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Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients

Section I: Introduction

The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) is an organization comprised of health care professionals representing the disciplines of medicine, nursing, pharmacy, dietetics, and nutrition science. The mission of A.S.P.E.N. is to serve as a preeminent, interdisciplinary, research-based, patient-centered clinical nutrition society throughout the world. A.S.P.E.N. vigorously works to support quality patient care, education, and research in the fields of nutrition and metabolic support in all health care settings.

Promulgation of safe and effective patient care by nutrition support practitioners is a critical role of the A.S.P.E.N. organization. To this end, in 1993, the A.S.P.E.N. Board of Directors published "Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients."[1] The guidelines were created in accordance with Institute of Medicine recommendations as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."[2] These clinical guidelines, designed for use by health care professionals who provide nutrition support services and their patients, offer clinical advice for managing adult and pediatric (including adolescent) patients in inpatient and outpatient (ambulatory, home, and specialized care) settings. The utility of the Guidelines is attested to by the frequent citation of this document in peer-reviewed publications and their frequent use by A.S.P.E.N. members and other nutrition care professionals in clinical practice, academia, research, and industry. They guide personal and professional clinical activities, they are helpful as educational tools, and they influence institutional practices and resource allocation.

In the Spring of 1999, the A.S.P.E.N. Board of Directors established the A.S.P.E.N. Clinical Guidelines Task Force to revise the 1993 Clinical Guidelines. Three objectives for the revised document were identified. These objectives determined the process, format, and content of this updated version:

1. The Guidelines must be factually up-to-date to reflect a current, evidence-based, best approach to the practice of nutrition support.
2. The Guidelines must support the clinical and professional activities of nutrition support practitioners by articulating evidence-based recommendations upon which to base personal and institutional practices and resource allocation.
3. The Guidelines should serve as a tool to help guide policy makers, health care organizations, insurers, and nutrition support professionals to improve the systems and regulations under which specialized nutrition support is administered.

Patients may be treated with specialized nutrition support in any care setting, including hospitals, nursing homes, rehabilitation facilities, and at home. For most patients, the duration of nutrition support therapy is relatively short (less than 6 weeks); for others, dependence upon parenteral or enteral feeding may be lifelong. These guidelines are intended to assist clinical practitioners who provide specialized nutrition support to patients in all care settings.

DEFINITIONS AND SUPPORTING MATERIALS

The A.S.P.E.N. Board of Directors has published a series of related documents. These include:

Definition of Terms Used in A.S.P.E.N. Guidelines and Standards. JPEN 19(1):1, 1995

Standards for Nutrition Support Hospitalized Pediatric Patients. Nutr Clin Pract 11:217–228, 1996

Standards for Nutrition Support Hospitalized Patients. Nutr Clin Pract 10(6):208–219, 1995

Standards for Nutrition Support for Residents of Long-Term Care Facilities. Nutr Clin Pract 12: 284–293, 1997

Standards for Home Nutrition Support. Nutr Clin Pract 14:151–162, 1999

Standards for Nutrition Support Pharmacists. Nutr Clin Pract 14:275–281, 1999

Standards of Practice for Nutrition Support Dietitians. Nutr Clin Pract 15:53–59, 2000

Standards of Practice for Nutrition Support Nurses. Nutr Clin Pract 16(1):56–62, 2001

Standards of Practice for Nutrition Support Physicians. Nutr Clin Pract 11:235–240, 1996

Correspondence and reprint requests: American Society for Parenteral and Enteral Nutrition, 8630 Fenton Street, Suite 412, Silver Spring, MD 20910-3805.

The Science and Practice of Nutrition Support: A Case Based Core Curriculum. American Society for Parenteral and Enteral Nutrition and Kendall Hunt Publishing Company, Dubuque, IA, 2001

The A.S.P.E.N. Nutrition Support Practice Manual. American Society for Parenteral and Enteral Nutrition, Silver Spring, MD, 1998

Clinical Pathways and Algorithms for Delivery of Parenteral and Enteral Nutrition Support in Adults. American Society for Parenteral and Enteral Nutrition, Silver Spring, MD, 1998

Safe Practices for Parenteral Nutrition Formulations. JPEN 22:49–66, 1998

Here are listed terms that frequently appear within this Guidelines document and have specific meanings:

Clinical guidelines: Systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.[2]

Nutrition screening: A process to identify an individual who is malnourished or who is at risk for malnutrition to determine if a detailed nutrition assessment is indicated.

Nutrition assessment: A comprehensive approach to defining nutrition status that uses medical, nutrition, and medication histories; physical examination; anthropometric measurements; and laboratory data. A formal nutrition assessment should provide all of the information necessary to develop an appropriate nutrition care plan. Because of the inextricable relationship between malnutrition and severity of illness and the fact that tools of nutrition assessment reflect both nutrition status and severity of underlying disease, an assessed state of malnutrition or presence of specific indicators of malnutrition in fact refers to the consequences of a combination of an underlying illness *and* associated nutritional changes and deficits.

Nutrition care plan: A formal statement of the nutrition goals and interventions prescribed for an individual using the data obtained from a nutrition assessment. The plan, formulated by an interdisciplinary process, should include statements of nutrition goals and monitoring parameters, the most appropriate route of administration of specialized nutrition support (oral, enteral, and/or parenteral) method of nutrition access, anticipated duration of therapy, and training and counseling goals and methods.

Pediatric: Patients ≤17 years old, including premature newborns, neonates, infants, toddlers, children, and adolescents.

Specialized nutrition support (SNS): Provision of nutrients orally, enterally, or parenterally with therapeutic intent. This includes, but is not limited to, provision of total enteral or parenteral nutrition support and provision of therapeutic nutrients to maintain and/or restore optimal nutrition status and health.

HOW TO USE THESE GUIDELINES

These clinical guidelines, designed for health care professionals who provide SNS services, offer clinical advice for managing adult and pediatric patients in the hospital or home. The guidelines are organized into the following sections:

1. Sections concerning issues generic to SNS in most or all patients (eg, nutrition assessment, nutrient requirements), subdivided into Adult and Pediatric discussions.
2. Disease-specific sections for Adults.
3. Disease-specific sections for Pediatrics.

With this 2002 revision, an attempt has been made, when possible, to have the Adult and Pediatric sections look and feel the same. Each section begins with a Background that presents general information necessary to understand the relevant physiologic and clinical issues. This is followed by a presentation of Evidence that summarizes the applicable clinical studies that can be used to guide clinical practice. Next comes a Special Issues or Considerations subheading where further evidence is presented about specialized, new, or controversial topics. The Practice Guidelines are then clearly stated in an active manner (eg, SNS *should* be administered . . .), and annotated with a Strength of Evidence classification (see below). Finally, each section is referenced. Space limitations prevented exhaustive referencing. Therefore, liberal use is made in the references of review articles, summary statements, and meta-analyses that do contain references to the primary sources.

Careful reading of the guideline statements with their associated strength of evidence classifications should highlight those clinical situations where there are strong data to support practice recommendations. Absence of data, however, does not necessarily mean that interventions are harmful or contraindicated. In situations where evidence based recommendations cannot be made because of a lack of relevant clinical studies, clinicians must still make the best possible decisions for their patients. Those areas where guidelines are classified as being based on class C data (formulated using expert opinion and editorial consensus) reflect an attempt to make the best recommendations possible within the context of the available data and expert clinical experience. These class C guidelines identify an agenda for critical, clinical research to more firmly establish SNS as an evidence-based specialty.

A thread running throughout many of the disease-specific guidelines is the rationale for choosing enteral over parenteral SNS or alternatively parenteral over enteral when a decision to use SNS has been made. The A.S.P.E.N. Board of Directors and the A.S.P.E.N. Clinical Guidelines Task Force struggled with this crucial issue. The generic data relevant to this decision are presented in the section entitled "Indications for Administration of Specialized Nutrition Support." In some specific clinical situations (eg, critical care, trauma), data support the use of enteral over parenteral nutrition because of improved outcomes and reduced complication rates. A critical review of the literature, however, offers little guidance in other areas. Nevertheless, because of data suggesting a lower cost for enteral nutrition (EN) than parenteral nutrition (PN) and because of general consensus that the gut should be used when possible, these guidelines

are biased toward recommending EN when feasible and reserving PN for those patients in whom the gut is not functional, enteral access is not possible, or the risk of EN-related complications (eg, aspiration) is unacceptably high.

Another fundamental issue that influences many of the discussions and recommendations in the Guidelines is the relationship between nutrition assessment, nutrition status, malnutrition, and severity of disease. It can be argued that a formal nutrition assessment does not define the presence and extent of *malnutrition* per se, but instead identifies the metabolic consequences of an underlying disease state as defined by parameters that are also deranged in a state of pure starvation. Therefore, when a nutrition assessment is performed on an ill patient, the results reflect metabolic consequences of *both* undernutrition *and* the underlying disease. In this document, the terms *malnutrition* and *nutrition risk* are used to identify clinical situations in which the parameters of the nutrition assessment (eg, weight loss, temporal wasting, hypoalbuminemia, etc) are abnormal as a result of the intermingled effects of both undernutrition and the underlying disease. In this context, the goals of SNS are to both treat malnutrition and to support the patient nutritionally and metabolically to prevent further physiologic deterioration while primary disease directed therapy is being administered.

The 2002 Guidelines update the original A.S.P.E.N. Clinical Guidelines first published nine years ago. To avoid a future gap in the timeliness of the guidelines, the A.S.P.E.N. Board of Directors is committed to continuously review them and update them on a rotating cycle.

STRENGTH OF EVIDENCE

The strength of the evidence supporting each guideline statement has been coded using a modified version of the method used by the Agency for Healthcare Research and Quality (AHRQ), US Department of Health and Human Services. After review of the references cited, the section authors and the Clinical Guidelines Task Force used the AHRQ criteria to classify the strength of the evidence supporting each guideline statement. The evidence supporting each statement is classified as follows:

A There is good research-based evidence to support the guideline (prospective, randomized trials).

B There is fair research-based evidence to support the guideline (well-designed studies without randomization).

C The guideline is based on expert opinion and editorial consensus.

The preference of the AHRQ to rely primarily on prospective randomized clinical trials as the basis for establishment of practice guidelines is appropriate because therapies that are accepted and widely used may subsequently be found lacking when such trials are conducted.[3] However, a major distinction between therapeutic trials of the efficacy of a drug or procedure and the feeding of nutrients known to be essential to the maintenance of human health and survival must be made. Withholding a drug or invasive procedure will not produce disease in otherwise healthy humans, whereas essential nutrients must be provided to both healthy and ill people. Patients with advanced malnutrition or who are at risk for becoming severely malnourished must be fed to prevent death by starvation. Some of the guideline statements that follow in this document were developed on the basis of expert opinion and editorial consensus (class C data) because of the ethical dilemma of conducting prospective randomized trials involving patients at risk for starvation.

DEVELOPMENT OF THE GUIDELINES

The 2002 A.S.P.E.N. "Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients" were developed in response to the need to factually update the 1993 Guidelines in light of new evidence. This opportunity was also used to improve the Guidelines' suitability to change institutional and clinical practices and resource allocation and to influence policy leaders, health care organizations, insurers, and SNS professionals. Although there are exceptions, such as the Clinical Efficacy Assessment Project of the American College of Physicians, most medical-practice guidelines in the United States are now developed by professional medical and other health care organizations having expertise in particular specialties. The advantage of this approach is that professionals who are familiar with the literature and the practice of health care in specific subspecialties prepare the guidelines. These individuals presumably have greater knowledge and more experience with the particular service or procedure. The disadvantage of this approach is that professional specialists may make biased judgments in the course of developing medical-practice guidelines that affect their own practice. A.S.P.E.N. considered the advantages and disadvantages and concluded that guidelines could be prepared objectively by experts in our Society. Care has been taken throughout the guidelines development process to assure objectivity as best as possible.

In the Spring of 1999, the A.S.P.E.N. Board of Directors established the Clinical Guidelines Task Force (CGTF). The members of the task force are as follows:

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The task force members were carefully selected for their experience, integrity, and knowledge of SNS.

Their backgrounds span all of the SNS disciplines (physicians, dietitians, nurses, and pharmacists) and the areas of expertise embodied within the guidelines. Their generous donation of time and expertise made completion of this document possible. The CGTF "met" frequently between September 1999 and August 2001 by conference call, e-mail, and (on two occasions) for intense 36-hour face-to-face discussions, review, and editing. The process was initiated by reviewing and revising the table of contents from the 1993 Guidelines. After approval of this new table of contents by the A.S.P.E.N. Board of Directors, it was used to divide up responsibility for actual writing of the components of the Guidelines. The CGTF members selected section authors and supervised the authors' efforts. The authors were selected for their detailed knowledge and experience in a chosen niche. These authors deserve the credit for reviewing the primary literature, synthesizing and summarizing it, and formulating the guideline statements. Without their detailed knowledge of the literature and current best practice, the document could not have been completed. The authors and the contributions for which they are credited are listed below:

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When the authors' drafts were completed, they were reviewed by the section editors (the members of the CGTF), edited and/or rewritten, and then reviewed twice by the members of the CGTF as a group. The entire document was then re-edited by the CGTF Chair. This four-times–edited draft was submitted to the A.S.P.E.N. Board of Directors and more than 180 experts in the field of nutrition support (including experts and organizations outside of A.S.P.E.N.) for content, format, and style review. These reviewers were also specifically asked to check each guideline statement for appropriateness, accuracy, and strength of evidence. This review phase stimulated a final cycle of editing by the CGTF and the CGTF Chair. The final document was then approved by the A.S.P.E.N. Board of Directors and submitted to the *Journal of Parenteral and Enteral Nutrition* for publication.

The members of the Clinical Guidelines Task Force, the A.S.P.E.N. Board of Directors, and the section authors feel that this document represents the current state of the art in provision of specialized nutrition support to adult and pediatric patients and provides an evidence-based rationale for the recommendations. We also hope that these Guidelines help highlight important areas for future clinical and translational research so that practitioners of nutrition support may provide even better care for patients in the future. The Chair, Co-Chair, and members of the Clinical Guidelines Task Force and the A.S.P.E.N. Board of Directors express their deep gratitude to all of the volunteers who contributed their time and expertise to make this document possible.

Notice: These A.S.P.E.N. Clinical Guidelines are general statements. They are based upon general conclusions of health professionals who, in developing such guidelines, have balanced potential benefits to be derived from a particular mode of medical therapy against certain risks inherent with such therapy. However, the professional judgment of the attending health professional is the primary component of quality medical care. The underlying judgment regarding the propriety of any specific procedure must be made by the attending health professional in light of all of the circumstances presented by the individual patient and the needs and resources particular to the locality. These guidelines are not a substitute for the exercise of such judgment by the health professional, but rather are a tool to be used by the health professional in the exercise of such judgment. These guidelines are voluntary and should not be deemed inclusive of all proper methods of care, or exclusive of methods of care reasonably directed toward obtaining the same results.

REFERENCES

1. A.S.P.E.N: Board of Directors. Guidelines for the Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients. JPEN 17:1SA-52SA, 1993
2. Committee to Advise Public Health Service on Clinical Practice guidelines (Institute of Medicine). Clinical Practice Guidelines: Directions for a New Program. National Academy Press, Washington, DC, 1990, p 58
3. Pocock SJ, Elbourne DR: Randomized trials or observational tribulations? New Engl J Med 342:1907–1909, 2000

Section II: Nutrition Care Process

The process of nutrition care may be broken down into a series of steps with feedback loops. These include nutrition screening, formal nutrition assessment, formulation of a nutrition care plan, implementation of the plan, patient monitoring, reassessment of the care plan and reevaluation of the care setting, and then either reformulation of the care plan or termination of therapy. These Guidelines suggest how each of these steps may be carried out to optimize clinical outcomes and cost-effectiveness. Frequent reference to Figure 1 while reviewing the guidelines can help orient the user to where within the overall plan of nutrition care specific guidelines fit.

Integral to the process of nutrition care and the administration of specialized nutrition support is the decision of route of administration of specialized nutrition support. Figure 2 presents an algorithm that may be used to determine whether the optimal route of nutrition support is enteral or parenteral in a specific clinical situation. In general, it is assumed that enteral support is preferable to parenteral support because enteral support is more cost-effective. The data that support this assumption are presented elsewhere in the document.

REFERENCES

1. A.S.P.E.N: Board of Directors: Standards for nutrition support: Hospitalized patients. Nutr Clin Pract 10:208–218, 1995
2. A.S.P.E.N: Board of Directors: Clinical Pathways and Algorithms for Delivery of Parenteral and Enteral Nutrition Support in Adults. A.S.P.E.N., Silver Spring, MD, 1998, p 5

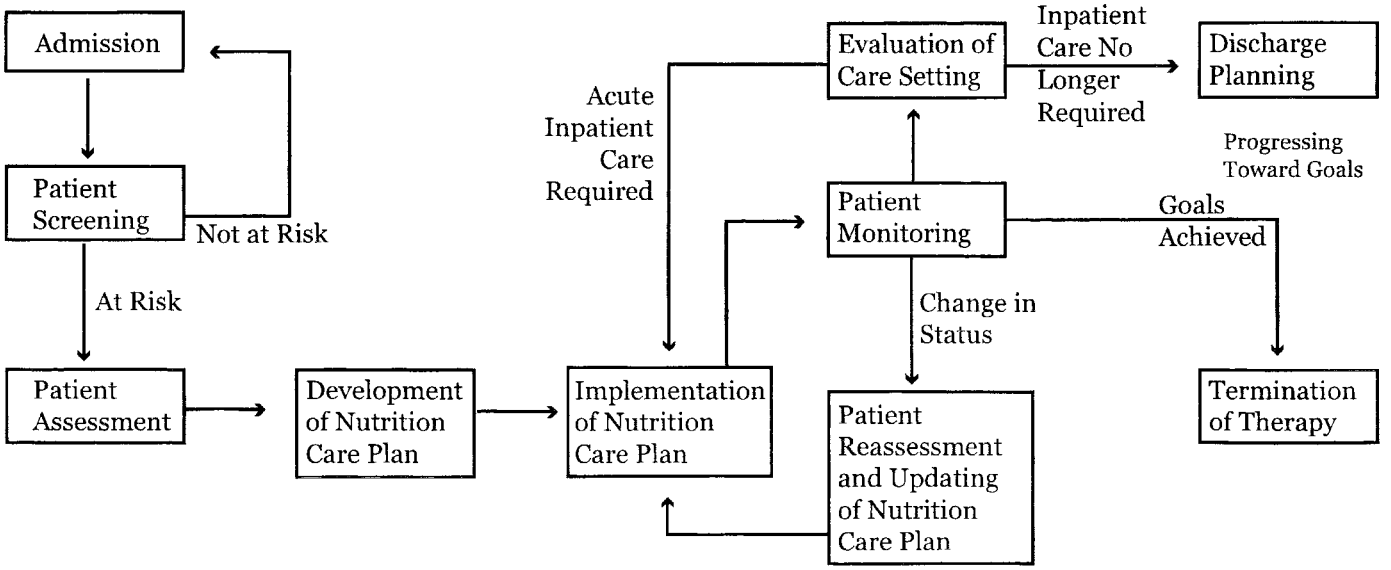

FIG. 1. The nutrition care process[1] (Taken From the A.S.P.E.N. Standards for Nutrition Support: Hospitalized Patients).

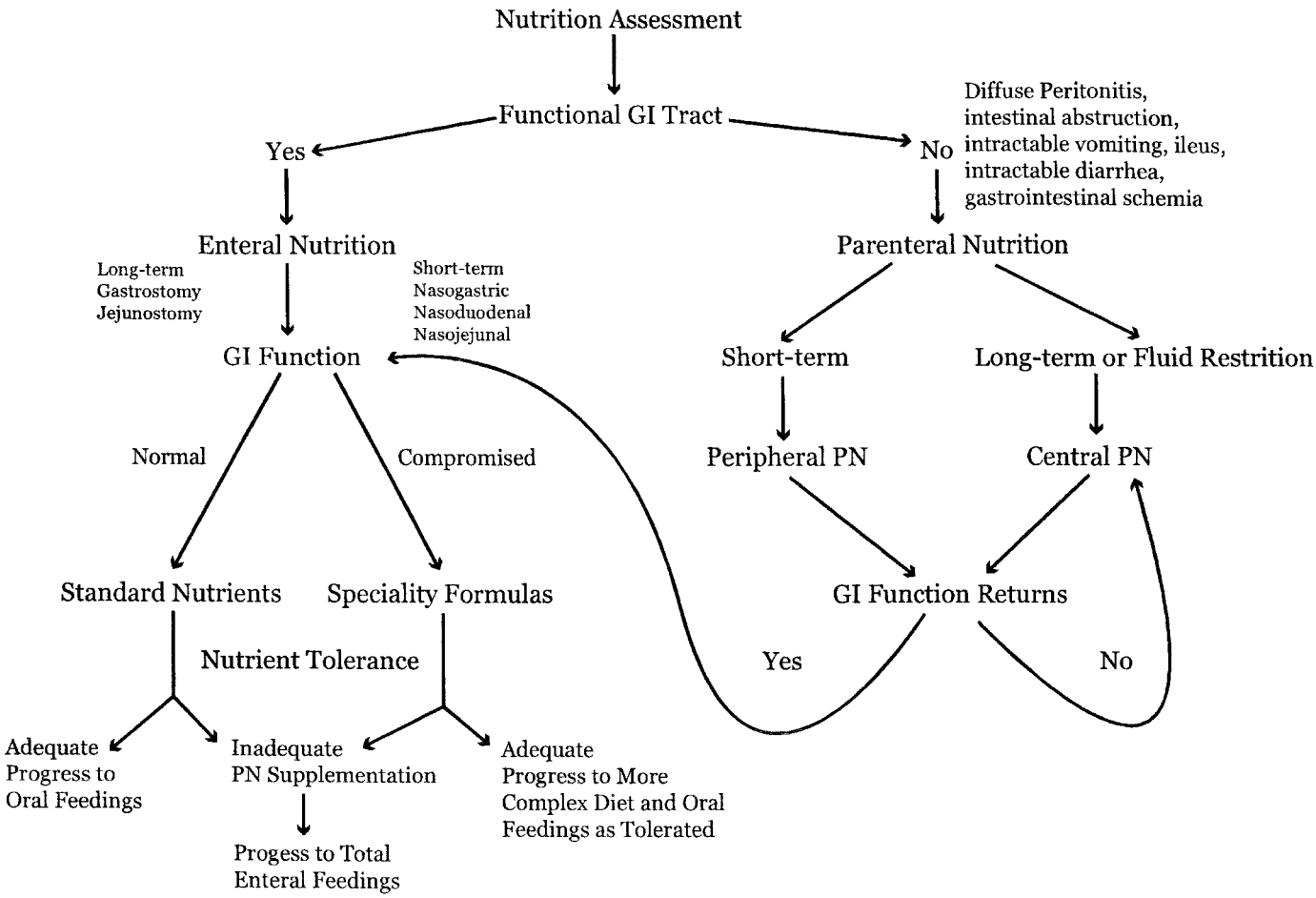

FIG. 2. Route of Administration of Specialized Nutrition Support[2] (Taken from the A.S.P.E.N. Clinical Pathways and Algorithms for Delivery of Parenteral and Enteral Nutrition Support in Adults).

Section III: Nutrition Assessment–Adults

NUTRITION SCREENING

Background

Malnutrition is defined as any disorder of nutrition status, including disorders resulting from a deficiency of nutrient intake, impaired nutrient metabolism, or over-nutrition.[1] The consequences of malnutrition are related to premorbid condition of the patient, the extent and length of time nutrient intake is inadequate, and the concurrent presence of other diseases or illnesses. Nutrient depletion is associated with increased mortality and morbidity.[2] Wound healing is delayed, complication rates are increased, and an increased rate of rehospitalization occurs in the presence of malnutrition.[3] Malnutrition is a common occurrence in hospitalized patients, with an incidence of 30–55%.[4] Malnourished hospitalized patients have been shown to have increased lengths of stay, with associated increased costs of care.[5,6] Factors indicative of malnutrition include: involuntary loss or gain of ≥10% of usual body weight within 6 months, or ≥5% of usual body weight in 1 month; body weight of 20% over or under ideal body weight, especially in the presence of chronic disease or increased metabolic requirements; and inadequate nutrition intake including an impaired ability to ingest or absorb food adequately.[1]

Nutrition screening identifies individuals who are malnourished or who are at risk for malnutrition. The purpose of the nutrition screening is to determine if a more detailed nutrition assessment is necessary.[7,8] Nutrition screening is a dynamic process to identify changes in a patient's condition that effect nutritional status.[9] The nutrition screen identifies risk factors that place a patient at nutrition risk and that may lead to nutrition related problems.[1]

Evidence

Subjective and objective data can facilitate early intervention and assist initiation of a formal nutrition assessment. These data may be obtained easily, quickly, and efficiently.[10] Objective data such as height, weight, weight change, primary diagnosis, and presence of comorbidities can be used in nutrition screening to indicate malnutrition or risk of malnutrition.[7] Adult nutrition screening tools designed for use by staff nurses have been tested for validity and reproducibility[11] and evaluated for ease of use, cost-effectiveness, and for validity, reliability, sensitivity, and specificity.[12]

Although few data are available from clinical studies, it makes sense that an effective nutrition screening can be used to efficiently identify those patients that may benefit from a more extensive formal nutrition assessment. It may be particularly important to aggressively screen elderly patients, because the elderly may experience eating or swallowing difficulties, adverse drug-nutrient interactions, alcohol abuse, depression, reduced appetite, functional disabilities, impaired taste and smell, and/or effects of polypharmacy.[7]

Practice Guidelines
Nutrition Screening

1. A nutrition screening incorporating objective data such as height, weight, weight change, primary diagnosis, and presence of comorbidities should be a component of the initial evaluation of all patients in ambulatory, hospital, home, or alternate site care settings. (C)
2. The health care organization should determine who will perform the screen and the elements to be included in the screen. (C)
3. A procedure for periodic nutrition re-screening should be implemented. (C)

REFERENCES

1. American Society for Parenteral and Enteral Nutrition Board of Directors: Definition of terms used in A.S.P.E.N. guidelines and standards. JPEN 19:1–2, 1995
2. Ireton-Jones C, Hasse J: Comprehensive nutritional assessment: The dietitian's contribution to the team effort. Nutrition 8:75–81, 1992
3. Ottery F: Nutritional screening and assessment in home care. Infusion September:36–45, 1996
4. Shopbell JM, Hopkins B, Shronts EP: Nutrition screening and assessment. IN The Science and Practice of Nutrition Support. Gottschlich MM (ed). Kendall/Hunt, Dubuque, IA, 2001, pp 107–140
5. Robinson G, Goldstein M, Levine GM: Impact of nutritional status on DRG length of stay. JPEN 11:49–52, 1987
6. Green MS, Rubinstein E, Amit P: Estimating the effects of nosocomial infections on the length of hospitalization. J Infect Dis 145:667–672, 1982
7. ADA's Definition for nutrition screening and assessment. J Am Diet Assoc 94:838–839, 1994
8. Nutrition Interventions Manual for Professionals Caring for Older Americans: Project of the American Academy of Family Physicians, The American Dietetic Association, and National Council on Aging. Washington, DC: Nutrition Screening Initiative, 1994

9. Barrocas A, Belcher D, Champagne C, et al: Nutrition assessment practical approaches. Clin Geriatr Med 11:675–713, 1995
10. Guidelines for initial nutrition screening. IN Suggested Guidelines of Nutrition and Metabolic Management of Adult Patients Receiving Nutrition Support. Winkler MF, Lysen L (eds). The American Dietetic Association, Chicago, 1993
11. Kovacevich DS, Boney AR, Braunschweig CL, et al: Nutrition risk classification: A reproducible and valid tool for nurses. Nutr Clin Pract 12:20–25, 1997
12. Arrowsmith H: A critical evaluation of the use of nutrition screening tools by nurses. Br J Nurs 12:1483–1490, 1999

NUTRITION ASSESSMENT

Background

Nutrition assessment is "a comprehensive approach to defining nutrition status that uses medical, nutrition, and medication histories; physical examination; anthropometric measurements; and laboratory data. Further, it includes the organization and evaluation of information to declare a professional judgment."[1] Evaluation of nutrition status consists of two components: nutrition assessment and metabolic assessment.[2] Nutrition assessment utilizes static measurements of body compartments and examines the alterations caused by undernutrition. Metabolic assessment includes the analysis of the structure and function of organ systems, of altered metabolism as it relates to the loss of lean body mass or other body compartments, and of the metabolic response to nutrition intervention (whether beneficial or harmful). The goals of a formal nutrition assessment are to identify patients who are malnourished or who are at risk for malnutrition; to collect the information necessary to create a nutrition care plan; and to monitor the adequacy of nutrition therapy.

There is an inextricable relationship between nutrition status and severity of illness. Severely ill patients, no matter what assessment tools are used, will be identified as being "malnourished." Whether this assessment in fact truly indicates malnutrition (a state induced by nutrient deficiency that may be improved solely by administration of nutrients) or is merely a reflection of the severity of the metabolic derangements caused by the underlying illness is arguable. Likely it reflects a combination of both malnutrition and the presence of an underlying disease process. When thought of in this context, the use of nutrition assessment tools to identify patients who are malnourished or at nutrition risk does not imply that nutrition support alone will reverse the problem. Rather, in the setting of malnutrition or nutrition risk, nutrition support is essential so that if the medical treatment is appropriate and effective, nutrients are available to prevent undernutrition and to facilitate disease directed therapy and promote recovery.[3,4] Because of the relationship between malnutrition and severity of illness and the fact that tools of nutrition assessment reflect both nutrition status and severity of underlying disease, an assessed state of malnutrition or the presence of specific indicators of malnutrition in fact refers to the consequences of a combination of both an underlying illness *and* associated nutritional changes and deficits.

The body mass index (BMI) accounts for differences in body composition by defining the level of adiposity according to the relationship of weight to height and eliminates the dependence on frame size. BMI is a useful assessment tool because it has a low correlation with height and high correlation with independent measures of body fat for adults (including the elderly). A BMI of 14 to 15 kg/m^2 is associated with significant mortality, less than 18.5 kg/m^2 is considered underweight, greater than 25 kg/m^2 connotes overweight, and a BMI greater than 30 kg/m^2 indicates obesity.[5,6]

Patient history and physical examination are required for an adequate nutrition assessment. The intensity of the assessment should match the severity of illness and degree of suspected malnutrition for the patient. The patient history should focus on weight (ideal, usual, and current weight, and recent weight loss), changes in eating habits and gastrointestinal function, the nature and severity of the underlying disease, and any unusual personal dietary habits or restrictions. The physical assessment can include the general appearance of the patient, noting the presence of edema, ascites, cachexia, obesity, skin changes, dry mucous membranes, petechiae or ecchymoses, poorly healing wounds, and glossitis, stomatitis, or cheilosis. Additionally, the patient's musculoskeletal system should be inspected and palpated, recognizing asymmetry may occur with a preexisting neurologic disorder such as stroke and that the size of muscles are exercise dependent. The temporalis muscles, deltoids, suprascapular and infrascapular muscles, the bulk and tone of the biceps, triceps, and quadriceps, and the interosseus muscles of the hands should be the areas of special attention.[7] The clinician can often easily identify loss of subcutaneous fat and muscle wasting in patients with severe underlying disease or those who are bedridden. The physical assessment may also help identify specific nutrient deficiencies. It should be focused on body areas with noticeable changes, such as hair-bearing areas, the oral mucosa, gravity-dependent areas, and peripheral sensation in the hands and feet. However, the clinical signs and symptoms of most nutrient deficiencies are not manifest until an advanced state of deficiency develops. If the signs and symptoms of a deficiency exist, it must be correlated with the patient's history and laboratory data to establish a deficiency diagnosis.

Serum proteins levels correlate with nutrition status and severity of illness.[3,4,8] The most often analyzed visceral proteins are serum albumin, transferrin, and prealbumin.[9] Studies have shown that hypoalbuminemia is associated with poor clinical outcomes.[5] Hypoalbuminemia is not a normal result of aging. Serum albumin level has been shown to be an independent risk factor for mortality of all causes in older persons.[1,9] Although albumin levels may have prognostic value, they have been found to be poor indicators of the adequacy of nutrition support.[9] Serum transferrin has a short half-life (8.8 days) and a relatively small body pool so it may more accurately reflect acute protein depletion and replenishment.[9] Transferrin has not been studied extensively in relation to nutrition status. Serial and frequent measurements of prealbumin

(half-life of 2 to 3 days) may help assess nutrition status changes in response to therapy.[9]

Indirect calorimetry and body composition analysis using a multitude of techniques have been suggested for clinical use to quantitatively measure energy needs and assess nutrition status. Although these techniques, especially indirect calorimetry, may be helpful in settings where nutrition requirements are difficult to estimate or when complications of over- or underfeeding are suspected, their routine use cannot be advocated. They are expensive and technically demanding, and methodologic biases may introduce errors in estimates obtained using these "quantitative" tools. None of these techniques has been demonstrated to effectively predict clinical outcome or improve the effectiveness of administration of SNS.[4,10]

Multifactorial prognostic indices have been developed that utilize objective measures of nutrition status. The Prognostic Nutrition Index (PNI) uses serum albumin and transferrin levels, triceps skin fold measurements, and delayed hypersensitivity skin test reactivity to predict the risk of operative morbidity and mortality in relation to nutrition status.[11] The Prognostic Inflammatory and Nutritional Index (PINI) uses markers of the inflammatory response (alpha 1 acid glycoprotein and C-reactive protein) in combination with nutrition assessment parameters (albumin and prealbumin) to predict infectious complications and death.[8] The Nutritional Risk Index (NRI), used in the Veterans Administration Cooperative Group study of preoperative parenteral nutrition, successfully stratifies operative morbidity and mortality using serum albumin and the ratio of current weight to usual weight.[12]

The nutrition care plan is the final component of the nutrition assessment. The care plan is used to organize the information obtained in the assessment and "to declare a professional judgment."[1] Many aspects of patient care such as consultation, treatments, medications, patient assessment and monitoring, education, and activity level are integrated into the nutrition care plan and coordinated with the overall care plan. The nutrition care plan should include nutrition goals and the route of administration of nutrition support. Goals of nutrition care/intervention are stated. Because nutrition status is dynamic, nutrition goals may be long term and/or short term. Goals should be set utilizing the clinical information as well as patient and/or caregiver wishes. In some cases, the nutrition care plan may not include a nutrition support regimen when the nutrition goal is palliative care. Nutrition goals should be measurable to evaluate the adequacy of the care plan. Monitoring of the effect of the nutrition intervention should be performed at regular intervals as defined in the nutrition care plan.

Evidence

Ideally, there should be data from clinical trials that address the hypothesis, "Formal, appropriate nutrition assessment results in the implementation of nutrition interventions that improve patient outcomes." Unfortunately, no such studies exist. As noted above, the PNI, the PINI, and the NRI all reliably predict morbidity in perioperative patients.[8,11,12] The only clinical method that has been validated as reproducible and that evaluates nutrition status (and severity of illness) by encompassing patient history and physical parameters is the subjective global assessment (SGA).[13,14] It may be used in a variety of clinical settings. With the SGA, data obtained from the patient's history and physical examination are subjectively weighted to classify the patient as well nourished, moderately malnourished, or severely malnourished. The SGA has been found to be a good predictor of complications in patients undergoing gastrointestinal surgery, liver transplantation, and dialysis.[5] The use of the SGA in critically ill patients has not been formally evaluated and future research in this area is needed. The use of SGA is more specific than sensitive and may miss some patients with mild degrees of malnutrition.[10]

Practice Guidelines *Nutrition Assessment*

1. A formal nutrition assessment should be carried out in any patient, independent of the care setting, who is identified by a nutrition screen as nutritionally at risk. (C)
2. In the absence of an outcomes validated approach to nutrition assessment, a combination of clinical (history and physical exam) and biochemical parameters should be used to assess the presence of malnutrition. (C)
3. A written summary should be created and made available to the patient's care providers which includes the following: The objective and subjective data collected for the nutrition assessment; the explicit nutrition risk stratification; and the specific recommendations to be incorporated into the nutrition care plan (protein, calorie, and micronutrient requirements, route of administration, and treatment goals and monitoring parameters). (C)

REFERENCES

1. ADA's definition for nutrition screening and assessment. J Am Diet Assoc 94:838–839, 1994
2. Guidelines for initial nutrition screening. IN Suggested Guidelines of Nutrition and Metabolic Management of Adult Patients Receiving Nutrition Support. Winkler MF, Lysen L (eds). The American Dietetic Association, Chicago, 1993
3. Kotler DP. Cachexia. Ann Intern Med 133:622–634, 2000
4. Trujillo EB, Chertow GM, Jacobs DO: Metabolic assessment. IN Parenteral Nutrition. Rombeau JL, Rolandelli RH (eds). WB Saunders, Philadelphia, 2001, pp 80–108
5. Charney P: Nutrition assessment in the 1990's, where are we now? Nutr Clin Pract 10:131–139, 1995
6. NHLBI Obesity Education Initiative Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—The evidence report. Obes Res 6(Suppl 2):51S–209S, 1998
7. Jeejeebhoy KN: Bulk or bounce: The object of nutritional support. JPEN 12:539–549, 1988
8. Shopbell JM, Hopkins B, Shronts EP: Nutrition screening and assessment. IN The Science and Practice of Nutrition Support. Gottschlich MM (ed). Kendall/Hunt, Dubuque, IA, 2001 pp 107–140

9. Ireton-Jones C, Hasse J: Comprehensive nutritional assessment: The dietitians contribution to the team effort. Nutrition 8:75–81, 1992
10. Klein S, Kinney J, Jeejeebhoy K, et al: Nutrition support in clinical practice: Review of published data and recommendations for future research directions. JPEN 21:133–156, 1997
11. Mullen, J, Buzby G, Waldman T, et al: Prediction of operative morbidity and mortality by preoperative nutritional assessment. Surg Forum 30:80–82, 1979
12. The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group: Perioperative total parenteral nutrition in surgical patients. N Engl J Med 325:525–532, 1991
13. Baker JP, Detsky AS, Wesson DE, et al: Nutritional assessment: A comparison of clinical judgment and objective measurements. N Engl J Med 306:969–972, 1982
14. Detsky AS, McLaughlin JR, Baker JP, et al: What is subjective global assessment of nutritional status? JPEN 11:8–13, 1987

Section IV: Nutrition Assessment—Pediatrics

MALNUTRITION AND ITS CONSEQUENCES

Background

Malnutrition is a pathologic state of varying severity with clinical features caused by deficiency, excess, or imbalance of essential nutrients. The cause may be primary (involving the quantity or quality of food consumed) or secondary (involving alterations in nutrient requirements, utilization, or excretion).

Historically, malnutrition in children has been defined using the terms marasmus and kwashiorkor. Marasmus develops after severe deprivation of calories and is characterized by weight loss and wasting of fat and muscle tissue. Low weight-for-height and a reduced height-for age are commonly observed. In the child with kwashiorkor, protein deficits outweigh calorie deficits. Edema due to visceral protein depletion occurs along with muscle wasting. Although some degree of growth failure may be present, weight-for-height may not be notably low secondary to retention of fluid in the extravascular compartment. Irritability, apathy, anorexia, and fatigue may be seen in both marasmus and kwashiorkor.

Currently, most forms of pediatric malnutrition are defined by the term protein-calorie malnutrition (PCM). PCM represents a state where features of both kwashiorkor and marasmus are present. In addition to growth impairment, physiologic alterations include electrolyte and micronutrient imbalances and reduced levels of serum proteins and albumin. Gastrointestinal function may be altered in children with protein-calorie malnutrition as well as immune function with impairment of cell-mediated immunity, phagocyte function, and complement systems.[1] For the child with chronic or acute disease, these effects may contribute to suboptimal response to medical and surgical therapy. In addition, cognitive and behavioral development may be adversely affected.

Excess intake of nutrients may also present a health hazard and can be considered a state of malnutrition. Overfeeding may lead to obesity, which may be characterized as weight for height above the 95th percentile for age or BMI greater than 30.0 kg/m^2.[1] The obese child is at risk for a variety of health problems including sleep apnea, hyperlipidemia, hepatic steatosis, and orthopedic problems.

Evidence

Primary malnutrition is a common cause of morbidity and mortality in the developing countries of the world where nearly 40% of children under 5 years of age are affected.[2] Malnutrition due to the effects of acute or chronic disease has been described in 44% of hospitalized children in the United States and is a frequently described problem in children with a variety of specific disease states in both the inpatient and outpatient settings.[3–7] Excessive intake of nutrients leading to obesity has increased significantly in the last 20 years, with the prevalence in children in the United States rising approximately 8%.[8]

The immediate and long-term consequences of malnutrition in children have been described. For the child with acute or chronic disease, poor nutrition status may have a negative effect on recovery or response to therapy.[4,5,8] For the developing fetus and very young infant, intrauterine and very early deprivation may have life long consequences.[9]

Special Considerations

Children throughout their developmental cycle have a growth imperative that makes them especially vulnerable to the impact of malnutrition. Children are additionally vulnerable because of their dependence on their adult caregivers to ensure that their nutrient needs are met. The nutrition status of the mother influences the growth and well being of the developing fetus.[9] The socioeconomic and psychological well being of the family influences the supply of food available to the child. Malnutrition due to an inadequate or inappropriate food supply may be a sign of child neglect or abuse.[10]

Practice Guidelines *Malnutrition and Its Consequences*

1. Prevention and early detection of malnutrition in children throughout the developmental cycle should be integrated into all health care encounters. (B)
2. Prevention and detection strategies should be adapted to the clinical setting and the needs of the pediatric patient. (C)
3. A family centered approach should be used for prevention and early detection of malnutrition to

address all the factors that may have an impact on the adequate delivery of nutrients to the child. (C)

REFERENCES

1. Torun B, Chew F: Protein-energy malnutrition. IN Modern Nutrition in Health and Disease. Shils ME, Shike M, Olson J, et al (eds). Lippincott, Williams & Wilkins, Media, PA, 1999
2. deOnis M, Blossner M: WHO Global database on child growth and malnutrition. WHO/NUT/97.4 Geneva, Switzerland: Programme of Nutrition. World Health Organization, 1997
3. Hendricks KM, Duggan C, Gallagher L, et al: Malnutrition in hospitalized pediatric patients. Current prevalence. Arch Pediatr Adolesc Med 149(10):1118–120, 1995
4. Sermet-Gaudelus I, Poisson-Salomon AS, Colomb V, et al: Simple pediatric nutritional risk score to identify at risk of malnutrition. Am J Clin Nutr 72(1):64–70, 2000
5. Reilly JJ, Weir J, McColl JH, et al: Prevalence of protein-energy malnutrition at diagnosis in children with acute lymphoblastic leukemia. J Pediatr Gastroenterol Nutr 29:194–197, 1999
6. Cameron JW, Rosenthal A, Olson AD: Malnutrition in hospitalized children with congenital heart disease. Arch Pediatr Adolesc Med 149:1098, 1995
7. Motil KJ, Phillips SM, Conkin CA: Nutritional assessment. IN Pediatric Gastroenterology. Wylie R, Hyams JS (ed). Philadelphia, 1999
8. Flegal KM, Troiano RR: Changes in the body mass index of adults and children in the US population. Int J Obesity 24: 807–818, 2000
9. Briassoulis G, Shekhar V, Thompson AE: Energy expenditure in critically ill children. Crit Care Med 28: 1166–1172, 2000
10. Scrimshaw NS: The relation between fetal malnutrition and chronic disease in later life: Good nutrition and lifestyle matter from womb to tomb. Br Med J 315:825–826, 1997
11. Dubowitz H: Child neglect: Guidance for pediatricians. Pediatr Rev 21:111–116, 2000

NUTRITION SCREENING–PEDIATRICS

Background

Pediatric patients have high nutrient needs for growth and development and low nutrient reserves when compared with adults.[1] Malnutrition continues to be a problem among pediatric surgical patients, with the prevalence noted in 1995 to be 25% in a pediatric tertiary care facility.[2] Nutrition screening is the first step in the nutrition care process: It allows identification of high risk individuals so that nutrition services can be provided in a timely manner to those with the greatest need.[3]

There has been little research on pediatric nutrition screening upon which to make evidence based practice recommendations. There is only one study that validates a nutrition screening method for pediatric patients.[4] Clinicians therefore have based their practice upon guidelines described by the Joint Commission for Accreditation of Healthcare Organizations (JCAHO). In lieu of evidence-based practice, these requirements will be described.

Nutrition screening is the process of using characteristics known to be associated with nutrition problems to determine if individuals are malnourished or at risk for malnutrition.[5] The screening process should be fast and efficient so that resources may subsequently be allocated to those patients with current problems or at risk. The JCAHO standard is that a nutrition screen be completed within 24 hours of admission, even on weekends and holidays.[5] Screening is also used to identify pediatric ambulatory patients at high nutrition risk who require more formal, extensive nutrition assessment.[5] Importantly, although these regulations have been implemented by most hospitals in order to comply with JCAHO standards, no evidence-based literature exists to support these standards, nor has it been shown that assessment within 24 hours of admission actually has an impact on the outcome of adult or pediatric hospitalized patients. To accomplish nutrition screening within JCAHO guidelines, a health care organization may decide on the components of the screen and who will complete the screen. The organization may choose to include the results of the screen in the medical record or choose to document by exception, noting only the results of those screens that identify malnutrition or nutrition risk, in the medical record.[5,6] Because of the 24-hour, 7-day-a-week time requirement for the initial nutrition screen, many organizations use staff nurses to complete the screen during the admission process. These screens are generally shorter in length than more in depth screens that include laboratory values, but have the advantage that they can be done efficiently and in a timely fashion. Data are not available concerning the reliability and reproducibility of nutrition screening performed by staff nurses in this population.

Periodic rescreening for patients who "passed" the initial nutrition screen should be performed. The patient's condition may change and nutrition problems develop.[5]

Evidence

Adult nutrition screening tools designed for use by staff nurses have been tested for validity and reproducibility[7] and evaluated for ease of use, cost-effectiveness, and facilitation of an action plan.[8]

A pediatric screening tool has been evaluated and validated in the pediatric intensive care setting. This screen identified patients at increased risk for adverse outcomes.[4] A pediatric risk score has been developed to be used within the first 48 hours of admission. The score, used to identify patients at risk for malnutrition, includes the following: anthropometric measurements, food intake, the ability to eat and retain food, medical condition, and symptoms interfering with feeding.[9] Bessler[10] has published a pediatric screening profile that uses weighted criteria including diagnosis, laboratory values, anthropometrics, diet, feeding ability, and clinical status to dictate the next step in the nutrition care process. This tool is used by dietetic technicians to determine priority level and follow-up. An organization may use several different screens for their varied populations.

