practice guidelines • Nutrition support recommendations followed • Incidence of underfeeding/overfeeding
Safety	Compliance with guidelines • Adherence to A.S.P.E.N. PN safety consensus recommendations • Tracking and reporting PN-related complications • Tracking and reporting PN-related errors Readmission rates for patients discharged on PN Reason for readmission: PN-related vs other medical issue

ASPEN, American Society for Parenteral and Enteral Nutrition; CLABSI, central line–associated bloodstream infection; CVAD, central venous access device; DVT, deep vein thrombosis; EN, enteral nutrition; PN, parenteral nutrition.

nutrition delivery for surgery and planned extubation as major contributing factors. Researchers have shown that when protocols are put into place, the initiation of nutrition in the PICU improves.[21] Clinical guidance and monitoring can be embedded into the electronic health record or through the development of web-based PN ordering systems.[22] Rapid-cycle hospital-based quality and safety improvement projects, which aim to implement and measure change in 3 months or less, can produce significant improvements, such as the reduction in CLABSIs reported in a British hospital using this methodology.[23]

Nutrition protocols have been effective quality improvement interventions, reducing the time to achieve nutrition goals, including transitioning off PN to full EN, while also lowering costs.[24,25] In a large tertiary pediatric institution, the

development and implementation of PN guidelines resulted in a marked reduction in PN courses that lasted less than 5 days, a cutoff that the authors used as an indicator of inappropriate PN use.[21] Overall, implementation of the PN guidelines reduced the percentage of short-course PN from 26.3% to 18.4%. This effect could be detected in multiple subspecialty units where short-term PN use was common. This change also lowered hospital costs and charges.[21] Instituting more specific nutrition protocols and assessing compliance will result in improved care over time.[19] Regarding daily management of PN, a report concerning a cohort of medical and surgical neonates noted that a considerable number of practitioners do not change PN components in response to abnormal blood results.[26] This suggests that the necessity for daily laboratory tests for monitoring parameters such as electrolytes is a question to be evaluated through quality improvement activities, particularly for the smallest preterm infants, who are at high risk of iatrogenic anemia. In consideration of the resources needed to administer PN, including personnel and cost, an area that remains unanswered is whether standardized PN admixtures in neonatal populations are safe and cost-effective.[27-30] With increased support for outcomes research in hospital settings, it should be expected that addressing nutrition will lead to improved care with fewer resources.

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Question 15: What are the areas for future research?

Research is the mechanism by which the science and practice of PN can be refined and advanced with the ultimate goal of

improving safety, efficacy, and patient care. It is also the key avenue to address historical concerns and emerging questions that have not been fully addressed by the existing evidence and recommendations. The members of this Consensus Task Force have extensively researched, reviewed, discussed, and debated the current (limited) evidence and common practice in the preparation of this document. During this process, they have also identified major gaps in existing knowledge and urgent issues requiring further research. These issues are summarized under 3 categories.

A. PN product-related issues:
   a. Increasing concern exists that ILE, especially soybean oil–based product, may be an important independent contributing factor in the development of PN-associated liver disease. Research should focus on confirming the primary contributing ingredients (eg, beta-sitosterol vs other sterols, omega-6 fatty acids, reduced vitamin E content), mechanisms, and clinical significance in children and adult patients.
   b. With the availability of ILE products that contain non–soybean oil (eg, fish oil, olive oil), future research should define their clinical benefits over soybean oil–based products. In addition, their safety and cost-effectiveness with long-term use in patients requiring HPN should be assessed.
   c. A parenteral vitamin D preparation, specifically calcidiol (whether it is derived from cholecalciferol or ergocalciferol) should be made commercially available for managing home PN patients with vitamin D deficiency.
   d. A modified version of parenteral multi–trace element preparations is urgently needed, as supported by the ASPEN Novel Nutrient Task Force, Parenteral Multi-Vitamin Multi–Trace Element Working Group, with research that continues to address the optimal dosing strategy for trace elements, especially in patients requiring HPN. Efforts should focus on the improved availability of single-entity products to allow appropriate dosing across varied settings and disease states.

B. Patient and/or disease-focused issues:
   a. It remains unknown how long a patient can withstand an absence of nutrient intake before detrimental clinical effects may ensue. The classic starvation model described by Keys does not represent the typical hospitalized patient who is likely experiencing disease state metabolism, thereby affecting nutrient metabolism. Future research should address the time course when nutrition support therapy should be initiated to prevent adverse clinical outcomes.
   b. The optimal timing of PN provision soon after birth in more mature preterm infants and strategies in improving their clinical outcomes require further investigation.
   c. Well-designed prospective research aimed to address the optimal timing to initiate PN therapy in pediatric patients when EN is not feasible should be conducted.
   d. With the increased provision of protein energy, especially in obese critically ill patients (eg, hypocaloric, high-protein nutrition support therapy), concerns exist regarding the safest maximum dose of parenteral amino acids. Future research should assess the short-term and long-term benefit of PN with high amino acids provision. Nitrogen balance or amino acid utilization should be assessed, if possible. More important, the safety, patient tolerability, and cost-effectiveness of high–amino acid PN should be carefully evaluated, preferably in prospective clinical trials.
   e. The impact of optimal serum glucose control, protection of the vascular access device, and attention to relative distribution of macronutrients on PN safety outcomes need to be explored for adult, pediatric, and neonatal populations.
   f. Further research to more clearly define the optimal use of PN (when and strategy to initiate PN) in the following clinical circumstances is urgently needed:
      i. PN in the acute phase of critical illness
      ii. Intradialytic PN
      iii. Home PN in obese patients
      iv. PN use in the palliative care setting
      v. PN use in in patients receiving chemotherapy
      vi. PN administration in the presence of bacteremia or fungemia not related to the CVAD

C. Administrative and policy-focused issues:
   a. The validity of the recommendation that when multilumen CVAD is used for PN, one lumen of the device should be dedicated exclusively for the PN administration should be confirmed, as this existing recommendation stems from a single study that showed a strong association between violations of the CVAD used to administer PN and infectious complications. The question of whether it is acceptable to administer PN through a lumen that has been previously used for other infusions remains unanswered. No research has examined this issue.
   b. There is a continued debate on the cutoff on osmolarity for peripheral PN. While the recommendation from ASPEN and the Infusion Nurses Society is to limit peripheral PN to a maximum osmolarity of 900 mOsm/L, some studies

have shown that admixtures up to 1000 mOsm/L may be tolerated. Prospective studies are needed that assess the tolerance of higher osmolarity, the role of infusion rate (ie, cycled vs continuous infusion), and the development of events related to vascular access, as a result of peripheral PN osmolarity. More important, it is crucial to understand what parameters and clinical end points best define "tolerance" of infusion.

c. In spite of the lacking in rigorous research data, a guiding policy in addressing the safety of delivering maintenance PN in terminally ill patients, especially those receiving comfort care, would be useful in directing resource utilization and improving the quality of future research that addresses outcomes.

d. Impact of PN education and competency demonstration on PN-associated complication development should be evaluated.

Finally, while some of the research questions proposed above should be addressed by well-designed clinical trials, the development of a national PN database may provide a useful mechanism to conduct important research related to the usage pattern, safety, effectiveness, and cost burden of PN therapy.