Practice Guidelines
Nutrition Screening—Pediatrics

1. A nutrition screen, incorporating objective data such as height, weight, weight change, primary diagnosis, and presence of comorbidities should be a component of the initial evaluation of all

pediatric patients in ambulatory, hospital, home, or alternate site care settings. (C)
2. The health care organization should determine the data elements to be included in the screening tool and who will perform the screen. (C)
3. A procedure for periodic nutrition re-screening should be established. (C)

REFERENCES

1. Marian, M: Pediatric nutrition support. Nutr Clin Pract 8:171–175, 1993
2. Hendricks, KM, Duggan, C, Gallagher, I, et al: Malnutrition in hospitalized pediatric patients: Current prevalence. Arch Pediatric Adolesc Med 149:1118, 1995
3. Klotz KA, Wessel LL, Hennies G: Goals of nutrition support and nutrition assessment. The A.S.P.E.N. Nutrition Support Practice Manual. A.S.P.E.N., Silver Springs, MD, 1998, pp 23–23
4. Mezoff A, Gamm L, Konek S, et al: Validation of a nutritional screen in children with respiratory synctial virus admitted to an intensive care unit. Pediatrics 97:543–546, 1996
5. Joint Commission for Accreditation of Healthcare Organizations: Comprehensive Accreditation Manual for Hospitals. Oakbrook Terrace, IL, JCAHO, 2000 standards, sections: GL-1, TX-4, PE 1.7.1, PE 1.3.1
6. Krasker GD, Balogen LB: JCAHO Standards: Development and relevance to dietetics practice. J Am Diet Assoc 95:240–243, 1995
7. Kovacevich DS, Boney AR, Braunschweig CL, et al: Nutrition risk classification: A reproducible and valid tool for nurses. Nutr Clin Pract 12:20–25, 1997
8. Arrowsmith H: A critical evaluation of the use of nutrition screening tools by nurses. Br J Nursing 12:1483–1490, 1999
9. Sermet-Gaudelus I, Poisson-Salomon AS, Colomb V, et al: Simple pediatric nutritional risk score to identify children at risk of malnutrition. Am J Clin Nutr 72:64–70, 2000
10. Bessler S: Nutritional assessment. IN Handbook of Pediatric Nutrition. Samour PQ, Helm KK, Lang CE (eds). Aspen Publishers, Gaithersburg, MD, 1999, p 19

NUTRITION ASSESSMENT—PEDIATRICS

Background

Nutrition assessment is the second stage of the nutrition care process. Nutrition screening identifies patients who require a comprehensive nutrition assessment.[1] The nutrition assessment describes the current nutrition status of the infant, child, or adolescent and facilitates the development of a nutrition care plan.

There is little research in the area of pediatric nutrition assessment upon which to formulate evidence-based practice guidelines. Clinicians are therefore obliged to follow the regulations set forth by the JCAHO, despite there being no outcomes-based data to support these guidelines.

The nutrition assessment is defined by JCAHO as a comprehensive process for defining an individual's nutrition status using medical, nutrition, and medication intake histories, physical examination, anthropometric measurements, and laboratory data.[1] As part of the nutrition care process, the assessment is completed and updated at specific intervals when warranted by the patient's needs or condition. The 2000 edition of the JCAHO Comprehensive Manual for Hospitals does not require a written prescription or order for nutrition assessment.[1]

According to JCAHO, the initial assessment should be performed and documented within a reasonable time frame as defined by the hospital.[1] A preadmission assessment may be done if completed no more than 30 days before an admission or readmission. The report must be included in the patient's record and any significant changes in the patient's condition documented at the time of admission.[1]

A qualified clinician with nutrition expertise should perform the nutrition assessment, using input from other members of the health care team. The following components should be considered as part of the assessment:

- Adequacy of previous and current nutrient intake[1];
- Current enteral diet or parenteral fluid prescription and the number of days with nothing per mouth[1];
- Feeding behavior and feeding skill development[2];
- Financial resources for food[2];
- Food intolerance or allergies[1];
- Growth evaluation using current anthropometric measurements and growth history according to appropriate growth charts[1,2];
- Medications that may affect nutrient status[1];
- Medical history including conditions that alter ingestion, digestion, absorption, or use of nutrients[1];
- Nutritional implications of laboratory tests[1];
- Physical examination including manifestations of nutrient deficiencies and excess[1] and assessment of development and activity level[2];
- Religious, cultural, ethnic, and personal food preferences[1]; and
- The family viewpoint regarding nutrition and feeding.[2]

The nutrition assessment can be viewed as an ongoing process, particularly in the acute care setting.[3] Clinical circumstances and medical or surgical management may change rapidly, altering the nutrition assessment. Some practitioners use a nutrition acuity rating to capture the intensity of the nutrition care plan and describe the timing of assessments.[4]

Feeding skill level may be impossible to assess in the acute setting. In the recuperative phase of treatment it may be the focus of the assessment, determining the feeding approach for the nutrition care plan. All of the components of the comprehensive assessment should be evaluated to properly understand the nutrition status of the child within their family setting.

Evidence

The comprehensive nutrition assessment is used to describe acute protein-calorie malnutrition (PCM). The presence of PCM correlates with increased surgical morbidity and mortality. Its prevalence is high in pediatric general surgical patients[5] and pediatric cardiac surgical patients.[6] The nutrition assessment can be an important part of the surgical evaluation process and demonstrates those perioperative patients at risk for PCM.[5,6]

There are many comprehensive articles and texts available to describe the nutrition assessment process for pediatrics.[2,7–17] The pediatric evaluation is very different from the assessment of adults in that growth

and development are essential factors that must be assessed and monitored. A Cochrane database review recently examined the evidence for growth monitoring. Despite worldwide attention on growth monitoring, there were only two studies available for review, both from developing countries.[18] No conclusions can be drawn.

Practice Guidelines
Nutrition Assessment—Pediatrics

1. A formal nutrition assessment should be carried out in any pediatric patient, independent of the care setting, who is identified by a nutrition screen as nutritionally at risk.(C)
2. The nutrition assessment should be patient specific and include evaluation of the medical course, medication history, nutritional history, feeding skill level, analysis of typical and current diet, physical examination, anthropomorphic measurements, and laboratory data. (C)
3. A written summary of the objective and subjective data collected for the nutrition assessment, of the explicit nutrition risk stratification, and of the specific recommendations to be incorporated into the nutrition care plan (protein, calorie, and micronutrient requirements, route of administration, and treatment goals and monitoring parameters) should be created and made available to the patient's care providers. (C)
4. Nutrition goals should be developed as a part of the nutrition care plan. (C)
5. The frequency of nutrition monitoring and re-assessment should be based on the patient's clinical course and upon an objective nutrition acuity rating. (C)

REFERENCES

1. Joint Commission for Accreditation of Healthcare Organizations: Comprehensive Accreditation Manual for Hospitals. Oakbrook Terrace, IL, JCAHO, 2000, TX-4, GL, PE 1.2, PE 1.7
2. Isaacs JC, Cialone J, Horsley JW, et al: Children with Special Needs: A Community Pocket Guide. American Dietetic Association, Chicago, IL, 1997
3. Baxter JP: Problems of nutritional assessment in the acute setting. Proc Nutr Soc 58:39–46, 1999
4. Williams CP, ed. Pediatric Manual of Clinical Dietetics. American Dietetic Association, Chicago, IL, 1998, pp 14–15
5. Cooper A, Jakobowski D, Spiker J, et al: Nutritional assessment: An integral part of the preoperative pediatric surgical evaluation. J Pediatr Surg 16:554–556, 1981
6. Leite HP, Fisberg M, Novo NF, et al: Nutritional assessment and surgical risk markers in children submitted to cardiac surgery. Rev Paul Med 113:706–714, 1995
7. Mascarenhas MR, Zemel B, Stallings VA: Nutritional assessment in pediatrics. Nutrition 14:105–115, 1998
8. Marian M: Pediatric nutrition support. Nutr Clin Pract 8:171–175, 1993
9. Klotz KA, Wessel LL, Hennies G: Goals of nutrition support and nutrition assessment. The A.S.P.E.N. Nutrition Support Practice Manual. A.S.P.E.N., Silver Springs, MD, 1998, p 23.3
10. Groh-Wargo S, Thompson M, Cox JH: Nutritional Care for High Risk Newborns, 3rd ed. Precept Press, Chicago, IL, 2000
11. Kessler D, Dawson P. Failure to Thrive and Pediatric Undernutrition: A Transdisciplinary Approach. Brookes, Baltimore, MD, 1998
12. Kleinman RE, ed. Pediatric Nutrition Handbook, 4th ed. American Academy of Pediatrics, Elk Grove Village, IL, 1999
13. Mitchell MK: Nutrition Across the Life Span. WB Saunders, Philadelphia, 1997, pp 28–48
14. Rickert V: Adolescent Nutrition: Assessment and Management. Chapman and Hall, New York, NY, 1995
15. Samour PQ, Helm KK, Lang CE, eds. Handbook of Pediatric Nutrition. A.S.P.E.N., Gaithersburg, MD, 1999
16. Williams CP, ed: Pediatric Manual of Clinical Dietetics. American Dietetic Association, Chicago, IL, 1998, pp 14–15
17. Leleiko NS, Luder E, Fridman M, et al: Nutritional assessment of pediatric patients admitted to an acute-care pediatric service utilizing anthropometric measurements. JPEN 10:166–168, 1986
18. Panpanich R, Garner P: Growth monitoring in children. Cochrane Database Syst Rev 2:CD001443, 2000

CREATION OF A NUTRITION CARE PLAN—PEDIATRICS

Background

The nutrition care plan serves as a template for nutrition therapy and should be integrated into the medical and surgical treatment care plans. The nutrition care plan should address all supplemental nutrients and oral, enteral, and parenteral nutrition modalities. It is developed to correct nutritional problems or reduce nutritional risks identified by the formal nutrition assessment. It also serves as an outline of sequential, reasonable, and achievable interventions and counseling for the infant, child, or adolescent within a given setting. A nutrition care plan is dynamic because of the changes in clinical status and shifting needs of growth and development that characterize pediatric patients.

A care plan consists of a nutrition assessment, identification of nutrition problems and/or potential nutrition risks, measurable goals or outcomes, education and intervention strategies, parameters for evaluating (monitoring) results, reassessment and modification of the care plan as needed, and recommendations for follow-up care.[1] Interventions are developed to meet established goals. The appropriate modality of nutrition intervention (oral, enteral, parenteral, or a combination) is considered first. Delivery site, method of administration, equipment, nutrient solution (composition and concentration), rate of delivery, and need for any additional additives are then addressed. Monitoring parameters are chosen relative to the goals and timing of specific interventions. Frequency of nutritional monitoring depends upon severity of clinical condition, degree of malnutrition, level of metabolic stress, and existing nutrient deficiencies (Table I). Monitoring parameters provide information for the evaluation of care plan outcomes. If the evaluation reveals that goals are not being met or that new problems/risks have arisen, the process repeats itself with reassessment and the modification of the care plan. The effectiveness of nutrition intervention is determined through periodic nutrition reassessment. Condition-specific and growth charts are integral components of any pediatric care plan.

Evidence

Whether oral, enteral, or parenteral nutrition is utilized, the presence of malnutrition, level of physiological stress, and level of gastrointestinal function need to be determined before setting goals. Calorie and protein goals will vary depending upon the desired out-

come, such as prevention of weight loss, minimal growth, normal growth velocity, or catch-up growth. Monitoring parameters may include measured actual nutrient delivery (calories and protein) compared with measured or estimated needs (Tables I and II). Abernathy et al[2] reported that adult patients fed by nasoenteric tube received only 61% of their caloric goals.

Children who are malnourished are at greater risk for infections and metabolic problems. All moderately to severely malnourished children should have serum potassium, phosphorus, magnesium, and glucose levels checked during the first week of refeeding because of metabolic alterations seen in the nutritional recovery syndrome.[3,4]

Goals of nutrition care should be stated in measurable behavioral or quantitative terms and be directly related to the effectiveness of nutrition interventions.[5]

TABLE I
Suggested care plan monitoring parameters and frequency for pediatric patients

Parameter	Suggested frequency	
	Initial/ hospitalized	Follow-up/outpatient
Growth		
Weight	Daily	Daily to q visit
Height/length	Weekly	Weekly to q visit
Head circumference	Weekly	Weekly to q visit
Body composition (TSF, bone age)	Initially	Monthly to annually
Metabolic (serum*)		
Electrolytes	Twice weekly	Weekly to q visit
BUN/creatinine	Weekly	Weekly to q visit
Minerals	Twice weekly	Weekly to q visit
Acid–base status	Until stable	As indicated
Albumin/prealbumin	Weekly	Weekly to q visit
Glucose	Daily to weekly	Weekly to q visit
Triglycerides†	Initially daily	Weekly to q visit
Liver function tests†	Weekly	Weekly to q visit
Complete blood count/differential	Weekly	Weekly to q visit
Platelets, PT/PTT†	Weekly	As indicated
Iron indices	As indicated	Biannually to annually
Trace elements	As indicated	Annually
Carnitine†	As indicated	As indicated
Folate/vitamin B-12	As indicated	As indicated
Ammonia†	As indicated	As indicated
Cultures	As indicated	As indicated
Metabolic (urine)		
Glucose†	Twice daily	Daily to weekly
Ketones†	Twice daily	Daily to weekly
Specific gravity	As indicated	As indicated
Urea nitrogen	As indicated	As indicated
Clinical calculations		
Fluid balance	Daily	As indicated
Weight velocity	Weekly	Weekly to q visit
Height velocity	Monthly	Monthly to q visit
Projected versus actual intake	Daily	Weekly to q visit
Clinical observation		
Developmental milestones	As indicated	Annually
Intake and output	Daily	As indicated
Administration system	6 times/day	2 times/day
Access site/dressing	6 times/day	2 times/day

Frequency depends on clinical condition.
*For metabolically unstable patients, need to check more frequently.
†For patients on parenteral nutrition.

TABLE II
Suggested monitoring during enteral nutrition support of infants

Parameter	Initial week	Hospitalization	Outpatient follow-up
Growth			
Calories, protein, vitamins, minerals	Daily	Weekly	Monthly
Weight for corrected age	Daily	Daily	Monthly
Height for corrected age	Initially	Weekly	Monthly
Head circumference for corrected age	Initially	Weekly	Monthly
Gastrointestinal			
Abdominal girth	3 hourly	8 hourly	PRN
Gastric residuals	2 hourly	8 hourly	PRN
Vomiting	Daily	Daily	Daily
Stools			
Frequency/consistency	Daily	Daily	PRN
Occult blood	Initially	PRN	PRN
Mechanical			
Tube placement	Initially	3–8 hourly	8 hourly
Nose care	8 hourly	8 hourly	8 hourly
Gastrostomy/jejunostomy site care	PRN	PRN	PRN
Metabolic			
Electrolytes	Daily until stable	Weekly	Monthly if stable
Glucose	Daily until stable	Weekly	Monthly if stable
BUN/creatinine	Initially	Weekly	Monthly if stable
Viceral proteins	Initially	2–4 weeks	Monthly if stable
Alk phos, trig	Initially	PRN	1–3 months
Minerals (Ca, P, Mg)	Initially and daily	Weekly	Monthly if stable
Hgb, Hct	Initially	PRN	1–3 months
Fluid intake/output	Daily	Daily	Daily
Urine specific gravity	Daily	Weekly	PRN

Adapted with permission: Davis A. Indications and techniques for enteral feeds. IN *Pediatric Enteral Nutrition.* Baker SB, Baker RD Jr, Davis A, ed. Aspen Publishers, Gaithersburg, MD, 1994.

Practice Guidelines
Creation of a Nutrition Care Plan—Pediatrics

1. Nutrition goals should include short-term and long-term objectives. (C)
2. A plan for monitoring the effect of nutrition interventions should be stated in the nutrition care plan. (C)

REFERENCES

1. Nutritional care process. IN Krause's Food, Nutrition, and Diet Therapy. Mahan LK, Escott-Stump S (eds). WB Saunders, Philadelphia, PA, 1996, p 403–423
2. Abernathy GB, Heizer WD, Holcombe BJ, et al: Efficacy of tube feeding in supplying energy requirements of hospitalized patients. JPEN 13:387–391, 1989
3. Solomon SM, Kirby DF: The refeeding syndrome: A review. JPEN 14:90–97, 1990
4. Mezoff AG, Gremse DA, Farrell MK: Hypophosphatemia in the nutritional recovery syndrome. Am J Dis Child 143:1111, 1989
5. August DA: Outcomes research in nutrition support: background, methods, and practical applications. IN Practice-oriented Nutrition Research. Ireton-Jones CS, Gottschlich MM, Bell SJ (eds). Aspen Publishers, Gaithersburg, MD, 1998, p 129–156

Section V: Administration of Specialized Nutrition Support

INDICATIONS FOR SPECIALIZED NUTRITION SUPPORT

Background

Specialized nutrition support (SNS) is defined as the provision of nutrients orally, enterally, or parenterally with therapeutic intent. Enteral nutrition (EN) involves the nonvolitional delivery of nutrients by tube into the gastrointestinal tract. Parenteral nutrition (PN) is the administration of nutrients intravenously. For individuals who cannot, should not, or will not eat adequately and in whom the benefits of improved nutrition outweigh the risks, SNS may be implemented. Patients who are malnourished or at significant risk for becoming malnourished should receive SNS. The administration of SNS is never an emergency; it should not be initiated until the patient is hemodynamically stable. A distinction between nutrition support as primary therapy for a disease versus its value as an adjunct to primary therapy is essential. SNS is used to treat malnutrition when present and to avoid the development of malnutrition resulting from insufficient energy and nutrient intake in the face of increased energy needs. Only in relatively uncommon circumstances is SNS used to treat specific disease manifestations (eg, altered protein intake in patients with renal failure or hepatic encephalopathy). This section reviews general issues generic to the decision to initiate SNS. Consult guideline statements in the metabolic and disease-specific sections regarding specific indications for the use of EN and PN in individual patients with specific metabolic conditions or diseases.

Evidence

Canned, liquid meal replacement beverages are widely available commercially. These products are used to supplement the nutrient intake of individuals who are unable to ingest adequate nutrients in the form of a standard oral diet. Two small studies suggest that ingestion of these beverages may have a role in improving the nutrition status of homebound elderly persons.[1,2] They have also been used soon after gastrointestinal and hip fracture surgery to improve nutritional parameters.[3,4] There are no data supporting routine use of commercial canned, meal replacement beverages.

A functioning gastrointestinal tract is required for the use of EN. A functioning gastrointestinal tract is of sufficient length and condition to allow adequate nutrient absorption. Contraindications to enteral feeding include diffuse peritonitis, intestinal obstruction, intractable vomiting, paralytic ileus, intractable diarrhea, and gastrointestinal ischemia.[5] Advances in administration of EN make its use possible in some patients with conditions previously felt to contraindicate its use (eg, acute pancreatitis and high-output enterocutaneous fistulae).

PN is an invasive therapy with inherent risks. Its purpose is to provide nutrition for individuals without adequate GI function.[6] The use of PN in specific disease conditions is discussed in detail in other sections of this document.

A major controversy in the field of nutrition support concerns the relative indications for the use of PN versus EN. Proposed advantages of EN include reduced cost, better maintenance of gut integrity, reduced infection, and decreased hospital length of stay.

It has been suggested that critically ill patients who do not receive enteral nutrients may experience translocation of intestinal flora and associated endotoxin release, which can activate inflammatory pathways. It is proposed that the resultant systemic activation contributes to the etiology, progression, and morbidity/mortality of multisystem organ failure. However, there are few human data to substantiate this.[7] Provision of enteral nutrients appears to help maintain mucosal structure and function of the intestine.[8] A number of trials have found reduced septic complications in abdominal trauma patients given EN when compared with PN.[9,10] Decreased rates of infection in enterally fed burn patients have been noted in two studies,[11,12] and comparable results have been achieved in comparisons of PN and EN administered to patients with severe head injury.[13–15]

Sufficient randomized, prospective, controlled trials with carefully matched patients receiving EN and PN are not available to conduct a meta-analysis comparing enteral and parenteral interventions across a wide variety of illnesses.[16] Therefore, no definitive conclusions about the superiority of EN over PN can be made in many disease states.[17] Many studies show an improved ability to meet nutrient goals with PN over EN, and there may be some clinical situations where even with a functional gut, it is not possible to administer adequate SNS other than with PN. It must be observed, however, that nutrient delivery is only an intermediate end point, and reliance on outcome data is preferable.

Costs, charges, and reimbursement for PN have all been found to be higher than those for EN by numerous

investigators.[18–20] There are no studies that show oral diets or EN to be more expensive than PN. However, it must also be acknowledged that true and accurate cost data (as opposed to charge based estimates) are hard to come by. Furthermore, it is very difficult to calculate true global costs (including complications, additional x-rays, monitoring, etc) of these therapies. Nevertheless, from a financial perspective, oral diets and EN are likely less costly than PN. In situations where there are no specific data demonstrating improved outcomes with PN over EN, EN therefore seems preferable on a cost basis.

Another controversial issue is the optimal timing of initiation of SNS. Initiation of enteral feedings early in the course of illness has been recommended to attenuate the stress response and improve feeding tolerance. Although there are reports of enteral feeding being well tolerated when initiated within 6 to 12 hours after injury,[21–23] these data suggest feasibility but not necessarily benefit. Many protocols exist for enteral feeding advancement, but these are largely untested. There appears to be no benefit to elaborate regimens for slow initiation of enteral feeding,[24] and newer studies show full feedings can usually be tolerated within 2 to 3 days of formula initiation.[21–23] EN is generally considered safe, but gastrointestinal, metabolic, and respiratory complications have been documented. Inappropriate formula advancement or feeding interruptions may result in underfeeding.[25] A reduced incidence of metabolic abnormalities and other improved outcomes of EN have been demonstrated when tube-fed patients are managed by an interdisciplinary team.[26–28] At least one study documented the cost-effectiveness of this approach.[28]

The number of days to wait before initiating PN is a complex, frequently asked question. There are no prospective, randomized, clinical trials that specifically address this issue. In many studies of the use of PN, the majority of patients are able to eat orally within 6 to 8 days; it is unlikely that these patients benefit from such short-duration PN. This is likely true even in malnourished patients.[29–31] It is also likely that patients who do not eat or receive SNS for more than 10 to 14 days after hospital admission or after surgery do have worse clinical outcomes, longer hospital stays, and higher costs of care.[8,29] Unfortunately, it is difficult to identify these patients prospectively. On the basis of these data, it does seem reasonable to initiate SNS in patients with inadequate oral intake for 7 to 14 days or in those patients in whom inadequate oral intake is expected over a 7- to 14-day period.

Practice Guidelines *Indications for Specialized Nutrition Support*

1. SNS should be used in patients who cannot meet their nutrient requirements by oral intake. (B)
2. When SNS is required, EN should generally be used in preference to PN. (B)
3. When SNS is indicated, PN should be used when the gastrointestinal tract is not functional or cannot be accessed and in patients who cannot be adequately nourished by oral diets or EN. (B)
4. SNS should be initiated in patients with inadequate oral intake for 7 to 14 days, or in those patients in whom inadequate oral intake is expected over a 7- to 14-day period. (B)

REFERENCES

1. Lipschitz DA, Mitchell CO, Steele RW, et al: Nutritional evaluation and supplementation of elderly subjects participating in a "meals on wheels" program. JPEN 9:343–347, 1985
2. Gray-Donald K, Payette H, Boutier V: Randomized clinical trial of nutritional supplementation shows little effect on functional status among free-living frail elderly. J Nutr 125(12):2965–2971, 1995
3. Delmi M, Rapin C-H, Bengoa J-M, et al: Dietary supplementation in elderly patients with fractured neck of the femur. Lancet 335:1013–1016, 1990
4. Keele AM, Bray MJ, Emery PW, et al: Two phase randomized controlled clinical trial of postoperative oral dietary supplements in surgical patients. Gut 40:393–399, 1997
5. A.S.P.E.N: Board of Directors. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. JPEN 17(Suppl):1SA–52SA, 1993
6. Shils ME, Brown RO. Parenteral nutrition. IN Modern Nutrition in Health and Disease, 9th ed. Shils ME, Olson JA, Shike M, Ross AC (eds). Williams and Wilkins, Baltimore MD, 1999, p 1658
7. Lipman TO: Bacterial translocation and enteral nutrition in humans: An outsider looking in. JPEN 19:156–165, 1995
8. Hernandez G, Velasco N, Wainstein C, et al: Gut mucosal atrophy after a short enteral fasting period in critically ill patients. J Crit Care 14:73–77, 1999
9. Moore FA, Feliciano DV, Andrassy RJ, et al: Early enteral feeding compared with parenteral, reduces postoperative complications. The results of a meta-analysis. Ann Surg 216:172–183, 1992
10. Kudsk KA, Croce MA, Fabian TC, et al: Enteral versus parenteral feeding: effects on septic morbidity following penetrating trauma. Ann Surg 215:503–513, 1992
11. Gottschlich MM, Jenkins M, Warden GD, et al: Differential effects of three enteral dietary regimens on selected outcome variables in burn patients. JPEN 14:225–236, 1990
12. Garrell DR, Razi M, Lariviere F, et al: Improved clinical status and length of care with low fat nutrition support in burn patients. JPEN 19:482–491, 1995
13. Norton JA, Ott LG, McClain C, et al: Intolerance to enteral feeding in the brain-injured patient. J Neurosurg 68:62–66, 1988
14. Grahm TW, Zadrozny DB, Harrington T: The benefits of early jejunal hyperalimentation in the head-injured patient. Neurosurgery 25:729–735, 1989
15. Borzotta AP, Pennins J, Papasadero B, et al: Enteral versus parenteral nutrition after severe closed head injury. J Trauma 37:459–468, 1994
16. Braunschweic C, Levy P, Sheean P, et al: Enteral versus parenteral nutrition: A meta analysis. Am J Clin Nutr 74:534–542, 2001
17. Lipman TO: Grains or veins: Is enteral nutrition really better than parenteral nutrition? A look at the evidence. JPEN 22:167–182, 1998
18. Adams S, Dellinger P, Wertz MJ, et al: Enteral versus parenteral nutritional support following laparotomy for trauma: A randomized prospective trial. J Trauma 26:882–891, 1986
19. Kotler DP, Fogleman L, Tierney A: Comparison of total parenteral nutrition and an oral, semielemental diet on body composition, physical function, and nutrition-related costs in patients with malabsorption due to acquired immunodeficiency syndrome. JPEN 22:120–126, 1998
20. Senkel M, Mumme A, Eickhoff U, et al: Early postoperative enteral immunonutrition: Clinical outcome and cost-comparison analysis in surgical patients. Crit Care Med 25:1489–1496, 1997
21. Braga M, Gianotti L, Vignali A, et al: Artificial nutrition after major abdominal surgery: Impact of route of administration and composition of the diet. Crit Care Med 26:24–30, 1998
22. Gianotti L, Braga M, Vignali A, et al: Effect of route of delivery and formulation of postoperative nutritional support in patients undergoing major operations for malignant neoplasms. Arch Surg 132:1222–1230, 1997
23. Rees RG, Keohane PP, Grimble GK, et al: Tolerance of elemental diet without starter regimen. Br Med J 290:1868–1869, 1985

24. McClave SA, Sexton LK, Spain DA, et al: Enteral tube feeding in the intensive care unit: Factors impeding adequate delivery. Crit Care Med 27:1252–1256, 1999
25. Brown RO, Carlson SD, Cowan GS, et al: Enteral nutritional support management in a university teaching hospital: team vs. nonteam. JPEN 11:52–56, 1987
26. Powers DA, Brown RO, Cowan GS, et al: Nutritional support team vs. nonteam management of enteral nutritional support in a veterans administration medical center teaching hospital. JPEN 10:635–638, 1986
27. Hassell JT, Games AD, Shaffer B, et al: Nutrition support team management of enterally fed patients in a community hospital is cost-beneficial. J Am Diet Assoc 94:993–998, 1994
28. Sandstrom R, Drott C, Hyltander A, et al: The effect of postoperative intravenous feeding (TPN) on outcome following major surgery evaluated in a randomized study. Ann Surg 217:185–195, 1993
29. Holter AR, Fischer JE: The effects of perioperative hyperalimentation on complications in patients with carcinoma and weight loss. J Surg Res 23:31–34, 1977
30. Sako K, Lore JM, Kaufman S, et al: Parenteral hyperalimentation in surgical patients with head and neck cancer: a randomized study. J Surg Oncol 16:391–402, 1981
31. Brennan MF, Pisters PW, Posner M, et al: A prospective randomized trial of total parenteral nutrition after major pancreatic resection for malignancy. Ann Surg 220:436–444, 1994

HOME SPECIALIZED NUTRITION SUPPORT

Background

The indications for home specialized nutrition support (HSNS) are similar to those for the use of specialized nutrition in the hospital setting. Home enteral nutrition (HEN) is used in patients requiring SNS when the gastrointestinal tract is functional. HEN is commonly used for swallowing disorders associated with strokes, neuromuscular illness, head and neck cancers, gastroparesis, and mild to moderate malabsorption.[1,2] Home parenteral nutrition (HPN) is reserved for patients who are unable to maintain an adequate nutrition status when fed via the gastrointestinal tract. Common indications for HPN include inflammatory bowel disease, nonterminal cancer, ischemic bowel, radiation enteritis, motility disorders of the bowel, bowel obstruction, high-output intestinal or pancreatic fistulae, celiac disease, hyperemesis gravidarium, and protein-losing enteropathy.[1,2] Although combined enteral and parenteral therapy is used in the hospital setting, it is rarely used in the home because this approach increases the complexity of care, and it is rarely covered by third-party payers (particularly Medicare and Medicaid).

Because of the expense of HEN and HPN, reimbursement issues may delineate and limit the options available to individual patients. HSNS is reimbursed under Medicare Part B (prosthetic device benefit provision) when specific conditions are satisfied (see below). These therapies may also be covered by state Medicaid programs, private insurance carriers, managed care payers, and other insurance entities. Medicare requires documentation of severe steatorrhea, malabsorption, short bowel syndrome, intestinal motility disorder or obstruction, or exacerbation of inflammatory bowel disease for HPN. Documentation includes one or more of the following: operative reports, x-ray studies, discharge summaries, fecal fat tests, and small bowel motility studies. Under certain circumstances malnutrition must be documented. Swallowing disorders, temporary impairment of gastric emptying, psychological and metabolic disorders such as severe cardiac, pulmonary, and renal disease are not covered for HPN. To be covered, Medicare also requires that the need for HPN be "permanent" (expected duration of therapy greater than 90 days). Many other payers require that similar standards be met for HPN. The total number of patients on HSNS is unknown. The Health Care Finance Administration has published data on parenteral and enteral nutrition use based on workload statistics from Blue Cross and Blue Shield of South Carolina, one of two fiscal intermediaries for Medicare, between 1986 and 1993. Blue Cross and Blue Shield of South Carolina managed 75% of the HSNS covered during the time of this survey. By adjusting this survey for the number of patients not covered by this payer, it was estimated that there were 40,000 patients on HPN and 152,000 on HEN in 1992.[1,3] HSNS data for non-Medicare patients has never been made public because home care providers and payers consider this information to be proprietary. In addition, a registry of patients on HSNS (North American Home Parenteral and Enteral Nutrition Patient Registry), which had provided useful information on these patients, was discontinued in 1993.

Evidence

Based on data from the North American Home Parenteral and Enteral Nutrition Patient Registry, the survival rate and rehabilitation of HSNS patients is highest in the pediatric age group (0 to 18 years) and lowest in those greater than 65 years of age.[4] Conversely, therapy-related complications are highest in the pediatric age group. The primary diagnosis for which HSNS is required is a predictor of outcome. Patients with inflammatory bowel disease have the highest 5-year survival rate, approximately 90%.[2] Patients who start HSNS when they are under 40 years of age are also more likely to do well, with a 5-year survival rate greater than 80%.[2] Complication rates and cost of treatment are higher for HSNS patients who are opiate and sedative dependent to control pain.[5] A majority of the complications that occur are related to the underlying disease for which the therapy is required. However, HSNS itself is associated with serious complications. These include catheter sepsis, metabolic abnormalities, organ dysfunction, and technical problems associated with feeding device placement. The use of clinical pathways for HSNS patients has been reported to facilitate more cost-effective care and to improve communication between home care clinicians and the patient's physician.[6]

Special Considerations

Some studies of the HSNS population have addressed quality of life issues. Many HSNS patients are not aware that a national support group, the OLEY Foundation, and other advocacy or support groups exist.[7] HSNS is perceived by patients to have a negative impact on their quality of life. Despite the fact that it is life saving for patients who have lost GI function, the technological and psychological burdens of HPN

are significant. In a study of HPN patients in Denmark, patients reported reduced strength for physical activity, feelings of depression and anger, loss of independence, and reduced social interaction.[8] Patients in the United States have reported problems with loss of friends, loss of employment, and depression.[9] Supportive interventions for HSNS patients should include financial evaluation and (when needed) psychosocial initiatives to improve self-esteem, manage depression, and enhance coping skills.

The cost of HSNS is substantial. Based on Medicare charges, HPN has been estimated to cost \$55,193 ± 30,596 annually, and HEN has been estimated to cost \$9605 ± 9237 annually.[10] Rehospitalizations, which cost up to \$140,220 per year for HPN patients and \$39,204 per year for HEN patients, occur an average of 0.52 to 1.10 times per year for HPN patients and 0 to 0.50 times per year for HEN patients.[10] Monitoring of therapy is important to prevent complications and to institute early intervention, but the cost of care to providers is also substantial. Industry providers have not published information on costs; however, the annual costs of case management to a hospital nutrition support team has been estimated at \$2070 per patient.[11]

Practice Guidelines
Home Specialized Nutrition Support

1. Home SNS should be used in patients who cannot meet their nutrient requirements by oral intake and who are able to receive therapy outside of an acute care setting. (B)
2. When HSNS is required, HEN is the preferred route of administration when feasible. (B)
3. When HSNS is indicated, HPN should be used when the gastrointestinal tract is not functional and in patients who cannot be adequately supported with HEN. (B)

REFERENCES

1. Howard L, Ament M, Fleming R, et al: Current use and clinical outcome of home parenteral and enteral n nutrition therapies in the United States. Gastroenterology 109:355–365, 1995
2. Scolapio JS, Fleming CR, Kelly DG, et al: Survival of home parenteral nutrition-treated patients: 20 years of experience at the Mayo Clinic. Mayo Clin Proc 74:217–222, 1999
3. Dickerson RN, Brown RO: Parenteral and enteral nutrition in the home and chronic care settings. Am J Managed Care 4:445–455, 1998
4. Howard L, Malone M: Clinical outcome of geriatric patients in the United States receiving home parenteral and enteral nutrition. Am J Clin Nutr 66:1364–1370, 1997
5. Richards DM, Scott NA, Shaffer JL, et al: Opiate and sedative dependence predicts a poor outcome for patients receiving home parenteral nutrition. JPEN 21:336–338, 1997
6. Ireton-Jones C, Orr M, Hennessy K: Clinical pathways in home nutrition support. J Am Diet Assoc 97:1003–1007, 1997
7. Smith CE, Curtas S: Research data: source of information for patient education materials. Nutrition 15:180–181, 1999
8. Jeppesen PB, Langholz E, Mortensen PB: Quality of life in patients receiving home parenteral nutrition. Gut 44:844–852, 1999
9. Smith CE: Quality of life in long-term total parenteral nutrition patients and their family caregivers. JPEN 17:501–506, 1993
10. Reddy P, Malone M: Cost and analysis of home parenteral and enteral nutrition. JPEN 22:302–310, 1998
11. Curtas S, Hariri R, Steiger E: Case management in home total parenteral nutrition: a cost-identification analysis. JPEN 20:113–119, 1996

Section VI: Normal Requirements—Adults

Background

The nutrient requirements for a group of otherwise normal adults unable to take adequate substrate through the oral route from foods, and needing SNS, should not differ from those consuming a usual diet. However, SNS is rarely given to "otherwise normal adults," and the dosing of required nutrients may differ with the route of administration and the formulation provided—given issues of bioavailability, physiologic regulatory mechanisms, and physicochemical characteristics of enteral or parenteral products. The nutritional requirements for adults who need SNS should be based on the results of the formal individualized nutrition assessment. The requirements for each nutrient may vary with nutrition status, disease, organ function, metabolic condition, medication use, and duration of nutrition support. Unfortunately, there are few studies that have critically evaluated the influence of nutrient dosing via SNS on body composition or function. Requirements are based on available information.

Evidence

Nutrient requirements for EN can reasonably be based on the Food and Nutrition Board, Dietary Reference Intakes (DRIs).[1–4] A requirement here is defined as the lowest continuing intake level of a nutrient that maintains a specified indicator of adequacy.[1–4] These nutrient standards are based on data generated from epidemiologic, depletion-repletion, and clinical studies, using appropriate indicators of nutrient adequacy, including clinical and functional outcome markers.[1–4] The inherent limitation to the application of the DRIs, or more specifically the Recommended Dietary Allowance (RDA)/Adequate Intake (AI) levels, is that they are designed to be met from a usual diet for healthy individuals to prevent deficiencies and, where the data exist, to minimize the risk from nutrition-related chronic disease and developmental disorders.[1–4] Although they take into account individual variability, they are not intended for use in people with acute or chronic disease. The RDA/AI values should be used as a guide for planning individual nutrient intake levels.[1–4] The uppermost RDA/AI value of each nutrient can serve as a reference point for SNS in nonpregnant/nonlactating adults. Previously published practice guidelines for parenteral nutrition formulations[5] can also provide a basis for prescribing parenterally administered nutrients.[6] The dosing ranges for enteral and parenteral nutrients provided (Tables I through III) are considered acceptable reference points to meet individual patients' estimated requirements. A dosing weight needs to be determined for each patient (ideally based on body cell mass or lean tissue, because actual body weight does not account for variations in water or fat content).[7]

Although energy is not itself a nutrient, it is provided for by the administration of macronutrients. Although there is no "standard" EN or PN formulation for a "normal" adult requiring SNS, surveys reveal that patients frequently receive standard formulas that provide excess energy.[7] Current energy allowances by the Food and Nutrition Board[8] and the World Health Organization[9] may overestimate or underestimate requirements for many individuals, given the variability both in energy expenditure and its measurement. The requirement for energy, in kilocalories (or kilojoules), is patient specific. Calories should be administered in an amount adequate to meet basal energy expenditures and provide for a level of physical activity to maintain a healthy body mass index. Basal energy expenditure can vary with disease state. In the absence of usual food selection and regulation of food intake, identifying energy needs during nutrition support requires indirect measurement or estimation of expenditures. Predictive equations to estimate energy requirements in healthy adults may be valuable.[10] This estimated amount should fall within a range of 20 to 35 kcal/kg (85–145 kJ/kg) daily. While providing the calories to meet energy needs, the daily dose of carbohydrates and lipids should not exceed 7 and 2.5 g/kg per day, respectively, to minimize adverse metabolic consequences.[5] Some data support the use of a maximum of lipid 1 g/kg/d intravenously, especially in critically ill patients.[11,12] The only recommendation regarding specific fatty acids is that 1% to 2% of daily

TABLE I
Daily electrolyte requirements[1,4,8]†

Electrolyte	Enteral	Parenteral
Sodium	500 mg (22 mEq/kg)*	1–2 mEq/kg
Potassium	2 g (51 mEq/kg)*	1–2 mEq/kg
Chloride	750 mg (21 mEq/kg)*	as needed to maintain acid-base balance with acetate
Calcium	1200 mg (30 mEq/kg)	5–7.5 mEq/kg
Magnesium	420 mg (17 mEq/kg)	4–10 mEq/kg
Phosphorus	700 mg (23 mEq/kg)	20–40 mEq/kg

energy requirements should be derived from linoleic acid (ω6) and about 0.5% of energy from α-linolenic acid (ω3) to prevent essential fatty acid deficiency. Guidelines for a few fatty acids in health have been suggested, as has a ratio for ω6:ω3 fatty acids.[13]

Protein needs cannot be determined solely from factorial and nitrogen balance data, but require amino acid turnover data and, ideally, data on metabolic and functional status to reflect protein's roles. The current recommendations for protein are based predominantly on nitrogen balance data, but not on optimal metabolic balance or metabolic function.[8,9] More recent data support levels of about 186 mg/kg per day of essential amino acids to make up 25% to 30% of protein intake.[14] Adequate energy substrate must be provided along with protein to assure its proper utilization. The use of SNS has actually led to a re-evaluation of the role of amino acids in health. Assessment of an individual's protein status helps determine individual requirements. For the unstressed adult patient with adequate organ function requiring SNS, 0.8 g/kg per day may be adequate, but requirements may rise with metabolic demands to levels of about 2 g/kg per day (or, rarely, even higher). Protein requirements based on fat-free mass may decrease with age.[15] Optimal intake of specific amino acids from the diet for health maintenance or improvement are being investigated, but the data available at this time do not allow for general recommendations for SNS beyond specific metabolic conditions.

Based on an appropriate assessment, water requirements are individualized to fluid balance and solute load. Alterations in fluid and electrolyte needs are managed in a patient-specific manner, taking into account disturbances of volume, concentration, and/or composition. The fluid requirement for adults is generally met with volumes of 30 to 40 mL/kg per day, or at 1 to 1.5 mL/kcal expended.[5,8] Enteral electrolyte doses follow RDA/AI reference values. The standard dosing ranges for parenteral electrolytes assumes normal organ function, without abnormal losses. Electrolyte content of parenteral nutrient stock solutions should be taken into consideration.

Vitamins and trace elements are essential nutrients that act as coenzymes and cofactors involved in metabolism. For EN, recommendations are based on the RDA/AI levels. Dosing beyond the RDA/AI values near the tolerable upper intake level is not generally supported by experimental data for most patients requiring SNS. The dosing guidelines for parenteral vitamins and trace elements should be considered as approximations of need.[5,16] The parenteral vitamin recommendations were intended to meet the needs of patients with increased requirements and should be given daily in patients with limited oral intake. Until the anticipated reformulation of parenteral multivitamin products to include vitamin K (as well as additional thiamin, pyridoxine, folate, and vitamin C), vitamin K should be administered in addition to the vitamin K–free multivitamin products currently used.[17] Micronutrients present as contaminants in parenteral products should also be taken into consideration.[18]

Although fiber, as defined by a variety of characteristics (viscosity, water dispersability, fermentability, bulk, and binding properties), is an important component of the diet with benefit on colonic function, specific dosing recommendations cannot be made for enteral nutrition at this time.

TABLE II
Daily vitamin requirements[1-4,8]†

Vitamin	Enteral	Parenteral
Thiamin	1.2 mg	3 mg
Riboflavin	1.3 mg	3.6 mg
Niacin	16 mg	40 mg
Folic acid	400 μg	400 μg
Pantothenic acid	5 mg	15 mg
Vitamin B-6	1.7 mg	4 mg
Vitamin B-12	2.4 μg	5 μg
Biotin	30 μg	60 μg
Choline	550 mg	not defined
Ascorbic acid	90 mg	100 mg
Vitamin A	900 μg	1000 μg
Vitamin D	15 μg	5 μg
Vitamin E	15 mg	10 mg
Vitamin K	120 μg	1 mg

TABLE III
Daily trace element requirement[1,3,8]†

Trace element	Enteral	Parenteral
Chromium	30 μg	10–15 μg
Copper	0.9 mg	0.3–0.5 mg
Fluoride	4 mg	Not well defined
Iodine	150 μg	Not well defined
Iron	18 mg	Not routinely added
Manganese	2.3 mg	60–100 μg
Molybdenum	45 μg	Not routinely added
Selenium	55 μg	20–60 μg
Zinc	11 mg	2.5–5 mg

†Tables give general ranges for safe administration of nutrients in generally healthy people. Nutrient prescriptions must be individualized for each patient and clinical situation.

Practice Guidelines
Normal Requirements—Adults

1. Determination of nutrient requirements should be individualized, based on assessment of body composition and function, and fall within acceptable ranges, while taking physiologic and pathophysiologic conditions into account. (B)

REFERENCES

1. Institute of Medicine, Food and Nutrition Board: Dietary reference intakes: calcium, phosphorus, magnesium, vitamin D, and fluoride. National Academy Press, Washington, DC, 1997
2. Institute of Medicine, Food and Nutrition Board: Dietary reference intakes: thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline. National Academy Press, Washington, DC, 1998
3. Institute of Medicine, Food and Nutrition Board: Dietary reference intakes: vitamin C, vitamin E, selenium, and carotenoids. National Academy Press, Washington, DC, 2000
4. Institute of Medicine, Food and Nutrition Board: Dietary reference intakes: Vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. National Academy Press, Washington, DC, 2001
5. National Advisory Group on Standards and Practice Guidelines for Parenteral Nutrition: Safe Practices for parenteral nutrition formulations. JPEN 22:49–66, 1998

6. American Medical Association Department of Foods and Nutrition, 1975: Multivitamin preparations for parenteral use: a statement by the nutrition advisory group. JPEN 3:258–262, 1979
7. Schloerb PR: Electronic parenteral and enteral nutrition. JPEN 24:23–29, 2000
8. National Research Council: Recommended dietary allowances, 10th ed. National Academy Press, Washington, DC, 1998
9. WHO (World Health Organization): Energy and protein requirements: Report of a joint FAO/WHO/UNU expert consultation. Technical Report Series 724. WHO: Geneva, 1985
10. Vinken AG, Bathalon GP, Sawaya AL, et al: Equations for predicting the energy requirements of healthy adults aged 18–81 y. Am J Clin Nutr 69:920–926, 1999
11. Nussbaum MS, Fischer JE: Parenteral nutrition. IN Nutrition in Critical Care. Zaloga GP (ed). Mosby-Year Book, St Louis, 1994, pp 371–397
12. Battistella FD, Widergren JT, Anderson JT, et al: A prospective, randomized trial of intravenous fat emulsion administration in trauma victims requiring total parenteral nutrition. J Trauma 43:52–60, 1997
13. Kris-Etherton PM, Taylor DS, Yu-Poth S, et al: Polyunsaturated fatty acids in the food chain in the United States. Am J Clin Nutr 71(Suppl):179S–188S, 2000
14. Young VR, Borgonha S: Adult human amino acid requirements. Curr Opin Clin Nutr Metab Care 2:39–45, 1999
15. Millward DJ, Fereday A, Gibson N, et al: Aging, protein requirements, and protein turnover. Am J Clin Nutr 66:774–786, 1997
16. American Medical Association Department of Foods and Nutrition: Guidelines for essential trace element preparations for parenteral use. A statement by an expert panel. JAMA 241: 2051–2054, 1979
17. Food and Drug Administration. Parenteral Multivitamin Products; Drugs for Human Use; Drug Efficacy Study Implementation; Amendment: Federal Register April 20, 2000. Vol 65, number 77: 21200–21201
18. Pluhator-Murton MM, Fedorak RN, Audette RJ, et al: Trace element contamination of total parenteral nutrition. JPEN 23:222–232, 1999

Section VII: Normal Requirements—Pediatrics

INTRODUCTION

This section is divided into two separate sections: fluid and energy needs and substrate requirements. The latter area includes protein, carbohydrate, and lipid requirements. Although fluid and energy are not nutrients, they clearly play a critical role in the nutritional care of infants and children. Additionally, the requirements are quite specific for various ages of children and disease states, as delineated below. Finally, many disease states have specific energy, fluid, and substrate requirements or restrictions.

This section discusses nutritional requirements predominately for the healthy child. Subsequent individual sections will highlight specific needs for individual disease states.

ENERGY

Background

The energy needs and reserves of infants and children are quite unique and have been reviewed by several authors.[1] Energy in a child is required for both maintenance of body metabolism as well as for growth. Estimated energy needs of an infant and older child are shown in Table I. Caloric requirements in an infant may be calculated in a variety of ways, including a modification of the Harris-Benedict equation, which has been designed for use in younger children and infants.[2,3] Energy requirements for most pediatric patients can also be calculated based on standard nomograms (eg, Recommended Daily Allowance [RDA] tables) or by indirect calorimetry.

Evidence

Energy requirements vary with age. Because of the great variability of energy needs, the World Health Organization Expert Consultation on Energy and Protein Requirements have recommended that "whenever possible energy requirements should be based on measurements of expenditure rather than intake."[4] Heird et al[5] have estimated that a 1-kg infant has only a 4-day nutritional reserve, and a full-term infant may live for no more than a month without nutrition. In general, infants require more calories if fed enterally rather than parenterally.[6] Methods to estimate the energy needs of infants and older children are well described.[7] Energy requirements before adolescence appear to differ between sexes, with lower energy needs in girls because of lower activity states.[8] Adolescence increases energy requirements. Bitar et al[9] showed that energy needs in adolescence vary with gender, body composition, and even the season. Administration of nutrition support will alter energy needs.

TABLE I
Estimated energy needs

Age (y)	Kilocalories (kcal/kg body weight)
0–1	90–120
1–7	75–90
7–12	60–75
12–18	30–60
>18	25–30

Special Considerations

Although each individual section will deal with specific disease states, there are some important energy considerations that should be mentioned here.

Unlike increased substrate utilization observed in adult surgical patients, substrate utilization has not been shown to increase substantially in neonates following surgery. In fact, previous estimates of early postoperative energy requirements apparently overstate needs. Administration of calories at 50% above REE levels to perioperative neonates leads to significant overfeeding.[10]

Johann-Liang et al[11] showed that energy intake, but not energy expenditure, in HIV-infected children was significantly reduced compared with age- and gender-matched controls. This suggests that there may be a benefit to increasing energy delivery to HIV-infected children who are growth impaired; however, studies are needed to confirm this.[11,12]

Practice Guidelines *Energy*

1. Energy needs in infants and children should be estimated using standard formulas or nomograms and then adjusted according to the clinical course of the child. (B)
2. Energy requirements should be adjusted depending on the route of SNS administration. (B)
3. Energy needs for patients undergoing surgical procedures should be based on indirect calorimetry or adjusted down from standard formulas to avoid overfeeding. (B)

REFERENCES

1. Wells JC: Energy metabolism in infants and children. Nutrition 14:817, 1998
2. Baker J, Detsky A, Wesson D: Nutritional assessment: A comparison of clinical judgment and objective measurements. N Engl J Med 306:969, 1982
3. Caldwell MD, Kennedy-Caldwell C: Normal Nutritional requirements. Surg Clin North Am 61:491, 1981
4. Anonymous: World Health Organization. Energy and protein requirements. Report of a joint FAO/WHO/UNU Expert Consultation. Geneva: World Health Organization WHO Technical Report Series No. 724, 1985
5. Heird W, Driscoll J, Schullinger J: Intravenous alimentation in pediatric patients. J Pediatr 80:351, 1972
6. Reichman B, Chessex P, Putet G, et al: Diet, fat accretion, and growth in premature infants. N Engl J Med 305:1495, 1981
7. Anonymous: National Academy of Sciences. Recommended Dietary Allowances. National Academy Press, Washington, DC, 1989, p 24
8. Goran MI, Gower BA, Nagy TR, et al: Developmental changes in energy expenditure and physical activity in children: Evidence for a decline in physical activity in girls before puberty. Pediatrics 101:887, 1998
9. Bitar A, Fellmann N, Vernet J, et al: Variations and determinants of energy expenditure as measured by whole-body indirect calorimetry during puberty and adolescence. AJCN 69:1209, 1999
10. Letton RW, Chwals WJ, Jamie A, et al: Early postoperative alterations in infant energy use increase the risk of overfeeding. J Pediatr Surg 30:988, 1995
11. Johann-Liang R, O'Neill L, Cervia J, et al: Energy balance, viral burden, insulin-like growth factor-1, interleukin-6 and growth impairment in children infected with human immunodeficiency virus. AIDS 14:683, 2000
12. Henderson RA, Talusan K, Hutton N, et al: Resting energy expenditure and body composition in children with HIV infection. J Acquir Immune Defic Syndr 19:150, 1998

FLUID AND ELECTROLYTES

Background

Fluid requirements. The standard method of calculating fluid requirements for pediatrics was described in an article published in 1957.[1] Fluid requirements are related to caloric expenditure, and caloric expenditure is determined by a simple formula using body weight:

100 kcal/kg for an infant 3 to 10 kg

1000 kcal + 50 kcal/kg for every kg over 10 kg for a child 10 to 20 kg

1500 kcal + 20 kcal/kg for every kg over 20 kg for a child over 20 kg

Approximately 40 mL/100 kcal per 24 hours replaces insensible losses and 60 mL/100 kcal replaces urinary losses. Serendipitously, 100 mL/100 kcal or 1 mL/kcal per 24 hours is needed to replace fluid losses.[2] Adjustments are made for pathologic situations (fever, stress, etc). This method of calculating fluid requirements is in very close agreement with several other methods based on formulas, body surface area, basal calories plus activity calories, and age. With the development of parenteral nutrition and of oral rehydration therapy, this method of calculating basal fluid needs remains valid and is used as the basis for fluid calculations.

Enteral and parenteral fluid requirements are essentially the same. In the absence of diarrhea, stool losses are minimal, implying that almost all of the ingested fluid is absorbed. However, if diarrhea is present, fluid loss can increase dramatically. Diarrhea should be taken into account and should be replaced milliliter for milliliter. Acute weight loss almost always reflects fluid loss; any acute weight deficit should be added to fluid requirements. When there are additional fluid losses (for instance from an ileostomy or biliary drain), this fluid should also be replaced on a daily basis. Fever increases insensible water loss via respiration and via the skin. For each degree of temperature above 38°C, insensible water loss is increased by 5 mL/kg per 24 hours.[3]

Electrolyte requirements. In an otherwise healthy child, essentially all electrolyte loss occurs via the urine. Therefore, recommendations for electrolyte requirements come from measurements of sodium, potassium, and chloride urinary losses in healthy children. As with fluids, unusual losses of electrolytes (diarrhea, stoma output, burns, exercise, diuretic therapy, renal abnormalities, etc) need to be considered. Electrolyte requirements may be summarized: sodium, 3 mEq/kg per day; potassium, 2 mEq/kg per day; chloride, 5 mEq/kg per day.[2]

Calcium. Because children synthesize new bone, they should be in continual positive calcium balance. The American Academy of Pediatrics, Committee on Nutrition recently updated their policy on calcium.[4] The Committee followed the recommendations for calcium intake of the National Academy of Sciences: 0 to 6 months, 210 mg/d; 6 months to 1 year, 270 mg/d; 1 to 3 years, 500 mg/d; 4 to 8 years, 800 mg/d; and 9 to 18 years, 1300 mg/d.[5] Administration of parenteral calcium is often limited by its solubility.

Fluid and electrolyte therapy in the neonate is different than in the older pediatric patient. Shifts in fluid and electrolytes from one compartment to another occur normally as the baby adjusts to extrauterine life. The aim of therapy is not to maintain balance, but to allow these shifts to occur while not letting them become exaggerated. The full-term newborn can lose up to 10% body weight during the first week of life, and the preterm infant can lose up to 20%. It can be difficult to decide when this weight loss is appropriate and when it becomes dangerous. The usual measures of kidney function such as creatinine and BUN are not helpful in the immediate postpartum period. They largely reflect clearance by the placenta and the mother.[6]

Evidence

Evidence concerning fluid and electrolyte needs in infants comes from relatively few well-performed studies. Alteration of total body water has been shown to be affected by the nutrition status of the child. In normal infants on PN, a decline in both total body water and extracellular fluid volume has been noted despite adequate weight gain.[15] This suggests that weight gain is due to actual tissue accretion and not just an increase in body fluid. In support of adequate electrolyte delivery to infants, strong evidence suggests that patients evidence failure to thrive if they develop sodium depletion. Sacher et al[16] have shown that the depletion of total body sodium in infants with obligate electrolyte losses from a small bowel stoma results in a plateau in

weight gain. Subsequent repletion of electrolytes results in resumption of growth.

Practice Guidelines
Fluid and Electrolytes

1. Fluid needs vary with the age and weight of the child and should be adjusted accordingly. (B)
2. Water and electrolyte requirements should be adjusted in pediatric patients undergoing surgical procedures or who have on-going losses from stomas or other sites. (B)

REFERENCES

1. Gamble JL. Chemical Anatomy. Physiology and Pathology of Extracellular Fluid. Cambridge, Harvard University Press, 1964
2. Fiorotto ML, Klish WJ: Total body electrical conductivity measurements in the neonate. Clin Perinatol 18:611–627, 1991
3. Ellis KJ, Shypailo RJ, Wong WW: Measurement of body water by multi-frequency bi0electrical impedance spectroscopy in a multiethnic pediatric population. Am J Clin Nutr 70:847–853, 1999
4. Forbes GB: Growth of lean body mass in man. Growth 36:325–338, 1972
5. Boineau FG, Lewy JE: Estimation of parenteral fluid requirements. Pediatr Clin N Am 37:257–264, 1990
6. Hill LL: Body composition, normal electrolyte concentrations, and the maintenance of normal volume, tonicity, and acid-base metabolism. Pediatr Clin N Am 37:241–256, 1990
7. Stokes JB: Disorders of the epithelial sodium channel: Insights into the regulation of extracellular volume and blood pressure. Kidney Int 56:2318–2333, 1999
8. Bello-Reuss E, Colindres RE, Pastoriza-Munoz E, et al: Effects of acute unilateral renal denervation in the rat. J Clin Invest 56:208–217, 1975
9. Holliday MA, Segar WE: The maintenance need for water in parenteral fluid therapy. Pediatrics 19:823–832, 1957
10. Chesney RW: Maintenance needs for water in parenteral fluid therapy. Pediatrics 102:399–400, 1998
11. Mirkin G: Insensible weight loss in infants with fever. Pediatrics 30:279, 1962
12. Calcium requirements of infants, children and adolescents. Policy statement. Pediatrics 104:1152–1157, 1999
13. Institute of Medicine, Food and Nutrition Board: Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. National Academy Press, Washington DC, 1997
14. Lorenz JM: Assessing fluid and electrolyte status in the newborn. National Academy of Clinical Biochemistry. Clin Chem 43:205–210, 1997
15. Coran AG, Drongowski RA, Wesley JR: Changes in total body water and extracellular fluid volume in infants receiving total parenteral nutrition. J Pediatr Surg 19:771, 1984
16. Sacher P, Hirsig J, Gresser J, et al: The importance of oral sodium replacement in ileostomy patients. Prog Pediatr Surg 24:226, 1989

PROTEIN REQUIREMENTS

Background

The protein requirements of neonates and children vary according to age (Table I). Optimal protein nutrition in this population is dependent on both the quantity of protein as well as its quality (amino acid composition). Adequate energy substrate must be provided along with protein to assure its proper utilization. The amount of protein necessary for neonates and children is higher than in adults when expressed in proportion to body weight. Neonates also potentially differ qualitatively from adults because of their limited capacity to synthesize certain amino acids. Although protein requirements are more difficult to define in the child than in the adult, data exist for guidelines to be articulated for premature neonates, full-term neonates, and children. The ideal dietary amino acid composition for these groups, however, remains controversial.

TABLE I
Estimates of protein requirements for healthy pediatric patients

Age of child	Protein requirements (g/kg/day)
Low birth weight	3 to 4
Full-term	2 to 3
1 to 10 years	1.0 to 1.2
Adolescence	
Boys	0.9
Girls	0.8
Critically ill child/adolescent	1.5

The protein needs of children may be assessed using multiple techniques. Methods include the analysis of growth and body composition, nitrogen balance, stable isotopic tracer techniques, and biochemical indices such as plasma amino acid concentrations. In full-term infants up to 6 months of age, protein requirements may also be estimated on the basis of the protein content of human milk consumed by normal children. Implicit in all of these methods is that energy requirements are met, as inadequate calorie administration will prevent protein anabolism.

Evidence

Immature humans have higher proportional protein requirements. Low-birth-weight neonates need approximately 2 to 4 g/kg per day of protein to maintain a growth rate similar to that in utero.[1] Premature neonates show adequate growth rates and nitrogen retention at protein allotments of approximately 3.0 g/kg per day.[2] The administration of protein in a range higher than 4 g/kg per day may result in abnormal amino acid profiles.[3] When protein 6 g/kg per day is given to low-birth-weight neonates, untoward effects such as azotemia, pyrexia, a higher rate of strabismus, and lower IQ have been reported.[4,5] Reviews suggest that the quantities of protein (or amino acids) needed for low birth weight or premature neonates approximate 3 to 4 g/kg per day.[6,7] The requirements of extremely low-birth-weight neonates are less well understood, but these patients have high rates of proteolysis and attaining adequate growth remains difficult.[8]

Well-established guidelines exist for the provision of protein to full-term neonates.[9,10] These estimates range from 2 to 3 g/kg per day. Although this range appears adequate for most neonates, those who are critically ill remain in profound negative protein balance despite provision of apparently adequate protein.[11] In well children from age 1 to 10 years, the recommended dietary allowance for protein remains relatively static, decreasing slowly from 1.2 to 1.0 g/kg per day.[9] During adolescence, boys have a slightly higher recommended dietary allowance than girls (0.9 and 0.8 g/kg per day, respectively).[9,10] Common clinical practice is to give hospitalized children, who are presumed to be under metabolic stress, 1.5 g/kg per day of protein.[7] Those children

who are manifesting catch-up growth may also require increased quantities of protein.

The optimal amino acid composition (protein quality) of pediatric diets has not been established. For full-term neonates to infants 12 months of age, breast milk affords a guide to ideal amino acid allotment. Histidine has been shown to be a conditionally essential amino acid in neonates up to age 6 months, and growth is compromised in its absence.[12] Cysteine has been suggested as possibly conditionally essential in low-birth-weight neonates because of the low activity of the enzyme cystathionase (which converts methionine to cysteine).[13] Both cysteine and its metabolite taurine are found in high concentrations in human milk, but are absent in commercial parenteral amino acid formulations. Although newer stable isotopic techniques are aiding to further define neonatal amino acid synthesis, histidine remains the only amino acid that, at present, must be considered conditionally essential in the newborn.

Practice Guidelines
Protein Requirements

1. Protein requirements should be adjusted according to the age of the child. (B)
2. Histidine is a conditionally essential amino acid for neonates and infants up to 6 months of age and should be specifically supplemented. (B)

REFERENCES

1. Zlotkin SH, Bryan MH, Anderson GH: Intravenous nitrogen and energy intakes required to duplicate in utero nitrogen accretion in prematurely born human neonates. J Pediatr 99:115–120, 1981
2. Kashyap S, Schulze KF, Forsyth M, et al: Growth, nutrient retention, and metabolic response in low birthweight infants fed varying intakes of protein and energy. J Pediatr 113:713–721, 1988
3. Benevenga NJ, Steele RD: Adverse effects of excessive consumption of amino acids. Annu Rev Nutr 4:157–161, 1984
4. Goldman HI, Fredenthal R, Holland B, et al: Clinical effects of two different levels of protein intake on low birth weight infants. J Pediatr 74:881–889, 1969
5. Goldman HI, Liebman OB, Fredenthal R, et al: Effects of early dietary protein intake on low-birth-weight infants: Evaluation at 3 years of age. J Pediatr 78:126–129, 1971
6. Heird WC, Kashyap S, Gomez MR: Protein intake and energy requirements of the infant. Semin Perinatol 15:438–448, 1991
7. Shew SB, Jaksic T: The metabolic needs of critically ill children and neonates. Semin Pediatr Surg 8:131–139, 1999
8. Kalhan SC, Iben S: Protein metabolism in the extremely low-birth weight infant. Clin Perinatol 27:23–56, 2000
9. Food and Nutrition Board, National Research Council: Recommended dietary allowances, 10th ed. National Academy Press, Washington, DC, 1989
10. Committee on Nutrition, American Academy of Pediatrics: Pediatric nutrition handbook, 4th ed. American Academy of Pediatrics, Elk Grove Village, IL, 1996
11. Keshan TH, Miller RG, Jahoor F, et al: Stable isotopic quantitation of protein metabolism and energy expenditure in neonates on and post extracorporeal life support. J Pediatr Surg 32:958–963, 1997
12. Snyderman SE: The protein and amino acid requirements of the premature infant. IN Visser HKA, Toreistra JA (eds). Nutrica Symposium: Metabolic Processes in the Fetus and Newborn Infant. Stenfert Kroese, Leiden, Netherlands, 1971, pp 128–143
13. Sturman JA, Gaull GE, Raiha NCR: Absence of cystathionase in human fetal liver: Is cysteine essential? Science 169:74–76, 1970

CARBOHYDRATES

Background

Carbohydrates are a major component of both EN and PN. Carbohydrates can be provided in one of three different ways: Monosaccharides (glucose and fructose), disaccharides (lactose, sucrose, and maltose); and complex carbohydrates (starches). Because the body is capable of forming sugars from both lipids as well as amino acids, there is no essential amount of carbohydrate needed. However, carbohydrates are required to prevent breakdown of somatic protein sources.[1]

Evidence

Much of the evidence for the use of carbohydrates is empiric. Standards have been established by the American Academy of Pediatrics and have a generally sound basis. A recent review has further defined the upper and lower boundaries of appropriate carbohydrate intake in relation to age.[2] The primary enteral carbohydrate delivered to neonates and young infants is lactose.[3] Preterm infants may be unable to digest certain carbohydrates, particularly lactose, because of inadequate intestinal lactase activity. Thus, in small preterm infants, formulas that have a 50/50 mixture of lactose and glucose polymers are indicated.[3]

Although somewhat empiric, stable infants should receive approximately 40% to 45% of their total caloric intake as carbohydrate. Parenteral nutrition for the neonate should begin administering approximately 6 to 8 mg/kg per minute of dextrose to maintain adequate serum glucose levels. Lesser amounts of glucose in a young neonate will lead to hypoglycemia because of inadequate hepatic production of glucose. Older neonates tolerate greater loads of glucose, provided it is administered through a central venous catheter (10 to 14 mg/kg per minute). Glucose intolerance in the premature infant is not uncommon and is not only manifested by hyperglycemia, but also quite commonly by hypertriglyceridemia.

Special Considerations

Hyperglycemia is a major adverse effect of carbohydrate administration in the immediate postoperative period. This problem is due to a decrease in insulin concentration and possibly due to an increase in gluconeogenesis.[4,5] Hyperglycemic states resolve much more quickly in neonates compared with adult postoperative patients. Glucose levels were found to be two times preoperative values after major surgery in neonates and returned to baseline levels after 12 hours.[6] Postsurgical hyperglycemia appears to be due to elevated levels of catecholamines.[7] Postoperative hyperglycemia also appears to be associated with increased production of both lactate and pyruvate.

Practice Guidelines
Carbohydrates

1. Carbohydrates should comprise 40% to 50% of the caloric intake in infants and children. (C)

2. Small amounts of carbohydrates should be used in infants and children who are not otherwise receiving nutrition support to suppress protein catabolism. (B)
3. In infants who are lactose tolerant, lactose should be the predominate enteral carbohydrate administered in the first 3 years of life. (B)
4. Preterm infants should receive a formula that has a 50/50 mixture of lactose and glucose polymers. (B)
5. For the neonate, carbohydrate delivery in PN should begin at approximately 6 to 8 mg/kg per minute of dextrose and be advanced, as tolerated to a goal of 10 to 14 mg/kg per minute. (B)
6. Carbohydrate administration should be closely monitored and adjusted in the postoperative period in neonates and children to avoid hyperglycemia. (B)

REFERENCES

1. Kien L: Carbohydrates. IN Tsang RC, Lucas A, Vauy R (eds). Nutritional Needs of the Preterm Infant, Scientific Basis and Practical Guidelines. Williams & Wilkins, Baltimore, 1993, pp 47
2. Kalhan SC, Kilic I: Carbohydrate as nutrient in the infant and child: Range of acceptable intake. Eur J Clin Nutr 53(Suppl 1):S94, 1999
3. American Academy of Pediatrics: CoN: Practical significance of lactose intolerance in children. Pediatrics 86(Suppl):643, 1990
4. Wilmore D: Glucose metabolism following severe injury. J Trauma 21:705, 1981
5. Watters J, Bessey P, Dinarello C: Both inflammatory and endocrine mediators stimulate host response to sepsis. Arch Surg 121:179, 1986
6. Elphick M, Wilkinson A: The effects of starvation and surgical injury on the plasma levels of glucose, free fatty acids, and neutral lipids in newborn babies suffering from various congenital anomalies. Pediatr Res 15:313, 1981
7. Anand K, Sippell W, Schofield N: Does halothane anaesthesia decrease the metabolic and endocrine stress response of newborn infants undergoing operation? Br Med J 296:668, 1988

LIPIDS

Background

Considerable controversy exists regarding the requirements for fat intake in children. As the debate about lipid recommendations has raged over the past two decades, the prevalence of obesity in children in the United States has increased alarmingly. Almost one quarter of US children are now overweight or obese, an increase of over 20% in the past decade.[1,2] There is concern that this change will translate into increased adult obesity and associated comorbidities such as hyperlipidemia, hypertension, and type II diabetes. As research data began pointing to a direct correlation between dietary fat and risk factors for cardiovascular disease, advice to the public at large, including children, was to reduce total fat, saturated fat, and cholesterol intake.

However, children, especially in the first several years of life, have nutrient requirements that differ markedly from those of adults. Concerns have been voiced that lowering fat intake in the growing child might result in decreased supply of omega-6 and omega-3 essential fatty acids, have adverse effects on normal growth and development, lead to adverse lipoprotein profiles, and increase intake of potentially harmful trans-fatty acids as saturated fats are replaced by polyunsaturated fats.[2] It appears that the amount of total fat ingested/administered may not be as critical a risk factor as the type of fat. Furthermore, evidence is building that specific dietary fatty acids may not only decrease the risk or severity of a number of chronic diseases, but may also play a role in therapy of specific diseases.[3] This section will principally focus on the evidence and recommendations for lipid requirements in full-term healthy infants and children.

Evidence

In the United States, multiple organizations such as the US Department of Agriculture, the Department of Health and Human Services Dietary Guidelines for Americans, the American and Heart Association, and the National Heart, Lung, and Blood Institute have recommended a "moderate-fat diet" consisting of <30% energy from total fat and <10% from saturated fat for everyone over the age of 2 years, with a gradual transition from an unrestricted to a moderate–fat diet occurring between 2 and 5–6 years.[4–6] However, the results of clinical studies examining the energy and nutrient adequacy of moderate-fat restricted diets for children have been inconsistent.[4]

Nutrient needs in general, and lipid needs in particular, are high in the first year of life, and dietary recommendations are well delineated. Fat intake should be unrestricted in the infant diet. Lipid needs in the second year of life, as most infants transition from predominantly breast milk/formula based diets to adult-style diets, have not been clearly defined. Most information suggests that fats in this age group not be restricted.[7] A recent longitudinal study of growth and infant nutrition conducted in the US found that the intake of some key nutrients during the period of dietary transition between 12 and 18 months of life was insufficient in infants on a low-fat diet.[8] In contrast, recent data presented from the Special Turku coronary Risk factor Intervention Project (STRIP), an ongoing longitudinal cohort study of more than 1000 children in Finland, reported that a low saturated fat and cholesterol diet begun before the age of 1 year resulted in lower LDL cholesterol and unchanged HDL cholesterol, with no adverse effects on growth, development (to age 5–6 years), or overall nutrient intake.[9] The differences between these two studies and others is probably related to study design and/or cultural issues in that the Finnish children received frequent follow-up and dietary assessment, whereas populations in the US are frequently "free living."[2]

Beyond age 2 years, recommendations from many organizations concur that there should be a slow transition from unrestricted dietary fat to a goal of <30% total fat and <10% saturated fat as a percentage of total energy intake. However, the details of this transition continue to be a point of debate. The American Academy of Pediatrics has agreed with USDA/HHS guidelines, recommending that the transition between unrestricted dietary fat and a moderate-fat diet occur by the age of 5 years.[7] A recent cross-sectional study of

2802 US children 4 to 8 years old reported that spontaneous consumption of diets with approximately 30% energy from fat did not significantly increase the risk for nutritional inadequacy, and high-fat diets did not consistently protect against inadequacy.[4] Other investigators, however, have echoed the recommendations made in the Canadian Dietary Guidelines, suggesting that the transition from high- to moderate-fat diets occur over the longer time frame of linear growth (adolescence).[10,11] The rationale for prolonging the transition from a high- to a moderate-fat diet has been to minimize the potential for adverse effects on growth, development, lipoprotein profiles, and immunologic function that might occur with a more rapid transition.[2] The most definitive statement regarding this approach is by Rask-Nissila et al.[13] This randomized, controlled study showed that 5-year-old children raised since infancy on a low-fat, low-cholesterol diet had equivalent neurologic development while having lower serum cholesterol levels compared with those receiving control diets.

To date, the data seem to indicate that emphasizing fat-modified diets by encouraging consumption of low-fat dairy products, fruits, vegetables, and grains does not compromise children's nutrition status, growth, and development.[12] It may be most important to emphasize avoidance of excess total caloric intake and promotion of increased physical activity, rather than making changes in very specific recommendations regarding fat intake in children.[2]

Similar to adults receiving SNS, it is recommended that 1% to 2% of energy should be derived from linoleic acid (ω6) and about 0.5% of energy from α-linolenic acid (ω3) to prevent essential fatty acid deficiency.[14]

Special Considerations

Characteristic findings in infants suffering from trauma or undergoing surgery are increases in circulating fatty acids, ketone bodies, and glycerol.[15] These changes are indicative of lipolysis and ketogenesis. These products appear to be a major source of energy after surgery. In fact, it is estimated that some 75% to 90% of postoperative energy requirements come from fat metabolism, with the remainder coming from protein stores. It appears that these changes are driven by a release of catecholamines starting intraoperatively.[16] A reversal of these changes has been demonstrated with the administration of halothane anesthesia, because halothane can suppress the catecholamine response.[17]

Practice Guidelines
Lipids

1. Full term infants up to 1 year of age should be allowed an unrestricted fat intake. (A.)
2. Children between 1 and 2 years of age should have very limited or no restrictions on fat intake (B)
3. Between age 2 and 5 to 6 years, children should transition from a high-fat diet to a fat-modified (moderate fat) diet (less than 30% of total energy from fats and less than 10% from saturated fats). (B)

REFERENCES

1. Ogden C, Troiano RP, Briefel R, et al: Prevalence of overweight among preschool children in the United States, 1971 through 1994. Pediatrics 99:el–el3, 1997
2. Deckelbaum RJ, Williams CL: Fat intake in children: Is there need for revised recommendations? J Pediatr 136(1):7–9, 2000
3. Deckelbaum RJ, Calder PC: Lipids in health and disease: Quantity, quality, and more. Curr Opin Nutr Metabol 3(2):93–94, 2000
4. Ballew C, Kuester S, Serdula M, et al: Nutrient intakes and dietary patterns of young children by dietary fat intakes. J Pediatr 136(2):181–187, 2000
5. Report of the Dietary Guidelines Advisory Committee for the 2000 Dietary Guidelines for Americans (in progress)
6. US Dept of Health and Human Services and US Dept of Agriculture: Nutrition and Your Health: Dietary Guidelines for Americans, 4th ed. US Dept of Health and Human Services and US Dept of Agriculture, Washington, DC, 402–519, 1995
7. American Academy of Pediatrics Committee on Nutrition Statement or: "Cholesterol in Childhood." Pediatrics101:145–147, 1998
8. Picciano MF, Smiciklas-Wright H, Birch LL, et al: Nutritional guidance is needed during dietary transition in early childhood. Pediatrics 106(1):109–114, 2000
9. Lagstrom H, Seppanen R, Jokinen E, et al: Influence of dietary fat on the nutrient intake and growth of children from 1 to 5 y of age: The Special Turku Coronary Risk Factor Intervention Project. Am J Clin Nutr 69:516–23, 1999
10. Olson RE: The folly of restricting fat in the diet of children. Nutr Today 30:234–245, 1995
11. Joint Working Group of the Canadian Pediatric Society and Health Canada. Nutrition recommendations update—Dietary fat and children. Ministry of Supply and Services. Publications Distribution, Health Canada, Ottawa, Ontario, Canada, 1993
12. Johnson R: Can children follow a fat-modified diet and have adequate nutrient intakes essential for optimal growth and development? J Pediatr 136(2):143–145, 2000
13. Rask-Nissila L, Jokinen E, Terho P, et al: Neurological development in 5-year old children receiving a low-saturated fat, low-cholesterol diet since infancy: A randomized controlled trial. JAMA 284:993, 2000
14. Uauy R, Hoffman DR: Essential fat requirements of preterm infants. AJCN 71:245S–250S, 2000
15. Anand K, Brown M, Causon R, et al: Can the human neonate mount an endocrine and metabolic response to surgery? J Pediatr Surg 20:41, 1985
16. Wolfe R, Herndon D, Peters E: Regulation of lipolysis in severely burned children. Ann Surg 206:214, 1987
17. Anand K, Sippell M, Aynsley-Green A: Randomized trial of fentanyl anesthesia in preterm babies undergoing surgery: Effects on the stress response. Lancet 1:243, 1987

MICRONUTRIENT REQUIREMENTS

Vitamins

Background. As complex organic substances, vitamins are considered essential contributors to human growth and health.[1] The essentiality of vitamins dictates a sustained exogenous intake (with perhaps the exception of vitamin D) in order to avoid deficiency. Classified by solubility, the lipid-soluble vitamins A, D, E, and K have the potential for storage and therefore the potential for toxicity. The water-soluble vitamins ascorbic acid and the B-complex vitamins are considered relatively nontoxic and are excreted when administered in excess.

Evidence. Both lipid- and water-soluble vitamins should be provided in PN solutions. The subcommittee

on Pediatric Parenteral Nutrient Requirements of the Committee on Clinical Practice Issues of The American Society for Clinical Nutrition published guidelines in 1988 outlining recommendations for vitamins in PN solutions for term infants and children (Table I).[2] Owing to limited product selection, the choice of multivitamin preparations differs for children less than and greater than 11 years of age. For children greater than 11 years, vitamin K should be provided in conjunction with a multivitamin package at a dose of 200 μg/d.[2] In addition to routine vitamin K supplementation, specific products may require supplemental dosing with other vitamins.

Carnitine, synthesized from methionine and protein bound lysine, is the requisite transporter of long chain fatty acids across the inner mitochondrial membrane for β-oxidation. Carnitine can be obtained through the diet, exogenous supplementation, and endogenous biosynthesis. Now a standard addition to many enteral formulas, carnitine may become conditionally essential in the neonate on long term PN secondary to limited biosynthetic capability and immature conservation mechanisms.[3] Carnitine supplementation should be provided once a deficiency has been confirmed.

Special considerations. Vitamin supplementation recommendations are provided below for stable pediatric patients and do not account for conditions of catabolic stress, ventilatory support, or organ dysfunction. The 1988 subcommittee recommendations also include suggested intakes for preterm infants. To avoid potential toxicity related to impaired metabolism, multivitamin preparations administered to the preterm infant should be formulated without propylene glycol or polysorbate, which may be found in adult formulations.[2]

Trace Elements

Background. Trace elements generally function as prosthetic groups of enzymes. Zinc, copper, chromium and manganese are all in the first transition series of metals in the periodic table, and therefore, have many physical and chemical properties in common. Selenium, chemically classified as a nonmetal, is an equally important nutrient. Cobalt, chromium, copper, iodine, manganese, molybdenum, selenium, and zinc are all considered to be essential micronutrients for support of normal human metabolic processes (Table II).[4]

TABLE I
Daily vitamin requirement—infants[2,3]

Vitamin	Enteral[a]	Parenteral[a]
Thiamin	0.3–0.4 mg	1.2 mg
Riboflavin	0.4–0.5 mg	1.4 mg
Niacin	5–6 mg (niacin equivalent)	17 mg
Folic acid	25–35 μg	140 μg
Pantothenic acid	2–3 mg*	5 mg
Vitamin B-6	0.3–0.6 mg	1 mg
Vitamin B-12	0.3–0.5 μg	1 μg
Biotin	10–15 μg*	20 μg
Ascorbic acid	30–35 mg	80 mg
Vitamin A	375 μg (retinol equivalent)	700 μg (retinol equivalent)
Vitamin D	7.5–10 μg (as cholecalciferol)	10 μg
Vitamin E	3–4 mg	7 mg
Vitamin K	5–10 μg	200 μg
Carnitine	No RDA	2–10 mg/kgc

TABLE II
Daily trace element requirement—infants[b]

Trace element	Enteral[a]	Parenteral[b]
Chromium	2.5 μg/kg*	0.2 μg/kg
Copper	No RDA	20 μg/kg
Iodide	40–50 μg	1 μg/kg
Iron	6–10 mg	Maintenance doses not well

Evidence. Routine addition of zinc, copper, selenium, chromium, and manganese to PN solutions is recommended to avoid deficiency.[5] Although not a conventional addition, molybdenum supplementation may be appropriate in long term TPN therapy.[6] The 1988 subcommittee recommendations identify trace element requirements in the term infant and child for zinc, copper, selenium, chromium, manganese and molybdenum.[2] Intakes for preterm infants are also suggested. The type of nutrition support (breast milk, enteral formula or PN) can influence the trace element status of the patient and should be considered when determining supplementation or analyzing levels.[7,8]

Special considerations. The provision of balanced nutrients will prevent both deficiency and toxicity. Trace element contamination must be considered when determining element supplementation. Blood concentrations of copper, chromium and manganese may become elevated because of contamination of TPN solutions by these metals.[2,9–12] In addition, specific disease states will necessitate adjustments in the elements provided. Copper and manganese should be administered cautiously, if at all, in patients with impaired biliary excretion or cholestatic liver disease.[7,13–15] Because of renal excretion of these elements, dosage reduction for selenium, molybdenum, and chromium should be evaluated in patients with renal dysfunction.[2,5] Additional zinc supplementation is necessary in conditions of increased losses, such as persistent diarrhea or excessive ileostomy drainage.[2,5]

Recently, Williams et al[13] reported on new recommendations for dietary fiber by the American Academy of Pediatrics Committee on Nutrition. For children older than 2 years of age, they recommend a minimum of 5 g/d of dietary fiber and children over 5 years of age should consume 10 g/d of dietary fiber.[16]

The widespread occurrence of iron deficiency anemia before the 1970s resulted in a 1976 statement by the American Academy of Pediatrics (AAP) Committee on Nutrition entitled "Iron Supplementation for Infants." Updated in 1989, and again in 1999, the AAP statement recommends using iron-fortified formula (4 to 12 mg/L of iron) from birth to 12 months in the absence of exclusive breast feeding.[17] Guidelines for parenteral supplementation using iron dextran are less clear and differ among the child and the term and preterm infant in conjunction with the total estimated duration of PN therapy. Additionally, iron replacement for documented deficiency and iron supplementation to maintain iron balance or meet fetal accretion rates are

dosed differently. Compatibility problems due to precipitation of iron phosphate and trivalent-induced instability of lipid emulsions must also be considered before iron supplementation using PN solutions.[18]

Practice Guidelines *Micronutrient Requirements*

1. Vitamins and trace elements should be components of all PN solutions and enteral formulas. (A)
2. Vitamin and trace element levels should be monitored periodically during long-term PN administration. (C)

REFERENCES

1. Linder MC: Nutrition and metabolism of vitamins. IN Nutritional Biochemistry and Metabolism with Clinical Applications, Linder MC (ed). Elsevier Science, New York, 1985, pp 69–131
2. Greene HL, Hambidge M, Schanler R, et al: Guidelines for the use of vitamins, trace elements, calcium, magnesium, and phosphorus in infants and children receiving total parenteral nutrition: report of the Subcommittee on Pediatric Parenteral Nutrient Requirements from the Committee on Clinical Practice Issues of The American Society for Clinical Nutrition. Am J Clin Nutr 48:1324–1342, 1988
3. Borum PR: Carnitine in neonatal nutrition. J Child Neurol 10(Suppl 2):2S25–2S31, 1995
4. Szwanek M, Khalidi N, Wesley JR: Trace elements and parenteral nutrition. Nutr Suppl Ser 7:8–14, 1987
5. Leung FY: Trace elements in parenteral micronutrition. Clin Biochem 28(6):561–566, 1995
6. Friel JK, MacDonald AC, Mercer CN, et al: Molybdenum requirements in low-birth-weight infants receiving parenteral and enteral nutrition. JPEN 23(3):155–159, 1999
7. Krachler M, Rossipal E, Micetic-Turk D: Concentrations of trace elements in sera of newborns, young infants, and adults. Biol Trace Element Res 68(2):121–135, 1999
8. Aquilio E, Spagnoli R, Seri S, et al: Trace element content in human milk during lactation of preterm newborns. Biol Trace Element Res 51(1):63–70, 1996
9. Frankel DA: Supplementation of trace elements in parenteral nutrition: Rationale and recommendations. Nutr Res 13:583–596, 1993
10. Moukarzel AA, Song MK, Buchman AL, et al: Excessive chromium intake in children receiving total parenteral nutrition. Lancet 339:385–388, 1992
11. Bougle D, Bureau F, Deschrevel G, et al: Chromium and parenteral nutrition in children. J Pediatr Gastro Nutr 17:72–74, 1993
12. Kurkus J, Alcock NW, Shiles ME: Manganese content of large volume parenteral solutions and of nutrient additives. JPEN 8:254–257, 1984
13. Reynolds AP, Kiely E, Meadows N: Manganese in long term pediatric parenteral nutrition. Arch Dis Child 71:527, 1994
14. Fell JME, Reynolds AP, Meadows N, et al: Manganese toxicity in children receiving long-term parenteral nutrition. Lancet 347–1218, 1996
15. Kafritsa Y, Fell J, Long S, et al: Long term outcome of brain manganese deposition in patients on home parenteral nutrition. Arch Dis Child 79(3):263–265, 1998
16. Williams CL, Bollella M, Wynder EL: A new recommendation for dietary fiber in childhood. Pediatrics 96:985, 1995
17. Anonymous: Iron fortification of infant formulas. American Academy of Pediatrics Committee on Nutrition. Pediatrics 104: 119–123, 1999
18. Allwood MC, Martin H, Greenwood M, et al: Precipitation of trace elements in parenteral nutrition mixtures. Clin Nutr 17:223, 1998

Section VIII: Access for Administration of Nutrition Support

ENTERAL ACCESS

Background

Enteral nutrition is indicated for patients with a functional gastrointestinal tract whose oral nutrient intake is insufficient to meet estimated needs. Selection of the proper enteral access device is based on the patients' gastrointestinal anatomy and function, anticipated duration of enteral nutrition, and the potential for aspiration. The nasoenteric tube is the most commonly used method of enteral access because it can be inserted into the stomach, duodenum, or the jejunum. These tubes are indicated for short-term (less than 4 weeks) use because they have low complication rates, are relatively inexpensive, and easy to place. They may also be used for interim access before placement of a long-term device. Tube enterostomies are indicated when long-term (greater than 30 days) feeding is anticipated or when obstruction makes nasal intubation impossible.[1]

Evidence

Access to the gastrointestinal tract can be attained at the bedside, endoscopically, under fluoroscopic or ultrasound guidance, or operatively. Bedside placement of an enteric (postpyloric) tube involves advancing the tube into the stomach and allowing it to migrate independently into the small bowel. Recent studies report success rates approaching 90% if pH monitoring is used.[2,3] Positioning patients in the right lateral decubitus position has not been demonstrated to increase spontaneous tube migration into the small bowel.[4] Prokinetic agents given before, but not after, tube insertion may facilitate tube passage into the small bowel.[5] Use of weighted tubes, pH sensors, magnets, and bioelectrical detection devices to facilitate tube placement can be of help to confirm tube location.[6–12] Fluoroscopic, sonographic, and endoscopic guidance are often used to achieve transpyloric tube placement when blind methods fail. These techniques have an 85 to 95% success rate for initial tube placement.[13–18] However, these tubes frequently dislodge or migrate back into the stomach, necessitating repeat tube insertion and increased costs.[19]

Tube placement can be confirmed by air insufflation, auscultation, aspiration of gastric or small bowel contents, or radiographically. In one study, the location of the feeding tube tip on 100 consecutive radiographs obtained within 4 hours of placement was analyzed. Eighty percent of tubes were in the stomach or duodenum, 19% in the esophagus, and 1% in the pleural space.[20] Because of the possibility of false positives and the potential for tube malposition in the tracheobronchial tree, radiographic confirmation of the position of the tube tip is recommended.[19,21–22]

Nasally placed tubes may predispose to nasopharyngeal ulcers, nasal septum necrosis, sinusitis, otitis, hoarseness, and vocal cord paralysis.[23] Small-bore feeding tubes made from polyurethane or silicone, in sizes from 5F to 12F, are soft, smooth, and more flexible than the stiff, large-bore nasogastric tubes designed for decompression and gastric drainage. These small tubes provide improved patient comfort and decrease the risk of nasal-tissue necrosis.

Patients requiring long-term EN should receive more permanent access. Gastrostomy is the most common method for long-term access because it eliminates nasal irritation, psychosocial stress of having a tube in the nose, and requirement for an infusion pump (intragastric feedings may be administered as a bolus in patients who tolerate it). Gastric tubes, because of their large diameter, can also be used for gastric decompression, pH monitoring, and medication delivery. Insertion can be performed surgically (with laparotomy or laparoscopy) or nonoperatively. Nonoperative placement of gastric feeding tubes (percutaneous endoscopic gastrostomy [PEG]) or with fluoroscopic guidance) is favored because it can be performed without general anesthesia and allows feedings to be administered soon after placement.[24–27] A meta-analysis of over 5000 cases found higher rates of successful tube placement for radiologic gastrostomy than for PEG, a lower complication rate than with PEG or surgery, and lower 30-day procedure-related mortality.[18]

Jejunostomies can be placed at the time of laparotomy in patients in whom access to the small bowel is desired. PEG tubes with a jejunal extension or direct percutaneous endoscopic placement provide additional options for obtaining access to the jejunum when simultaneous gastric decompression is desired.[28] These tubes have a high rate of mechanical dysfunction and dislodgment and are not advocated for long-term use.[29] A skin level or low-profile device placed through a mature gastrostomy offers long-term EN patients a less obtrusive gastric tube. Preplacement marking for optimal gastrostomy and jejunostomy tube site locations is recommended to decrease complications of therapy and to promote patient self-care.[30] Complica-

tions associated with tube enterostomies include perforation, hemorrhage, wound infection, bowel obstruction, bowel necrosis, and stomal leakage. Tube migration may lead to erosion of the exit site and leakage of gastric or intestinal contents onto the surrounding skin.

There is considerable controversy regarding the preferred site for EN delivery. Gastric feedings require intact gag and cough reflexes and adequate gastric emptying. Small bowel access is indicated in clinical conditions in which tracheal aspiration, reflux esophagitis, gastroparesis, gastric outlet obstruction, or previous gastric surgery precludes gastric feedings, or when early postoperative feeding after major abdominal procedures is planned. Prevention of aspiration entails identification of high-risk patients, elevation of the head of the bed, careful monitoring of tube feeding delivery and patient tolerance, and adequate airway management. Studies have not consistently demonstrated a benefit of small bowel feedings over gastric feedings to prevent aspiration.[31–36] However, lack of an accepted definition of clinically significant aspiration makes interpretation of these studies difficult. The physical presence of a nasogastric tube across the lower esophageal sphincter probably impairs sphincter function and promotes reflux of gastric contents.[37] Pharmacologic intervention with antireflux agents has been used to decrease the risk of gastric reflux, but it has not been shown to decrease the frequency of nosocomial pneumonia or affect the mortality rate of critically ill patients receiving EN.[38]

Gastric residuals are frequently used to monitor safety and effectiveness of tube feedings. Gastric motility is affected by disease, mechanical obstruction, and medications (including paralytic agents). There is no agreement regarding the acceptable volume of gastric residual for monitoring tube feedings.[39,40] The level of residual volume of concern in the critically ill patient appears to be 200 mL with a nasogastric tube located in the antrum or fundus or 100 mL for surgical or endoscopic gastrostomy tubes located on the anterior gastric wall.[41] McClave et al[41] compared gastric residuals in critically ill patients, stable gastrostomy-fed patients, and normal healthy volunteers. They found that there was a peak in residual volumes early in the study, with a subsequent reduction in those volumes over time. Lin and Van Critter,[40] using a computer simulated model, found that gastric residual volumes after tube feeding reach a plateau similar to that found in the postprandial stomach. It is probably prudent to check gastric residuals every 4 to 5 hours when initiating feedings until a plateau of less than 50 mL has been achieved.[40,42] One high residual volume should not prompt stopping the feeding but instead to monitor for signs and symptoms of intolerance.[43] Patients with persistently elevated gastric residual volumes may benefit from a tube placed beyond the ligament of Treitz.

All feeding tubes are subject to mechanical complications, especially clogging. Clogging is caused by viscous formulas, inappropriate medication administration, formula residue, and inadequate flushing. Tubes should be flushed with at least 20 to 30 mL warm water every 4 hours during continuous feedings and before and after intermittent feedings and medications.[44] Fluids with an acidic pH such as cranberry juice can precipitate protein and cause tube clogging.[45] When water fails to declog feedings tubes, use of papain, combinations of activated pancreatic enzymes and sodium bicarbonate mixed with water, or declogging devices has been successful.[46]

Special Considerations

A significant discrepancy is often seen between prescribed and delivered calories; that is, the volume of tube feeding received, expressed as a percentage of the goal intake is often less than 100%.[47–49] Reasons for inadequate tube feeding include slow advancement of infusion rates, interruptions of feedings due to tube displacement or gastric residuals, withholding of feedings for operative and diagnostic procedures, medication administration, physician underprescription, and routine nursing procedures.[42,48,50] EN protocols allow standardized management of tube feedings and also help educate practitioners on the importance and monitoring of outcomes. Several studies have demonstrated that tube feeding delivery is improved with EN protocols.[51–53]

Practice Guidelines *Enteral Access*

1. Decisions regarding access for EN should be made considering the effectiveness of gastric emptying, gastrointestinal anatomy, and aspiration risk. (B)
2. Nasoenteric tube placement should initially be attempted using a spontaneous or other bedside placement technique; if this is unsuccessful, fluoroscopic or endoscopic guidance should be used. (A)
3. Radiographic confirmation of the feeding tube tip position should be obtained after placement of a nasogastric or nasoenteric access tube. (B)
4. Gastric residuals should be checked frequently when feedings are initiated and feedings should be held if residual volumes exceed 200 mL on two successive assessments. (A)
5. Feeding tubes should routinely be flushed with 20 to 30 mL of warm water every 4 hours during continuous feedings and before and after intermittent feedings and medication administration. (A)
6. Standardized protocols for enteral nutrition ordering, administration, and monitoring should be utilized. (B)

REFERENCES

1. American Gastroenterological Association Technical Review on Tube Feeding for Enteral Nutrition. Gastroenterology 108:1282–1301, 1995
2. Cohen LD, Alexander DJ, Catto J, et al: Spontaneous transpyloric migration of a ballooned nasojejunal tube: a randomized controlled trial. JPEN 24:240–243, 2000
3. Zaloga GP: Bedside method for placing small bowel feeding tubes in critically ill patients. Chest 100:1643–1646, 1991

4. Marian M, Rappaport W, Cunningham D, et al: The failure of conventional methods to promote spontaneous transpyloric feeding tube passage and the safety of intragastric feeding in the critically ill ventilated patient. Surg Gynecol Obstet 176:475–479, 1993
5. Kittinger JW, Sandler RS, Heizer WD: Efficacy of metoclopramide as an adjunct to duodenal placement of small-bore feeding tubes: a randomized, placebo-controlled, double-blind study. JPEN 11:33–37, 1987
6. Thurlow PM: Bedside enteral feeding tube placement into duodenum and jejunum. JPEN 10:104–105, 1986
7. Gabriel SA, Ackerman RJ, Castresana MR: A new technique for placement of nasoenteral feeding tubes using external magnetic guidance. Crit Care Med 25:641–645, 1997
8. Davis TJ, Sun D, Dalton ML: A modified technique for bedside placement of nasoduodenal feeding tubes. J Am Coll Surgeons 178:407–409, 1994
9. Salasidis R, Fleiszere, Johnston R: Air insufflation technique of enteral tube insertion: A randomized, controlled trail. Crit Care Med 26:1036–1039, 1998
10. Cresci G, Grace M, Park M, et al: Accurate and timely blind bedside placement of post-pyloric feeding tubes using an electromagnetic navigation device. Nutr Clin Pract 14:101, 1999
11. Lord LM, Weiser-Maimone A, Pulhamus M, et al: Comparison of weighted vs. unweighted enteral feeding tubes for efficacy of transpyloric intubation. JPEN 17:271–273, 1993
12. Ahmed W, Levy H, Kudsk K, et al: The rates of spontaneous transpyloric passage of three enteral feeding tubes. Nutr Clin Pract 14:107–110, 1999
13. Minard G: Enteral access. Nutr Clin Pract 9:172–182, 1994
14. Gutierrez ED, Balfe DM: Fluoroscopically guided nasoenteric feeding tube placement: Results of a 1-year study. Radiology 178:759–762, 1991
15. Patrick PG, Marulendra S, Kirby DF, et al: Endoscopic nasogastric-jejunal feeding tube placement in critically ill patients. Gastrointest Endosc 45:72–76, 1997
16. Bosco JJ, Gordon F, Zelig M, et al: A reliable method for the endoscopic placement of a nasoenteric feeding tube. Gastrointest Endosc 40:740–743, 1994
17. Hernandez-Soocorro CR, Marin J, Ruiz-Santana S, et al: Bedside sonographic-guided versus blind nasoenteric feeding tube placement in critically ill patients. Crit Care Med 1996, 24:1690–1694
18. Wollman B, D'Agostino HB, Walus-Wigle JR, et al: Radiologic, endoscopic, and surgical gastrostomy: An institutional evaluation and meta-analysis of the literature. Radiology 197:699–704, 1995
19. Chen MY, Ott DJ, Gelfand DW: Nonfluoroscopic, postpyloric feeding tube placement: Number and cost of plain films for determining position. Nutr Clin Pract 15:40–44, 2000
20. Benya R, Langer S, Mobarhan S: Flexible nasogastric feeding tube tip malposition immediately after placement. JPEN 108–109, 1990 VOLUME
21. Welch SK, Hanlon MD, Waits M, et al: Comparison of four bedside indicators used to predict duodenal feeding tube placement with radiography. JPEN 18:525–530, 1994
22. Bankier AA, Wiesmayr MN, Henk C, et al: Radiographic detection of intrabronchial malpositions of nasogastric tubes and subsequent complications in intensive care unit patients. Intensive Care Med 23:406–410, 1997
23. Sofferman RA, Haisch CE, Kirchner JA, et al: The nasogastric tube syndrome. Laryngoscope 100:962–968, 1990
24. Baskin WN, Johansen JF: An improved approach to the delivery of enteral nutrition in the intensive care unit. Gastrointest Endosc 42:161–165, 1995
25. Larson DE, Burton DD, Schroeder KW, et al: Percutaneous endoscopic gastrostomy: Indications, success, complications and mortality in 314 consecutive patients. Gastroenterology 93:48–52, 1987
26. Grant JP: Comparison of percutaneous endoscopic gastrostomy with Stamm gastostomy. Ann Surg 207:598–603, 1988
27. Apelgren KN, Zambos J: Is percutaneous better than open gastrostomy?: A clinical study in one surgical department. Am Surg 55:596–600, 1989
28. Shike M, Latkany L, Gerdes H, et al: Direct percutaneous endoscopic jejunostomies for enteral feeding. Nutr Clin Pract 12(Suppl):S38–S42, 1997
29. Shapiro T, Minard G, Kudsk KA: Transgastric jejunal feeding tubes in critically ill patients. Nutr Clin Pract 12:164–167, 1997
30. Hanlon MD: Pre-placement marking for optimal gastrostomy and jejunostomy tube site locations to decrease complications and promote self care. Nutr Clin Pract 13:167–171, 1998
31. Lazarus BA, Murphy JB, Culpepper L: Aspiration associated with long-term gastric versus jejunal feeding: A critical analysis of the literature. Arch Phys Med Rehab 71:46–53, 1990
32. Montecalvo MA, Steger KA, Farber HW, et al: Nutritional outcome and pneumonia in critical care patients randomized to gastric versus jejunal tube feedings. Crit Care Med 20:1377–1387, 1992
33. Strong RM, Condon SC, Solinger MR, et al: Equal aspiration rates for postpylorus and intragastric-placed small bore nasoenteric feeding tubes: A randomized, prospective study. JPEN 16:59–63, 1992
34. Fox KA, Mularski KA, Sarfati MR: Aspiration pneumonia following surgically placed feeding tubes. Am J Surg 170:564–567, 1995
35. Methany N, Eisenberg P, Spies M: Aspiration pneumonia in patients fed through nasoenteral tubes. Heart Lung 15:256–261, 1986
36. Mullen H, Roubenoff RA, Roubenoff R: Risk of pulmonary aspiration among patients receiving enteral nutrition support. JPEN 16:160–164, 1992
37. Saxe JM, Ledgermwood MD, Lucas CE, et al: Lower esophageal sphincter dysfunction precludes safe gastric feeding after head injury. J Trauma 37:581–584, 1994
38. Yavagal DR, Karnad DR, Oak JL: Metoclopramide for preventing pneumonia in critically ill patients receiving enteral tube feeding: A randomized controlled trial. Crit Care Med 28:1408–1411, 2000
39. Heyland D, Cook, DJ, Winder B, et al: Enteral nutrition in the critically ill patient: A prospective survey. Crit Care Med 23:1055–1060, 1995
40. Lin HC, VanCritters GW: Stopping enteral feeding for arbitrary gastric residual volumes may not be physiologically sound: results of a computer simulated model. JPEN 21:280–289, 1997
41. McClave SA, Snider HL, Lowen CC, et al: Use of residual volumes as a marker for enteral feeding intolerance: Prospective blinded comparison with physical examination and radiographic findings. JPEN 16:99–105, 1992
42. McClave SA, Sexton LA, Spain DA, et al: Enteral tube feeding in the intensive care unit. Factors impeding adequate delivery. Crit Care Med 27:1252–1256, 1999
43. Murphy LM, Bickford V: Gastric residuals in tube feeding: How much is too much? Nutr Clin Pract 14:304–306, 1999
44. Scanlan M, Frisch S: Nasoduodenal feeding tubes: Prevention of occlusion. J Neurosci Nurs 24:250–259, 1992
45. Methany N, Eisenberg P, McSweeney M: Effect of feeding tube properties and three irrigants on clogging rates. Nurs Res 37:165–169, 1998
46. Frankel EH, Enow NB, Jackson KC, et al: Methods of restoring patency to occluded feeding tubes. Nutr Clin Pract 13:129–131, 1998
47. Petnicki PJ: Cost savings and improved patient care with use of a flush enteral feeding pump. Nutr Clin Pract (Suppl) 1998, 13:S39–41
48. Echevarria CG, Winkler MF: Enteral feeding challenges in critically ill patients. Top Clin Nutr 16:37–42, 2000
49. Woodcock N, Zeigler D, Palmer MD, et al: Enteral versus parenteral nutrition: A pragmatic study. Nutrition 17:1–12, 2001
50. Stechmiller J, Treolar DM, Derrico D, et al: Interruption of enteral feedings in head injured patients. J Neurosci Nurs 26:224–229, 1994
51. Chapman G, Curtas S, Meguid M: Standardized enteral orders attain caloric goals sooner: A prospective study. JPEN 16:149–151, 1992
52. Adams S, Batson S: A study of problems association with the delivery of enteral feedings in critically ill patients in five ICUs in the UK. Intensive Care Med 23:261–266, 1997
53. Spain DA, McClave SA, Sexton LK, et al: Infusion protocol improves delivery of enteral tube feeding in the critical care unit. JPEN 23:288–292, 1999

PARENTERAL ACCESS

Background

Parenteral nutrition administration requires central venous access in order to provide nutrients at greater concentrations than is possible through peripheral veins. PN is appropriate when SNS is indicated and a contraindication to the use of EN is present or EN is not tolerated. Selection of the most appropriate parenteral access device is based on the patient's vascular access history, venous anatomy, coagulation status, the anticipated duration of PN, the care setting (hospital versus other), and the nature of the underlying disease. For hospitalized patients, temporary percutaneous central venous catheters are often most appropriate. For long-term therapy in a nonhospital setting, subcutaneously tunneled percutaneous catheters or implanted subcutaneous infusion ports are most commonly used. When selecting a long-term access device, consideration should be given to the patient's activity level, body-image concerns, physical ability to care for the catheter, cognitive function, and caregiver involvement.

Evidence

Percutaneously inserted catheters advanced into the superior vena cava (SVC) are the route of choice for the delivery of PN. Catheters inserted through the femoral veins are associated with higher risk of venous thrombosis and catheter-related sepsis and are not recommended for PN.[1]

Access to the SVC can be gained through the internal jugular vein, the subclavian vein, or through peripheral veins in the arm. Internal jugular vein catheters are associated with a higher rate of local hematoma formation, arterial injury, and catheter-associated blood stream infections than subclavian vein catheters.[2,3] Subclavian vein catheters are associated with a higher risk of pneumothorax during insertion than internal jugular vein catheters.[2,4] A prospective, randomized trial comparing 102 centrally inserted subclavian catheters versus peripherally inserted central catheters (PICC) for PN demonstrated a significantly higher rate of thrombophlebitis, malposition on insertion, and difficulties during insertion with PICC lines but no difference in overall rate of infection, dislodgement, or line occlusion.[5] These findings are consistent with other reports comparing PICC and non-PICC venous access in which an increased incidence of local complications, leaking catheters, phlebitis, and malposition is noted.[6–8] PICCs are used, however, with increasing frequency in many institutions. It is likely that increased experience with their use will lead to decreased complication rates.

Catheter tip misplacement during insertion of CVCs is not infrequent. The use of fluoroscopy during catheter insertion allows immediate repositioning of the catheter tip into its correct location in the SVC.[9] A chest radiograph should be obtained after the insertion procedure to document catheter placement and rule out a pneumothorax.[10] A postprocedure chest x-ray yields little benefit if the internal jugular vein or an upper extremity vein is used for access by interventional radiology using fluoroscopic guidance.[11]

Catheter-related infections and mechanical complications can occur after placement of a CVC. Catheter-related sepsis occurs in 5 to 8 per 1000 patient days and is associated with morbidity, mortality, and increased medical costs.[12–15] Guidelines for the management of intravascular catheter-related infections have been jointly prepared by the Infectious Diseases Society of America, the American College of Critical Care Medicine and the Society of Healthcare Epidemiology of America,[16] and the Hospital Infection Control Practices Advisory Committee.[17] An evidence-based review on prevention of catheter infection during PN has also been published.[18] The treatment of catheter-related sepsis involves catheter removal and appropriate antibiotic coverage although success in managing catheter infection with antibiotics alone has been reported.[13] Prophylactic catheter exchange over a guide wire has not been shown to decrease the risk of catheter-associated infection.[19]

Several strategies have been investigated to decrease the risk of catheter-associated sepsis. Use of full-barrier precautions during catheter insertion (mask, cap, sterile gloves, long-sleeve gowns, and sheet drapes) reduces the incidence of catheter-related infections compared with the use of only sterile gloves and small drapes alone.[20] Skin preparation with chlorhexidine results in a lower incidence of microbial colonization of catheters than with povidone iodine.[21] Antibiotic prophylaxis during catheter insertion has not been demonstrated to reduce the incidence of catheter-related blood stream infection.[22] Prophylactic use of antibiotic ointment at the catheter exit site encourages the development of resistant flora and should be avoided.[13,14] No differences in catheter-associated sepsis were detected in comparisons of transparent film dressings with gauze dressings.[13]

Reductions in catheter-associated sepsis have been reported when the devices were cared for by specially trained nurses and when catheter manipulation was minimized.[13] The use of catheters for multiple therapeutic and diagnostic purposes, the use of accessory devices (manometers, pressure transducers, flush solutions, stopcocks and "piggy-back" infusion sets), and the infusion of blood products or intravenous medications increases the risk of bacteremia.[13,14] One large single institution review found that PN therapy was the most important risk factor for developing sepsis.[8] Colonization of catheter hubs as well as the skin surrounding the insertion site are the source of most catheter-related infections.[15] Greater catheter hub manipulation increases the risk for contamination. Catheter hubs and sampling ports should be disinfected before they are accessed.[13] Early studies of needleless systems demonstrated an association between the development of infection, site care, and frequency of end-cap changes. Risk factors associated with catheter-related blood stream infections included patients who were allowed to shower and wet the exit site and weekly end-cap changes. The risk of blood stream infection decreases with use of rigorous aseptic technique and when end-caps are replaced every 2 days.[22,23] A pro-

spective study investigating the microbial contamination of needleless connectors and standard entry port caps connected to the hubs of CVCs immediately after insertion found no difference in contamination rates.[24]

Central venous catheters impregnated with chlorhexidine and silver sulfadiazine or with minocycline and rifampin are associated with a lower rate of blood stream infection than untreated catheters.[13,25] Because of the higher cost of these catheters it is probably reasonable to restrict their use to institutions or units with particularly high infection rates.[26,27]

Clinically relevant catheter-related thrombosis is a late complication of long-term use of CVCs. Occlusion may occur because of the formation of a fibrin sleeve or thrombin sheath, or partial or total vascular mural thrombosis.[28] Heparin-bonded catheters have been associated with a significant reduction in thrombosis.[29] Prophylactic use of anticoagulants has been shown to decrease the risk of catheter-associated venous thrombosis in patients with long-term catheters.[30]

The selection of a vascular access device for home PN involves multiple issues including patient preferences, device characteristics, frequency of infusions, and duration of therapy. Subcutaneously tunneled (Hickman or Broviac) catheters or implanted subcutaneous infusion ports are most commonly used for home PN administration. PICCs are increasingly being used because of the ease and economy of bedside placement. No one device has been shown to provide the lowest rate of complications with the greatest therapeutic benefit and ease of maintenance for all patients.[31]

Practice Guidelines *Parenteral Access*

1. Parenteral nutrition should be delivered through a catheter located with its distal tip in the superior vena cava or right atrium. (A)
2. A chest x-ray should be obtained after catheter insertion unless internal jugular or upper extremity IV access is obtained by interventional radiology techniques. (B)
3. Full-barrier precautions should be used during the insertion of central lines. (B)
4. Skin preparation before catheter insertion should be performed using chlorhexidine. (B)
5. Catheter hubs and sampling ports should be disinfected before access for medication administration and blood drawing. (C)
6. Central catheters should not be exchanged routinely over guide wires. (A)
7. The use of antimicrobial-impregnated catheters is recommended in high risk patients and high risk care settings. (B)
8. Low dose anticoagulant therapy should be used in patients requiring long-term catheterization. (B)
9. Specialized nursing teams should care for venous access devices in patients receiving PN. (B)

REFERENCES

1. Trottier SJ, Veremakis C, O'Brien J, et al: Femoral deep vein thrombosis associated with central venous catheterization: results from a prospective, randomized trial. Crit Care Med 23:52–59, 1995
2. Sznajder JI, Zveibil FR, Bitterman H, et al: Central vein catheterization, failure and complication rates by three percutaneous approaches. Arch Intern Med 146:259–261, 1986
3. Mermel L: Central venous catheter-related infections and their prevention: Is there enough evidence to recommend tunneling for short-term use? Crit Care Med 26:1315–1316, 1998
4. Macdonald S, Watt AJ, McNally D, et al: Comparison of technical success and outcome of tunneled catheters inserted via the jugular and subclavian approaches. J Vasc Interv Radiol 11:225–231, 2000
5. Cowl CT, Weinstock JV, Al-Jurf A, et al: Complications and cost associated with parenteral nutrition delivered to hospitalized patients through either subclavian or peripherally-inserted central catheters. Clin Nutr 19:237–243, 2000
6. Duerksen DR, Papineau N, Siemens J, et al: Peripherally inserted central catheters for parenteral nutrition: A comparison with centrally inserted catheters. JPEN 23:85–89, 1999
7. Smith JR, Friedell ML, Cheatham ML, et al: Peripherally inserted central catheters revisited. Am J Surg 176:208–211, 1998
8. Ng PK, Ault MJ, Ellrodt AG, et al: Peripherally inserted central catheters in general medicine. Mayo Clin Proc 72:225–233, 1997
9. Pomp A, Caldwell MD Feitelson M: Seldinger technique for central venous catheter insertions, a prospective study of 200 cases. Clin Nutr 6(Suppl):103, 1987
10. Miller JA, Singireddy S, Maldjian P, et al: A reevaluation of the radiographically detectable complications of percutaneous venous access lines inserted by four subcutaneous approaches. Am Surg 65:125–130, 1999
11. Cardi JG, West JH, Stavropoulos SW: Internal jugular and upper extremity central venous access in interventional radiology: Is a post-procedure chest radiograph necessary? Am J Roentgenol 174:363–366, 2000
12. Forchielli ML, Gura K, Anessi-Pessina E, et al: Success rates and cost-effectiveness of antibiotic combinations for initial treatment of central-venous-line infections during total parenteral nutrition. JPEN 24:119–125, 2000
13. Mermel LA: Prevention of intravascular catheter-related infections. Ann Intern Med 132:391–402, 2000
14. Gosbell IB: Central venous catheter related sepsis: epidemiology, pathogenesis, diagnosis, treatment and prevention. Int Care World 11:54–59, 1994
15. Sitges-Serra A, Girvent M: Catheter-related bloodstream infections. World J Surg 23:589–595, 1999
16. Mermel LA, Farr BM, Sherertz RJ, et al: Guidelines for the management of intravascular catheter-related infections. Clin Infect Dis 32:1249–1272, 2001
17. Pearson ML: Guideline for prevention of intravascular device-related infections. Part 1. Intravascular device-related infections: an overview. The Hospital Infection Control Practices Advisory Committee. Am J Infect Control 24:262–277, 1996
18. Attar A, Messing B: Evidence-based prevention of catheter infection during parenteral nutrition. Curr Opin Clin Nutr Metab Care 4:211–218, 2001
19. Cook D, Randolph A, Kernerman P, et al: Central venous catheter replacement strategies: A systematic review of the literature. Crit Care Med 25:1417–1424, 1997
20. Raad II, Hohn DC, Gilbreath BJ, et al: Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. Infect Control Hosp Epidemiol 15:231–238, 1994
21. Maki DG, Ringer M Alvarado CJ: Prospective randomized trial of povidone iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. Lancet 338:339–343, 1991
22. Do AN, Ray BJ, Banerjee SN, et al: Bloodstream infection associated with needleless device use and the importance of infection-control practices in the home health care setting. J Infect Dis 179:442–448, 1999
23. Hanchett M, Kung LY: Do needleless intravenous systems increase the risk of infection? J Intraven Nurs 22:117–121, 1999
24. Seymour VM, Dhallu TS, Moss HA, et al: A prospective clinical study to investigate the microbial contamination of a needless connector. J Hosp Infect 45:165–168, 2000

25. Maki DG, Stolz SM, Wheeler S, et al: Prevention of central venous catheter-related bloodstream infection by use of an antiseptic-impregnated catheter. A randomized, controlled trial. Ann Intern Med 127:257–266, 1997
26. Darouiche RO, Raad II, Heard SO, et al: A comparison of two antimicrobial-impregnated central venous catheters. Catheter study group. N Engl J Med 340:1–8, 1999
27. Veenstra DL, Saint S, Sullivan SD: Cost-effectiveness of antiseptic-impregnated central venous catheters for the prevention of catheter-related bloodstream infection. JAMA 282:554–560, 1999
28. Arenas-Marquez H, Anaya-Prado R, Barrera-Zepeda LM, et al: Complications of central venous catheters. Curr Opin Clin Nutr Metab Care 4:207–210, 2001
29. Marin MG, Lee JC, Skurnick JH: Prevention of nosocomial blood stream infections: Effectiveness of antimicrobrial-impregnated heparin-bonded central venous catheters. Crit Care Med 28:3332–3338, 2000
30. Bern MM, Lokich JJ, Wallach SR, et al: Very low doses of warfarin can prevent thrombosis in central venous catheters. A randomized prospective trial. Ann Intern Med 112:423–428, 1990
31. Orr ME: Vascular access device selection for parenteral nutrition. Nutr Clin Pract 14:172–177, 1999

MONITORING FOR EFFICACY

Background

Considerable cost and serious complications are associated with specialized nutrition support (SNS). Regular monitoring and meticulous care are necessary to ensure successful outcomes. Monitoring patients maintained on SNS is necessary to determine efficacy of specialized nutrition therapy; detect and prevent complications; evaluate changes in clinical condition; and document clinical outcomes.[1] These guidelines address monitoring by the health care team to determine efficacy or adequacy of the nutrition therapy with attention to specific end points. These endpoints should be defined based on the patient's disease, condition, setting, and wishes.[2,3]

Evidence

Once it is determined that a patient will receive SNS, goals for the nutrition support should be set with specific markers and outcomes to be measured. These goals may include maintenance or repletion of lean body mass, reduction in morbidity and mortality, improvement in quality of life, or optimization of clinical outcomes such as reduction of hospital length of stay and cost.

Many studies of patients receiving SNS have used surrogate markers of nutrition status as clinical outcomes. Energy balance, body composition analyses, body weight measurements, anthropometry, serum protein concentrations, protein balance, functional status, focused physical examination, and growth velocity (in pediatric patients) are all parameters that have been used to assess nutrition status and efficacy of SNS.[2,4–9] Nitrogen balance has often been used to monitor the nutritional efficacy of SNS.[4,7–9] Many of these parameters are influenced by ongoing illness or injury, and thus it may not clearly reflect changes in the individual's nutritional status.[2] Nutritional status, however, is an intermediate marker; the ultimate goal of SNS is to improve clinical outcomes. Clinical outcome monitoring using end points such as quality of life, morbidity and mortality, length of hospital stay, and cost is much more relevant. There have been numerous clinical outcome studies of patients receiving SNS that utilize nutritional efficacy markers in their monitoring or reassessment protocols. These have included large, prospective randomized trials in trauma patients,[10–14] ICU patients,[15,16] and perioperative patients.[17] Nitrogen balance, serum proteins, and energy balance were most often used in these studies to measure nutritional efficacy of the SNS.

Unfortunately, there are no studies available that specifically investigate the effect of monitoring nutritional efficacy of SNS on clinical outcomes (morbidity, mortality, quality of life). That is, there are no studies that demonstrate or refute the hypothesis that, "Clinical monitoring of patients receiving SNS to assess nutritional effects of therapy improves patient outcomes." There are, however, some data suggesting a relationship between nutrition efficacy monitoring and improved cost-effectiveness. These studies include three prospective trials. Two randomized trials investigated enhanced SNS versus standard SNS[18,19] in a heterogeneous group of patients, and one study looked at early EN versus no nutrition intervention in gastrointestinal surgical patients.[20] In all three studies, nutrition efficacy was monitored and the incidence of complications was an outcome that was measured. In all three studies, the intervention groups had significantly fewer complications and lower costs compared with standard therapy. In one study,[18] nitrogen balance was also used as an outcome variable, and positive nitrogen balance was associated with decreased costs as well.

Monitored parameters should be compared to the goals of the nutrition care plan and documented.[21] Focused, serial nutrition status reassessment is important. Specifically, nutrient content of SNS administered should be regularly compared with predicted energy and protein needs. Changes in clinical condition and activity level may require periodic recalculation of energy requirements. If the patient is not responding appropriately, indirect calorimetry may be used to guide changes in energy intake.[22] The patient should be evaluated periodically to determine whether continued SNS therapy is needed. Readjustments of the nutrition prescription may be necessary if oral intake has improved.[23,24]

Practice Guidelines *Monitoring for Efficacy*

1. Nutrition and outcome goals should be stated in the nutrition assessment prior to the initiation of SNS. (C)
2. Nutritional and outcome parameters should be measured serially during SNS therapy. (B)
3. Periodic comparison of nutritional and outcome measures with SNS goals should occur to monitor efficacy of therapy. (C)

REFERENCES

1. A.S.P.E.N Board of Directors: Standards of practice: Nutrition support nurse. Nutr Clin Pract 16:56–62, 2001
2. Klein S, Kinney J, Jeejeebhoy K, et al: Nutrition support in clinical practice: Review of published data and recommendations for future research directions. JPEN 21:133–156, 1997
3. A.S.P.E.N Board of Directors: Standards for nutrition support physicians. Nutr Clin Pract 11:235–240, 1996
4. Church JM, Hill GL: Assessing the efficacy of intravenous nutrition in general surgical patients: Dynamic nutritional assessment with plasma proteins. JPEN 11:135–139, 1987
5. Bernstein LH, Leukhardt-Fairfield CJ, Pleban W, et al: Usefulness of data on albumin and prealbumin concentrations in determining effectiveness of nutritional support. Clin Chem 35(2): 271–274, 1989
6. Sawicky CP, Nippo J, Winkler MF, et al: Adequate energy intake and improved prealbumin concentration as indicators of the response to total parenteral nutrition. J Am Diet Assoc 92(10): 1266–1268, 1992
7. Fletcher JP, Little JM, Guest PK: A comparison of serum transferrin and serum prealbumin as nutritional parameters. JPEN 11(2):144–147, 1987
8. Starker PM, LaSala PA, Forse RA, et al: Response to total parenteral nutrition in the extremely malnourished patient. JPEN 9(3):300–302, 1985
9. Iapichino G, Radrizzani D, Solca M, et al: The main determinants of nitrogen balance during total parenteral nutrition in critically ill injured patients. Intensive Care Med 10(5):251–254, 1984
10. Moore EE, Jones TN: Benefits of immediate jejunostomy feeding after major abdominal trauma: a prospective, randomized study. J Trauma 26:874–881, 1986
11. Moore FA, Moore EE, Kudsk KA, et al: Clinical benefits of an immune-enhancing diet for early postinjury enteral feeding. J Trauma 37(4):607–615, 1994
12. Kudsk KA, Croce MA, Fabian TC, et al: Enteral vs. parenteral feeding: Effects on septic morbidity after blunt and penetrating abdominal trauma. Ann Surg 215(5):503–513, 1992
13. Bastow MD, Rawlings J, Allison SP: Benefits of supplementary tube feeding after fractured neck of femur: A randomized controlled trial. British Med J 287:1589–1592, 1983
14. Taylor SJ, Fettes SB, Jewkes C, et al: Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. Crit Care Med 27(11):2594–2595, 1999
15. Bower RH, Cerra FB, Bershadsky B, et al: Early enteral administration of a formula (Impact) supplemented with arginine, nucleotides, and fish oil in intensive care unit patients: Results of a multicenter, prospective, randomized, clinical trial. Crit Care Med 23(3):436–449, 1995
16. Montecalvo MS, Steger KA, Farber HW, et al: Nutritional outcome and pneumonia in critical care patients randomized to gastric versus jejunal tube feedings. Crit Care Med 20(10):1377–1387, 1992
17. VA Total Parenteral Nutrition Cooperative Study Group: Perioperative total parenteral nutrition in surgical patients. N Engl J Med 325(8):525–532, 1991
18. MacBurney M, Young LS, Ziegler TR, et al: A cost-evaluation of glutamine-supplemented parenteral nutrition in adult bone marrow transplant patients. J Am Diet Assoc 94(11):1263–1266, 1994
19. Senkal M, Zumtobel V, Bauer KH, et al: Outcome and cost-effectiveness of perioperative enteral immunonutrition in patients undergoing elective upper gastrointestinal tract surgery: A prospective randomized study. Arch Surg 134(12):1309–1316, 1999
20. Hedberg AM, Lairson DR, Aday LA, et al: Economic implications of an early postoperative enteral feeding protocol. J Am Diet Assoc 99(7): 802–807, 1999
21. A.S.P.E.N: Board of Directors: Standards for nutrition support: Hospitalized patients. Nutr Clin Pract 10:208–219, 1995
22. Skipper A, Millikan KW: Parenteral nutrition implementation and management. IN Merritt RJ (ed). The A.S.P.E.N. Nutrition Support Practice Manual. A.S.P.E.N., Silver Spring, MD, 1998, pp 9.1–9.9
23. A.S.P.E.N: Board of Directors. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. JPEN 17:1SA–52SA, 1993
24. A.S.P.E.N: Board of Directors. Clinical Pathways and Algorithms for Delivery of Parenteral and Enteral Nutrition Support in Adults. A.S.P.E.N., Silver Spring, MD, 1998

MONITORING FOR COMPLICATIONS

Background

Although SNS can be a useful and life-saving therapy in a variety of settings, both EN and PN may cause significant complications. These complications can be minimized through diligent patient monitoring by nutrition support professionals.

Evidence

The refeeding syndrome is a complication that may arise during aggressive administration of SNS.[1,2] Although more commonly reported in association with PN, the refeeding syndrome may also occur in the setting of EN and even oral feeding. The refeeding syndrome can be life threatening if not treated promptly. At greatest risk for the syndrome are chronically, semistarved marasmic patients whose bodies have adapted largely to use of free fatty acids and ketone bodies as energy sources. Rapid reintroduction of large amounts of carbohydrate feedings can result in metabolic abnormalities, including hypophosphatemia, hypokalemia, and hypomagnesemia. In particular, hypophosphatemia has been considered a hallmark of the refeeding syndrome. Hypophosphatemia is associated with the hematologic, neuromuscular, cardiac, and respiratory dysfunction in severe cases. Another common sequelum of the refeeding syndrome is fluid retention due to the antinatriuretic effect of increased insulin concentrations. Sudden expansion of extracellular fluid can lead to cardiac decompensation in severely marasmic patients. Alternatively, administration of dextrose may cause significant hyperglycemia, which may in turn result in osmotic diuresis and dehydration. Close monitoring of serum phosphate, magnesium, potassium, and glucose are imperative when SNS is initiated, particularly in malnourished patients.[3]

Both hyperglycemia and hypoglycemia are potential complications of SNS. In one study, the incidence of hyperglycemia (defined as a blood glucose greater than 200 mg/dL) during PN was 7% in patients given less than or equal to 5 mg/kg per minute of dextrose, whereas 49% of patients receiving greater than 5 mg/kg per minute of dextrose developed hyperglycemia.[4] In this study, patients with a history of diabetes mellitus or glucose intolerance, patients receiving systemic corticosteroids, and patients with sepsis or multisystem organ failure were excluded; the incidence of hyperglycemia would be expected to be even higher in these patients. The extreme scenario of hyperglycemia is hyperosmolar hyperglycemic state (hyperosmolar nonketotic coma). Mortality has been quoted to be 0% in patients less than 50 years of age and 14% in those more than 50 years of age.[5] Harbingers of impending hyperosmolar hyperglycemic state include elevated

blood glucose and osmolality in the absence of ketones. Confusion, dizziness, lethargy, and other neurologic signs may precede frank obtundation and coma. Periodic clinical examinations and close monitoring of blood glucose and urine glucose can minimize these complications.

Patients with pre-existing diabetes or significant physiologic stress may develop hyperglycemia upon initiation of PN. Because hyperglycemia has been shown to be associated with decreased measures of immune function and increased risk of infectious complications, efforts to monitor and control blood glucose during SNS are prudent.[6]

Rebound hypoglycemia upon discontinuation of parenteral nutrition has been reported, although this is an extremely uncommon event. Some experts continue to recommend that, particularly for patients receiving large amounts of insulin along with their PN, the PN infusion rate be cut in half for the last two hours prior to discontinuation. This approach can avoid the need for careful blood glucose monitoring during discontinuation of PN.

Acid–base abnormalities are commonly seen in the patient receiving SNS. In a quality assurance study from a busy nutrition support service based in a large hospital, found carbon dioxide content was abnormal up to 13% of the time. In the same study, blood chloride values were unacceptable between 1% and 7% of the time.[7] In most cases, severe abnormalities are not due to the nutrition regimen itself but rather to the patient's underlying condition. Many of the current commercially available intravenous amino acid solutions contain large amounts of endogenous acetate, which tend to be alkalinizing. Metabolic acid–base abnormalities may at least partially be addressed by manipulating the acetate and chloride content of the PN solution. Periodic monitoring of serum electrolytes can avoid problems before they pose a danger to the patient.

Hypertriglyceridemia may occur in some patients receiving intravenous fat emulsion; if unnoticed and untreated, this may lead to the development of pancreatitis and altered pulmonary function.[8] These complications can be avoided by prudent monitoring of serum triglyceride levels during the administration of fat-containing PN.

Excessive carbon dioxide production in patients receiving SNS may lead to difficulty with ventilatory support and weaning. This complication occurs less commonly now than in the past with the use of less aggressive feeding regimens. Early literature attributed the excess carbon dioxide production to overfeeding with dextrose calories.[9] Subsequently it was found that reduced energy administration typical of current PN and EN regimens does not cause significant carbon dioxide overproduction.[10] A warning sign of excessive carbon dioxide production is an elevation in the respiratory quotient as measured by indirect calorimetry, (especially if this value exceeds unity).

Hepatobiliary complications may arise during administration of PN.[11] The incidence is uncertain. Steatosis or fatty liver may occur early, whereas cholestasis typically occurs later (months or years) in the course of therapy. Hepatic steatosis is reversible with discontinuation of PN. The chronic, irreversible, cholestatic liver disease sometimes seen with long-term PN can lead to liver failure and death. Many potential etiologic factors for these liver abnormalities have been postulated; the cause is generally multifactorial. Careful monitoring of liver function tests can help to identify these problems early, when changes in PN prescription may allow resolution.

Metabolic bone disease, which may present with bone pain and fractures, occurs with unknown frequency in patients receiving PN.[12] Early studies revealed an incidence of 29% or more in long-term patients. Recent availability of rapid, reproducible and relatively inexpensive techniques for measuring bone density should help to recognize this complication early. Risk factors for development of metabolic bone disease include chronic systemic glucocorticoid use, short bowel syndrome, menopause, and positive family history of bone disease; patients with these and other risk factors should be closely monitored.[13]

Vascular access sepsis in patients receiving PN is a common complication. There is no monitoring that can be routinely performed to detect the development of sepsis prospectively. Careful symptomatic and laboratory monitoring (fever, constitutional symptoms, technical complications with the vascular access device, hyperglycemia) can help recognize an episode of sepsis early.

Gastroesophageal reflux and pulmonary aspiration are potential complications of EN. Significant aspiration can lead to pneumonia and death in an already debilitated patient; aspiration is considered to be one of the most serious complications of EN. Although postpyloric feedings are frequently preferred by clinicians over gastric feedings in patients with impaired gag reflex or neurologic compromise, hard evidence to support that aspiration risk is decreased by postpyloric tube placement is lacking.[14,15] Two factors commonly quoted as putting a patient at risk for aspiration are presence of a nasoenteric feeding tube and supine patient positioning. Lack of a truly reliable bedside method for detection of aspiration makes study of this complication difficult. Increasing gastric residuals and vomiting are warning signs that aspiration may occur, although aspiration may be asymptomatic especially in an obtunded patient.

Gastrointestinal complications are common during EN. Depending on the definition used, the incidence of diarrhea occurs in 21% to 72% of patients receiving EN.[16] In this study, the frequency of overall enteral feeding patient days in which diarrhea occurred was 2% to 26%, again varying with the definition of diarrhea.[16] Severe diarrhea can lead to life-threatening fluid and electrolyte abnormalities. Common causes of diarrhea in this population include concomitant medications (eg, sorbitol-containing medications, prokinetic agents), underlying illness predisposing to malabsorption, and *Clostridium difficile* colitis. Tube feeding–related causes may include enteral feeding formula content (eg, fiber or lactose content) and administration technique. Contamination of enteral feeding

tubes, delivery sets, and formula with microbes can occur. Studies have looked at the frequency and importance of such contamination. Issues investigated included the use of tap versus sterile water to reconstitute formulas or rinse tubing, whether enteral delivery sets, were rinsed and the length of time delivery sets were utilized.[17] There is no consensus on optimizing many of these variables.

Practice Guidelines *Monitoring for Complications*

1. Malnourished patients at risk for refeeding syndrome should have serum phosphorus, magnesium, potassium and glucose levels monitored closely at initiation of SNS. (B)
2. In patients with diabetes or risk factors for glucose intolerence, SNS should be initiated with a low dextrose infusion rate and blood and urine glucose monitored closely. (C)
3. Blood glucose should be monitored frequently upon initiation of SNS, after any change in insulin dose, and until measurements are stable. (B)
4. Serum electrolytes (sodium, potassium, chloride, and bicarbonate) should be monitored frequently upon initiation of SNS until measurements are stable. (B)
5. Patients receiving intravenous fat emulsion should have serum triglyceride levels monitored until stable and when changes are made in the amount of fat administered. (C)
6. Liver function tests should be monitored periodically in patients receiving PN. (A)
7. Bone densitometry should be performed upon initiation of long-term SNS and periodically thereafter. (C)
8. Postpyloric placement of feeding tubes should be considered in patients at high risk for aspiration who are receiving EN. (C)

REFERENCES

1. Solomon SM, Kirby DF: The refeeding syndrome: A review. JPEN 14:90–97, 1990
2. Brooks MJ, Melnik G: The refeeding syndrome: An approach to understanding its complications and preventing its occurrence. Pharmacotherapy 15:713–726, 1995
3. Marik P, Bedigian MK: Refeeding hypophosphatemia in critically ill patients in an intensive care unit: A prospective study. Arch Surg 131:1043–1047, 1996
4. Rosmarin DK, Wardlaw GM, Mirtallo J: Hyperglycemia associated with high, continuous infusion rates of total parenteral nutrition dextrose. Nutr Clin Pract 11:151–156, 1996
5. Kaminski MV Jr: A review of hypersomolar hyperglycemic nonketonic dehydration (HHND): Etiology, pathophysiology and prevention during intravenous hyperalienation. JPEN 2(5):690–698, 1978
6. McMahon MM, Rizza RA: Nutrition support in hospitalized patients with diabetes mellitus. Mayo Clinic Proc 71:587–594, 1996
7. Owens JP, Geibig CB, Mirtallo JM: Concurrent quality assurance for a nutrition-support service. Am J Hosp Pharm 46:2469–2476, 1989
8. Sacks GS: Is IV lipid emulsion safe in patients with hypertriglyceridemia? Adult patients. Nutr Clin Pract 12:120–123, 1997
9. Askanazi J, Nordenstrom J, Rosenbaum SH, et al: Nutrition for the patient with respiratory failure. Anesthesiology 54:373, 1981
10. Talpers SS, Romberger DJ, Bunce SB, et al: Nutritionally associated increased carbon dioxide production. Excess total calories vs. high proportion of carbohydrate calories. Chest 102:551–555, 1992
11. Quigley EMM, Marsh MN, Shaffer JL, et al: Hepatobiliary complications of total parenteral nutrition. Gastroenterology 104: 286–301, 1993
12. Jeejeebhoy KN: Metabolic bone disease and total parenteral nutrition: A progress report. Am J Clin Nutr 67:186–187, 1998
13. Seidner DL, Licata A: Parenteral nutrition-associated metabolic bone disease: Pathophysiology, evaluation, and treatment. Nutr Clin Pract 15:163–170, 2000
14. Lazarus BA, Murphy JB, Culpepper L: Aspiration associated with long-term gastric versus jejunal feeding: A critical analysis of the literature. Arch Phys Med Rehabil 71:46–53, 1990
15. Elpern EH: Pulmonary aspiration in hospitalized adults. Nutr Clin Pract 12:5–13, 1997
16. Bliss DZ, Guenter PA, Settle RG: Defining and reporting diarrhea in tube-fed patients–what a mess! Am J Clin Nutr 55:753–759, 1992
17. Eisenberg PG: Causes of diarrhea in tube-fed patients: A comprehensive approach to diagnosis and management. Nutr Clin Pract 8:119–123, 1993

Section IX: Drug–Nutrient Interactions

DRUG–NUTRIENT INTERACTIONS

Background

Medications are frequently prescribed for patients receiving SNS.[1] Unrecognized interactions between drugs and nutrients may lead to unexpected, poor outcomes.[2] Some interactions may be acute in onset.[3] Other interactions may develop over years before they become evident (eg, osteoporosis).[4] A drug nutrient interaction involves the alteration of the kinetics or dynamics of a drug or nutritional element or a compromise in nutrition status as a result of the action or side effect of a drug. Both the kinetic (absorption, metabolism, disposition, or elimination) and/or the dynamic effect (clinical/physiological) of a drug (eg, phenytoin) or a nutritional element (eg, folic acid) may be altered as a result of the interaction. Decreased tetracycline absorption caused by complex with dairy products is a well-known interaction. Reduced elimination of potassium by cyclosporine and spironolactone and retention of lithium by a sodium-rich diet are also examples of drug–nutrient interactions of this type.

Direct physical contact between drug molecules and nutrition elements in either the delivery system (eg, infusion tubing and/or bags) or during the compounding process is an interaction that takes place outside of the body. These are the most commonly observed interactions in nutrition support patients. They are characterized by a hydrolytic process involving the direct mixing of an EN formula and the vehicles used in oral liquid medications (eg, syrup),[5] physical incompatibility between intravenously administered drugs and PN admixtures,[6] or the addition of a drug into an infusion device containing intravenous lipid emulsion resulting in the disruption of the emulsion.[7]

In the absence of parenteral access and an inability to take medications orally, the feeding tube invariably becomes a route for medication delivery. Medications are available in multiple dosage forms: solid (tablets, capsules), and liquid (elixirs, syrups, suspensions, solutions) enteral forms; and parenteral forms. Most solid dosage forms require manipulation for administration via enteral feeding tubes. Dosage forms of medications are developed to maintain the integrity of the drug product and facilitate its bioavailability. Any manipulation of the tablet, capsule, or liquid may influence drug bioavailability; this needs to be considered when delivering drug therapy by the enteral tube. For example, sustained release or enteric-coated preparations should not be crushed for administration via a feeding tube.[8] Occasionally, patients with feeding tubes may be able to swallow oral medications, avoiding potential bioavailability and mechanical tube problems.

Medications may be added to PN formulations in an effort to decrease fluid requirements, reduce the need for Y-site injections, reduce the possibility of line contamination due to manipulation, and decrease labor time required for drug administration. Although these reasons may seem compelling, the physiochemical complexity of PN formulations makes their interactions with parenteral medications a very challenging compatibility dilemma. A recent publication on safe practices for PN formulations emphasizes the number and complexity of problems that have been reported.[9] The most common factors influencing compatibility of PN formulations with drugs include the drug pH, solubility, concentration, light sensitivity, and specific formulation.[10] Published information regarding drug–PN physical incompatibilities in these instances is limited, and applying the available information to a given patient's needs is difficult due to the variety of medication concentrations used clinically.[11,12]

Evidence

Schneider and Mirtallo[1] found that over 75% of the drugs administered to 600 patients receiving PN were capable of interfering with SNS. Drug–nutrient interactions result in derangements in fluid and electrolyte homeostasis, changes in vitamin status, and disturbances in acid–base balance.[13] Recognition of these drug–nutrient interactions may assist the clinician to prevent metabolic complications and to achieve desired therapeutic outcomes.

Alteration in sodium homeostasis is a common electrolyte disorder induced by medications. In one study, almost 20% of all hypernatremic episodes identified during hospitalization were related to EN and PN.[14] Parenteral medications available as sodium salts and delivered in normal saline are factors that contribute to hypernatremia. Drugs may stimulate inappropriate secretion of antidiuretic hormone. Renal[15,16] and gastrointestinal[13] losses of sodium are frequent causes of hyponatremia.

Hypophosphatemia occurs in 20% to 40% of patients receiving SNS.[17] Certain agents, such as some antacids or sucralfate, can bind phosphorus in the gastroin-

testinal tract and decrease serum phosphate concentrations. Urinary phosphate excretion is increased by corticosteroids and thiazide diuretics, sometimes necessitating phosphate supplementation. Insulin administration may also cause a shift of phosphate into the intracellular space.

Hyperglycemia is a common metabolic complication of SNS. Management of this problem with insulin or dietary modification of glucose intake is a difficult challenge that can be complicated by medications that interfere with pancreatic function (eg, cyclosporine A) or stimulate gluconeogenesis (eg, corticosteroids).[18,19] Continuous infusions of propofol can lead to administration of significant calories and to hypertriglyceridemia.[20]

Occlusion of the feeding tube is a frequent complication of EN. Administration of syrups, medications with a low pH, or oleaginous liquid medications can disrupt the stability of the EN formula and cause enteral tube occlusion.[5] Liquid medications may be preferred for patients with feeding tubes. However, gastrointestinal intolerance has been observed with liquid medications that are hyperosmolar,[21] contain sorbitol, or contain other ingredients like polyethylene glycol.[22] Limiting sorbitol intake is difficult since it is not a requirement for the manufacturer to list its presence on the medication label.

Bioavailability of medications administered via enteral feeding tubes is a concern. The EN formula itself may influence medication bioavailability. The EN formula or a component can adversely effect the absorption, metabolism or excretion of a medication; this has been observed with phenytoin.[2] All medications given directly into the stomach, duodenum or jejunum require an appropriate fluid flush (water, normal saline) before and after each administration. Leff and Roberts[23] found that drug bioavailability improved when proper flushing techniques were used.

Diarrhea is a frequent complication of EN. The incidence of this complication is increased in patients receiving antibiotics. Guenter et al[24] found that diarrhea occurred in 41% of enteral tube fed patients receiving antibiotics versus 3% in those that did not. In the antibiotic group with diarrhea, 50% of stool cultures were positive for *Clostridium difficile* toxin. This is a frequent complication that complicates the use of EN.

Physical incompatibilities in PN solutions may lead to patient death. This has occurred as a result of pulmonary deposition of calcium phosphate precipitates.[25] Intravenous administration of substantial amounts of large (>5 μm) particles resulting from an incompatibility is dangerous and potentially life threatening and must be considered when evaluating compatibility issues with PN. It should also be noted that once a precipitate has formed, it is highly unlikely it will redissolve, especially calcium phosphate.[26] Further, there may be pharmaceutical factors in the patient environment that promote incompatibilities. For example, excessive heat and light (direct sunlight) can initiate incompatibilities. Incompatibilities have also been reported to occur when PN is administered to patients with higher core temperatures (25°C versus 37°C) and pH values (formulation pH of 6.0 versus physiologic pH of 7.4) than that of the solution.[27]

The physical compatibility of 102 drugs with 2-in-1 PN solutions in a manner that simulates y-site administration has been evaluated.[11] It was found that 20 drugs (including commonly used drugs such as amphotericin B, acyclovir, sodium bicarbonate, and ciprofloxacin) were incompatible with the PN solutions, resulting in formation of precipitates, haziness, or discoloration. The physical compatibility of 106 drugs with 3-in-1 PN admixtures in a manner simulating y-site administration was also studied.[12] It was found that 23 drugs were incompatible with the admixtures either by formation of a precipitate or emulsion disruption with separation of oil and water phases. Many of the incompatibilities were observed immediately after mixing, which is different than observed with the 2-in-1 solutions. It is interesting to note that compatibility differed for 3-in-1 admixtures versus 2-in-1 solutions, emphasizing that compatibility in one formulation does not predict compatibility in the other. It is also worth noting that many of these interactions and incompatibilities may be noted simply by careful inspection of the PN formulas for precipitates, discoloration, haziness, or breaking of the emulsion.[9]

Special Considerations

Drug–nutrient interactions involve a myriad of real and potential problems in patients receiving SNS. So common are some that reporting their clinical consequences is not pursued. As such, this limits the evidence needed to develop comprehensive guidelines. For PN, each institution, whether providing acute or chronic care, has different compounding methods. These institutional practices often vary from the methods used in published compatibility trials. The order of mixing of the components of PN may also differ and affect compatibility. Incompatibilities are also more common at higher drug concentrations. Guidelines for compounding and professional practices intended to foster consistent procedures and processes have been published and should be followed.[9] For co-administration of medications with PN, the United States Pharmacopeia provides specific recommendations that address not only compatibility but also efficacy.[28] Finally, long-term PN formula stability (>48 hours) and compatibility data are sparse, especially in the home care environment, and are in need of further research.

Practice Guidelines
Drug–Nutrient Interactions

1. Medication profiles of patients receiving SNS should be reviewed for potential effects on nutrition and metabolic status. (B)
2. Medications co-administered with EN should be reviewed periodically for potential incompatibilities. (B)

3. When medications are administered via an enteral feeding tube, the tube should be flushed before and after each medication is administered. (B)
4. Liquid medication formulations should be used, when available, for administration via enteral feeding tubes. (C)
5. EN patients who develop diarrhea should be evaluated for antibiotic-associated causes, including *C. difficile*. (B)
6. Co-administration or admixture of medications known to be incompatible with PN should be prevented. (A)
7. In the absence of reliable information concerning compatibility of a specific drug with an SNS formula, the medication should be administered separately from the SNS. (B)
8. Each PN formulation compounded should be inspected for signs of gross particulate contamination, discoloration, particulate formation, and phase separation at the time of compounding and before administration. (B)

REFERENCES

1. Schneider PJ, Mirtallo JM: Medication profiles in TPN patients. Nutr Supp Serv 3:40–46, 1983
2. Gauthier I, Malone M: Drug-food interactions in hospitalized patients. Methods of prevention. Drug Saf 18(6):383–393, 1998
3. Bauer LA: Interference of oral phenytoin absorption by continuous nasogastric feedings. Neurology 132(5):570–572, 1982
4. Shane E, Rivas M, McMahon DJ, et al: Bone loss and turnover after cardiac transplantation. J Clin Endocrinol Metab 82(5): 1497–1506, 1997
5. Cutie AJ, Altman E, Lenkel L: Compatibility of enteral products with commonly employed drug additives. JPEN 7:186–191, 1983
6. Niemiec PW, Vanderveen TW: Compatibility considerations in parenteral nutrient solutions. Am J Hosp Pharm 41:893–911, 1984
7. Bullock C, Clark JH, Fitzgerald JF, et al: The stability of amikacin, gentamicin, and tobramycin in total nutrient admixtures. JPEN 13:505–509, 1989
8. Mitchell JF: Oral dosage forms that should not be crushed, 1998 update. Hosp Pharm 33:399–415, 1998
9. National Advisory Group on Standards and Practice Guidelines for Parenteral Nutrition: Safe practices for parenteral nutrition formulations. JPEN 22:49–66, 1998
10. Anonymous: Parenteral admixture incompatibilities: An introduction. Int J Pharm Compound 1:165–167, 1997
11. Trissel LA, Gilbert DL, Martinez JF, et al: Compatibility of parenteral nutrient solutions with selected drugs during simulated Y-site administration. Am J Health-Syst Pharm 54:1295–1300, 1997
12. Trissel LA, Gilbert DL, Martinez JF, et al: Compatibility of medications with 3-in-1 parenteral nutrition admixtures. JPEN 23:67–74, 1999
13. Driscoll DF: Drug-induced metabolic disorders and parenteral nutrition in the intensive care unit: a pharmaceutical and metabolic perspective. Drug Intell Clin Pharm 23:363–371, 1989
14. Snyder NA, Feigal DW, Arieff AI: Hypernatremia in elderly patients: A heterogeneous, morbid, and iatrogenic entity. Ann Intern Med 107:309–319, 1987
15. Nanji AA: Drug-induced electrolyte disorders. Drug Intell Clin Pharm 17:175–185, 1983
16. Sunyecz L, Mirtallo JM: Sodium imbalance in a patient receiving total parenteral nutrition. Clin Pharm 12:138–149, 1993
17. Sacks GS, Walker J, Dickerson RN, et al: Observations of hypophosphatemia and its management in nutrition support. Nutr Clin Pract 9:105–108, 1994
18. Pandit MK, Burke J, Gustafson AB, et al: Drug-induced disorders of glucose tolerance. Ann Intern Med 118:529–539, 1993
19. Knapke CM, Owens JP, Mirtallo JM: Management of glucose abnormalities in patients receiving total parenteral nutrition. Clin Pharm 8:136–144, 1989
20. Lowery TS, Dunlap AW, Brown RO, et al: Pharmocologic influence on nutrition support therapy: Use of propofol in a patient receiving combined enteral and parenteral nutrition support. Nutr Clin Pract 1996:147–149
21. Dickerson RN, Melnik G: Osmolality of oral drug solutions and suspensions. Am J Hosp Pharm 45:832–834, 1988
22. Lutomski DM, Gora ML, Wright SM, et al: Sorbitol content of selected oral liquids. Ann Pharmacother 27:269–274, 1993
23. Leff RD, Roberts RJ: Enteral drug administration practices: report of a preliminary survey. Pediatrics 81:549–551, 1988
24. Guenter PA, Settle G, Perlmutter S, et al: Tube feeding-related diarrhea in acutely ill patients. JPEN 15:277–280, 1991
25. Food and Drug Administration: Safety Alert: Hazards of precipitation associated with parenteral nutrition. Am J Hosp Pharm 51:1427–1428, 1994
26. Allwood MC, Kearney MC: Compatibility and stability of additives in parenteral nutrition admixtures. Nutrition 14:697–706, 1998
27. Robinson LA, Wright BT: Central venous catheter occlusion caused by body-heat-mediated calcium phosphate precipitation. Am J Hosp Pharm 39:120–121, 1982
28. Total parenteral nutrition/total nutrient admixture. USP DI Update, Vol I and II. United States Pharmacopeial Convention Inc, Rockville, MD, 1996, pp 66–71
29. Chan, L: Redefining drug-nutrient interactions. NCP 15(5):245–252, 2000

SECTION X: Life Cycle and Metabolic Conditions

PREGNANCY

Background

The correlation between maternal nutrition and healthy babies has been well established.[1] Adequate nutrition before and during pregnancy is necessary to achieve optimal health of the pregnant mother and her baby. Maternal malnutrition can have a profound effect on the growth and development of the unborn child and lead to poor pregnancy outcomes, including low-birth-weight infants, intrauterine growth retardation, and increased prenatal morbidity and mortality.[2,3] Women with a low prepregnancy weight-for-height are at greatest risk for giving birth to a low-birth-weight infants when maternal weight gain is inadequate.[1]

During normal pregnancy, nutrient absorption is not adversely affected. Conditions that may impair absorption, have an impact on gastrointestinal function, or increase the demand for nutrients during pregnancy include hyperemesis gravidarum, pancreatitis, cholecystitis, motility disorders, small bowel obstruction, inflammatory bowel disease, short bowel syndrome, and trauma.

Evidence

Maternal weight gain is a key indicator of the adequacy of maternal and fetal nutrition status.[4] Current recommendations for optimum weight gain during pregnancy are based on body mass index (BMI = weight (kg)/height^2 (m^2)). Normal BMI values range from 20 to 26; a value greater than 26 or less than 20 is designated as overweight or underweight, respectively.[1] The Committee on Nutritional Status and Weight Gain During Pregnancy recommends a total weight gain of 28 to 40 pounds for underweight women compared with a gain of 15 to 25 pounds for overweight women. Normal weight women are encouraged to gain 25 to 35 pounds. The rate of weight gain should be 2 to 5 pounds (total) in the first trimester, increasing to 0.5 to 1 pound each week in the second and third trimesters.[1] Teenagers who are within 2 years postmenarche and black women should gain in the upper range to reduce the prevalence of low-birth-weight infants in these groups. The recommendation for women bearing twins is 35 to 45 pounds.

Additional calories and protein are required during pregnancy to meet the demands of both mother and fetus and achieve optimum weight gain. The National Research Council has established recommended daily allowances (RDAs) for oral intake. Pregnant women should receive approximately 300 additional calories per day during the second and third trimester to meet the increased demands of pregnancy.[5] An additional 10 to 14 g of protein per day is needed to support fetal growth and development.[5] Conditions such as physiologic stress, trauma, and sepsis may require increased intake of calories and protein to achieve the desired weight gain.

Women with symptoms affecting nutrient intake, evidence of fluid and/or electrolyte imbalance or who are unable to achieve adequate weight gain during pregnancy are at nutrition risk and should undergo formal nutrition assessment with development of a nutrition care plan.[4] In addition to the nutrition assessment data obtained for nonpregnant patients, prepregnancy weight, weight history during pregnancy, measurement of fundal height, fetal ultrasound, and urine ketones are useful in evaluation of nutrition status and fetal growth.[4] The interpretation of biochemical indices for assessment of nutrition status must allow for changes in values associated with the normal physiologic changes of pregnancy.[4]

Indications for SNS in pregnancy are the same as for nonpregnant patients. If the gastrointestinal tract is functional, EN should be considered before initiating PN. Russo-Stieglitz et al[6] evaluated the perinatal outcomes and complications of PN in pregnancy. Sixteen of 26 patients required PN for hyperemesis gravidarum. They reported favorable fetal outcomes. Maternal complications included hyperglycemia and central venous catheter complications. Large controlled studies are lacking; however, numerous case reports support the safety and effectiveness of PN during pregnancy.[7–16]

Special Considerations

When conventional approaches using diet modifications and supplementations to attain adequate weight gain are unsuccessful, SNS may become necessary.

Maternal hyperglycemia is associated with increased fetal morbidity.[17–20] Maternal blood glucose levels should be maintained within the range of approximately 90 to 120 mg/dL.[17] Blood glucose monitoring should be performed during and after SNS infusions.

Maternal folic acid deficiency contributes to the

development of neural tube defects. The United States Public Health Service recommends that all women who are capable of becoming pregnant should consume 0.4 mg/d of folic acid for the purpose of reducing their risk of having a pregnancy affected with neural tube defects. Specific folate supplementation is recommended for women who previously have had an infant or fetus with a neural tube defect. These women should be advised to take supplemental folic acid, 0.4 mg/d, at the time they decide to become pregnant.[21] Pregnant women should consume 0.6 mg/d of folate.[22]

There is no apparent correlation between premature labor or increased uterine irritability and lipid infusion using currently available soybean and soybean/safflower lipid emulsions.[6,9,23,24]

Practice Guidelines *Pregnancy*

1. Pregnant women are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. In pregnant women who require SNS, baseline needs should be supplemented with an additional 300 kcal/d and 10 to 14 g/d of protein during the second and third trimester. (B)
3. PN is indicated for pregnant patients at risk for malnutrition because of a nonfunctioning gastrointestinal tract or inability to tolerate EN. (C)
4. Maternal blood glucose should be maintained within the range of 90 to 120 mg/dL. (C)
5. Intravenous lipid emulsions may be used safely in pregnant women to provide a source of isotonic nonprotein calories and avoid essential fatty acid deficiency. (C)
6. All women of child-bearing age who are capable of becoming pregnant should consume at least 0.4 mg/d of folic acid, using specific supplementation if necessary. (A)

REFERENCES

1. Institute of Medicine (IOM) Subcommittee on Nutritional Status and Weight Gain During Pregnancy. Nutrition During Pregnancy. National Academy Press, Washington, DC, 1990
2. Smith CA: Effects of maternal under nutrition upon newborn infants in Holland: 1944–1945. J Pediatr 30:229–243, 1947
3. Naeve RL: Weight gain and the outcome of pregnancy. Am J Obstet Gynecol 135:3–9, 1979
4. Wagner BA, Worthington PA, Russo-Stieglitz, et al: Nutritional management of hyperemesis gravidarum. Nutr Clin Pract 15(2): 153–155, 65–76, 2000
5. National Research Council (NRC). Recommended Dietary Allowances, 10th ed. National Academy Press, Washington, DC, 1989
6. Russo-Stieglitz KE, Levine AB, Wagner BA, et al: Pregnancy outcome in patients requiring parenteral nutrition. J Maternal Fetal Med 8:164–167, 1999
7. Chevreau N, Anthony PS, Kessinger K: Managing hyperemesis gravidarum with home parenteral nutrition: treatment parameters and clinical outcomes. Infusion 5(8):22–28, 1999
8. Wiedner LC, Fish J, Talabiska DG, et al: Total parenteral nutrition in pregnant patient with hyperemesis gravidarum. Nutrition 9(5): 446–449, 1993
9. Levine MG, Esser D: Total parenteral nutrition for the treatment of severe hyperemesis gravidarum: maternal nutritional effects and fetal outcome. Obstet Gynecol 72(1):102–107, 1988
10. Charlin V, Borghesi L, Hasbun, et al: Parenteral nutrition in hyperemesis gravidarum. Nutrition 9(1): 29–32, 1993
11. Caruso A, De Carolis S, Ferrazzani S, et al: Pregnancy outcome and total parenteral nutrition in malnourished pregnant women. Fetal Diagn Ther 13:136–140, 1998
12. Hatjis CG, Meis PJ: Total parenteral nutrition in pregnancy. Obstet Gynecol 66(4):585–588, 1985
13. Greenspoon JS, Rosen DJD, Ault M: Use of the peripherally inserted central catheter for parenteral nutrition during pregnancy. Obstet Gynecol 81(5):831–834, 1993
14. Mamel JJ, Kuznicki M, Carter M, et al: Total parenteral nutrition during pregnancy in a patient requiring long-term nutrition support. Nutr Clin Pract 13:123–128, 1998
15. Wolk RA, Rayburn WF: Parenteral nutrition in obstetric patients. Nutr Clin Pract 5:139–152, 1990
16. Watson LA, Bommarito AA, Marshall JF: Total peripheral parenteral nutrition in pregnancy. JPEN 14(5):485–489, 1990
17. Moore TR: Diabetes in pregnancy. In Maternal-Fetal Medicine, 4th ed., Creasy RK, Resnik R (eds). WB Saunders, Philadelphia, 1999, p 964
18. Philipps AF: Carbohydrate metabolism in the fetus. IN Fetal and Neonatal Physiology, Polin RA, Fox WW (eds). WB Saunders, Philadelphia, 1998, pp 560–573
19. Skyler JS, O'Sullivan MJ, Holsinger KK: The relationship between maternal glycemia and macosomia. Diabetes Care 3:3, 1980
20. Sosenko IR, Kitzmiller JL, Loo SW, et al: The infant of the diabetic mother. N Engl J Med 301:16, 1979
21. Centers for Disease Control: Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. MMWR 41(no. RR-14):1–7, 1992
22. Subcommittee on Interpretation and Uses of Dietary Reference Intakes and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Dietary reference intakes: Applications in dietary assessment. National Academy Press, Washington, DC, 2001
23. Amato P, Quercia RA: A historical perspective and review of the safety of lipid emulsion in pregnancy. Nutr Clin Pract 6:189–192, 1991
24. Greenspoon JS, Safarik RH, Hayashi JT, et al: Parenteral nutrition during pregnancy: lack of association with idiopathic preterm labor or preeclampsia. J Reprod Med 39(2): 89–91, 1994

NEONATOLOGY: PREMATURE INFANT

Background

Premature neonates are categorized by birth weight and gestational age. Table I summarizes the terminology used to classify premature infants[1];

Numerous physiologic factors differentiate preterm and term infants. Preterm infants have: low carbohy-

TABLE I
Terminology used to classify premature infants[1]

Term	Definition
Low birth weight (LBW)	Birth weight <2500 g
Very low birth weight (VLBW)	Birth weight <1500 g
Extremely low birth weight (ELBW)	Birth weight <1000 g
Preterm	Gestational age <38 weeks
Small-for-gestational age (SGA)	<10th percentile (birth weight for gestational age)
Appropriate-for-gestational age (AGA)	>10th and <90th percentile (birth weight for gestational age)
Large-for-gestational age (LGA)	>90th percentile (birth weight for gestational age)
Intrauterine growth restriction (IUGR)	Abnormally slow rate of fetal growth

drate and fat stores; elevated metabolic rates due to a higher percentage of metabolically active tissue; high evaporative losses; and immature gastrointestinal systems. Because of these differences, the nutrition needs of this population differ from term infants. PN, incorporating protein, carbohydrate and fat infusion, should be started as soon as clinically possible, preferrably on the first day of life, to prevent a starvation state, normalize serum glucose levels, and improve protein balance.[2] Nutrient delivery is provided in quantities to promote growth matching in utero accretion rates.

Evidence

Early parenteral nutrition (PN) support in the extremely low birth weight (ELBW) and very low birth weight (VLBW) infants, beginning on day 1 of life, is advocated for numerous reasons. Infusing parenteral amino acids and glucose decreases protein catabolism when compared with glucose infusion alone.[3] A decrease in the incidence of hyperglycemia and hyperkalemia has been documented when amino acid infusions are begun on day 1 of life.[4] Experimental evidence indicates that amino acid infusion may enhance glucose-stimulated insulin secretion, aiding the prevention and treatment of hyperglycemia.[1]

Protein requirements in ELBW and VLBW infants are dependent on the clinical situation and nutrition goals at any given time. In the first weeks of life, 1 to 1.5 g/kg per day of protein intake should prevent protein catabolism.[2] To promote in utero growth rates, 3.5 to 3.85 g/kg per day protein is required.[5] Term infants can achieve positive nitrogen balance at a protein level of 2.5 g/kg per day.

Energy intake also effects nitrogen balance. Glucose and fat calories must be administered concurrently to promote anabolism. Fifty to 60 kcal/kg per day meets minimal energy requirements in ELBW infants, but the maximal protein accretion rate is achieved at 100 to 120 kcal/kg per day intake in most preterm infants.[2]

Glucose administration in ELBW and VLBW infants to meet basal requirements can be predicted from endogenous glucose production, which approximates 6 mg/kg per minute. The upper limit of intake is dependent on the infant's maximal glucose oxidative capacity. This rate is estimated to be 12 to 13 mg/kg per minute.[6] Along with intravenous lipid emulsion, this amount of glucose is sufficient to achieve caloric goals for weight gain.

Intravenous fat administration should be initiated within the first 3 days of life to prevent fatty acid deficiency. A deficiency state can be avoided with as little as 0.5 to 1 g/kg per day of fat emulsion.[7] Maximally tolerated fat delivery in the preterm population is 3 g/kg per day. There is little clinical evidence to support the practice of gradually increasing daily fat intake to promote lipid clearance.[8] Lipid emulsion delivered over 24 hours by constant infusion maximizes lipid clearance.[9]

Aggressive SNS, using both parenteral and enteral support, in VLBW infants has recently been explored.[10] It was hypothesized that improved energy intake has an impact on growth, pulmonary morbidity, hospital stay, and feeding morbidity. Growth in early life and at discharge were significantly improved in the aggressively fed group.

The benefits of EN as little as 0.5 to 1 mL/h via a tube feeding, to ELBW and VLBW infants are well documented. EN promotes normal gut motility, improved feeding tolerance, lactase activity and reduces the risk of sepsis.[11] The risk of necrotizing enterocolitis in this population can be minimized by avoiding rapid advancement of the feeding regimen.

Perinatal SNS may have long-term consequences in preterm infants. Reports from a randomized feeding trial of standard term formula versus preterm formula indicate that infants fed standard term formula have lower verbal IQ scores and overall IQ scores.[12] This cohort of preterm infants has been compared with age appropriate term infants at 8 to 12 years of age.[13] Former preterm infants were shorter and weighed less than their full-term peers. There was no difference in bone mineralization found between the groups once bone mineral content was adjusted for body weight. Maximizing linear growth potential in the preterm population may be essential in improving bone mineralization.[14,15]

Practice Guidelines *Neonatology: Premature Infant*

1. Preterm infants are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. When indicated, PN should be started in preterm infants on day 1 of life, if clinically possible. (B)
3. Concurrent EN in infants receiving PN should be started as soon as clinically possible. (C)
4. Protein should be given to stable ELBW and VLBW infants at a rate of 3.5 to 3.85 g/kg per day. (B)
5. Energy should be administered at a rate of 100 to 120 kcal/kg per day to stable preterm infants anabolism. (A)
6. Intravenous glucose administration should be advanced as tolerated to 10 to 13 mg/kg per minute to meet caloric goals. (A)
7. Intravenous fat emulsion should be administered over 24 hours up to a maximum rate of 3 g/kg per day. (B)

REFERENCES

1. Hay WW Jr: Assessing the effect of disease on nutrition of the preterm infant. Clin Biochem 29:399–417, 1996
2. Thureen PJ, Hay WW Jr: Intravenous nutrition and postnatal growth of the micropremie. Clin Perinatol 27:197–234, 2000
3. Battaglia FC, Thureen PJ: Nutrition of the fetus and premature infant. Nutrition 13:903–907, 1997
4. Micheli J-L, Schutz Y, Junod S, et al: Early postnatal intravenous amino acid administration to extremely low-birth-weight infants. IN Hay WW Jr (ed). Seminars in Neonatal Nutrition and Metabolism, vol. 2, Ross Products Division, Abbott Laboratories, Columbus, OH, 1994, pp 1–3
5. Ziegler EE: Protein in premature feeding. Nutrition 10:69–72, 1994

6. Jones MO, Pierro A, Hammond P, et al: Glucose utilization in the surgical newborn infant receiving total parenteral nutrition. J Pediatr Surg 28:1121–1124, 1993
7. Foote KD, MacKinnon MJ, Innis S: Effect of early introduction of formula versus fat free parenteral nutrition on essential fatty acid status of preterm infants. Am J Clin Nutr 54:93, 1992
8. Brans YW, Andrew DS, Carrillo DW, et al: Tolerance of fat emulsions in very-low-birth-weight neonates. Am J Dis Child 142:145, 1988
9. Spear ML, Stahl GE, Paul ME, et al: Effect of heparin dose and infusion rate on lipid clearance and bilirubin binding in premature infants receiving intravenous fat emulsions. J Pediatr 112: 94, 1988
10. Wilson DC, Cairns P, Halliday HL, et al: Randomised controlled trial of an aggressive nutritional regimen in sick very low birth weight infants Arch Dis Child Fetal Neonatal Ed 77:F4–F11, 1997
11. Newell SJ: Enteral feeding of the micropremie. Clin Perinatol 27:221–234, 2000
12. Lucas A, Morley R, Cole TJ: Randomised trial of early diet in preterm babies and later intelligence quotient. Br Med J 317: 1481–1487, 1998
13. Fewtrell MS, Prentice A, Jones SC, et al: Bone mineralization and turnover in preterm infants at 8–12 years of age: The effect of early diet. J Bone Miner Res 14:810–820, 1999
14. Lucas A, Fewtrell MS, Prentice A, et al: Effects of growth during infancy and childhood on bone mineralization and turnover in preterm children aged 8–12 years Acta Paediatr 89:148–153, 2000
15. MS, Cole TJ: Fetal origins of adult disease-the hypothesis revisited. Br Med J 319:245–249, 1999

NEONATOLOGY: PEDIATRIC UNDERNUTRITION (FAILURE TO THRIVE)

Background

Despite increases in the prevalence of childhood obesity in the United States,[1] pediatric undernutrition remains an important clinical and public health problem. The prevalence of undernutrition can range from 1% to 10% in different clinical settings.[2] Among low-income children, recent national data document linear growth retardation in 8%;[3] 12% of children live in households classified as food insecure with moderate or severe hunger.[4] Undernutrition may be associated with decreases in immune function and physical activity, motor and cognitive delay, and poor school performance.[2] Effects of undernutrition on behavior and cognitive processes rarely can be isolated from social and environmental variables[5,6]; however, these "effects" may also relate to emotional responses to stress rather than irreversible effects on brain function.[7,8] Infant undernutrition has been identified as an independent risk factor for neglect in preschool years,[9] and, in combination with neglect, associated with lower levels of cognitive function than either condition alone.[10]

The term "failure to thrive" (FTT), lacks consistent definition[11] limiting scientific study across populations.[12] FTT is considered a clinical indicator of nutrition status,[13] reflecting organic, nonorganic, or mixed etiology.[14] The term "pediatric undernutrition" currently is preferred, emphasizing growth delay and de-emphasizing broad etiologic categories.[2]

Undernutrition has been defined in clinical practice as weight-for-age or weight-for-height less than the fifth percentile on the NCHS/WHO growth charts.[15] For surveillance purposes, weight-for-age or weight-for-height are converted to a standard deviation score (Z-score)[16,17] using software available from the Centers for Disease Control and Prevention[18]; undernutrition is classified as a Z score less than −2.0, a cutoff equivalent to the 2.3 percentile.[19] The recently released, 2000 NCHS growth curves reflect the racial/ethnic composition of the US population,[20] and the third rather than fifth percentile can be used to classify undernutrition, because it more closely approximates a Z score of less than −2.0. The updated charts also include body mass index (BMI) curves, to aid early identification of obesity.[20] FTT also has been defined as a fall of two or more major centile lines on reference curves once a stable weight pattern has been reached,[12] failure to gain weight on two successive measurements,[19] or as a decrease in Z score.[21,22] A consensus definition specifying the magnitude or time interval of growth delay is lacking.[22]

Type and severity of undernutrition previously have been differentiated as mild, moderate, and severe, and as wasting (acute) malnutrition and stunting (chronic) malnutrition, using the Waterlow criteria.[23] Short stature may indicate past nutritional deficits or long-term, continuing processes; because this distinction has different implications for intervention, the term "chronic" malnutrition is now discouraged.[19] Furthermore, the Waterlow criteria and other criteria based on percent of median[23] are age biased,[21,24] and Z score decrements are recommended to classify severity of underweight, wasting, and stunting.[19]

Risk factors for developing undernutrition in the United States include low birth weight[25] and chronic diseases of infancy as well as complex social factors including poverty, parental stress, parental health beliefs,[25] excess fruit juice consumption,[26] and parent-child interaction difficulties.[27] Oral-motor dysfunction and poor feeding skills may also play a role in the development of undernutrition.[28,29]

Evidence

Assessment of undernutrition is initiated by history and physical exam.[12,30] Nutrition history, including feeding behavior and environment, should be included in the formal nutrition evaluation. Family history should include biological parent heights and weights and sibling growth patterns. Social history should cover parental age, life stresses, economic supports (eg, means-tested benefit programs) and domestic violence. When one risk factor is identified, others need to be thoroughly evaluated because multiple risk factors may have a cumulative detrimental effect on cognitive function.[10] A review of systems should be performed to rule out underlying medical conditions.

Anthropometric measurements should be carefully obtained and plotted on growth charts. Maximum weight attained between 4 and 8 weeks of age is a better predictor of weight at 1 year of age than birth weight and should be used in place of birth weight as the reference percentile.[31] Corrected age should be used with premature infants until 24 months for weight, 40 months for height, and 18 months for head circumference.[32]

A comprehensive physical examination including inspection and palpation of hair, skin, oral mucosa, muscle, and subcutaneous fat stores is a fundamental part of the assessment. Attention to eye contact, vocalization, response to cuddling, and interest in the environment can give insight into the presence or absence of psychosocial or environmental deprivation.[30] Observation of a feeding allows for assessment of both the parent-child dynamic and oral-motor or swallowing difficulties.[30] Ideally, a formal psychosocial evaluation of the child's behavior and relationship with caregivers and environment, as well as cultural variables, is performed by a trained professional on the multidisciplinary team.[33]

Management of undernutrition ideally takes place in the outpatient setting. The goal of treatment is weight gain. This is generally achieved by increased caloric intake.[34] Catch up weight gain (rate of weight gain that exceeds average weight gain for a given age group) may require 50% greater calories and protein than is required for normal growth.[34] Catch up growth calorie needs can be calculated as follows: kcal/kg needed = RDA kcal/kg (age appropriate) × ideal weight/actual weight, using fiftieth percentile as ideal weight. Catch up growth protein requirements can be calculated similarly using the age appropriate RDA for protein. The best way to increase caloric intake is by increasing caloric density of formula for infants and with high calorie additives (peanut butter, whole milk, etc) for children. Intake of low caloric density foods such as soft drinks and juices should be decreased. Attention must of course be paid to medical conditions, nutrition requirements, gastrointestinal tolerance, and renal solute load when developing a feeding plan.[34,35]

Close monitoring should be performed regularly (weekly to monthly) with anthropometry and plotting on growth curves. Triceps skinfold is a useful measurement to monitor because changes in weight and skinfold occur most rapidly in the course of nutrition rehabilitation.[34] Most children treated for undernutrition gain weight and grow well. Nonetheless, one fourth to one half of infants diagnosed with failure to thrive will remain small.[30]

A multidisciplinary approach to evaluation and treatment of children with undernutrition has been associated with faster weight gain than treatment in the primary care setting alone.[36] Extensive laboratory testing is of limited value in most cases of undernutrition,[37] and testing is clearly not indicated for all patients. Physical examination and history should guide the selection of tests. Appropriate screening laboratory tests may include hematocrit, urinary analysis and culture, BUN, calcium, electrolytes, HIV antibody, and Mantoux tubercillin skin test.[30]

The role of home visits has been evaluated in several recent studies with varying results. In the primary care setting, the use of home health visitors has been associated with faster growth,[29,38] improved home environments and mothers' perceived stress,[38] and better language skills development.[39] The utility of a home health visitor for children attending failure to thrive specialty clinics is less clear, with one study showing no additional benefit of home intervention on growth or development.[40]

In preterm low-birth-weight infants, regular home health visits do not decrease the incidence of undernutrition.[41] When undernutrition does develop in this population, home health visits are associated with higher IQ scores at 36 months of age.[41] In stunted children, psychosocial intervention has been shown to confer additional benefits on cognitive development when compared with nutrition supplementation alone.[42] Among preterm infants with low birth weights, home environments have been found to be less stimulating in those who develop undernutrition.[43]

Approximately 1.7 million children in the United States have elevated lead levels.[44,45] Blood lead levels are negatively associated with linear growth, and prevalence of high blood lead levels is greater among children with growth delay.[46,47] Iron deficiency affects 3% of young children.[48] Although not linked directly to growth deficiency, iron deficiency can lead to increased absorption of lead (and other toxins) from the gastrointestinal tract[46] and may be accompanied by zinc deficiency.[46] Although there is limited evidence that zinc supplementation enhances growth in US children with undernutrition, supplementation has been associated with improved linear growth in developing countries.[49]

Practice Guidelines
Neonatology: Pediatric Undernutrition (Failure to Thrive)

1. Clinicians should define pediatric undernutrition as either: weight for age or weight for height less than the third percentile (less than −2.0 weight for age or weight for height Z-score) on the 2000 NCHS growth charts or a fall across two or more centile lines on the NCHS growth charts once a stable growth pattern has been reached. (B)
2. Severity of wasting and stunting should be assessed (Z score less than −2.0 [moderate], less than −3.0 [severe]) and past or continuing causes of growth delay documented. (B)
3. A careful history and physical exam should be performed to assess risk factors for undernutrition and to evaluate resources available to treat undernutrition. (C)
4. A multidisciplinary team approach, including a dietitian, social worker, nurse, behavior specialist, and physician, should be convened to diagnose, treat, and monitor undernourished patients. (B)
5. Periodic re-evaluation of nutrition status should be performed using anthropometric and clinical examination assessment tools. (B)

REFERENCES

1. Troiano RP, Flegal KM: Overweight children and adolescents; description, epidemiology and demographics. Pediatrics 27:225–234, 1998
2. Kessler D: Failure to thrive and pediatric undernutrition: Historical and theoretical context. IN Kessler D, Dawson P (eds).

Failure to Thrive and Pediatric Undernutrition. Paul H. Brookes Publishing Co, Baltimore, MD, 1999
3. Healthy People 2010 Conference Edition. US Department of Health and Human Services, 2000
4. Federal Interagency Forum on Child and Family Statistics (Federal Interagency Forum on Child and Family Statistics): Nation's Children Gain in Many Areas, July 13, 2000
5. . Metallinos-Katsaras E, Gorman KS: Effects of undernutrition on growth and development. IN Kessler D, Dawson P (eds). Failure to Thrive and Pediatric Undernutrition. Paul H. Brookes Publishing Co, Baltimore, MD, 1999
6. Gorman KS: Malnutrition and cognitive development: Evidence from experimental/quasi-experimental studies among the mild-to-moderately malnourished [Review]. J Nutr 125(8 Suppl): 2239S–2244S, 1995
7. Levitsky DA, Strupp BJ: Malnutrition and the brain: Changing concepts, changing concerns. J Nutr 124:2212S–2220S, 1995
8. Strupp BJ, Levitsky DA: Enduring cognitive effects of early malnutrition: a theoretical appraisal. J. Nutr 125:2221S–2232S, 1995
9. Skuse DH, Gill D, Reilly S, et al: Failure to thrive and the risk of child abuse: a prospective population survey. J Med Screening 2(3):145–149, 1995
10. Mackner LM, Starr RH Jr, Black MM: The cumulative effect of neglect and failure to thrive on cognitive functioning. Child Abuse Negl 21(7):691–700, 1997
11. Wilcox WD, Nieburg P, Millller DS: Failure to thrive: A continuing problem of definition. Clin Pediatr 28:391–394, 1989
12. Duggan C: Failure to thrive: Malnutrition in the outpatient setting. IN Walker WA, Watkins JB (eds). Nutrition in Pediatrics: Basic Science and Clinical Applications. BC Decker, Inc, Hamilton, Ontario, 1996
13. Peterson KE, Chen LC: Defining undernutrition for public health purposes in the United States. J Nutr 120(8):933–942, 1990
14. Homer C, Ludwig S: Categorization of etiology of failure to thrive. Am J Dis Child 135:848–851, 1981
15. Hamill PVV, Drizd T, Johnson CL, et al: Physical growth: National Center for Health Statistics percentiles. Am J Clin Nutr 32:607–629, 1979
16. Dibley MJ, Goldsby JB, Staehling NW, et al: Development of normalized curves for the international growth reference: Historical and technical considerations. Am J Clin Nutr 46:736–748, 1987
17. Dibley MJ, Staehling NW, Neiberg P, et al: Interpretation of Z-score anthropometric indicators derived from the international growth reference. Am J Clin Nutr 46:749–762, 1987
18. Dean AG, Dean JA, Coulombier D, et al: Epi Info, Version 6: A Word-Processing, Database, and Statistics Program for Public Health on IBM-compatible Microcomputers. Centers for Disease Control and Prevention, Atlanta, GA, 1995
19. World Health Organization: Physical Status: The Use and Interpretation of Anthropometry, WHO Technical Report Series No. 854, Geneva: WHO, 1995, pp 198–224, Chapter 5: Infants and children; section 5.3 and 5.4
20. NCHS: New pediatric growth charts provide tool to ward off future weight problems. National Center for Health Statistics, Division of Data Services, Hyattsville, MD, 2000
21. Peterson KE, Rathbun JM, Herrera MG: Growth data analysis in failure to thrive treatment and research. IN Drotar D (ed). New Directions in Failure to Thrive: Implications for Research and Practice. Plenum Press, New York, 1985
22. Sherry B: Epidemiology of inadequate growth. IN Kessler D, Dawson P (eds). Failure to Thrive and Pediatric Undernutrition. Paul H. Brookes Publishing Co., Baltimore, MD, 1999
23. Waterlow JC, Buzina R, Keller W, et al: The presentation and use of height and weight data for comparing the nutritional status of groups of children under the age of 10 years. Bull WHO 55(4):489–498, 1977
24. Gorstein J: Assessment of nutritional status: Effects of different methods to determine age on the classification of undernutrition. Bull WHO 67:143–150, 1989
25. Pugliese MT, Weyman-Daum M, Moses N, et al: Parental health beliefs as a cause of nonorganic failure to thrive. Pediatrics 80(2):175–182, 1987
26. Smith MM, Lifshitz F: Excess fruit juice consumption as a contributing factor in nonorganic failure to thrive. Pediatrics 93(3): 438–443, 1994
27. Rathbun JM, Peterson KE: Nutrition in failure to thrive. IN Grand RJ, Sutphen JL, Dietz WH (eds). Pediatric Nutrition: Theory and Practice. Butterworths, Boston, 1987
28. Reilly SM, Skuse DH, Wolke D, et al: Oral-motor dysfunction in children who fail to thrive: Organic or non-organic? Dev Med Child Neurol 41(2):115–122, 1999
29. Wright C, Birks E: Risk factors for failure to thrive: A population-based survey. Child Care Health Dev 26(1):5–16, 2000
30. Kirkland RT. Failure to Thrive. IN McMillan JA, DeAngelis CD, Feigin RD, et al (eds). Oski's Principals and Practices of Pediatrics. Lippincott Williams and Wilkins, Baltimore, 1999
31. Edwards AG, Halse PC, Parkin JM, et al: Recognizing failure to thrive in early childhood. Arch Dis Child 65(11):1263–1265, 1990
32. Bithoney WG, Dubowitz H, Egan H: Failure to thrive/growth deficiency. Pediatr Rev 13(12):453–460, 1992
33. Black M, Cureton P, et al: Behavior Problems in Feeding: Individual, Family and Cultural Influences. IN Kessler D, Dawson P (eds). Failure to Thrive and Pediatric Undernutrition. Paul H. Brookes Publishing Co., Baltimore, MD, 1999
34. Peterson KE, Washington J, Rathbun JM: Team management of failure to thrive. J Am Diet Assoc 84(7):810–815, 1984
35. Cunningham KF, McLaughlin M. Nutrition. IN Kessler D, Dawson P (eds). Failure to Thrive and Pediatric Undernutrition. Paul H. Brookes Publishing Co, Baltimore, MD, 1999
36. Bithoney WG, McJunkin J, Michalek J, et al: The effect of a multidisciplinary team approach on weight gain in nonorganic failure-to-thrive children. J Dev Behav Pediatr 12(4):254–258, 1991
37. Sills RH: Failure to thrive. The role of clinical and laboratory evaluation. Am J Dis Child 132(10):967–969, 1978
38. Reifsnider E: Reversing growth deficiency in children: The effect of a community-based intervention. J Pediatr Health Care 12(6 Pt 1):305–312, 1998
39. Black MM, Dubowitz H, Hutcheson J, et al: A randomized clinical trial of home intervention for children with failure to thrive. Pediatrics 95(6):807–814, 1995
40. Raynor P, Rudolf MC, Cooper K, et al: A randomised controlled trial of specialist health visitor intervention for failure to thrive. Arch Dis Child 80(6):500–506, 1999
41. Casey PH, Kelleher KJ, Bradley RH, Kellogg KW, Kirby RS, Whiteside L: A multifaceted intervention for infants with failure to thrive. A prospective study. Arch Pediatr Adolesc Med 148(10):1071–1077, 1994
42. Grantham-McGregor SM, Walker SP, Chang SM, et al: Effects of early childhood supplementation with and without stimulation on later development in stunted Jamaican children. Am J Clin Nutr 66(2):247–253, 1997
43. Kelleher KJ, Casey PH, Bradley RH, et al: Risk factors and outcomes for failure to thrive in low birth weight preterm infants [published erratum appears in Pediatrics 92(1):190, 1993]. Pediatrics 91(5):941–948, 1993
44. Satcher D: Screening young children for lead poisoning: Guidance for state and local public health officials. Atlanta, Centers for Disease Control and Prevention
45. Pirkle JL, Brody DJ, Gunter EW, et al: The decline in blood lead levels in the United States. JAMA 272:284–291, 1994
46. Cutts D, Geppert J: Anemia, lead exposure, renal disease and dental caries. IN Kessler D, Dawson P (eds). Failure to Thrive and Pediatric Undernutrition. Paul H. Brookes Publishing Co, Baltimore, MD, 1999
47. Ballew C, Khan LK, Kaufmann R, et al: Blood lead concentration and children's anthropometric dimensions in the Third National Health and Nutrition Examination Survey (NHANES III), 1988 to 1994. J Pediatr 134(5):623–630, 1999
48. Looker AC, Dallman PR, et al: Prevalence of iron deficiency in the United States. JAMA 277:973–976, 1997
49. Brown KH, Peterson JM, Allen LH: Effect of zinc supplementation on children's growth: A meta-analysis of intervention trials. Bibliotheca Nutritio et Dieta 54:76–83, 1998

GERIATRICS

Background

The physiologic changes that occur with advancing age affect nutritional requirements, independent of disease or rehabilitation demands.[1]

The major physiologic changes that occur are as follows: a reduction in lean body mass, a decline in bone density, an increase in total body fat with a redistribution of fat stores, and a decrease in total body water. These physiologic alterations occur in all people as they age. They occur at different rates among individuals dependent upon nutritional intake throughout earlier life stages,[1] the presence and progression of chronic disease, and episodes of acute illness.

Distinguishing between physiologic age-induced changes and nutritional deficiencies may be difficult. These abnormalities alter physical strength and the functional and cognitive capacity of the elderly. The basal requirements to maintain homeostasis, the demands of chronic disease, and the extraordinary needs of acute illness make the provision of nutrition care to elderly patients challenging.

Evidence

Lower calorie intake and immobility contribute to reduced retention of dietary nitrogen, therefore requiring more dietary protein to achieve nitrogen balance in older subjects.[2] Surgery, sepsis, long bone fractures, and unusual losses such as those that occur with burns or gastrointestinal disease increase the need for dietary protein beyond the augmented needs induced by age and immobility. Often, clinicians have been wary of providing adequately high levels of protein for fear of precipitating renal disease. There is no evidence that dietary protein impairs renal function in individuals who do not have preexisting renal disease.[3]

The ability to metabolize carbohydrates declines with age.[4] Fasting blood glucose levels tend to increase slowly over time to a mean of 140 mg/dL for individuals over age 65. As such, carbohydrate intake should be approximately 55% to 60% of total calories with an emphasis on complex carbohydrates to enhance colon motility.

Subclinical deficiencies of water-soluble vitamins, particularly vitamin B-12, vitamin B-6, folate and ascorbic acid are likely in elderly persons.[5] Epidemiologic studies show that low vitamin levels in elderly subjects are associated with declining cognitive function.[5] Vitamin B-12 and folate stores may be low due to decreased absorption induced by gastric mucosal atrophy[6] or diets low in fat that reduce vitamin B-12 intake. Ribaya-Mercado[7] found that normal vitamin B-6 doses were insufficient to replete stores in depleted elderly subjects, suggesting higher doses are required to replete vitamin deficient states in this age group. There is an age-related decrease in whole blood, serum, and plasma leukocyte ascorbic acid levels although absorption appears normal in elderly subjects. For vitamin C, repletion of stores occurs rapidly with usual replacement doses.

Limited exposure to sunlight, the use of sunscreens, and intake of dairy products contribute to low vitamin D levels in the elderly. These low levels are associated with poor bone density and reduced muscle strength as well as function.[5] Along with vitamin D, calcium requirements have attracted much attention in recent years. Recommended dietary intake has increased from 800 to 1200 or 1500 mg/d to reduce the risk of osteoporosis.

Dehydration can be very debilitating in elderly persons. Adaptation to inadequate fluid intake and increased requirements due to fever and excessive heat is impaired. Symptoms of dehydration, hypotension, elevated body temperature, constipation, nausea, vomiting, mucosal dryness, decreased urine output, and mental confusion are rarely attributed to fluid imbalances and are, therefore, often overlooked. A reasonable estimate of fluid needs for elderly persons is approximately 30 mL/kg actual body weight with a minimum intake for all healthy older adults being 1500 mL/d.[8] Inadequate fluid intake in the institutionalized elderly results from impaired access to dietary fluid, voluntary restriction of fluid to avoid incontinence, and inadequate fluid in SNS.[9]

Malnutrition is a problem that often goes unrecognized in elderly patients.[10] Because of the physiologic changes that occur with advancing age, standard nutrition assessment parameters may not be appropriate for older adults.[11–14] Few of the standard measures of nutrition status have reference values for adults over 60 years of age. For older adults, nutrition assessment should include evaluation of physical status, including a review of anthropometric measures, biochemical assessment, oral health status, and medication review; functional status including activities of daily living and instrumental activities of daily living; cognitive and psychologic function; and socioeconomic factors.[11–14] It is important to recognize that indicators for older adults are often reflective of something different than they are for younger patients. Low serum cholesterol, for example, may indicate a serious medical problem independent of heart disease.[15] The elderly may be subclinically undernourished and may require more time to respond appropriately to a physiologic stress (trauma, surgery, sepsis), thereby influencing their nutrition status.[10,16]

Special Considerations

The use of specialized nutrition support (SNS) in elderly patients requires consideration of the physiologic changes that occur with age, cognitive status, polypharmacy and potential drug interactions, hydration status, and prognosis. Many older individuals have living wills, durable medical power of attorney assignments, and multiple comorbidities. Careful consideration of the long-term prognosis is necessary for older patients; if there is a reasonable expectation of recovery, aggressive nutrition intervention is a legitimate option. Nutrition support used to extend life

or prolong dying is generally an undesirable intervention and often eliminated as an option in living wills.

Practice Guidelines
Geriatrics

1. Elderly patients (age greater than 65 years) are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Age and life style parameters should be used to assess the nutrition status of elderly persons. (C)
3. Potential drug-nutrient interactions should be assessed in all elderly patients receiving medications. (B)
4. Diet and SNS prescriptions for elderly persons should take into consideration altered nutrient requirements observed in this age group. (B)

REFERENCES

1. Chernoff R: Demographics of aging. IN Chernoff R (ed). Geriatric Nutrition: The Health Professional's Handbook, 2nd ed. Aspen Publishers, Inc, Gaithersburg MD, 1999, pp 1–12
2. Campbell WW, Crim MC, Dallal GE, et al: Increased protein requirements in elderly people: New data and retrospective reassessments. Am J Clin Nutr 60:501–509, 1994
3. Carter WJ: Macronutrient requirements for elderly persons. IN Chernoff R (ed): Geriatric Nutrition: The Health Professional's Handbook, 2nd edition, Gaithersburg MD, Aspen Publishers, Inc, 1999, pp 13–26
4. American Diabetes Association: Nutrition recommendations and principles for people with diabetes mellitus. Diabetes Care 21(suppl 1):S32–S36, 1998
5. Rosenberg IH, Miller JW: Nutritional factors in physical and cognitive functions of elderly people. Am J Clin Nutr 55:1237S–1243S, 1992
6. Suter PM: Vitamin status and requirements of the elderly. IN Chernoff R (ed). Geriatric Nutrition: The Health Professional's Handbook, 2nd ed. Aspen Publishers, Inc, Gaithersburg MD, 1999, pp 27–62
7. Ribaya-Mercado JD, Russell RM, Morrow FD, et al: Vitamin B-6 deficiency elevates serum insulin in elderly subjects. Ann NY Acad Sci 531–533, 1990
8. Holben DH, Hassell JT, Williams JL, et al: Fluid intake compared with established standards and symptoms of dehydration among elderly residents of a long-term care facility. J Am Diet Assoc 99(11):1447–1450, 1999
9. Chernoff R: Nutritional requirements and physiological changes in aging: Thirst and fluid requirements. Nutr Rev 52(8)II:S3–S5, 1994
10. Sullivan DH, Sun S, Walls RC: Protein-energy undernutrition among elderly hospitalized patients: A prospective study. J Am Diet Assoc 281(21):2013–2019, 1999
11. Mitchell CO, Chernoff R: Nutritional assessment of the elderly. IN Chernoff R (ed). Geriatric Nutrition: The Health Professional's Handbook, 2nd ed. Aspen Publishers, Inc, Gaithersburg MD, 1999, pp 382–415
12. Guigoz Y, Vellas B, Garry PJ: Assessing the nutritional status of the elderly: The Mini Nutritional Assessment as part of the geriatric evaluation. Nutr Rev 54(1Pt 2):S59–S65, 1996
13. Morrow FD: Assessment of nutritional status in the elderly: Application and interpretation of nutritional biochemistries. Clin Nutr 5:112–120, 1986
14. Finucane P, Rudra T, Hsu R, et al: Markers of the nutritional status in acutely ill elderly patients. Gerontology 34:304–309, 1988
15. Rudman D, Mattson DE, Nagraj HS, et al: Prognostic significance of serum cholesterol in nursing home men. JPEN 12:155–158, 1988
16. Sullivan DH, Walls RC, Lipschitz DA: Protein-energy undernutrition and the risk of mortality within 1 yr of hospital discharge in a select population of geriatric rehabilitation patients. Am J Clin Nutr 53:599–605, 1991

OBESITY

Background

Obesity is the most common chronic disease in the United States, and its incidence is increasing at an alarming rate. Recent data document that over 50% of adults are overweight [with a BMI 25 to 29 (kg/m^2)], 15% are obese (BMI 30–34, WHO Class I), 5% are seriously obese (BMI 35–40, WHO Class II), and 3% have clinically severe obesity (BMI > 40, WHO Class III).[1]

The physical, psychological, and economic burden that severe obesity places on those afflicted and on society is enormous. Obesity is an independent risk factor for death from all causes and is associated with numerous potentially life-threatening comorbid conditions, including type 2 diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, obstructive sleep apnea, and several forms of malignancy.[2] Mortality from obesity increases with BMI.[3] It is estimated that obesity causes in excess of 300,000 premature deaths each year in the United States, second only to tobacco usage.[4] In addition, obesity is associated with numerous life style-limiting complications, such as arthritis, gastroesophageal reflux, gallstones, urinary stress incontinence, venous stasis disease, abdominal wall hernias, infertility, and depression.[2]

Obesity may also affect the outcome of hospitalized patients. Obese patients have a higher incidence of wound infections and hernias than lean counterparts and may have a higher incidence of respiratory, cardiac, and thromboembolic complications, although these latter associations are much less clearly defined.[5]

Because of the prevalence of obesity, obese individuals are frequently encountered in the hospital setting. A retrospective review of general, thoracic, urologic, and gynecologic surgical patients noted that 37% of the elective adult surgical population were overweight [BMI > 27 (kg/m^2)] and 17% were severely overweight (BMI > 31).[6] Thus, an estimate for the incidence of obesity of 35% to 40% for the hospitalized population in general is probably reasonable, if not low. Nevertheless, considerable confusion exists regarding whether, when, how, and what to feed, hospitalized obese patients.[7]

Evidence

Obesity and malnutrition are not mutually exclusive. In fact, obesity can be considered a form of malnutrition (overnutrition). Obese individuals should be assessed using the same approach as nonobese patients, based on history, physical exam, and laboratory studies. Catabolic illness (trauma, burns, sepsis), prolonged ventilator dependence, cancer (especially if receiving chemotherapy or radiation therapy), and

involuntary recent weight loss increase the risk for malnutrition and significant loss of lean body mass. On the other hand, significant voluntary weight loss in a monitored, balanced-deficit program does not appear to increase risk for nutrition-related adverse outcome.[8]

Nutrition support should be initiated expeditiously in obese patients with illnesses that produce significant catabolism. For patients who were relatively healthy before the onset of their current illness or those undergoing elective surgery support should be considered after a period of 5 to 7 days without oral intake, especially if it does not appear likely that the individual will be consuming greater than 50% of estimated needs within the next 3 to 4 days. Starvation or "letting them live off their fat" is not an appropriate strategy. It places these patients at risk for loss of lean body mass because metabolic stress and results in "mixed fuel" (carbohydrate, protein, and fat) utilization, as opposed to the response seen with simple starvation.[9]

The most accurate method for determining nutritional requirements in obese individuals is indirect calorimetry.[10,11] However, because indirect calorimetry is expensive to perform and not universally available, the development of prediction equations that would be more widely applicable has been advocated.

Predictive equations based on normal populations, such as the Harris-Benedict equations, have been shown to underestimate the resting energy expenditure of obese individuals when IBW is used and overestimate energy expenditure when actual body weight is used in the equations.[12,13] This has resulted in controversy regarding the most appropriate weight to be used when calculating energy needs—IBW or actual body weight.[14] Some clinicians use an "adjusted" body weight [(actual BW × 0.25) + IBW], which represents an attempt to account for the increase in lean body mass seen in the obese patient.[15]

In addition to the Harris-Benedict equations, which can be used in acutely-ill patients in conjunction with "stress factors," several other equations have been devised for estimating energy needs which may be applicable in obese patients.[13–17] However, studies comparing the accuracy of predictive formulas with indirect calorimetry have found their utility to be limited.[18,19]

Special Considerations

Starvation or semi-starvation has been successfully used as a treatment for obesity in otherwise healthy obese individuals for some time.[20] Adaptive changes during starvation reduce energy requirements and allow fat depots to be utilized for energy, while sparing muscle protein from excessive catabolism. In this setting, the administration of adequate amounts of exogenous protein (approximately 1 g/kg IBW) results in nitrogen equilibrium or positive nitrogen balance.[21,22]

Hypocaloric feeding of obese hospitalized patients has several theoretical advantages, including: avoidance of complications related to impaired glucose/insulin metabolism, improved ventilatory dynamics, positive nitrogen balance, and enhanced protein anabolism, wound healing, and immune function.

Data concerning the safety and efficacy of hypocaloric nutritional regimens in acutely ill obese patients is accumulating. Four prospective studies have been performed to date demonstrating that obese patients given hypocaloric nutrition support can achieve positive nitrogen balance comparable to controls.[23–25] In addition, others have advocated the use of various hypocaloric regimens in hospitalized obese patients with varying degrees of metabolic stress.[26–29] Although not specifically studied, such a high-protein regimen should probably not be administered to patients with significant renal or hepatic dysfunction, which generally mandates some restriction of protein intake, to avoid severe azotemia (BUN > 100 mg/dL) and hepatic encephalopathy.

Determination of the route of administration of SNS is also similar to that in nonobese patients. If no contraindication to EN exists, this should be attempted first. Parenteral access and long-term enteral access can be difficult in obese patients. Central venous cannulation tends to be increasingly difficult because, as body fat increases, the normal anatomic landmarks are obscured.[50] When placing enteral access devices such as gastrostomy or jejunostomy tubes, careful consideration must be given to placement of the tube exit site in relation to skin creases.

Practice Guidelines *Obesity*

1. Obese patients are at nutrition risk, and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. When possible, energy requirements of obese patients should be assessed using indirect calorimetry because predictive equations have considerable limitations in estimating energy requirements in obese patients. (B)
3. Hypocaloric nutrition regimens with supplemental protein are recommended in the treatment of mild to moderately stressed obese patients. (A)

REFERENCES

1. Flegal KM, Carroll MD, Kuczmarski RJ, et al: Overweight and obesity in the United States: Prevalence and trends 1960–1994. Int J Obes 22:39–46, 1998
2. Pi-Sunyer FX: Medical hazards of obesity. Ann Intern Med 119: 655–660, 1993
3. Hubert H, Feinleib M, McNamara PM, et al: Obesity as an independent risk factor for cardiovascular disease: A 26-year follow-up of participants in the Framingham heart study. Circulation 67:968–977, 1983
4. Kushner RF: Body weight and mortality. Nutrition Rev 51:127–136, 1993
5. Flancbaum L, Choban PC: Surgical implications of obesity. Ann Rev Med 49:215–234, 1998
6. Choban PS, Heckler R, Burge J, et al: Nosocomial infections in obese surgical patients. Am Surg 61:1001–1005, 1995
7. Ireton-Jones CS, Francis C: Obesity: nutrition support practice and application to critical care. Nutr Clin Pract 10:144–149, 1995
8. Martin LF, Tjiauw-Ling T, Holmes DA, et al: Can morbidly obese patients safely lose weight preoperatively? Am J Surg 169:245–253, 1995

9. Cerra FB: Hypermetabolism, organ failure, and metabolic support. Surgery 10:1–14, 1987
10. Flancbaum L, Choban PS, Sambucco S, et al: Comparison of indirect calorimetry, the Fick method, and prediction equations in estimating energy requirements in critically ill patients. Am J Clin Nut 69:461–466, 1999
11. Brandi LS, Bertolini R, Calafa M: Indirect calorimetry in critically ill patients: Clinical applications and practical advice. Nutrition 13:349–35, 1997
12. Pavlou KN, Hoefer MA, Blackburn GL: Resting energy expenditure in moderate obesity. Ann Surg. 203:136–141, 1986
13. Daly JM, Heymsfield SB, Head CA, et al: Human energy requirements: Overestimation by widely used prediction equation. Am J Clin Nutr 42:1170–1174, 1985
14. Ireton-Jones CS, Turner WW Jr: Actual or ideal body weight: which should be used to predict energy expenditure? J Am Diet Assoc 91:193–195, 1991
15. Wilken K: Adjustment for obesity. ADA Renal Practice Group Newsletter, Winter 1984,
16. Ireton-Jones CS: Evaluation of energy expenditure in obese patients. Nutr Clin Pract 4:127–129, 1989
17. Ireton-Jones, Turner WW Jr, Liepa GU, et al: Equations for the estimation of energy expenditure in patients with burns with special reference to ventilatory status. J Burn Care Rehabil 33–333, 1992
18. Amato P, Keating KP, Quericia RA, et al: Formulaic methods of estimating caloric requirements in mechanically ventilated obese patients: A reappraisal. Nutr Clin Pract 10:229–230, 1995
19. Glynn CC, Greene GW, Winkler MF, et al: Predictive versus measured energy expenditure using limits-of-agreement analysis in hospitalized obese patients. JPEN 23:147–154, 1999
20. Bray GA: The obese patient. WB Saunders Company, Philadelphia, PA, 1976
21. Strang JM, McClugage HB, Evans FA: Further studies in the dietary correction of obesity. Am J Med Sci 179:687–694, 1930
22. Strang, JM, McClugage HB, Evans FA: The nitrogen balance during dietary correction of obesity. Am J Med Sci 181:336–349, 1931
23. Dickerson RN, Rosato EF, Mullen JL: Net protein anabolism with hypocaloric parenteral nutrition in obese stressed patients. Am J Clin Nutr 44:747–755, 1986
24. Burge JC, Goon A, Choban PS, et al: Efficacy of hypocaloric total parenteral nutrition in hospitalized obese patients: A prospective, double-blind randomized trial. JPEN 18:203–207, 1994
25. Choban PS, Burge JC, Scales D, et al: Use of hypocaloric parenteral nutrition in obese hospitalized patients: A double-blind, randomized, prospective trial. Am J Clin Nutr 66:546–550 ,1997
26. Boschert K, Dickerson RA, Kudsk KA, et al: Clinical outcome of hypocaloric enteral tube feeding in obese trauma ICU patients [Abstract]. Nutr Clin Pract 15:S12, 2000
27. Pasulka PS, Kohl D: Nutrition support of the stressed obese patient. Nutr Clin Pract 4:130–132, 1989
28. Baxter JK, Bistrian BR: Moderate hypocaloric parenteral nutrition in the critically ill, obese patient. Nutr Clin Pract 4:133–135, 1989
29. Shikora SA, Muskat PC: Protein-sparing, modified-fast total parenteral nutrition formulation for a critically-ill, morbidly obese patient. Nutrition 10:155–158, 1994
30. Shikora SA: Nutrition support of the obese patient. Nutr Clin Care 2:231–238, 1999

DIABETES MELLITUS

Background

Diabetes Mellitus (DM) is a serious metabolic disorder caused by an absolute (type 1) or a relative (type 2) lack of insulin that may lead to alterations in metabolism of carbohydrate, protein, and fat. In addition, serious illness may cause hyperglycemia in patients without a prior diagnosis of diabetes or may worsen blood glucose control in critically ill patients who have preexisting DM.[1] This is thought to be due to release of various inflammatory mediators, cytokines, and hormones. The stress response leads to peripheral insulin resistance along with increased proteolysis and gluconeogenesis and resulting hyperglycemia. Near normal glucose control is the goal in ambulatory, healthy subjects with type 1 and type 2 diabetes in order to prevent or delay the development of microvascular complications (in the retina, kidney, and peripheral nerves). There is increasing evidence that glucose control is important in hospitalized patients because hyperglycemia can adversely affect immune function and fluid balance.

Appropriate nutrition therapy is a vital component in the treatment of DM. Timely nutrition assessment and initiation of medical nutrition therapy may help to prevent the development of complications over the long run. In the past, individuals with DM were instructed to follow strict diets containing specific amounts of foods with careful monitoring of carbohydrate intake and complete avoidance of simple carbohydrates, including sucrose. Recommendations for carbohydrate have been liberalized with emphasis placed on intake of complex carbohydrates and fiber. The American Diabetes Association recommends that for otherwise healthy patients, protein comprise 10% to 20% of total calories, with no specific guidelines for carbohydrate and fat other than to individualize intake based on eating habits and goals of therapy.[2,3] Recommendations for macronutrient formulation of EN or PN do not differ from standard dietary recommendations for diabetic patients.[4] It is probably more important to avoid overfeeding total calories.[5,6]

The major goal in patients with diabetes receiving SNS is optimal blood glucose control and the avoidance of hyper- and hypoglycemia and the sequelae of metabolic alterations such as fluid imbalance and dehydration, ketoacidosis, and hyperosmolar hyperglycemic state (hyperosmolar nonketotic coma), infection, and neurological injury.[4] Indications for SNS in diabetic patients are not different from nondiabetic patients in need of such therapy. Patients with permanent injury or stroke or those recovering from surgery, acute illness, or trauma may require short-term EN until safe transition to oral diet can be made. In patients in whom tube feeding is contraindicated or in situations of tube feeding intolerance, PN may be used.

Evidence

Multicenter trials have shown that intensive insulin therapy using multiple injections per day can lead to decreased risk for long-term complications in ambulatory, healthy individuals with type 1 diabetes and for people with type 2 diabetes.[10,11] During short-term hospitalization, hyperglycemia can adversely affect fluid balance and immune function. Studies document that hyperglycemia is associated with abnormalities in white cell and complement function. Increasing clinical evidence links hyperglycemia with increased risk for infection. A retrospective review of patients undergoing cardiac operation found a significant relationship between elevated blood glucose levels 48 hours after surgery and increased risk for deep wound infection in patients with DM. Implementation of a strict protocol

for blood glucose management in the postoperative period led to a significant decrease in deep wound infections.[7] Several prospective studies found that postoperative hyperglycemia in patients with DM was related to a significant increase in the incidence of infections.[8,9] It appears reasonable to aim for a blood glucose range of 100 to 200 mg/dL while minimizing the incidence of hypoglycemia.[12–14] Because intensive insulin therapy may increase the risk for hypoglycemia, it is important to closely monitor blood glucose levels when providing SNS to individuals with DM.

The use of EN and PN poses special challenges in managing blood glucose levels. A retrospective analysis of 65 patients with DM who required SNS over a 10-year period found that one third of patients with type 2 diabetes required insulin during PN; patients with type 1 diabetes required an increase from their preadmission insulin dose during PN.[15] The likelihood of a patient requiring a major change from preadmission diabetes therapy depended on severity of the underlying illness, the amount of calories provided, and the type of feeding (PN). Insulin therapy may also need to be adjusted or initiated in patients not previously requiring insulin. Initial insulin requirements for EN can be estimated based on the percentage of usual intake being provided by the feeding solution. As with PN, basal insulin requirements should be provided along with sliding scale coverage while feedings are being advanced. If the feeding is providing 25% of usual intake, then 15% to 25% of usual insulin can be given, with increases in daily insulin dose based on feeding rate and blood glucose levels. Regular insulin should be used until tolerance of EN is demonstrated. The dose and frequency of administration of intermediate-acting varies with the route of SNS administration. Glucose levels should be monitored until they stabilize.[16] Insulin infusion should be initiated if glucose goals cannot be achieved with subcutaneous administration. Oral diabetic agents are appropriate for use in stable patients with type 2 diabetes who have normal hepatic and renal function and are receiving EN.

When initiating PN, insulin therapy should be continued in patients with type 1 diabetes and in patients with type 2 diabetes who previously required insulin. Insulin therapy should be initiated in patients with blood glucose levels consistently greater than 200 mg/dL. It is recommended that initially 0.1 unit of regular insulin be added for each gram of dextrose in PN solutions in order to meet basal insulin requirements.[17] Parenteral dextrose should be kept constant until blood glucose levels are controlled. Depending on the level of glucose control, patients may require increased insulin in the PN, additional subcutaneous insulin, or an insulin infusion. Because there is a variable amount of insulin binding to PN bags and tubing, depending on materials used, it is important to be aware of this and adjust insulin dosage accordingly.

Gastroparesis, abnormal gastric emptying, and impaired small bowel motility occur in a significant number of persons with DM and may be exacerbated by poor blood glucose control. Gastroparesis may make glucose control more difficult.[18] The presence of gastroparesis requires special consideration in designing and implementing SNS. Alterations in gastric emptying may lead to difficulty achieving adequate blood glucose control due to mismatching of insulin action and nutrient absorption. Pharmacologic treatment of gastroparesis is possible. Gastroparesis in and of itself is not an indication for PN. Enteral feedings can be successfully administered using postpyloric feeding access along with promotility agents or a venting gastrostomy if needed. If EN is used, the initial formula should contain only moderate amounts of fat (30% of total calories) and should be fiber free, because both fat and fiber may slow gastric emptying.

Special Considerations

Special formulas have been developed and marketed for use in patients with DM. Several studies have examined glycemic response while feeding enteral formulations that are lower in carbohydrate and higher in fat content compared with standard products.[19] Although one study reported an improved glycemic response to the lower carbohydrate formula, another demonstrated that glycemic response was variable in each patient.[20,21] The results of these studies are difficult to apply to most clinical settings, because subjects consumed small amounts of formula over time or were given one meal but were not enterally fed. A study comparing enteral feedings of standard and diabetic formulas in nursing home residents with DM failed to show a significant difference in plasma glucose or Hgb A1c.[22] Dietary fiber intake may also play a role in blood glucose management, although further research is needed to determine the most appropriate form (soluble or insoluble) and amount of fiber needed.[23] Based on available research, there is not sufficient evidence at this time to recommend routine use of specialized enteral formulas for patients with DM or abnormal glucose control. More research is needed on the effect of different types of fat on long-term outcomes in enterally fed patients with DM.[19]

Practice Guidelines *Diabetes Mellitus*

1. Patients with diabetes mellitus are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (A)
2. In ambulatory, otherwise healthy people with diabetes mellitus, strict glucose control is recommended to decrease the incidence of diabetes-related complications. (A)
3. Blood glucose levels should be maintained in the 100 to 200 mg/dL range in hospitalized patients with diabetes mellitus. (A)
4. The macronutrient composition of EN and PN provided to patients with DM should be individualized and avoid administration of excess calories. (B)

REFERENCES

1. Rayfield EJ, Ault MJ, Keusch GT, et al: Infection and diabetes: the case for glucose control. Am J Med 72:439–450, 1982
2. American Diabetes Association: Nutrition recommendations and principles for people with diabetes mellitus. Diabetes Care 22(Suppl 1):S42–S45, 1999
3. Garg A, Bantle J, Henry R, et al: Effects of varying carbohydrate content of diet in patients with NIDDM. JAMA 271:1421–1428, 1994
4. Wright J: Total parenteral nutrition and enteral nutrition in diabetes. Curr Opin Clin Nutr Met Care 3:5–10, 2000
5. American Diabetes Association: Maximizing the role of nutrition in diabetes management. American Diabetes Association, Alexandria, VA, 1994
6. Parillo M, Rivellese AA, Ciardullo AV, et al: A high monounsaturated fat/low carbohydrate diet improves peripheral insulin sensitivity in non-insulin dependent diabetic patients. Metabolism 41:1371–1378, 1992
7. Zerr KJ, Furnary AP, Grunkemeier GL, et al: Glucose control lowers the risk of wound infection in diabetics after open heart operations. Ann Thorac Surg 63:356–361, 1997
8. Pomposelli JJ, Baxter JK, Babineau TJ, et al: Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. JPEN 22:77–81, 1998
9. Golden SH, Peart-Vigilance C, Kao WH, et al: Perioperative glycemic control and the risk of infectious complications in a cohort of adults with diabetes. Diabetes Care 22:1408–1414, 1999
10. DCCT Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications of insulin-dependent diabetes mellitus. N Engl J Med 329:977–986, 1993
11. UK Prospective Diabetes Study (UKPDS) Group: Intensive blood control with sulfonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 352:837–853, 1998
12. Baxter JK, Babineau TJ, Apovian CM, et al: Perioperative glucose control predicts increased nosocomial infection in diabetics Crit Care Med 18:S207, 1990
13. DCCT Research Group: Hypoglycemia in the diabetes control and complications trial. Diabetes 46:271–286, 1997
14. Hirsch IB, Paauw DS, Brunzell J: Inpatient management of adults with diabetes. Diabetes Care 18:870–878, 1995
15. Park RH, Hansell DT, Davidson LE, et al: Management of diabetic patients requiring nutritional support. Nutrition 8:316–320, 1992
16. McMahon MM, Hurley DL: Enteral nutrition and diabetes mellitus. IN Rombeau JL, Rolandelli RH (eds). Clinical Nutrition: Enteral and Tube Feeding, 3rd ed. WB Saunders, Philadelphia, 1997
17. McMahon MM: Management of hyperglycemia in hospitalized patients receiving parenteral nutrition. Nutr Clin Pract 12:35–38, 1997
18. Horowitz M, Wishart JM, Jones KL, et al: Gastric emptying in diabetes: An overview. Diabetes Med 13(Suppl):S16–S22, 1996
19. Coulston AM: Enteral nutrition in the patient with diabetes mellitus. Curr Opin Nutr Met Care 3:11–15, 2000
20. Peters AL, Davidson MB, Isaac RM: Lack of glucose elevation after simulated tube feeding with low carbohydrate, high fat enteral formula in patients with type I diabetes. Am J Med 87:178–182, 1989
21. Peters AL, Davidson MB: Effects of various enteral feeding products on post-prandial blood glucose response in patients with type I diabetes. JPEN 16:69–74, 1992
22. Craig LD, Nicholson S, Silverstone FA, et al: Use of a reduced-carbohydrate, modified-fat enteral formula for improving metabolic control and clinical outcomes in long-term care residents with Type 2 diabetes: Results of a pilot study. Nutrition 14:529–534, 1998
23. Thomas BL, Laine DC, Goetz FC: Glucose and insulin response in diabetic subjects: Acute effects of carbohydrate level and the addition of soy polysaccharide in defined formula diets. Am J Clin Nutr 48:1048–1052, 1988

ETHICAL AND LEGAL ISSUES

Introduction

Specialized nutrition support is provided when patients are unable to take adequate hydration or nutrients independently by mouth. SNS is considered a medical therapy. Withholding or withdrawing SNS often involves different considerations than other life-sustaining therapies, in part because of emotional, religious, and symbolic meanings. Since this organization last published ethical and legal guidelines about SNS,[1] little has changed in the legal or ethical approaches to withholding or withdrawing specialized nutrition support. However, additional evidence has accumulated about the natural course of certain subsets of patients who may require this support. This information has significant implications for caregivers.

The use of SNS involves understanding the medical indications, including benefits and burdens. Next, it involves applying these interventions in a moral, ethical, and legal construct that is satisfactory to patients, families, and caregivers.

Evidence

Consideration of the ethical and legal aspects of delivering SNS first requires choosing therapy that is medically appropriate. There are a wide variety of patients who may require SNS. Some authors make a distinction between those who cannot *physically* or *metabolically* take adequate hydration and nutrients from those who *choose* not to eat or drink. In general, it is medically indicated and ethically required to administer specialized nutrition to patients with anatomic or metabolic diseases. The ethical, legal, and moral debates surround patients with fatal diseases, progressive dementia, and persistent vegetative state.

When deciding to administer SNS, caregivers need to know the risk of intervention as well as the evidence regarding use in selected populations. For example, recent evidence has shown that gastrostomy tubes are of doubtful effectiveness in the late stages of cancer or AIDS.[2] In addition, studies have shown that hospitalized patients who require gastrostomy tube placement have a high complication rate, and patients with dementia who require gastrostomy tubes due to anorexia have a high 30-day and 1-year mortality.[3–5] This information enables members of the health care team to advise patients and their families about the medical appropriateness of these therapies. Health care professionals have come to propose a more prudent use of SNS in these populations.[6,7] There remains a need for additional studies of costly and potentially hazardous nutrition support interventions.[8]

In an otherwise psychologically competent and informed adult, choosing not to eat or drink (eg, political protest) is an autonomous decision that should be respected by physicians and caregivers, even if it results in the person's death. This is supported legally and ethically in the United States[9–11] but not every-

where (eg, in Israel, societal respect for individual life is considered more important than individual autonomy, and patients may be fed against their will).[12] Patients with anorexia nervosa or dementia have psychological disorders that result in malnutrition. It is considered legal and ethical to administer specialized nutrition to patients with these disorders, although it may not always be effective medically. Patients who forcibly remove enteral or intravenous feeding tubes may be considered to have refused this method of feeding, but if their psychological competence is in doubt, they may be restrained for ongoing feeding. Patients who are deemed psychologically competent and remove their feeding tubes or intentionally tamper or contaminate them should be allowed to refuse this therapy.

Much of the debate about administration of SNS would be avoided if every patient had an unambiguous living will outlining advance directives and if this document were used appropriately. This document would indicate whether (and for how long) patients would desire certain treatments and services. The Patient Self-Determination Act of 1990 mandated that all health care institutions receiving Medicare and Medicaid funding must provide patients with written information regarding their state's law about advance directives as well as their individual rights to refuse treatment.[13] Unfortunately, despite this legislation, most patients do not have a living will, and many patients with living wills do not specify nutritional needs in their directives. Even when a well-executed advance directive is available, family dynamics, cultural differences between caregivers and patients, and many other factors may have the practical effect of negating the directives. When an advance directive is not available, an identified durable power of attorney for health care is legally authorized to make decisions about withholding or withdrawing therapies.[14] In the absence of an unambiguous living will or durable power, the courts have identified surrogates to act as decision-makers. This occurs in a defined order, usually consisting of the patient's spouse, followed by any adult children, followed by parents.

Many times, surrogate decision makers do not know the wishes of the patient and must rely on the guidance of experienced clinicians and caregivers. It is important that caregivers consider the social and cultural implications of feeding and understand the medical, ethical, and legal ramifications in order to help patients and families make the best decisions about their care. When it remains unclear what the patient would have desired, guidelines from the Hastings Center provide assistance in surrogate decision-making. These guidelines require evaluating the burdens and benefits of an intervention from the patient's perspective and choosing therapies with a higher benefit-to-burden ratio. When it is uncertain what this ratio is, the guidelines recommend administering the intervention.[1]

In the case of young children, parents have a moral and legal obligation to provide the necessary care for them. This care includes nutrition support in the form of hydration or feeding. Federal law provides additional protection for infants, for whom adequate nourishment and hydration is mandated even in irreversible coma, presumably because of the completely dependent nature of all newborns. Withdrawal of this support, once started, may be discussed by caregivers and requested by parents. If there is a disagreement, ethics consultation and mediation should occur before seeking legal involvement and review.[1,15]

Although withdrawing and withholding treatment are equally justifiable from an ethical and legal perspective, it is often harder for caregivers to withdraw support already initiated than to withhold it.[11] This is due to concern that withdrawing therapy in patients with end-stage disease may hasten their death. However, it is important to understand that withdrawal of hydration or SNS often allows death from the natural course of the disease itself. Although physicians generally believe it is ethical to withdraw nutrition and hydration in certain patients,[16] significant debate continues whether dying patients suffer from thirst or hunger at the end of life.[17–19]

Fears about withdrawing treatment that has already started may prevent initiation of therapies in patients with poor or uncertain prognoses and therefore deprive a patient of potential benefit. An approach to this concern may be to start such therapy with defined goals and end points, thereby limiting the therapy prospectively.[1]

In cases in which there is disagreement or uncertainty about the course of action for a patient who requires artificial hydration or feeding, an ethics consultation should be obtained. Many hospitals now support a diverse group of professionals and lay people who constitute an ethics consultation service. Individuals with specific expertise in nutrition support should be members of this group.[20] This group may provide an analysis of the special circumstances of individual cases, offer opinions, mediation skills, and if necessary, recommend legal involvement.[21] Recent work has demonstrated that effective use of ethics consultation may be cost saving as well.[22]

Practice Guidelines *Ethical And Legal Issues*

1. Legally and ethically, SNS should be considered a medical therapy. (A)
2. Care providers should be familiar with current evidence of the benefits and burdens of SNS. (C)
3. Patients should be encouraged to have living wills and/or advance directives and to discuss with their loved ones their wishes in the event of a serious or terminal accident or disease. (C)
4. Adult patients or their legally authorized surrogates have the right to accept or to refuse SNS. (A)
5. The benefits and burdens of SNS, and the interventions required to deliver it, should be considered before offering this therapy. (B)
6. Institutions should develop clear policies regarding the withdrawal or withholding of SNS and

communicate these policies to patients in accordance with the Patient Self-Determination Act. (A)

REFERENCES

1. A.S.P.E.N Board of Directors: Ethical and legal issues in specialized nutrition support. JPEN 17(Suppl):50SA–52SA, 1993
2. Powell-Tuck J: Nutrition support in advanced cancer. J Roy Soc Med 90(11):591–592, 1997
3. Abuksis G, Mor M, Segal N, et al: Percutaneous endoscopic gastrostomy: High mortality rates in hospitalized patients. Am J Gastroenterol 95(1):128–132, 2000
4. Sanders DS, Carter MJ, D'Silva J, et al: Survival analysis in percutaneous endoscopic gastrostomy feeding: A worse outcome in patients with dementia. Am J Gastroenterol 95(6):1472–1475, 2000
5. Nair S, Hertan H, Pitchumoni CS: Hypoalbuminemia is a poor predictor of survival after percutaneous endoscopic gastrostomy in elderly patients with dementia. Am J Gastroenterol 95(1): 133–136, 2000
6. Finucane TE, Christmas C, Travis K: Tube feeding in patients with advanced dementia: A review of the evidence. JAMA 282(14):1365–1370, 1999
7. Gillick MR: Rethinking the role of tube feeding in patients with advanced dementia. N Engl J Med 342(3):206–210, 2000
8. August DA: Creation of a specialized nutrition support outcomes research consortium: If not now, when? JPEN 20(6):394–400, 1996
9. Quill TE, Byock IR: Responding to intractable terminal suffering: the role of terminal sedation and voluntary refusal of food and fluids. ACP-ASIM End-of-Life Care Consensus Panel. American College of Physicians-American Society of Internal Medicine [erratum in Ann Intern Med 20;132(12):1011, 2000]. Ann Intern Med 132(5):408–414, 2000
10. Snyder L: Life, death, and the American College of Physicians: The Cruzan case. Ann Intern Med 112(11):802–804, 1990
11. American College of Physicians: Ethics Manual, 4th ed. Ann Intern Med 128(7):576–594, 1998
12. Glick SM: Unlimited human autonomy–a cultural bias? N Engl J Med 336(13):954–956, 1997
13. Areen J: Advance directives under state law and judicial decisions. Law Med Health Care 1–2:91–100, 1991
14. Annas GJ: The health care proxy and the living will. N Engl J Med 324(17):1210–1213, 1991
15. Mayo TW: Forgoing artificial nutrition and hydration: Legal and ethical considerations. Nutr Clin Pract 11(6):254–264, 1996
16. Payne K, Taylor RM, Stocking C, et al: Physicians' attitudes about the care of patients in the persistent vegetative state: A national survey. Ann Intern Med 125(2):104–110, 1996
17. McCann RM, Hall WJ, Groth-Juncker A: Comfort care for terminally ill patients. The appropriate use of nutrition and hydration. JAMA 272(16):1263–1266, 1994
18. Vullo-Navich K, Smith S, Andrews M, et al: Comfort and incidence of abnormal serum sodium, BUN, creatinine and osmolality in dehydration of terminal illness. Am J Hosp Palliat Care 15(2):77–84, 1998
19. Printz LA: Terminal dehydration, a compassionate treatment. Arch Intern Med 152(4):697–700, 1992
20. Dorner B, Gallagher-Allred C, Deering CP, et al: The "to feed or not to feed" dilemma. J Am Diet Assoc 97(10 Suppl 2):S172–S176, 1997
21. La Puma J, Schiedermayer D, Siegler M: How ethics consultation can help resolve dilemmas about dying patients. West J Med 163(3):263–267, 1995
22. Heilicser BJ, Meltzer D, Siegler M: The effect of clinical medical ethics consultation on healthcare costs. J Clin Ethics 11(1):31–38, 2000

QUALITY OF LIFE

Background

As attention has shifted from purely life-saving technologies to those that improve patients' experiences, health care professionals are paying increased attention to the quality of life of their patients. Health-related quality of life (HRQOL) has become an increasingly important consideration in the treatment of patients. However, this field of research is relatively new, and there is insufficient evidence to support the issuance of practice guidelines for use of HRQOL tools in routine practice. There is also insufficient evidence to differentiate between various nutrition support interventions in specific therapeutic areas based solely on HRQOL information. This discussion will highlight the importance of HRQOL methodologies in refining and improving nutrition support therapies in the future.

HRQOL has been defined as "patients' appraisals of their current level of functioning and satisfaction with it compared with what they perceive to be ideal."[1] This definition incorporates "the impairments, functional states, perceptions, and social opportunities that are influenced by disease, injury, treatment, or policy."[2]

The purpose of HRQOL measurement is not to evaluate symptoms; rather it is used to describe the patient's subjective experience. As such it is critical to keep in mind that HRQOL should incorporate those aspects (often called domains) of their life that are affected by their health. In general, these domains include physical, psychological, social and spiritual components. A narrower subset of domains is typically assessed to focus on those domains likely to be influenced by the intervention of interest.

Nutrition intervention can affect a variety of domains, either by improving health status or through factors associated with treatment.[3–9] Physically, important domains may include physical functioning, activities of daily living, recreation, and fatigue. In the psychological/emotional area important domains include depression, anxiety/fear, body image, and independence. The social area may incorporate family and marital relationships, sexual life, and social interactions. Additional domains may well include financial status, appetite/eating/hunger, symptoms, and overall or general health.

A number of tools have been used to assess HRQOL. These can be divided into two groups: generic HRQOL measures, which are designed to be used across a wide range of diseases, and disease-targeted measures, which are developed to focus on a specific disease. Generic measures are often less sensitive than disease-targeted measures, but have the advantage that they can be used to make comparisons across a number of diseases. Examples of generic measures that have been used for patients receiving nutrition therapy include: the Short Form-36 (SF-36), the EuroQol EQ-5D, the Profile of Mood States, the Nottingham Health Profile, the Quality of Well-Being scale, the Sickness Impact Profile (SIP), Rosenberg's Self Esteem scale, the Norton scale, and the Barthel Activities of Daily Living Index. Disease-targeted measures have included: the QOL for liver transplants, the Inflammatory Bowel Disorder QOL form (IBDQOL), and the European Organization for Research and Treatment of Cancer (EORTC) core questionnaire, along with the head and neck and the esophageal modules of the EORTC.

Evidence

HRQOL research in nutrition support is still in its infancy. Currently HRQOL investigations do not lead to any solid conclusions. There are, however, two areas of research where HRQOL methods have shed some light. First, using cross-sectional HRQOL data (observations for multiple patients at a single point in time), researchers have shown that patients requiring nutrition support have worse HRQOL compared with those not requiring support. Second, longitudinal HRQOL data (observations for each patient at multiple points in time) show that SNS generally leads to improved HRQOL.

More specifically, cross-sectional data analysis shows that (1) patients receiving HPN are worse off than the normal population and have a HRQOL comparable or worse than those with chronic renal failure treated by dialysis[10–15]; (2) patients receiving HPN may be worse off than patients with anatomical or functional short bowel disease not receiving HPN[16,17]; (3) opiate-dependent patients are worse off than non–opiate-dependent patients receiving HPN[18]; and (4) caregivers of patients on long-term HPN have lower HRQOL.[10]

HRQOL improvements related to nutrition support show by longitudinal evaluations that (1) nutrition support may provide HRQOL improvement, although the burden of invasive support may be associated with some decline in psychosocial domains[19–24]; (2) patients with weight in the less-than-desirable range experience HRQOL improvements with HPN, whereas patients with weight in the desirable range do not[25]; (3) patients who receive an intestinal transplant experience better HRQOL than those receiving HPN[16,17]; and (4) an oral, semi-elemental diet provides better HRQOL outcomes than TPN in AIDs patients.[26]

Special Considerations

In an ideal academic environment, one would develop a disease- or nutrition-specific HRQOL tool and then validate it in the appropriate patient population. The time and resources necessary for this approach in each and every disease state is generally not available. In our resource-constrained environment, researchers may be best served by using a modular approach in which the core HRQOL measure remains the same and only disease-specific components change for the specific disease of interest. The core may consist of a generic measure and a nutrition-targeted component. The generic measure is useful for making comparisons across populations and to evaluate unpredicted HRQOL effects. The nutrition-targeted component includes those domains not assessed by the generic measure and would focus on nutrition-specific effects such as fatigue, body image, and symptoms. The nutrition-targeted component can consist of scales from existing measures (for example, the fatigue scale from the Functional Assessment of Cancer Therapy (FACT) and the sexual function scale from the Medical Outcomes Study).

In addition to the core HRQOL measure, researchers may include a disease-targeted measure. Such tools focus on the specific disease (ie, cancer, inflammatory bowel disease, AIDs, etc). Examples of disease-targeted measures include the EORTC (with appropriate modules), the FACT, and the IBDQOL.

Practice Guidelines
Quality of Life

1. The subjective patient experience receiving SNS should be measured with an HRQOL tool. (B)
2. A nutrition support HRQOL tool should include generic and disease targeted measures for either cross-section and/or longitudinal observations. (C)

REFERENCES

1. Cella DF, Tulsky DS: Measuring quality of life today: Methodological aspects. Oncology 5:29–38, 1990
2. Patrick DL, Erickson P: Health Status and Health policy: Quality of life in Health Care Evaluation and Resource Allocation. Oxford University Press, New York, 1993
3. Detsky AS, McLaughlin JR, Abrams HB, et al: Quality of life of patients on long term total parenteral nutrition at home. J Gen Intern Med 1:26–33, 1986
4. Herfindal ET, Bernstein LR, Kudzia K, et al: Survey of home nutritional support patients. JPEN 13:255–261, 1989
5. Malone M: Quality of life of patients receiving home parenteral or enteral nutrition support. PharmacoEconomics 5(2):101–108, 1994
6. Maunder RG, Cohen Z, McLeod RS, et al: Effect of intervention in inflammatory bowel disease on health-related quality of life: A critical review. Qual Life IBD Treat 38(11):1147–1161, 1995
7. Grindel CG, Whitmer K, Barsevick A: Quality of life and nutritional support in patients with cancer. Cancer Pract 4(2): 81–87, 1996
8. Kotler DP: Management of nutritional alterations and issues concerning quality of life. J Acquir Immune Defic Synd Human Retrovirol 16(Suppl 11):S30–S35, 1997
9. Richards DM, Irving MH: Cost-utility analysis of home parenteral nutrition. Br J Surg 83:1226–1229, 1996
10. Smith CE: Quality of life in long-term total parenteral nutrition patients and their family caregivers. JPEN 17(6): 501–506, 1993
11. Carlson GL, Maguire G, Williams N, et al: Quality of life on home parenteral nutrition: A single centre study of 37 patients. Clin Nutr 14:219–228, 1995
12. Richards DM, Irving MH: Assessing the quality of life on patients with intestinal failure on home parenteral nutrition. Gut 40:218–222, 1997
13. Reddy P, Malone M. Cost and outcome analysis of home parenteral and enteral nutrition. JPEN 22(5):302–310, 1998
14. Jeppesen PB, Langholz E, Mortensen PB: Quality of life in patients receiving home parenteral nutrition. Gut 44:844–852, 1999
15. Schneider SM, Pouget I, Staccini P, et al: Quality of life in long-term home enteral nutrition patients. Clin Nutr 19(1):23–28, 2000
16. Rovera GM, DiMartini A, Schoen RE, et al: Quality of life of patients after intestinal transplantation. Transplantation 66(9): 1141–1145, 1998
17. DiMartini A, Rovera GM, Graham TO, et al: Quality of life after small intestinal transplantation and among home parenteral nutrition patients. JPEN 22(6):357–362, 1998
18. Richards DM, Scott NA, Shaffer JL, et al: Opiate and Sedative Dependence Predicts a Poor Outcome for patients Receiving Home Parenteral Nutrition: JPEN 21(6): 336–338, 1997
19. King LA, Carson LF, Konstantinides RN, et al: Outcome assessment of home parenteral nutrition in patients with gynecologic malignancies: What have we learned in a decade of experience? Gynecol Oncol 53:377–382, 1993

20. Siskind MS, Lien Y-HH: Effect of intradialytic parenteral nutrition on quality of life in hemodialysis patients. Int J Artifical Organs 16(8):599–603, 1993
21. Edwards MW, Drexler AM, Aboulafia DM, et al: Efficacy of total parenteral nutrition in a series of end-stage AIDS patients: A case-control study. AIDS Patient Care STDs 11(5):323–329, 1997
22. Torelli GF, Campos AC, Meguid MM: Use of TPN in terminally ill cancer patients. Nutrition 15(9):665–667, 1999
23. Beattie AH, Prach AT, Baxter JP, et al: A randomised controlled trial evaluating the use of enteral nutritional supplements postoperatively in malnourished surgical patients. Gut 46:813–818, 2000
24. Roberge C, Tran M, Massoud C, et al: Quality of life and home enteral tube feeding: A French prospective study in patients with head and neck or oesophageal cancer. Br J Cancer 82(2): 263–269, 2000
25. Jamieson CP, Norton B, Lakeman M, et al: The quantitative effect of nutrition support on quality of life in outpatients. Clin Nutr 16:25–28, 1997
26. Kotler DP, Fogleman L, Tierney AR: Comparison of total parenteral nutrition and an oral, semielemental diet on body composition, physical function, and nutrition-related costs in patients with malabsorption due to acquired immunodeficiency syndrome. JPEN 22(3):120–126, 1998

SECTION XI: Specific Guidelines for Disease—Adults

CARDIAC DISEASE

Background

Cardiac cachexia is a syndrome of severe malnutrition that occurs in a minority of patients with New York Heart Association class III or IV congestive heart failure (CHF). It involves depletion of lean body mass (including vital organs such as the heart) leading to declines in performance status and immune function. Presence of cachexia is associated with decreased survival in patients with congestive heart failure. A classic description of cardiac cachexia was published by Pittman and Cohen in 1964.[1]

The cause of cardiac cachexia is multifactorial.[2] The fatigue seen in CHF patients leads to decreased physical activity that in turn leads to decreased lean body mass. Anorexia is a common finding and may be related to drug therapy, bowel edema leading to gastrointestinal hypomotility and nausea, and restriction to a bland, low-sodium diet. The bowel edema may also result in nutrient malabsorption in the intestine. Dyspnea may lead to increases in resting energy expenditure in this population. Increase in energy expenditure may also be related to the compensatory activation of the sympathetic nervous system.

Recent research has focused on the role of cytokines in the pathogenesis of cardiac cachexia.[3] In particular, elevated circulating levels of tumor necrosis factor-alpha (TNF) have been demonstrated in patients with severe CHF, especially in those with cachexia. Although elevation of TNF might initially have a beneficial effect by accelerating catabolism of muscle tissue to provide substrates for a hepatic acute-phase response, continued elevation leading to continued loss of lean body mass is deleterious.

Postoperative open heart surgery patients with complications are another population with potential need for nutritional support.[4] In one study, 5% of patients undergoing cardiopulmonary bypass (CPB) developed postoperative complications necessitating PN.[5] Only a minority of open heart surgery patients will demonstrate the frank cardiac cachexia of congestive heart failure described above.

Evidence

A correlation between preoperative malnutrition and increased postoperative morbidity (such as infectious complications, respiratory failure, pneumonia, arrhythmias, and renal failure) and mortality has been shown in some although not all studies in cardiac surgery patients. Abel et al,[6] in 100 consecutive adults undergoing cardiac surgery, found no strong correlations between anthropometric or biochemical measurements of malnutrition or decreased cell-mediated immunity and postoperative morbidity and mortality. They did point out, however, that most of their patients had arteriosclerotic disease and were not at high risk for cachexia. They concluded that routine nutrition assessment is of little value in management of these patients. In a more recent study, Ulicny et al prospectively examined 221 adult cardiac surgery patients.[7] They found no significant correlations between visceral protein status, acute phase protein response, or delayed hypersensitivity reaction and development of sternal wound infection. Again, however, most of their patients had normal preoperative nutrition status.

Several recent studies have identified a correlation between blood glucose control and incidence of postoperative infectious complications, especially sternal wound infections. In addition, Babineau et al[5] demonstrated a higher prevalence of diabetes and hyperglycemia in patients requiring PN after CPB compared with CPB patients not requiring PN. Other authors have suggested that a prolonged time to enteral alimentation after coronary bypass grafting is a risk factor for the development of postoperative infections.[8]

The objectives for nutrition management of patients with chronic congestive heart failure include reduction in the workload of the heart, maintenance of dry weight, and maintenance of optimal nutrition status.[9] General nutrition intervention includes sodium and fluid management. Although sodium and fluid restriction are often necessary, each situation must be assessed individually. For example, a sodium depletion syndrome may sometimes occur, especially in elderly patients put on strict sodium restriction. In addition, supplementation of magnesium and potassium may be necessary in patients receiving diuretics.

Although theoretically SNS might be useful in achieving and maintaining better nutrition status in patients with cardiac cachexia, clinical trial data supporting this hypothesis are scarce. Heymsfield and Casper studied continuous nasogastric feeding to promote accrual of lean body mass in undernourished patients with moderate to severe CHF.[10] Over a

2-week period, patients had a net loss of extracellular fluid with a gain in lean body mass; cardiac function was unchanged.

Paccagnella et al studied the effects of nutrition support pre- and postoperatively in six patients with malnutrition secondary to severe mitral valve disease and congestive heart failure.[11] Four of the patients received oral food plus PN for 2 weeks preoperatively and for 3 weeks postoperatively, whereas two of the patients only received the PN postoperatively. Hemodynamic function, oxygen consumption, and carbon dioxide production were not adversely affected by the PN. Visceral protein levels were improved in these patients at week 2 or 3 postoperatively compared with 2 weeks preoperatively. Other clinical findings included a decrease in anorexia and proteinuria over the study period. The authors concluded that nutrition support could be safely given to such patients and that such support improves clinical status.

In an early study of the effect of nutrition support in malnourished patients on outcome after cardiac surgery, Abel et al gave PN containing approximately 1000 kcal and 5 g nitrogen per day to 20 patients for 5 days immediately postoperatively.[12] There was no effect on morbidity and mortality in comparison to malnourished and nonmalnourished controls not receiving PN. The malnourished patients in this study were truly depleted, having a weight loss of at least 4.5 kg over 12 months, a body weight less than 85% of ideal, or giving a clinical impression of malnutrition on the basis of physical examination.

In a more recent study, Otaki studied 25 patients with New York Heart Association Class IV heart failure with body weights less than 80% of ideal.[13] Eighteen of the patients were given 5 to 8 weeks of preoperative PN containing 1000 kcal and 6 g nitrogen daily. The other 7 patients were not given preoperative PN. Patients receiving PN had a mortality rate of 17% compared with 57% for those without PN. Patients with preoperative nutrition support also had significant decreases in the incidence of postoperative respiratory failure.

Special Considerations

Nutrition assessment of the patient with cardiac cachexia may be challenging. Excess extracellular fluid as well as malnutrition may contribute to decreases in visceral protein markers such as albumin and transferrin. Although total body weight may be decreased when compared with premorbid body weight, the excessive extracellular fluid may mask weight loss. An entire spectrum of malnutrition occurs in patients with chronic congestive heart failure; on one end of the spectrum are the classic cases of cardiac cachexia with severe loss of lean body mass, whereas other cases are less pronounced. A loss of greater than 10% of lean body mass has been used to define cardiac cachexia; unfortunately, in the clinical setting a good estimation of loss of lean body mass may be very difficult to determine. This definition is felt to be helpful, however, because at this level reduced immune function can generally be documented.[2]

In the post-CPB patient requiring SNS, pancreatitis may develop. Babineau and colleagues reported a mild form of pancreatitis characterized by hyperlipasemia and early intolerance to EN into the stomach or duodenum in post-CPB patients.[14] The incidence of symptomatic hyperlipasemia was 1.3%. Although these authors did not recommend avoidance of enteral feeding in the critically ill patient post CPB, they did recommend caution with monitoring of the serum lipase and consideration of feeding distal to the ligament of Treitz.

Patients requiring PN after cardiac surgery have been shown to have a higher prevalence of volume overload, hyponatremia, metabolic alkalosis, and uremia compared with similar patients not requiring PN. These factors should be taken into account when formulating SNS for this population. For example, use of concentrated stock solutions to decrease fluid load and decrease the acetate to chloride ratio in the solution should be considered.

A serious but potentially fatal rare complication of early jejunal feeding after surgery in trauma patients is bowel necrosis. Some research indicates that decreased mesenteric blood flow is a risk factor for development of this complication,[15] although another series of case reports does not corroborate these findings.[16] Because of the potential for this serious complication, many clinicians are hesitant to initiate jejunal feedings in a patient who is hemodynamically unstable and thus may not have good blood flow to the gastrointestinal tract. Although this issue has not been studied specifically in the cardiac surgery population, a prudent approach would be to delay jejunal feedings until the patient is hemodynamically stable and to monitor closely for abdominal distention after initiation of tube feedings.

Practice Guidelines *Cardiac Disease*

1. Patients with cardiac cachexia or who develop complications after CPB are at nutrition risk, and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. The use of PN should be reserved for those cardiac patients having postoperative complications that preclude use of the gastrointestinal tract. (C)
3. In the cardiac surgery patient, EN should be deferred until the patient is hemodynamically stable. (C)

REFERENCES

1. Pittman JG, Cohen P: The pathogenesis of cardiac cachexia. N Engl J Med 271:403–409, 1964
2. Freeman LM, Roubenoff R: The nutrition implications of cardiac cachexia. Nutr Rev 52:340–347, 1994
3. Anker SD, Coats AJS: Cardiac cachexia. A syndrome with impaired survival and immune and neuroendocrine activation. Chest 115:836–847, 1999
4. Ulicny KS, Hiratzka LF: Nutrition and the cardiac surgical patient. Chest 101:836–842, 1992

5. Babineau TJ, Bollinger WS, Forse RA, et al: Nutrition support for patients after cardiopulmonary bypass: required modifications of the TPN solution. Ann Surg 228:701–706, 1998
6. Abel RM, Fisch D, Horowitz J, et al: Should nutritional status be assessed routinely prior to cardiac operation? J Thorac Cardiovasc Surg 85:752–757, 1983
7. Ulicny KS: Sternotomy infection: poor prediction by acute phase response and delayed hypersensitivity. Ann Thor Surg 50:949–958, 1990
8. Ford EG, Baisden CE, Matteson ML, et al: Sepsis after coronary bypass grafting: Evidence for loss of the gut mucosal barrier. Ann Thor Surg 52:514–517, 1991
9. Hughes C, Kostka P: Chronic congestive heart failure. IN Modern Nutrition in Health and Disease, 9th ed. Shils ME, Olson JA, Shike M, et al (eds). Williams and Wilkins, Philadelphia, 1999, pp 1229–1234
10. Heymsfield SB, Casper K: Congestive heart failure: Clinical management by use of continuous nasoenteric feeding. Am J Clin Nutr 50:539–544, 1989
11. Paccagnella A, Calo MA, Caenaro G, et al: Cardiac cachexia: Preoperative and postoperative nutrition management. JPEN 18:409–416, 1994
12. Abel RM, Fischer JE, Buckley MJ, et al: Malnutrition in cardiac surgical patients: Results of a prospective, randomized evaluation of early postoperative parenteral nutrition. Arch Surg 111: 45–50, 1976
13. Otaki M: Surgical treatment of patients with cardiac cachexia—An analysis of factors affecting operative mortality. Chest 105:1347–1351, 1994
14. Babineau TJ, Hernandez E, Forse RA, et al: Symptomatic hyperlipasemia after cardiopulmonary bypass: implications for enteral nutritional support. Nutrition 9:237–239, 1993
15. Smith-Choban P, Max MH: Feeding jejunostomy: a small bowel stress test? Am J Surg 155:112–117, 1988
16. Schunn DCG, Daly JM: Small bowel necrosis associated with postoperative jejunal tube feeding. J Am Coll Surg 180:410–416, 1995

PULMONARY DISEASE

Background

Nutrition and pulmonary disease are closely related. Alterations in nutrition status will have an impact on pulmonary function and conversely, pulmonary function can alter nutrition status. Pulmonary disease as presented here will address chronic obstructive pulmonary disease (COPD) and acute respiratory distress syndrome (ARDS)

COPD is an obstructive airway disease limiting airflow which occurs either by destruction of alveoli (emphysema), by a narrowing of small airways (chronic bronchitis), or from a combination of both processes. Patients with COPD frequently demonstrate clinical sequalae of both emphysema and chronic bronchitis.

Malnutrition in COPD is common. The incidence of altered nutrition status ranges from 19% to 74%, with a greater incidence in hospitalized patients with acute respiratory failure.[1,2] Decreases in albumin, transferrin, and prealbumin concentrations occur in COPD patients with acute respiratory failure.[2] Weight loss occurs frequently in COPD. Weight loss is caused by increased resting energy expenditure, reduced nutrient intake, and inefficient fuel metabolism.[1] Weight loss is known to occur in up to 50% of COPD patients who require hospitalization and is an independent predictor of mortality. Loss of both fat mass and fat-free mass occur, with the depletion of fat-free mass carrying functional implications.[1,3]

Malnutrition in COPD adversely affects pulmonary function. Respiratory muscle strength is impaired in malnourished COPD patients.[4] Both ventilatory drive and the response to hypoxia are decreased in malnourished COPD patients.[5] Alteration in immune function occurs in malnourished COPD patients and may influence the frequency and severity of pulmonary infections.[3,5]

Nutrition assessment in patents with COPD is necessary to identify those with a higher risk of an adverse outcome. A thorough nutrition history, including evaluation of weight history, nutrient intake, and medication usage will help to develop nutrition goals.[3] Nutrition assessment via a multiparameter approach has been shown to be useful in identifying malnutrition in the COPD patient with acute respiratory failure.[2]

ARDS is characterized by severe hypoxemia, diffuse pulmonary infiltrates, and reduced pulmonary compliance. The degree of hypoxemia is defined by the ratio of arterial oxygen concentration to fractional inspired oxygen (PaO_2/FiO_2) with a ratio equal to or less than 200 diagnostic for ARDS. The etiology of ARDS is multifactorial with sepsis being the predominant underlying cause.[6] Inflammatory mediators, including prostaglandins and leukotrienes derived from arachidonic acid metabolism, are implicated in acute lung injury.[7]

Critical illness can result in altered nutrition status secondary to the inflammatory response. Marked protein catabolism in the absence of exogenous intake can result in respiratory muscle impairment and decreased visceral proteins, factors that may be obstacles to weaning ventilatory support.[8]

Evidence

The strong association between nutrition and lung function has been appreciated for many years. In fact, it is often stated that, "death from starvation is death from pneumonia." It is clear that patients with protein-calorie malnutrition have an increased incidence of pneumonia, respiratory failure, and ARDS.[8] At the same time, many patients with COPD have unintentional weight loss.

SNS is used frequently in patients with COPD, acute respiratory failure, and ARDS. Unless other clinical conditions or complications are present, patients with COPD can improve their nutritional status with oral supplements or enteral tube feeding. Patients with acute respiratory failure or ARDS rarely meet their nutritional needs orally so they often receive EN or, in cases where the gastrointestinal tract is not functional or accessible, PN.

Nutrition assessment in pulmonary disease is challenging.[9] In COPD, overfeeding with resultant production of excess carbon dioxide is the primary concern. A number of disease specific predictive formulas have been developed to estimate energy requirements in these patients, but none has been clinically validated.[9] Indirect calorimetry has also been advocated, but is not of proven benefit.[10] The situation is similar in patients with ARDS; predictive equations exist and indirect calorimetry is advocated, but there is no proven optimal approach to nutrition assessment or estimation of caloric requirements.[9,10]

Each of the macronutrients used in SNS has an individual respiratory quotient (RQ) when metabolized

for energy. RQ is determined by dividing the CO_2 produced by the O_2 consumed metabolizing the substrate. The individual RQs for glucose, protein, and fat oxidation are approximately 1.0, 0.8, and 0.7, respectively. The lower RQ for fat oxidation has created interest in using it as a major energy component in patients where excessive CO_2 production is undesirable. Decreased CO_2 production and a lower RQ have been demonstrated when patients have 50% of nonprotein calories provided as lipid compared with 100% glucose in an overfed state. However, when total calories are provided in moderate amounts (eg, 30% above basal energy expenditure), manipulation of the macronutrients has little effect on CO_2 production, minute ventilation, and presumably RQ.[11–14] The production of excessive CO_2 secondary to nutrition support occurs when patients are overfed (eg, two times basal energy expenditure in patients with uncomplicated respiratory failure).[11]

Most patients with acute respiratory failure and many with ARDS can receive EN because their gastrointestinal tract is accessible and functional. Several EN products were developed with a high-fat, low-carbohydrate composition because of the theoretical advantage of the lower CO_2 production from fat oxidation. Controlled trials in stable outpatients with COPD have demonstrated decreased CO_2 production, O_2 consumption, and RQ in patients receiving a high-fat enteral formula compared with a high-carbohydrate enteral formula; however, the data do not demonstrate improved clinical outcomes.[15,16] Patients with acute respiratory failure who received high-fat EN also have demonstrated decreased CO_2 production and RQ when compared with those receiving a high-carbohydrate enteral formulation. One study of high fat EN did show significant reductions in both $PaCo_2$ before extubation and time receiving mechanical ventilation, although the sample size was quite small.[17]

Because ARDS is associated with elaboration of inflammatory cytokines such as interleukin-1, interleukin-6, and interleukin-8, nutrition formulations have been developed containing fatty acids that can potentially downregulate the inflammatory response. One study compared the use of a high-fat enteral formulation supplemented with n-3 fatty acids (fish oil and borage oil) and antioxidants with a standard high-fat enteral formulation. The patients receiving this immune-modulating enteral formula spent less time receiving mechanical ventilation, less time in the intensive care unit, and a decreased incidence of organ failure.[7]

Special Considerations

Patients with COPD often have accompanying weight loss. Although decreased nutrient intake secondary to the work of breathing had long been suspected as the primary cause of this weight loss, it is now clear that weight-losing COPD patients are hypermetabolic.[18] This demonstrates a poor adaptive response to weight loss. Most patients with other disease states will demonstrate a decrease in resting energy expenditure after weight loss.

Moderate doses of each of the macronutrients appear to be optimal when providing SNS to patients with pulmonary disorders.[11] Both glucose and protein administration have been shown to stimulate ventilatory drive independently after a period of semi-starvation. However, excessive glucose administration (>5mg/kg per minute) clearly increases CO_2 production to levels making it difficult to wean patients from mechanical ventilation. Excessive protein administration theoretically could stimulate ventilatory drive to the point of patient fatigue. Rapid administration of intravenous lipid (3 mg/kg per minute) may cause significant increases in pulmonary vascular resistance in patients with ARDS.[19]

Fluid accumulation and pulmonary edema in patients with ARDS are associated with a poor clinical outcome.[20] Therefore, it is prudent to use a fluid-restricted nutrient formulation in patients whose hemodynamic status necessitates fluid restriction.

Phosphate is essential for the synthesis of ATP and 2,3 DPG, both of which are critical for optimal pulmonary function. Normal diaphragmatic contractility is dependent on adequate provision of phosphate. Therefore, particular attention to phosphate balance is necessary in the patient with underlying pulmonary disease or acute respiratory failure. Length of hospital stay and time receiving mechanical ventilation is increased in critically ill patients who become hypophosphatemic when compared with those patients who do not develop this metabolic complication.[21] Phosphate replacement in patients with hypophosphatemia receiving SNS is crucial.[22]

Practice Guidelines *Pulmonary Disease*

1. Patients with COPD or ARDS are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Energy intake should be kept at or below estimated needs in patients with pulmonary disease and demonstrated carbon dioxide retention. (B)
3. Routine use of modified carbohydrate and fat nutrition formulations in patients with pulmonary disease is not warranted. (B)
4. Provision of a modified enteral formulation containing n-3 fatty acids may be beneficial in the patient with early ARDS. (B)
5. A fluid-restricted nutrient formulation should be used in patients with ARDS whose hemodynamic status necessitates fluid restriction. (B)
6. Serum phosphate levels should be monitored closely in patients with pulmonary disease. (B)

REFERENCES

1. Congleton J: The pulmonary cachexia syndrome: aspects of energy balance. Proc Nutr Soc 58:321–328, 1999
2. Laaban JP, Kouchakji B, Dore MF, et al: Nutritional status of patients with chronic obstructive pulmonary disease and acute respiratory failure. Chest 103:1362–1368, 1993

3. Donahoe M: Nutritional aspects of lung disease. Resp Care Clin NA 4(1):85–111, 1998
4. Gosker HR, Wouters E, van der Vusse G, et al: Skeletal muscle dysfunction in chronic obstructive pulmonary disease and chronic heart failure: Underlying mechanisms and therapy perspectives. Am J Clin Nutr 71:1033–1047, 2000
5. Pingleton SK: Enteral nutrition in patients with respiratory disease. Eur Respir J 9:364–370, 1996
6. Bernard GR, Artigan A, Brigham KL, et al: The American-European Consensus Conference on ARDS: Definitions, mechanisms, relevant outcomes and clinical trial coordination. Am J Resp Crit Care Med 149:818–824, 1994
7. Gadek J, DeMichele S, Karlstad M, et al: Specialized enteral nutrition improves clinical outcomes in patients with or at risk or acute respiratory distress syndrome: a prospective, blinded, randomized, controlled multicenter trial. Crit Care Med 27:1409–1420, 1999
8. Radrizzani D, Iapichino G: Nutrition and lung function in the critically ill patient. Clin Nutr 17:7–10, 1998
9. Hogg J, Lapholz A, Reid-Hector J: Pulmonary disease. IN The Science and Practice of Nutrition Support. A Core Curriculum. Gottschlich MM (ed). Kendall/Hunt, Dubuque, IA, 2001, pp 491–516
10. Sherman MS: Parenteral nutrition and cardiopulmonary disease. IN Clinical Nutrition: Parenteral Nutrition. Rombeau JL, Rolandelli RH (eds). WB Saunders, Philadelphia, 2000, pp 335–352
11. Talpers SS, Romberger DJ, Bunce SB, et al: Nutritionally associated increased carbon dioxide production: excess total calories vs. high proportion of carbohydrate calories. Chest 102:551–555, 1992
12. Sullivan DJ, Marty TL, Barton RG: A case of overfeeding complicating the management of adult respiratory distress syndrome. Nutrition 11:375–378, 1995
13. Kiiski R, Takala J: Hypermetabolism and efficiency of CO_2 removal in acute respiratory failure. Chest 105; 1198–1203, 1994
14. Van den Berg B, Stam H: Metabolic and respiratory effects of enteral nutrition in patients during mechanical ventilation. Intensive Care Med 14:206–211, 1988
15. Kuo CD, Shiao GM, Lee JD: The effects of high fat and high carbohydrate diet loads on gas exchange and ventilation in COPD patients and normal subjects. Chest 104:189–196, 1993
16. Akrabawi SS, Mobarhan S, Stoltz RR, et al: Gastric emptying, pulmonary function, gas exchange, and respiratory quotient after feeding a moderate versus high fat enteral formula meal in chronic obstructive pulmonary disease patients. Nutrition 12:260–265, 1996
17. Al-Saady NM, Blackmore CM, Bennet ED: High fat, low carbohydrate enteral feeding lowers $PaCO_2$ and reduces the period of ventilation in artificially ventilated patients. Intensive Care Med 15:290–295, 1989
18. Schols AM, Soeters PB, Mostert R, et al: Energy balance in chronic obstructive pulmonary disease. Am Rev Respir Dis 143: 1248–1252, 1991
19. Venus B, Smith RA, Patel C, et al: Hemodynamic and gas exchange alterations during Intralipid infusion in patients with adult respiratory distress syndrome. Chest 95:1278–1281, 1989
20. Simmons RS, Berdine GG, Seidenfeld JJ, et al: Fluid balance and the adult respiratory distress syndrome. Am Rev Respir Dis 135:924–929, 1987
21. Marik PE, Bedigian MK: Refeeding hypophosphatemia in critically ill patients in an intensive care unit. Arch Surg 131:1043–1047, 1996
22. Clark CL, Sacks GS, Dickerson RN, et al: Treatment of hypophosphatemia in patients receiving specialized nutrition support using a graduated dosing scheme: Results from a prospective clinical trial. Crit Care Med 23:1504–1511, 1995

LIVER DISEASE

Background

Protein calorie malnutrition (PCM) and nutritional deficiencies are common in liver diseases, especially when severe hepatocellular dysfunction occurs, because the liver plays a pivotal role in the metabolism, storage, and distribution of nutrients. Liver disease can be divided into several categories that include duration (acute vs chronic), pathophysiology (hepatocellular vs cholestasic), and etiology (viral, alcohol, toxin, autoimmune). Cirrhosis occurs when chronic injury leads to irreversible scarring of the liver. Malnutrition has been most extensively studied in patients with end stage cirrhosis; a modest amount of information regarding nutrient status is available concerning patients with acute alcoholic hepatitis, cholestatic liver disease, and fulminant hepatic failure.

Mortality is increased when malnutrition occurs in patients with either acute or chronic liver diseases.[1,2] Assessment of PCM in the setting of liver disease is particularly difficult because many of the common nutrition assessment parameters (eg, serum albumin) are directly affected by hepatic dysfunction even in the absence of undernutrition. The assessed presence of PCM in liver disease patients reflects true malnutrition, severity of liver disease, or a combination of both. The presence of factors associated with PCM has been associated with a poor prognosis in patients awaiting liver transplantation, in cirrhosis with decompensation, and in cirrhotics undergoing abdominal surgery.[3–5] Preoperative malnutrition has also been associated with increased operative blood loss, longer intensive care unit length of stay, increased mortality, and higher total hospital charges after liver transplantation.[6] Whether PCM is an independent predictor of survival or just a reflection of the severity of liver disease remains controversial.[7]

The prevalence of PCM in patients with liver disease has been reported to range from 10% to 100%. This broad range reflects a variety of factors that include etiology, severity and type of liver disease, the methods used to perform the nutrition assessment, and the setting where these surveys were performed. PCM has been noted to be as low as 20% for patients with compensated alcoholic liver disease in the community and as high as 100% in hospitalized patients with acute alcoholic hepatitis.[8] More recent surveys report the prevalence of PCM to range from 27% to 87% in patients with cirrhosis.[9]

The pathophysiology of malnutrition in liver disease is complex and often includes multiple processes. Gastrointestinal symptoms which limit food intake are common and include anorexia, early satiety secondary to ascites, altered taste due to zinc and magnesium deficiency, nausea, and vomiting.[10] Dietary intake may also be limited through the prescription of protein and salt restricted diets. Fat malabsorption secondary to the diminished production of bile acids can occur in cholestatic liver disease or when pancreatic exocrine insufficiency accompanies alcoholic liver disease. Malabsorption can occur with drugs such as lactulose and neomycin or when severe portal hypertension leads to protein losing enteropathy.

Altered amino acid metabolism is a hallmark of liver disease, characterized by low levels of circulating branched-chain amino acid (BCAA; leucine, isoleucine and valine) and elevated levels of circulating aromatic

amino acids (AAA; phenylalanine, tyrosine, and tryptophan) and methionine. Endogenous leucine flux, an indicator of protein breakdown, and leucine oxidation are increased in the postabsorptive state, and whole body protein synthesis in response to a meal is attenuated.[11]

The metabolism of carbohydrate and fat is also altered in cirrhosis and can be characterized as a more rapid transition from the fed to the starved pattern of substrate use. After an overnight fast, patients with stable cirrhosis derive approximately 75% of their calories from fat, as opposed to only 35% for healthy controls.[12] One of the mechanisms responsible for this metabolic pattern is the presence of marked insulin resistance which occurs with cirrhosis.[13]

Increased nutritional requirements may occur acutely in cirrhosis (eg, due to ascites generation, spontaneous bacterial peritonitis, or variceal hemorrhage).[14] Muller et al, in a study of 123 stable patients with various stages and etiologies of liver disease, found that resting energy expenditure, when expressed per unit of lean body mass, was increased, normal or decreased in 18%, 51%, and 31% of the patients, respectively, when compared with noncirrhotic controls.[12] The degree of increased energy requirement correlated with diminished body cell mass but not with the etiology or duration of liver disease in this study. Biochemical parameters, such as bilirubin or albumin, were not predictive of hypercatabolism. Estimates of the caloric needs of patients with cirrhosis, when based on the Harris-Benedict equation, are frequently inaccurate, tending to underestimate the caloric needs of patients with cirrhosis by 15% to 18% when compared with measurement using indirect calorimetry.[15]

Nutrition assessment of patients with liver disease is difficult because many of the traditional indices of nutrition status are altered in liver disease independent of nutrition status (eg, serum albumin, prothrombin time, and ideal body weight). Although adverse outcomes are associated with the presence of one or more indices of malnutrition, no single nutrition parameter is able to consistently identify patients with cirrhosis who are likely to experience poor outcomes. A multivariate approach to nutrition assessment is recommended. The subjective global assessment (SGA) of nutrition status, modified for patients with cirrhosis, is a simple, reproducible and validated method that includes nutrition history, physical examination and simple anthropometrics.[16] In addition, because of the frequency of micronutrient deficiencies in this population, serum levels of zinc, vitamins A, D, E, and prothrombin time should also be periodically measured.

Evidence

Nutritional deficiencies are common among patients with compensated cirrhosis and ubiquitous in patients with decompensated liver disease. Although protein calorie malnutrition is often the most clinically apparent manifestation of malnutrition in this population, deficiencies of micronutrients, particularly of vitamins A, D, E, and K[17] and zinc,[18] are also prevalent.

Although there is overwhelming evidence that the incidence of complications of liver disease increases with malnutrition, the impact of nutrition therapy on outcomes in patients with liver disease varies with the indication.[19–23]

The multifactorial wasting condition that is so frequently encountered in patients with Child-Pugh-Turcotte class B and C cirrhosis may predispose to encephalopathy (skeletal muscle is the second largest site of ammonia metabolism) and other complications of liver disease. Fortunately, muscle wasting/negative nitrogen balance has been shown to be ameliorated by the administration of 1.0 g/kg per day of standard protein.[24] The preferential early utilization of fat and protein that occurs in patients with cirrhosis can be ameliorated by frequent feeding. A late evening meal has been shown to have a positive effect on nitrogen balance in patients with cirrhosis when compared with an equicaloric diet without a late evening meal.[25]

The particularly high prevalence of malnutrition among patients with alcoholic liver disease and the association of negative nitrogen balance with subsequent mortality has led to a relatively large number of clinical trials of nutrition therapies in this group. Despite initial promise, the aggregated evidence suggests that parenterally and/or enterally administered SNS (with or without branched-chain amino acid–enriched preparations) does not confer a medium or long-term survival benefit to patients with acute alcoholic hepatitis.[26] It is important to note, however, that patients with alcoholic hepatitis who do not achieve a positive nitrogen balance have very poor survival rates, although cause and effect have not been demonstrated. Administration of a nitrogen balance maintaining diet, using standard amino acid mixtures/food preparations, with concomitant replacement of potassium, phosphate, magnesium, and thiamine should be considered in patients hospitalized with alcoholic liver disease.

Even subclinical hepatic encephalopathy, present in approximately 75% of patients with cirrhosis, can attenuate quality of life and should be treated. Lactulose administration and replacement of zinc, when deficient, are almost always sufficient therapy. Protein restriction is rarely necessary in the short-term and never in the medium or long term. Branched-chain amino acid–enriched, aromatic amino acid–deficient nutrition supplements are the most extensively studied and utilized nutrition therapy in patients with liver disease.[27–29] This is based on the theory that higher levels of aromatic amino acids generate false neurotransmitters, promoting encephalopathy. Of the nine published randomized, controlled trials of the use of branched-chain amino acid–enriched formulas to treat hepatic encephalopathy, six demonstrated no benefit, two found improved morbidity but unaltered mortality, and the ninth found significant improvements in both mortality and response of encephalopathy. Thus there is no consensus concerning the use of branched-chain amino acid–enriched supplements in the treatment of acute hepatic encephalopathy. Conversely, these supplements appear to be of clear benefit to patients with cirrhosis who exhibit evidence of chronic hepatic encephalopathy and who are intolerant of standard protein sources.

For acute, overt hepatic encephalopathy, acute withdrawal of protein from the diet while precipitating causes of encephalopathy are sought, has been shown to be a cornerstone of therapy. The administration of a disaccharide, such as lactulose or lactitol, has been repeatedly demonstrated to be effective and safe therapy.[30] Zinc, deficiency of which is a near constant finding in patients with advanced stages of liver disease, may be supplemented empirically, as there is reasonable evidence that supplementation is associated with improvement in amino acid metabolism and clinical grade of encephalopathy.[31]

After successful reversal of hepatic encephalopathy, nitrogen balance–maintaining quantities of standard proteins should be reintroduced into the diet. In the unusual patient who is not able to tolerate at least 1.0 g/kg/per day of standard protein without becoming encephalopathic, despite optimal pharmacological therapy, nutritional supplementation with vegetable proteins and, if necessary, branched-chain amino acid–enriched formulas should be considered. Both of these agents have been shown to produce clinical improvement in chronic hepatic encephalopathy while allowing adequate amounts of protein to be consumed. Medium- and long-term protein restriction are contraindicated in patients with cirrhosis.

Special Considerations

Fulminant hepatic failure is associated with a 1- to 4-fold increase in the rate of protein catabolism, with a concomitant loss of capacity for ammonia removal.[32] In addition, glucose metabolism is greatly altered, a condition characterized by diminished insulin sensitivity, high levels of insulin and glucagon, and a tendency to develop hypoglycemia.[33] Unfortunately, the ideal method of preventing hypoglycemia and glucopenic brain injury has not been established. Certainly, blood glucose levels require frequent monitoring; continuous infusions of 10% to 20% dextrose should be initiated after the onset of hypoglycemia. Almost every other facet of nutrition therapy in the setting of fulminant hepatic failure is controversial. Although branched-chain amino acid–enriched and medium chain triglyceride–supplemented preparations offer theoretical advantages over standard amino acid and lipid preparations, the relative benefits of these nutrients in the support of patients with fulminant hepatic failure have not been formally studied in a randomized, controlled fashion. Intuitively, patients with fulminant hepatic failure who require prolonged hospitalization seem to merit nutrition support and are usually given it. Such support is, however, empiric in terms of composition and route.

Fan et al, in a large randomized, controlled study, demonstrated that patients undergoing resection of hepatocellular carcinoma who received 14 days of perioperative intravenous nutrition support in addition to their oral diet, experienced lower overall postoperative morbidity when compared with a control group not receiving SNS (34% *versus* 55%; relative risk, 0.66), predominantly because of fewer septic complications.[34] There was also a reduction in the requirement for diuretic agents to control ascites, less weight loss after hepatectomy, and less deterioration of liver function among patients receiving perioperative nutrition support. These benefits were seen predominantly in the patients with underlying cirrhosis who underwent major hepatectomy. Based on these results, perioperative nutrition support should be considered in patients undergoing liver resection for hepatocellular carcinoma associated with cirrhosis.

Practice Guidelines *Liver Disease*

1. Patients with liver disease are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Nutrition assessment in patients with liver disease should include screening for micronutrient deficiencies, including vitamins A, D, E, and K, and zinc. (B)
3. Patients with cirrhosis should divide their caloric intake into 4 to 6 meals per day, including a late evening snack. (B)
4. Protein restriction should be implemented for the acute management of overt hepatic encephalopathy. (A)
5. Protein restriction should not be implemented chronically in patients with liver disease. (B)
6. Use of branched-chain amino acid–enriched diets and SNS formulas is only indicated in chronic encephalopathy unresponsive to pharmacotherapy. (B)
7. Perioperative nutrition support should be used in patients undergoing liver resection for hepatocellular carcinoma associated with cirrhosis. (A)

REFERENCES

1. Abad-Lacruz A, Cabre E, Gonzalez-Huix F, et al: Routine tests of renal function, alcoholism, and nutrition improve the prognostic accuracy of Child-Pugh score in nonbleeding advanced cirrhotics. Am J Gastroenterol 88:382–387, 1993
2. Chedid A, Mendenhall CL, Gartside P, et al: Prognostic factors in alcoholic liver disease. VA Cooperative Study Group. Am J Gastroenterol 86:210–216, 1991
3. Madden AM, Bradbury W, Morgan MY: Taste perception in cirrhosis. Its relationship to circulating micronutrients and food preferences. Hepatology 26:40–48, 1997
4. Kalman DR, Saltzman JR: Nutrition status predicts survival in cirrhosis. Nutr Rev 54:217–219, 1996
5. Selberg O, Bottcher J, Tusch G, et al: Identification of high- and low-risk patients before liver transplantation. A perspective cohort study of nutritional and metabolic parameters in 150 patients. Hepatology 25:652–657, 1997
6. Ricci P, Therneau TM, Malinchoc M, et al: A prognostic model for the outcome of liver transplantation in patients with cholestatic liver disease. Hepatology 25:672–677, 1997
7. Merli M, Riggio O, Dally L: Does malnutrition affect survival in cirrhosis? PINC Hepatol 23:1041–1046, 1996
8. Morgan MY: Alcohol and nutrition. Br Med Bull 38:21–29, 1982
9. McCullough AJ, Bugianesi E: Protein calorie malnutrition and the etiology of cirrhosis. Am J Gastroenterol 92:734–738, 1997
10. Gloria L, Cravo M, Camilo ME, et al: Nutritional deficiencies in chronic alcoholics. Relation to dietary intake and alcohol consumption. Am J Gastroenterol 92:485–489, 1997
11. McCullough AJ, Mullen KD, Tavill AS, et al: In vivo differences between the turnover rates of leucine and leucine's ketoacid in stable cirrhosis. Gastroenterology 103:571–578, 1992

12. Muller MJ, Lautz HU, Plogmann B, et al: Energy expenditure and substrate oxidation in patients with cirrhosis. The impact of cause, clinical staging and nutritional state. Hepatology 15:782–794, 1992
13. Petrides AS, Groop LC, Riely CA, et al: Effect of physiologic hyperinsulinemia on glucose and lipid metabolism in cirrhosis. J Clin Invest 88:561–570, 1991
14. Charlton MR. Energy and protein metabolism in alcoholic liver disease. Clin Liver Dis 2:781–798, 1998
15. Shanbhogue RL, Bistrian BR, Jenkins RL, et al: Resting energy expenditure in patients with end-stage liver disease and in normal population [see comments]. JPEN 11:305–308, 1987
16. Hasse J, Strong S, Gorman MA, et al: Subjective global assessment. Alternative nutrition-assessment technique for liver-transplant candidates. Nutrition 9:339–343, 1993
17. DiCecco SR, Wieners EJ, Wiesner RH, et al: Assessment of nutritional status of patients with end-stage liver disease undergoing liver transplantation. Mayo Clin Proc 64:95–102, 1989
18. Bode JC, Hanisch P, Henning H, et al: Hepatic zinc content in patients with various stages of alcoholic liver disease and in patients with chronic active and chronic persistent hepatitis. Hepatology 8:1605–1609, 1988
19. Bienia R, Ratcliff S, Barbour GL, et al: Malnutrition and hospital prognosis in the alcoholic patient. JPEN 6:301–303, 1982
20. Garrison RN, Cryer HM, Howard DA, et al: Clarification of risk factors for abdominal operations in patients with hepatic cirrhosis. Ann Surg 199:648–655, 1984
21. Blendis LM, Harrison JE, Russell DM, et al: Effects of peritoneovenous shunting on body composition. Gastroenterology 90:127–134, 1986
22. Shaw BW Jr, Wood RP, Gordon RD, et al: Influence of selected patient variables and operative blood loss on six-month survival following liver transplantation. Semin Liver Dis 5:385–393, 1985
23. Goldberg S, Mendenhall C, Anderson S, et al: VA Cooperative Study on Alcoholic Hepatitis. IV. The significance of clinically mild alcoholic hepatitis—describing the population with minimal hyperbilirubinemia. Am J Gastroenterol 81:1029–1034, 1986
24. Gabuzda GJ, Shear L: Metabolism of dietary protein in hepatic cirrhosis. Nutritional and clinical considerations. Am J Clin Nutr 23:479–487, 1970
25. Swart GR, Zillikens MC, van Vuure JK, et al: Effect of a late evening meal on nitrogen balance in patients with cirrhosis of the liver. Br Med J 299:1202–1203, 1989
26. Fulton S, McCullough AJ: Treatment of alcoholic hepatitis. Clin Liver Dis 2:799–820, 1998
27. Marchesini G, Bianchi G, Rossi B, et al: Nutritional treatment with branched-chain amino acids in advanced liver cirrhosis. J Gatroenterol 35:S1–S12, 2000
28. Riordan SM, Williams R: Treatment of hepatic encephalopathy. N Engl J Med 337:473–479, 1997
29. Fabbri A, Magrini N, Bianchi G, et al: Overview of randomized clinical trials of oral branched-chain amino acid treatment in chronic hepatic encephalopathy. JPEN 20:159–164, 1996
30. Butterworth RF: Complications of cirrhosis III. Hepatic encephalopathy. J Hepatol 32:171–180, 2000
31. Marchesini G, Fabbri A, Bianchi G, et al: Zinc supplementation and amino acid-nitrogen metabolism in patients with advanced cirrhosis. Hepatology 23:1084–1092, 1996
32. O'Keefe SJ, Abraham RR, Davis M, et al: Protein turnover in acute and chronic liver disease. Acta Chir Scand 507(Suppl):91–101, 1981
33. Vilstrup H, Iversen J, Tygstrup N: Glucoregulation in acute liver failure. Eur J Clin Invest 16(3):193–197, 1986
34. Fan ST, Lo CM, Lai EC, et al: Perioperative nutrition support in patients undergoing hepatectomy for hepatocellular carcinoma. N Engl J Med 1994

PANCREATITIS

Background

Pancreatitis is a common disorder. The incidence of pancreatitis appears to be increasing. Biliary obstruction by gallstones accounts for about 45% of the cases of acute pancreatitis (AP) and alcohol is the cause in another 35%. The remaining 20% is divided between idiopathic and miscellaneous causes.[1] The inflammatory response associated with acute pancreatitis can lead to a spectrum of pancreatic injury that ranges from mild edema to necrosis. Significant ischemia of the gland predisposes to severe hemorrhage and necrosis, which in turn, predisposes to secondary infection.[2–4] The severity of the injury determines the prognosis and dictates the therapy.[5]

Chronic pancreatitis (CP) results in fibrosis and permanent glandular insufficiency while in AP pancreatic function nearly always returns to normal.[6] Prolonged heavy alcohol consumption is the most common cause of CP, whereas many of the other cases are due to cystic fibrosis or nutritional and inherited forms of the disease. Patients can present with abdominal pain, maldigestion, and diabetes mellitus. The diagnosis of CP is based on both radiographic and functional testing. Pancreatic enzyme concentrations in the blood are often normal.

Most patients with AP have a mild, self-limiting illness that resolves with several days of supportive therapy.[7,8] Depending on the cause, these patients are usually not malnourished and are able to eat within 5 to 7 days, so nutrition support is unnecessary.[9] The cumulative effects of repeated attacks of chronic relapsing pancreatitis can lead to malnutrition.[5] Pancreatitis can lead to hypocalcemia and hypomagnesemia, liver function abnormalities, and abnormalities of a number of other metabolic parameters. Approximately 5% to 15% of patients develop necrotizing pancreatitis that predisposes them to complications and can have a mortality rate of 5% to 20%.[8–12] This severe form of the disease induces a catabolic state similar to that seen in trauma and sepsis, resulting in rapid weight loss and increased morbidity and mortality.[13,14] Combinations of clinical and laboratory parameters such as those described by Ranson[10] and others[15] and by the APACHE II scoring system are used to determine the severity of pancreatitis and to assess prognosis.[16] Severe pancreatitis is characterized by the presence of three or more Ranson criteria or eight or more APACHE II points.[17] Estimating the severity of the pancreatitis is important to the assessment of the need for SNS. In patients with severe pancreatitis by Ranson criteria, measured energy expenditure has been shown to be as high as 50% greater than the resting energy expenditure as calculated by the modified Harris-Benedict equation.[18] The most accurate measurement of caloric requirements is with indirect calorimetry.

CP may result in malnutrition. Energy requirements in underweight patients with CP may be 15% to 30% above the expected range compared with the Harris-Benedict equation.[19,20] The cause of this is unknown. It has been suggested that moderate fat diets and pancreatic enzyme replacement be given when steatorrhea is present.[21] Low-fat diets, along with pancreatic enzymes, are advised if steatorrhea does not improve. Patients should abstain from alcohol when AP or CP are present. Deficiencies in vitamin A and E have been identified in CP.[22] Deficiencies in vitamin C, riboflavin, thiamin, and nicotinic acid have been shown in alcohol

induced CP.[23] Steatorrhea can lead to malabsorption of calcium, magnesium and zinc. Vitamin B-12 malabsorption is common, but deficiency is rare. Supplementation for these micronutrients should be undertaken when deficiency is present. Diabetes should be managed to control blood sugars. Pain management can improve oral intake.

SNS does not consistently limit disease activity in patients with pancreatitis and therefore cannot be considered as primary therapy. Nutrition support for patients with severe pancreatitis may prevent nutrient deficiencies and preserve lean body mass and functional capacity when nutrient intake falls below needs.[24,25] This distinction between nutrition support as primary therapy for the disease versus its value as an adjunct to primary therapy is essential. The rationale and criteria for using nutrition support in the setting of pancreatitis is similar to that for other diseases. It is used to treat malnutrition when present and to avoid the development of malnutrition resulting from insufficient energy intake in the face of increased energy needs.

Evidence

One of the major goals of the therapy of pancreatitis is to limit pancreatic secretion. This has led to the belief that bowel rest might be useful as a primary treatment for pancreatitis. Although bowel rest certainly decreases pain, there are no clinical trials that have shown that it decreases the morbidity or mortality of the disease.[26,27] The belief that pancreatic rest is beneficial probably explains why PN has been the usual method of nutrition support in pancreatitis.

PN does not stimulate pancreatic secretion.[28–30] Despite this potential benefit of PN, it is infrequently needed as an adjunct to the supportive treatment of pancreatitis. In patients with mild disease who will probably be able to eat within 7 days, it is unnecessary. In more severe pancreatitis when SNS is indicated, EN is less expensive, reduces the incidence of infection, and may preserve gut integrity and gut barrier and immune function.[31] It facilitates transitional feeding. If the GI tract is functioning normally, EN is well tolerated. The degree of pancreatic stimulation depends on the location of the feeding tube in the gastrointestinal tract and the composition of the feeding. Less stimulation occurs the more distally the EN is delivered.[32] The advantages of EN observed in patients with trauma and sepsis have led to its use in patients with AP.[33] Patients receiving EN have outcomes similar to those seen in patients receiving PN. EN is safe, effective, and less expensive than PN in patients with mild to moderate AP.[34,35]

In severe pancreatitis, patients fed an elemental formula via a nasojejunal feeding tube have significantly fewer septic events and fewer complications overall. Enteral feeding of a semi-elemental low triglyceride diet is safe and cheaper than PN.[34]

Patients with AP expected to resolve clinically over a period of 5 to 7 days likely do not require SNS. In patients who are unable to tolerate oral intake or who are anticipated to be undernourished for a prolonged period, SNS is appropriate. Enteral feeding should be attempted first in the minority of patients with pancreatitis who require SNS. If enteral feeding increases pain, ascites or fistulous output it should be discontinued. Patients with mild-to-moderate AP allowed an oral diet of clear liquids and nutritional supplements in addition to EN show improvement in markers of disease activity.[35] Nutrition needs can safely be provided by EN in patients with acute pancreatitis. Recent data confirm earlier studies that suggested feeding jejunostomies are safe and effective and that formulas low in fat are tolerated best. Patients given EN do better than those given PN.[36] PN should be reserved for those patients requiring SNS who are not able to tolerate EN.

Special Considerations

Pseudocysts, intestinal and pancreatic fistulae, pancreatic abscesses, and pancreatic ascites are known complications of acute pancreatitis that occur in up to 25% of patients.[1] Complications such as these can make enteral feeding impossible. PN should be used along with appropriate treatment for each or these complications. Bowel rest with PN can lead to clinical and radiographic improvement of pseudocysts, but PN-related complications, mostly catheter-related infections, makes the overall utility, as a primary treatment for pseudocysts, questionable.[37]

Case reports of lipid emulsions causing AP have raised some concern regarding lipid administration in patients with pancreatitis.[21] Fortunately, most patients tolerate glucose- and lipid-based formulas quite well.[38] Because hypertriglyceridemia-induced pancreatitis is rare unless serum concentrations exceed 1000 mg/dL, it is suggested that lipid emulsions be withheld from patients with triglyceride concentrations exceeding 400 mg/dL.[39] PN administration without lipid emulsions beyond 2 weeks is not advised because of the risk of development of essential fatty acid deficiency.

Practice Guidelines *Pancreatitis*

1. Patients with pancreatitis are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. SNS should not be used routinely in patients with mild to moderate acute pancreatitis. (B)
3. SNS should be used in patients with acute or chronic pancreatitis to prevent or to treat malnutrition when oral energy intake is anticipated to be inadequate for 5 to 7 days. (B)
4. EN is the preferred route of SNS in patients with pancreatitis and should be attempted before initiating PN. (A)
5. PN should be used in patients with pancreatitis if SNS is indicated and EN is not tolerated. (B)
6. Intravenous lipid emulsions are safe in acute pancreatitis provided triglyceride levels are monitored and remain below 400 mg/dL. (B)

REFERENCES

1. Steinberg W, Tenner S: Acute pancreatitis. N Engl J Med 330: 1198–1210, 1994
2. Klar E, Messmer K, Warshaw AL, et al: Pancreatic ischaemia in experimental acute pancreatitis: Mechanisms, significance and therapy. Br J Surg 77:1205–1210, 1990
3. Beger HG, Bittner R, Block S, et al: Bacterial contamination of pancreatic necrosis: a prospective clinical study. Gastroenterology 91:433–438, 1986
4. Gerzof SG, Banks PA, Robbins AH, et al: Early diagnosis of pancreatic infection by computed tomography-guided aspiration. Gastroenterology 93:1315–1320, 1987
5. Helton WS: Intravenous nutrition in patients with acute pancreatitis. IN Clinical Nutrition: Parenteral Nutrition. Rombeau JL, Caldwell MD (eds). WB Saunders, Philadelphia, 1993, pp 442–461
6. Banks PA: Acute and chronic pancreatitis. IN Gastrointestinal and Liver Disease. Feldman M, Scharschmidt BF, Sleisenger MH (eds). WB Saunders, Philadelphia, PA, 1998, pp 809–862
7. Levelle-Jones M, Neoptolemos JP: Recent advances in the treatment of acute pancreatitis. Surg Ann 22:235–261, 1990
8. Dammann HG, Dreyer M, Walter TA, et al: Prognostic indicators in acute pancreatitis: Clinical experience and limitations. IN Acute Pancreatitis. Beger HG, Buchler M (eds). Springer-Verlag, Berlin, Germany, 1987, pp 181–197
9. Sax HC, Warner BW, Talamini MA, et al: Early total parenteral nutrition in acute pancreatitis: Lack of beneficial effects. Am J Surg 153:117–124, 1987
10. Ranson JHC, Rifkind KM, Roses DM, et al: Prognostic signs and the role of operative management in acute pancreatitis. Surg Gynecol Obstet 139:69–81, 1974
11. Beger HG: Surgical management of necrotizing pancreatitis. Surg Clin N Am 69:529–549, 1989
12. Allardyce DB: Incidence of necrotizing pancreatitis and factors related to mortality. Am J Surg 154:295–299, 1987
13. Feller JH, Brown RA, Toussant GPM, et al: Changing methods in the treatment of severe pancreatitis. Am J Surg 127:196–201, 1974
14. Voitk A, Brown RA, Echave V, et al: Use of an elemental diet in the treatment of complicated pancreatitis. Am J Surg 125:223–227, 1973
15. Blaney SL, Imrie CW, O'Neil J, et al: Prognostic factors in acute pancreatitis. Gut 25:1340–1346, 1984
16. Knaus WA, Draper EA, Wagner DP, et al: APACHE II: a severity of disease classification system. Crit Care Med 13:818–829, 1985
17. Summary of the international symposium on acute pancreatitis. Atlanta, GA, September 11–13, 1992. Arch Surg 128:586–590, 1993
18. Bouffard YH, Delafosse BX, Annant GJ, et al: Energy expenditure during severe acute pancreatitis. JPEN 13:26–29, 1989
19. Dickerson RN, Vehe KL, Mullen JL, et al: Resting energy expenditure in patients with pancreatitis. Crit Care Med 19:484–490, 1991
20. Hebuterne X, Hastier P, Peroux JL, et al: Resting energy expenditure in patients with alcoholic chronic pancreatitis. Dig Dis Sci 41:533–539, 1996
21. Seidner DL, Fuhrman MT: Nutrition Support in Pancreatitis. IN The Science and Practice of Nutrition Support: A Case-Based Core Curriculum. Gottschlich MM (ed). American Society for Parenteral and Enteral Nutrition. Kendall-Hunt Publishing, Dubuque, IA, 2001, pp 553–574
22. Dutta SK, Bustin MP, Russell RM, et al: Deficiency of fat-soluble vitamins in treated patients with pancreatic insufficiency. Ann Intern Med 1982, 97:549–552
23. Van Gossum A, Closset P, Noel E, et al: Deficiency in antioxidant factors in patients with alcohol-related chronic pancreatitis. Dig Dis Sci 41:1225–1231, 1996
24. Grant JP, James S, Grabowski V, et al: Total parenteral nutrition in pancreatic disease. Ann Surg 200:627–631, 1984
25. Kudsk KA, Campbell SM, O'Brien T, et al: Postoperative jejunal feedings following complicated pancreatitis. Nutr Clin Pract 5:14–17, 1990
26. Ranson JHC: Acute pancreatitis: pathogenesis, outcome, and treatment. Clin Gastroenterol 13:843–863, 1984
27. Kirby DF, Craig RM: The value of intensive nutritional support in pancreatitis. JPEN 9:353–357, 1985
28. Konturek SJ, Tasler J, Cieszkowski M, et al: Intravenous amino acids and fat stimulate pancreatic secretion. Am J Physiol 236: E676–E684, 1979
29. Kelly GA, Nahrwold DL: Pancreatic secretion in response to an elemental diet and intravenous hyper-alimentation. Surg Gynecol Obstet 143:87–91, 1976
30. Edelman K, Valenzuela JE: Effect of intravenous lipid on human pancreatic secretion. Gastroenterology 85:1063–1066, 1983
31. Cerra FB, Benitez MR, Blackburn GL, et al: Applied nutrition in ICU patients: a consensus statement of the American College of Chest Physicians. Chest 111:769–78, 1997
32. Ragins H, Levenson SM, Singer R, et al: Intrajejunal administration of an elemental diet at neutral pH avoids pancreatic stimulation. Am J Surg 126:606–614, 1973
33. McClave SA, Greene LM, Snider HL, et al: Comparison of the safety of early enteral vs. parenteral nutrition in mild acute pancreatitis. JPEN 21:14–20, 1997
34. Kalfarentzos F, Kehagias J, Mead N, et al: Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial. Br J Surg 84:1665–1669, 1997
35. Windsor ACJ, Kanwar S, Li AGK, et al: Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. Gut 42:431–435, 1998
36. Pennington CR: Feeding the inflamed pancreas. Gut 42:315–316, 1998
37. Jackson MW, Schuman BM, Bowden TA, et al: The limited role of total parenteral nutrition in the management of pancreatic pseudocyst. Am Surg 59:736–739, 1993
38. Silberman H, Dixon NP, Eisenberg D: The safety and efficacy of a lipid-based system of parenteral nutrition in acute pancreatitis. Am J Gastroenterol 77:494–497, 1982
39. Adamkin DH, Gelke KN, Andrews BF: Fat emulsions and hypertriglyceridemia. JPEN 8:563–567, 1984

SHORT-BOWEL SYNDROME

Background

Short-bowel syndrome (SBS) occurs when a combination of loss of bowel due to resection and/or dysfunction of the remaining bowel reduces intestinal absorption such that fluid, electrolyte, macronutrient, mineral, and vitamin needs cannot be met through use of standard oral or enteral feedings.[1] This syndrome occurs most commonly after surgery for Crohn's disease and mesenteric infarction in adults. Symptoms of SBS include large volume diarrhea, thirst, and weight loss. Although malabsorption is primarily the result of a decrease in intestinal surface area, a decrease in intestinal transit time contributes to the pathophysiology of this condition. Both nutrient and fluid absorption are compromised.[2] The colon and ileocecal valve decrease intestinal transit time; however, in SBS both the colon and ileocecal valve may have been resected. The function of the residual proximal small bowel is also important for absorption. Iron and most water-soluble vitamins are absorbed in the proximal jejunum. Deficiencies are found in only the most severe cases of short bowel. The terminal ileum is where vitamin B-12 and bile salts are absorbed. When 100 cm or more of the terminal ileum has been resected, monthly B-12 injections are eventually required.[3] Bile salts are required for micellar solubilization of dietary fat and fat-soluble vitamins. After extensive ileal resections, bile salts are malabsorbed, resulting in significant fat and fat soluble vitamin malabsorption.

Complications of SBS include dehydration and weight loss from malabsorption of fluids and macronu-

trients (carbohydrate, fat, and protein); electrolyte, mineral, and trace element deficiencies; metabolic bone disease (osteoporosis and osteomalacia) from calcium and vitamin D malabsorption; cholelithiasis because of inadequate bile salt reserves[4]; and nephrolithiasis. Oxalate nephrolithiasis develops in the setting of steatorrhea and the presence of an intact colon. Dietary oxalate usually binds to calcium and is excreted in the stool as an insoluble complex. In SBS, oxalate remains in a free unbound form that is easily absorbed in the colon, because calcium has a greater affinity for unabsorbed fatty acids.[5] Patients with end-jejunostomies, on the other hand, are more prone to uric acid renal stones from recurrent episodes of dehydration.

Two other entities that can occur in the pathophysiology of short bowel are gastric acid hypersecretion and D-lactic acidosis. The acute acid hypersecretory state after intestinal resection is usually transient (3 to 6 months) and unrelated to the length of intestinal resection.[6] The increased gastrointestinal acid load inactivates normal digestive enzymes such as pancreatic lipase and deconjugates intraluminal bile salts, which further impairs fat and fat soluble vitamin absorption. D-lactic acid is produced by the fermentation of malabsorbed carbohydrates in the colon.[7] Humans lack the enzyme necessary to metabolize D-lactic acid. D-lactic acidosis should be suspected when there is unexplained metabolic acidosis in a patient with short bowel and colonic continuity. Management involves the use of carbohydrate-restricted diets.

After intestinal resection, the remaining intestine undergoes both structural and functional changes that increase nutrient and fluid absorption. These changes are collectively termed intestinal adaptation.[8] These changes begin to occur immediately after surgery and may continue for up to 2 years, or occasionally even longer. The process of intestinal adaptation is promoted by luminal nutrients. Besides having a direct trophic effect on the intestine, luminal nutrients stimulate both pancreatic and intestinal peptide secretion, which promotes growth and function of the residual intestine.[9]

Evidence

The immediate postoperative period after intestinal resection is characterized by significant fluid and electrolytes losses. Most patients require PN for 1 or more months after massive intestinal resection. Patients with less than 100 cm of small bowel distal to the ligament of Treitz and without a colon often require PN for an indefinite period. In contrast, 50 cm of small bowel may suffice for adequate oral nutrition after a period of adaptation if most of the colon is preserved.[10] During the initial adaptive phase, intravenous fluids and nutrients should be administered to match losses and maintain nitrogen balance. Hypersecretion of gastric acid during this phase can result in significant fluid loss and should be treated with intravenous H_2-receptor antagonists, which can be placed in the PN formulation.[11] If stool volume increases with oral intake, antidiarrheal agents should be used.[2] The goal is to keep stool losses less than approximately 2 L/d per day, if possible. Oral rehydration solutions, which contain approximately 90 mEq/kg per liter of sodium, can also be used to help maintain fluid and electrolyte homeostasis postoperatively.[12] During the transitional feeding period, the oral diet should be advanced slowly using small, frequent feedings of solid food. The PN is reduced gradually as oral intake increases and the diarrhea decreases. From this point forward the dietary management of the short bowel patient varies, depending on the presence or absence of a colon.

The colon is a very important digestive organ. It has the ability to absorb both fluid and electrolytes and has slower transit time in comparison with the small intestine. The colon also has the capability to salvage energy by converting complex carbohydrates to short-chain fatty acids through bacterial fermentation in the colonic flora.[13] Noordgard et al[14] compared an isocaloric diet of 60:20% or 20:60% carbohydrate to fat in eight short-bowel patients with colons and six patients with end-jejunostomies. Patients with colons fed a high-carbohydrate, low-fat diet had reduced loss of total calories compared with the low-carbohydrate, high-fat diet. In contrast, patients with end-jejunostomies excreted equal amounts of calories on the high- and low-carbohydrate diets. The study confirms the findings of previous studies that patients with end-jejunostomies do not require a high-carbohydrate diet.[15–16] With regard to the type of carbohydrate, complex carbohydrates are preferable to simple carbohydrates. Simple carbohydrates may result in significant osmotic diarrhea in patients with SBS and are not fermented to short-chain fatty acids. Marteau et al compared the tolerance of a diet providing 20 g/d of lactose to a lactose-free diet in 14 patients with SBS.[17] Eight patients had a colon and 6 patients had an end-jejunostomy. The presence of lactose did not cause symptoms of intolerance, nor worsening of diarrhea in either group. Patients with short bowel and colonic continuity should also be placed on a low-oxalate diet, especially if they are prone to oxalate nephrolithiasis or have high 24-hour urinary oxalate levels.[5]

Fat-soluble vitamins (vitamins A, D, K, E) should be monitored; these vitamins should be supplemented if deficient. Water-soluble vitamins can usually be replaced with a daily oral multivitamin because they are primarily absorbed in the proximal small intestine. Monthly injections of vitamin B-12 should be given when the terminal ileum has been resected.[3] In patients with continued weight, electrolyte, and fluid loss, PN is required even though some gut stimulation with oral or EN feedings is continued. The PN should provide macronutrients, vitamins, minerals, and trace elements in amounts sufficient to maintain normal growth, development, and lean body mass. As the intestine continues to adapt after resection, PN may be reduced or discontinued. Careful monitoring during this period of weight, fluid status, volume of diarrhea, and blood chemistries is essential.

Ambulatory patients with SBS absorb less (one-third to one-half less) calcium, magnesium, and zinc than normal individuals.[18] Net negative calcium balance occurs before osteopenia is detected by bone mineral density scans. Urinary magnesium falls before serum

Mg is low.[19] Patients with extensive small bowel resection requiring PN have even lower absorption of these divalent ions and require intravenous replacement.[20]

Treatment of ambulatory patients is usually successful with oral therapy. The preparations with the highest content of calcium and magnesium (calcium carbonate and magnesium oxide) are the least soluble and have the lowest available content of the elemental ions. Thus, their use balances large delivery [400 mg of calcium/g of calcium carbonate; 360 mg magnesium (15 mEq)/600 mg of magnesium oxide] against uncertain solubility and absorption. Other preparations of calcium include acetate, citrate, lactate, gluconate, glubionate, and phosphate salts. The carbonate salt is recommended for initial therapy. The diet should be supplemented with 800 mg of elemental calcium while following the 24 urinary calcium excretion to ensure that it is brought into the normal range. If this fails, other more soluble salts, such as citrate or glubionate, are used. Magnesium oxide can be used initially to add 360 to 720 mg of elemental magnesium, remembering that it can cause diarrhea. Other preparations include acetate, citrate, aspartate, hydroxide, lactate, and gluconate salts. The most soluble of these are the acetate, lactate, and gluconate forms; the latter is most readily available in the United States. The 500-mg tablet dose of magnesium gluconate contains only 29 mg of elemental magnesium, so the liquid preparation (54 mg/5 mL) is generally preferred.[21]

Special Considerations

PN in the setting of SBS is associated with complications, including catheter sepsis and liver disease.[22] To wean patients from the need for PN, methods of "intestinal rehabilitation" designed to increase the absorptive capacity of the remaining intestine have been studied. The combination of various trophic factors including glutamine, human recombinant growth hormone and a high-carbohydrate, low-fat diet was shown in an uncontrolled study of 8 patients with SBS to significantly increase water, electrolyte, and carbohydrate absorption after 3 weeks of administration.[23] The same authors expanded their study with an additional 31 patients using the same treatment regimen.[24] Forty percent of the treated patients were able to discontinue parenteral nutrition. Because the study was uncontrolled, it is not clear whether the glutamine, growth hormone, diet, or other factors contributed to the favorable outcome. There have since been two controlled studies using this same treatment in patients with SBS, which did not find positive effects using this specific treatment.[25,26]

Small bowel transplantation is also an option. Graft survival has progressively increased. Rejection of the graft and post transplant related lymphoma remaining the biggest challenges after small bowel transplantation.[27] Currently, the 5-year survival with PN is better than graft survival after small bowel transplantation.[22,27] Therefore, PN remains the treatment of choice in patients with SBS who can not be maintained orally or enterally. Potential candidates for small bowel transplantation would include those with PN associated liver failure or recurrent catheter sepsis and lack of venous access.[27]

Progressive, cholestatic liver failure may arise in patients with SBS who are PN dependent. The risk of this complication appears proportional to the length of bowel resected. Weaning of PN if at all possible is the preferred method of treatment.

Practice Guidelines *Short-Bowel Syndrome*

1. Patients undergoing extensive bowel resection or with short bowel syndrome are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Patients with SBS and an intact colon should receive diets rich in complex carbohydrates and low in fat. (A)
3. A low oxalate diet should be given to patients with SBS and an intact colon. (A)
4. Monthly vitamin B-12 injections should be given to patients with greater than 100 cm of the terminal ileum resected. (A)
5. PN should be administered to patients with SBS if nutritional requirements cannot be met by oral or EN feeding. (A)

REFERENCES

1. Scolapio JS, Fleming CR: Short bowel syndrome. Gastroenterol Clin N Am 27:467–479, 1998
2. Scolapio JS, Camilleri MC: Motility considerations in short bowel syndrome. Dig Dis15:253–262, 1997
3. Gerson CD, Coben N, Janowitz HD: Small intestinal absorptive function in regional enteritis. Gastroenterology 64:907, 1973
4. Manji N, Bistrian BR, Mascioli EA, et al: Gallstone disease in-patients with severe short bowel syndrome dependent on parenteral nutrition. JPEN 13:461–464, 1989
5. Dobbins JW, Binder HJ: Importance of the colon in enteric hyperoxaluria. N Engl J Med 296:298–301, 1977
6. Windsor CW, Fejfar J, Woodward DA: Gastric secretion after massive small bowel resection. Gut 10:779–786, 1969
7. Stolberg L, Rolfe R, Gitlin N, et al: D-lactic acidosis due to abnormal gut flora. N Engl J Med 306:1344–1348, 1982
8. Williamson RC: Intestinal adaptation: Structural, functional, and cytokinetic changes. N Engl J Med 298:1393–1402, 1978
9. Dowling RH: Small bowel adaptation and its regulation. Scand J Gastroenterology 74:53–74,1982
10. Lennard-Jones JE: Review article: Practical management of the short bowel. Aliment Pharmacol Ther 8:563–577, 1994
11. Cortot A, Fleming CR, Malagelada JR: Improved nutrient absorption after cimetidine in short bowel syndrome with gastric hypersecretion. N Engl J Med 300:79–80, 1979
12. Lennard-Jones: Oral rehydration solutions in short bowel syndrome. Clin Therap 12:129–137, 1990
13. Nordgaard I, Hansen BS, Mortensen PB: Colon as a digestive organ in patients with short bowel. Lancet 343:373–376, 1994
14. Nordgaard I, Hansen BS, Mortensen PB: Importance of colonic support for energy absorption as small-bowel failure proceeds. Am J Clin Nutr 64:222–231, 1996
15. Woolf GM, Miller C, Kurian R, et al: Diet for patients with a short bowel: High fat or high carbohydrate. Gastroenterology 84:823–828, 1983
16. McIntyre PB, Fitchew M, Lennard-Jones JE: Patients with a high jejunostomy do not need a special diet. Gastroenterology 91:25–33, 1986

17. Marteau P, Messing B, Arrigoni E, et al: Do patients with short-bowel syndrome need a lactose-free diet? Nutrition 13:13–16, 1997
18. Woolf GM, Miller C, Kurian R, et al: Nutritional absorption in short bowel syndrome. Evaluation of fluid, calorie, and divalent cation requirements. Dig Dis Sci 32:8–15, 1987
19. Fleming CR, George L, Stoner GL, et al: The importance of urinary magnesium values in patients with gut failure. Mayo Clin Proc 71:21–24, 1996
20. Ladefoged K, Nicolaidou P, Jarnum S: Calcium, phosphorus, magnesium, zinc, and nitrogen balance in patients with severe short bowel syndrome. Am J Clin Nutr 33:2137–2144, 1980
21. Alpers DH, Stenson WF, Bier DM: Manual of Nutritional Therapeutics, 4th ed. Lippincott Williams & Wilkins, Baltimore, MD, Chapter 7 (in press)
22. Scolapio JS, Fleming CR, Kelly D: Survival of home parenteral nutrition patients: Twenty-years of experience at the Mayo Clinic. Mayo Clinic Proc 74:217–222, 1999
23. Byrne TA, Morrissey TB, Nattakom TV, et al: Growth hormone, glutamine, and a modified diet enhance nutrient absorption in patients with severe short bowel syndrome. JPEN 19:296–302, 1995
24. Byrne TA, Persinger RL, Young LS, et al: A new treatment for patients with short-bowel syndrome. Growth hormone, glutamine, and a modified diet. Ann Surg 222:243–254; discussion 254–255, 1995
25. Scolapio JS, Camilleri M, Fleming CR, et al: Effect of growth hormone, glutamine, and diet on adaptation in short-bowel syndrome: A randomized, controlled study. Gastroenterology 113: 1074–1081, 1997
26. Szkudlarek J, Jeppesen PB, Mortensen PB: Effect of high dose growth hormone with glutamine and no change in diet on intestinal absorption in short bowel patients: a randomised, double blind, crossover, placebo controlled study. GUT 47:199–205, 2000
27. Abu-Elmagd K, Reyes J, Todo S, et al: Clinical intestinal transplantation: new perspectives and immunologic considerations. J Am Coll Surg 186:512–525, 1997

INFLAMMATORY BOWEL DISEASE

Background

Inflammatory bowel disease (IBD) includes both Crohn's disease (CD) and ulcerative colitis (UC). CD can involve any portion of the alimentary tract from the mouth to the anus. Inflammation of the bowel is patchy and involves the full thickness of the intestine. Fistulae to other segments of involved bowel, adjacent organs (bladder, uterus),and skin are common, occurring in 20% to 40% of patients.

Ulcerative colitis (UC) is a mucosal disease restricted to the colon. UC begins in the rectum and is found in a continuous distribution without interspersed normal mucosa.

Malnutrition in CD, and to a somewhat lesser extent in UC, is common.[1] Depending on severity of disease, weight loss has been reported in 65% to 78% of those with CD and in 18% to 62% of those with UC. Hypoalbuminemia is encountered in 25% to 80% of patients with CD and in 26% to 50% of those with UC. Anemia occurs in about half of patients with CD, primarily the result of malabsorption, and in up to 80% of those with UC, largely caused by blood loss. Electrolytes are often depleted as a result of diarrhea in both CD and UC. Vitamin and mineral deficiencies are usually more prominent in CD, but this is variable depending on the location and degree of disease involvement. Mechanisms contributing to malnutrition in IBD include decreased food intake due to discomfort and diarrhea being exacerbated by eating, as well as to dietary restrictions, malabsorption of nutrients (primarily in CD), increased gastrointestinal losses associated with denudation of mucosa and bleeding, increased nutrient requirements resulting from fever and inflammation, and drug-nutrient interactions.

Proposed roles for SNS in CD have included correction of malnutrition, use as primary therapy to induce remission or to limit amount of surgical resection, perioperatively as an adjunct to decrease postoperative complications, to reverse growth retardation in children, to induce healing of enterocutaneous fistulae, and to provide long term nutrition in those with short bowel syndrome. In UC, the use of nutrition support has been directed toward achieving clinical remission to avoid surgery.

Evidence

Prospective studies have evaluated the role of PN as primary therapy in CD. PN induces remission during acute attacks of CD, but upon resuming oral nutrition recurrence rates are high and do not justify the cost or risk associated with PN.[2–4]

There is no therapeutic benefit of bowel rest in CD. Prospective studies have compared the role of PN with bowel rest to EN.[5,6] Clinical remission rates were similar, with no evidence that bowel rest with PN had any advantage in management of patients with active CD.

Meta-analysis of 16 prospective randomized trials showed that the frequency of clinical remission after treatment with steroids was 80% compared with 60% after treatment with an elemental or polymeric diet alone.[7–9] Pooled data of studies comparing polymeric and elemental formulas showed no advantage for elemental diets (65% *versus* 61% remission rates).[8,9]

Although it had been proposed that IBD is associated with markedly increased caloric requirements, it has been demonstrated that in both inactive CD and in the setting of active disease, total energy expenditure is not significantly different than expected in normals.[10,11] Although resting energy expenditure is increased in active CD, activity level in these patients is decreased, making total energy expenditure identical to normals.[11]

Published studies do not support the concept that improved nutrition status coupled with bowel rest induce clinical remission and avoid colectomy in UC.[2,3]

Special Considerations

High output CD fistulae may result in altered nutrition status. Fluid, electrolyte, and zinc deficiencies may be particularly prominent.[12] Although approximately 38% of fistulae close spontaneously with bowel rest and PN, fistulae frequently recur when oral intake is resumed.[13]

In some patients with very extensive CD, prolonged use of PN may be required when the oral or EN feeding is not tolerated. PN is usually indicated for a limited period of time until remission can be achieved with steroids or surgical intervention is performed.

Preoperative PN in CD has been investigated primarily in retrospective studies. These have shown fewer postoperative complications,[14] an improved clin-

ical course,[15] and a decreased length of bowel requiring resection, but at the expense of a longer hospitalization.[16] The latter study showed no significant difference in postoperative complications. It appears that the use of preoperative PN should be restricted to severely malnourished patients with CD who cannot tolerate EN and who are scheduled for elective or semi-elective procedures.

The only indication for dietary modification in patients with IBD is in CD when a nonobstructive stricture precludes a normal, well-balanced diet. In this case, restriction of fiber is indicated.

There may be a role for specific nutrients in UC. An association has been observed between folic acid supplementation and a decreased relative risk of development of cancer or dysplasia in UC.[18] Randomized controlled trials of omega-3 fatty acids as a nutritional supplement in UC provide evidence for a role in decreasing disease activity and in reducing steroid requirements.[19–21]

Practice Guidelines
Inflammatory Bowel Disease

1. Patients with IBD are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. EN should be used in CD patients requiring SNS. (B)
3. PN should be reserved for those patients with IBD in whom EN is not tolerated. (B)
4. In cases of fistulae associated with CD, a brief course of bowel rest and PN should be attempted. (B)
5. Peri-operative SNS is indicated in patients with IBD who are severely malnourished and in whom surgery may be safely postponed. (B)
6. SNS and bowel rest should not be used as primary therapies for UC or CD. (A)

REFERENCES

1. Kelly DG, Fleming CR: Nutritional considerations in inflammatory bowel diseases. Gastroenterol Clin N Am 24:597–611, 1995
2. Dickinson RJ, Ashton MG, Axon ATR, et al: Controlled trial of intravenous hyperalimentation and total bowel rest as an adjunct to the routine therapy of acute colitis. Gastroenterology 79:1199–1204, 1980
3. McIntyre PB, Powell-Tuck J, Wood SR, et al: Controlled trial of bowel rest in the treatment of severe acute colitis. Gut 27:481–485, 1986
4. Shiloni E, Coronado E, Freund HR: Role of total parenteral nutrition in the treatment of Crohn's disease. Am J Surg 157: 180–185, 1989
5. Lochs H, Meryn S, Marosi L, et al: Has total bowel rest a beneficial effect in treatment of Crohn's disease? Clin Nutr 2:61–64, 1983
6. Greenberg GR, Fleming CR, Jeejeebhoy KN, et al: Controlled trial of bowel rest and nutrition support in the management of Crohn's disease. Gut 29:1309–1315, 1988
7. Trallori M, D'Albasio G, Milla M, et al: Defined-formula diets versus steroids in the treatment of active Crohn's disease. Scand J Gastroenterol 31:267–272, 1996
8. Fernandez-Barares F, Cabre E, Esteve-Comas M, et al: How effective is enteral nutrition in inducing clinical remission in active Crohn's disease? A meta-analysis of the randomized controlled trials. JPEN 19:356–362, 1995
9. Griffiths A, Ohlsson A, Sherman P, et al: Meta-analysis of enteral nutrition as a primary treatment of active Crohn's disease. Gastroenterology 108:1056–1067, 1995
10. Chan AT, Fleming CR, O'Fallon WM, et al: Estimated versus measured basal energy requirements in patients with Crohn's disease. Gastroenterology 91:75–78, 1986
11. Stokes MA, Hill GL: Total energy expenditure in patients with Crohn's disease: Measurement by the combined body scan technique. JPEN 17:3–7, 1993
12. Yamazaki Y, Fukushima T, Sugita A, et al: The medical, nutritional and surgical treatment of fistulae in Crohn's disease. Jpn J Surg 20:376–383, 1990
13. Afonso JJ, Rombeau JL: Nutritional care for patients with Crohn's disease. Hepato-gastroenterology 37:32–41, 1990
14. Rombeau JL, Barot LR, Williamson CE, et al: Preoperative total parenteral nutrition and surgical outcome in patients with inflammatory bowel disease. Am J Surg 143:139–143, 1982
15. Eisenberg HW, Turnbull JRB, Weakley FL: Hyperalimentation as preparation for surgery in transmural colitis (Crohn's disease). Dis Colon Rectum 17:469–475, 1974
16. Lashner BA, Evans AA, Hanauer SB: Preoperative total parenteral nutrition for bowel resection in Crohn's disease. Dig Dis Sci 34:741–774, 1989
17. Wilschanski M, Sherman P, Pencharz P: Supplementary enteral nutrition maintains remission in paediatric Crohn's disease. Gut 38:543–548, 1996
18. Lashner B, Provencher K, Seidner D, et al: The effect of folic acid supplementation on the risk for cancer or dysplasia in ulcerative colitis. Gastroenterology 112:29–32, 1997
19. Aslan A, Triadafilopoulos, G: Fish oil fatty acid supplementation in active ulcerative colitis: A double-blind, placebo-controlled, crossover study. Am J Gastroenterol 87:432–437, 1992
20. Hawthorne AB, Daneshmend TK, Hawkey CJ, et al: Treatment of ulcerative colitis with fish oil supplementation: a prospective 12 month randomised controlled trial. Gut 33:922–928, 1992
21. Lorenz R, Weber PC, Szimnau P, et al: Supplementation with n-3 fatty acids from fish oil in chronic inflammatory bowel disease—a randomized, placebo-controlled, double-blind cross-over trial. J Intern Med 225:225–232, 1989

SOLID ORGAN TRANSPLANTATION

Background

The United Network of Organ Sharing (UNOS) estimates that the number of solid organ transplants performed over the past decade has almost doubled to nearly 22,000 annually.[1] Unfortunately, because of a limited number of donor organs, the number of recipients awaiting transplant is approximately 72,000, a more than a three-fold increase over the same time.

Malnutrition prior to transplantation has been shown to increase morbidity and mortality after solid organ transplant.[2–5] Nutrition assessment in these patients is dependent on a carefully performed history and physical examination. Objective measures such as body weight, anthropometric measures, and visceral protein levels may be less sensitive in detecting the degree of malnutrition as a result of fluid imbalance, organ dysfunction, and surgical stress.[6–10]

Nutrition care may need to be modified depending on the time in relation to transplantation. Patients can be stratified into three stages: pretransplant, peri-operative, and posttransplant. Clinical guidelines for specific diseases should be followed for patients in the pretransplant stage. Immediately after transplantation, the goal of nutrition support is to promote wound healing, support the body's ability to fight infection, and to allow for rehabilitation.[11] EN can be used in most

patients requiring SNS after organ transplant. PN may be necessary in malnourished patients with severe cytomegalovirus esophagitis and gastroenteritis, azathioprine induce pancreatitis, small bowel obstruction, fistula formation, gastrointestinal bleeding, chylous ascites, and in the immediate postoperative stage of small bowel transplantation. Finally, the long-term care of patients during the posttransplant stage can be complicated by obesity, hypertension, diabetes mellitus, hyperlipidemia, and osteoporosis.[12–15] A comprehensive program to care for patients undergoing solid organ transplant should address all of these issues.

Evidence

Protein and energy requirements are affected by the stress of surgery, the use of immune modulating medications, postoperative complications, and episodes of acute rejection. Peri-operative energy requirements are similar to those necessary to support uncomplicated surgical procedures of a similar magnitude. There requirements are generally 130 to 150% of basal energy expenditure as determined by the Harris Benedict equation or 35 kcal/kg of body weight.[2,6,16–20] Requirements may transiently increase as a result of sepsis or acute rejection. Although energy requirements are often estimated, they can be most reliably determined using indirect calorimetry.

Balance studies suggest that protein requirements after transplantation are modestly elevated, ranging from 1.5 to 2 gm/kg per day. This level of intake is in part necessary because of the losses associated with surgical wounds, drains, and fistulae, and the increase in protein catabolism associated with corticosteroid use.[21–23] Protein requirements can decrease to 1 gm/kg as the dose of corticosteroids is reduced to maintenance levels.[24]

There are only a few prospective controlled trials investigating the role of SNS in solid organ transplantation. Each involves the management of patients after liver transplant. Reilly et al[25] demonstrated a decrease in intensive care unit length of stay in a group of patients receiving PN compared with patients who received intravenous fluids. Wicks et al[26] compared EN to PN and was unable to show a difference in time to an oral diet, intestinal permeability or infectious complications. Hasse et al[27] found that EN reduced the occurrence of viral infections after transplant compared with intravenous fluid. In all cases EN was delivered via nasojejunal feeding tube. These results suggest that SNS provides a modest benefit for malnourished patients after liver transplantation and that EN is medically equivalent to PN.

SNS should be administered cautiously to avoid postoperative hyperglycemia. Hyperglycemia has been shown to impair wound healing and increase the risk of infection. Hyperglycemia after transplant is due to insulin resistance associated with surgical stress, infection, and corticosteroid administration.[28] The immune modulators tacrolimus and cyclosporine can contribute to hyperglycemia by inhibiting insulin secretion by the pancreas.[13]

Hyperlipidemia, a potential long-term complication after transplantation, can be particularly problematic since it has been linked to transplant graft vasculopathy. This can result in coronary artery disease, chronic rejection, and vanishing bile duct syndrome in heart, kidney and liver transplant, respectively.[12] A variety of factors can contribute to this problem including underlying genetic abnormalities, dietary factors, obesity, diabetes mellitus and corticosteroids.[21,29,30]

Special Issues

Experimental animal studies suggest that specific nutrients may be used to modify outcomes after organ transplant. Supplemental arginine and n-3 polyunsaturated fatty acids, alone and in combination, have been shown to improve survival after transplantation in animal models.[31–33] Growth hormone, insulin-like growth factor-1 (IGF-1) and homocysteine have been shown in similar models to improve graft and recipient survival.[34–36] Nucleotide-free diets have been shown to enhance immunity and improve graft and host survival.[37] Although there is often little control over the nutrition status of the donor, nutritional repletion of donor swine has been shown to improve survival in the recipient animals.[38,39] The nutrient status of the donor may become a more important issue in the future with transplants from living-related donors.

Practice Guidelines *Solid Organ Transplantation*

1. Patients in any stage of the transplant process are at nutrition risk, and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. In the perioperative transplant period, patients should receive energy substrate similar to that required in all postoperative patients. (B)
3. In the perioperative transplant period, patients should receive 1.5 to 2.0 g/kg per day protein. (B)
4. SNS should be provided to malnourished patients with complications or delayed oral intake after solid organ transplant. (B)
5. Metabolic and nutrition complications of transplantation, including obesity, hypertension, diabetes mellitus, hyperlipidemia, and osteoporosis, should be treated with appropriate dietary and pharmacologic interventions. (C)

REFERENCES

1. http: //www.unos.org
2. Frazier OH, Van Buren CT, Poindexter SM, et al: Nutritional management of the heart transplant recipient. J Heart Transplant 4:450–452, 1998
3. Selberg O, Bottcher J, Tusch G, et al: Identification of high and low risk patients before liver transplantation: A prospective cohort study of nutritional metabolic parameters in 150 patients. Hepatology 25:652–657, 1997
4. Harrison J, McKiernan J, Neuberger JM: A prospective study on the effect of recipient nutritional status on outcome in liver transplantation. Transpl Int 10:369–374, 1997
5. Pikul J, Sharpe MD, Lowndes R, et al: Degree of preoperative

malnutrition is predictive of postoperative morbidity and mortality in liver transplant recipients. Transplantation 57:469–472, 1994
6. Poindexter SM: Nutrition support in cardiac transplantation. Top Clin Nutr 7:12–16, 1992
7. DeCecco SR,Wieners EJ, Wisner RH, et al: Assessment of nutritional status of patients with end-stage liver disease undergoing liver transplantation. Mayo Clin Proc 64:95–102, 1989
8. Hasse J, Strong S, Gorman MA, et al: Subjective global assessment: Alternative nutritional assessment technique for liver transplant candidates. Nutrition 9:339–343, 1993
9. Baron P, Waymack JP: A review of nutrition support for transplant patients. Nutr Clin Pract 8:12–18, 1993
10. Lowell JA, Beindorff ME: Nutritional assessment and therapy in abdominal organ transplantation. IN Nutritional Support: Theory and Therapeutics. Shikora S, Blackburn G (eds). Chapman & Hall, Glasgow, Scotland, 1997, pp 422–488
11. Hasse JM: Recovery after organ transplantation in adults: The role of postoperative nutrition therapy. Top Clin Nutr 13:15–26, 1998
12. Kobashigawa JA, Kasiske BL: Hyperlipidemia in solid organ transplantation. Transplantation 63:331–338, 1997
13. Jindal RM: Post-transplant diabetes mellitus: A review. Transplantation 58:1289–1298, 1994
14. Perez R: Managing nutrition problems in transplant patients. Nutr Clin Pract 8:228–232, 1993
15. Meier-Kriesche H: Obesity and long-term allograft survival. Transplantation 68:1294–1297, 1999
16. Delafosse B, Faure JL, Biouffard Y, et al: Liver transplantation-energy expenditure, nitrogen loss, and substrate oxidation rate in the first two postoperative days. Transplant Proc 21:2453–2454, 1989
17. Shanbhogue RLK, Bistrian BR, Jenkins RL, et al: Increased protein catabolism without hypermetabolism after human orthotopic liver transplantation. Surgery 101:146–149, 1997
18. Ragsdale D: Nutritional program for heart transplantation. J Heart Transplant 6:228–233, 1987
19. Zabielski P: What are the calorie and protein requirements during the acute postrenal transplant period? Support Line 14:11–13, 1992
20. Kowalchuk D: Nutritional management of the pancreas transplant patient. Support Line 14:10–11, 1992
21. Steiger U, Lippuner K, Jensen EX, et al: Body composition and fuel metabolism after kidney grafting. Eur J Clin Invest 25:809–816, 1995
22. Seagraves A, Moore EE, Moore FA, et al: Net protein catabolic rate after kidney transplantation: Impact of corticosteroid immunosuppression. JPEN 10:453–455, 1986
23. Hoy WE, Sargent JA, Freeman RB, et al: The influence of glucorticoid dose on protein catabolism after renal transplantation. Am J Med Sci 291:241–247, 1986
24. Hasse JM, Weseman RA: Solid organ transplantation. IN The Science and Practice of Nutrition Support. A Core Curriculum. Gottschlich MM (ed). Kendall/Hunt, Dubuque, IA, 2001, pp 107–140
25. Reilly J, Mehta R, Teperman L, et al: Nutritional support after liver transplantation: A randomized prospective study. JPEN 14:386–391, 1990
26. Wicks C, Somasundaram S, Buarnason I, et al: Comparison of enteral feeding and total parenteral nutrition after liver transplantation. Lancet 344:837–840, 1994
27. Hasse JM, Blue LS, Liepa GU, et al: Early enteral nutrition support in patients undergoing liver transplantation. JPEN 19:437–443, 1995
28. Driscoll DF, Palombo JD, Bistrian BR: Nutritional and metabolic considerations of the adult liver transplant candidate and organ donor. Nutrition 11:255–263, 1995
29. Moore R, Thomas D, Morgan E, et al: Abnormal lipid and lipoprotein profiles following renal transplantation. Transplant Proc 25:1060–1061, 1993
30. Palmer M, Schaffner F, Thung SN: Excessive weight gain after liver transplantation. Transplantation 51:797–800, 1991
31. Alexander JW, Levy A, Custer D, et al: Arginine fish oil, and donor-specific transfusions independently improve cardiac allograft survival in rats given subtherapeutic doses of cyclosporine. JPEN 22:152–155, 1998
32. Elzinga L, Kelley VE, Houghton DC, et al: Model of experimental nephrotoxicity with fish oil as the vehicle for cyclosporine. Transplantation 43:271–274, 1987
33. Otto DA, Kahn DR, Hamm HW, et al: Improved survival of heterotopic cardiac allografts in rats with dietary omega-3 polyunsaturated fatty acids. Transplantation 50:193–198, 1990
34. Ducloux D, Fournier V, Rebibou JM, et al: Hyperhomocysteinemia in renal transplant recipients with and without cyclosporine. Clin Nephrol 49:232–235, 1998
35. Cole DE, Ross HJ, Evovski J, et al: Correlation between total homocysteine and cyclosporine concentrations in cardiac transplant recipients. Clin Chem 44:2307–2312, 1998
36. Alexander JW, Valente JF, Greenberg NA, et al: Dietary amino acids as new and novel agents to enhance allograft survival. Nutrition 15:130–134, 1999
37. Van Buren CT, Kulkami AD, Schandle VB, et al: The influence of dietary nucleotides on cell-mediated immunity. Transplantation 36:350–352, 1983
38. Sadamori H, Tanaka N, Yagi T, et al: The effects of nutritional repletion on donors for liver transplantation in pigs. Transplantation 60:317–321, 1995
39. Ishikawa T, Yagi T, Ishine N, et al: Energy metabolism of the grafted liver and influence of preretrival feeding process on swine orthotopic liver transplantation. Transplantation 29:397–399, 1997

GASTROINTESTINAL FISTULAE

Background

Gastrointestinal fistulae result in diversion of intestinal contents to the skin or to another hollow viscous such as the urinary bladder, vagina, or another part of the gastrointestinal tract. They occur as a result of Crohn's disease, abscess, surgery, trauma, ischemia, irradiation, and/or tumor. The pathophysiologic consequences are determined by the site of the fistula in the gastrointestinal tract, the site to which contents are diverted, and the volume of fluid diverted. Even small quantities of intestinal fluid may cause urinary or vaginal infection, skin irritation, or malabsorption. High-output fistulae, defined as loss of greater than 500 mL of fluid daily, are usually the result of enterocutaneous fistulae involving the proximal gastrointestinal tract. They may cause substantial losses of fluid (500 to 4000 mL/d), electrolytes, protein, energy, vitamins, and trace minerals resulting in dehydration, acid-base imbalance, electrolyte imbalance, and malnutrition. These losses, together with food restriction to minimize symptoms and hypercatabolism resulting from sepsis, cause profound nutrient depletion and death if not corrected. Mortality from gastrointestinal fistulae results from sepsis, malnutrition, and electrolyte imbalance, often after several attempts to close the fistula surgically. For external gastrointestinal tract fistulae, mortality rates of 40% to 65% before 1970[1–5] have generally declined to 5% to 21%.[1,6–9] Recent reports suggest no further decline in mortality rate but possibly further improvement in the rate of nonsurgical (spontaneous) closure.[7] Spontaneous closure rates from 15% to 80% are reported.[1,7,10,11] Malnutrition, other physiologic disturbances, and mortality are proportionately less in moderate-output fistulae (200 to 500 mL/d) and low-output fistulae (<200 mL/d).

Evidence

Most postoperative fistulae will heal without further surgery in the absence of distal obstruction,

loss of bowel continuity, adjacent abscess, foreign body, cancer, or Crohn's disease. There are no reported prospective, randomized, controlled clinical trials comparing the results of treatment which includes SNS (EN or PN) with controls not receiving SNS for any type of gastrointestinal fistula.

The improvement in mortality, especially for patients with high output fistulae, over the past 40 years, can be attributed to improvements in intensive care, antibiotic therapy, wound care, operative techniques, and possibly SNS. Edmunds et al[2] noted a 43% mortality and significant malnutrition (47%, defined as serum protein less than 5.6 g/100 mL and/or weight loss of greater than 15 pounds) among 157 fistula patients seen at Massachusetts General Hospital between 1946 and 1959. However, overall mortality was not increased in the malnourished group with one exception. Patients with lower bowel fistulae did have an increased mortality related to a high prevalence of cancer and malnutrition. Nonrandomized, prospective studies comparing the results for fistula patients treated with nutrition support, primarily PN, with results for historical controls suggested significant benefits from PN.[12–15] Reber et al[16] reviewed results of fistulae treated between 1968 and 1971 when 35% of the patients received PN with results from 1972 to 1977 when 71% received PN. Neither mortality nor spontaneous closure rates differed between the two groups.

Soeters et al[6] reviewed records of all 247 gastrointestinal-cutaneous fistula patients seen at Massachusetts General Hospital from 1960 to 1975. Compared with the results obtained by Edmunds[2] from the same institution from 1946 to 1959 (43% mortality), overall mortality was 15% for the period 1960 to 1970 when technology had improved but SNS was seldom used. Mortality remained 21% in the period 1970 to 1975 when 57% of the patients received PN. Mortality was 25% among those receiving PN and 16% among those not receiving PN in this retrospective, nonrandomized study. Significant malnutrition, defined as serum protein less than 6 g/100 mL and/or weight loss greater than 7 kg was present in 87% of the 119 patients seen in 1960 to 1970 and 51% of the 128 patients seen in 1970 to 1975. There were significant correlations between malnutrition, sepsis, and mortality. Because the decrease in mortality occurred prior to the frequent use of PN, it cannot be attributed to PN.

Studies have shown a correlation between intake of greater than 1600 kcal/d and decreased mortality.[3,17] Such correlations may or may not indicate that nutrition support improves outcome. The correlations could occur as a result of difficulty achieving calorie goals in the sickest patients, so that the ability to achieve adequate nutrient intake by the enteral or parenteral route may be a marker for less severe disease. Alternatively, physicians who are most diligent about providing nutrition support for patients may provide better management in other ways.

Currently, uncontrolled infection is the major cause of mortality among patients with gastrointestinal fistulae and should be a primary focus of attention. Starvation of otherwise healthy individuals will lead to death in about 60 days, and infection and excessive losses from high output fistulae can reasonably be expected to reduce the time for death from starvation to 30 days. Therefore, even in the absence of randomized, controlled clinical data, nutrition support with EN or PN should not be delayed beyond 7 to 14 days in patients with gastrointestinal fistulae who are not eating.

Special Considerations

Whether treatment with TPN and bowel rest increases the incidence of spontaneous fistula closure or reduces the incidence of postoperative complications among fistula patients is unclear. The primary role of SNS in management of gastrointestinal fistulae is supportive, that is, to prevent or treat malnutrition and debilitation.[8] Administration of octreotide plus PN did not increase the incidence of spontaneous closure (81% *versus* 85%) but decreased the mean time to closure from 20.4 to 13.9 days in one study[18]; other studies have shown no beneficial effect.[19] Some studies suggest that PN itself may decrease upper gastrointestinal tract secretions.[8,20]

High output intestinal fistulae may result in excessive losses of some nutrients, especially protein, zinc, copper, and several vitamins. Therefore, although there are no controlled studies to support the practice, it is appropriate for the nutrient prescription for such patients to include 1.5 to 2.0 g of protein/kg/per day in the absence of renal or liver failure and 10 to 15 mg of zinc/liter of fistula fluid lost. Some have recommended that patients with high output fistulae receive two times the recommended daily allowance (RDA) for vitamins and trace minerals and 5 to 10 times the RDA for vitamin C,[1,11] but there are no data to support this practice.

EN is often the preferred method of SNS in patients with gastrointestinal fistulae. Patients with fistulas involving the esophagus, stomach, or duodenum can be fed into the jejunum using a nasojejunal tube, gastrojejunal tube, or a jejunostomy.[3,21,22] Patients with fistulae at least 4 feet distal to the ligament of Treitz have been supported with gastric feeding.[21] It is not clear whether monomeric or low-fat products are better tolerated than polymeric. In a dog model, a monomeric diet produced significantly less output from an ileal fistula than a regular diet but significantly more than parenteral nutrition.[23] Patients with gastrointestinal fistulae in association with recent complicated abdominal surgery, marked malnutrition or other serious comorbid conditions may benefit from several months of SNS, given at home if possible.[24]

Practice Guidelines *Gastrointestinal Fistulae*

1. Patients with enterocutaneous fistulae are at nutrition risk and should undergo formal nutrition assessment and development of a nutrition care plan. (B)
2. EN, proximal or distal to the fistula, should be

used in patients who cannot meet their nutritional needs by oral intake and who are malnourished or expected to have inadequate oral intake for 7 to 14 days or more. (B)

3. When SNS is required, PN should be reserved for those patients in whom enteral intake must be restricted. (C)

REFERENCES

1. Dudrick SJ, Maharaj AR, McKelvey AA: Artificial nutritional support in patients with gastrointestinal fistulas. World J Surg 23:570–576, 1999
2. Edmunds LH Jr, Williams GM, Welch CE: External fistulas arising from the gastro-intestinal tract. Ann Surg 152:445–470, 1960
3. Chapman R, Foran R, Dunphy JE: Management of intestinal fistulas. Am J Surg 108:157–164, 1964
4. Halversen RC, Hogle HH, Richards RC: Gastric and small bowel fistulas. Am J Surg 118:968–972, 1969
5. Nassos TP, Broasch JW: External small bowel fistulas: current treatment and results. Surg Clin N Am 51:687–692, 1971
6. Soeters PB, Ebeid AM, Fischer JE: Review of 404 patients with gastrointestinal fistulas. Impact of parenteral nutrition. Ann Surg 190:189–202, 1979
7. Rose D, Yarborough MF, Canizaro PL, et al: One hundred and fourteen fistulas of the gastrointestinal tract treated with total parenteral nutrition. Surg Gynecol Obstet 163:345–350, 1986
8. Meguid MM, Campos ACL: Nutritional management of patients with gastrointestinal fistulas. Surg Clin N Am 76:1035–1080, 1996
9. McIntyre PB, Ritchie JK, Hawley PR, et al: Management of enterocutaneous fistulas: a review of 132 cases. Br J Surg 71:293–296, 1984
10. Benson DW, Fischer JE. Fistulas. IN Total Parenteral Nutrition. JE Fischer (ed). Little, Brown and Company, Boston, 1991, pp 253–262
11. Berry SM, Fischer JE: Classification and pathophysiology of enterocutaneous fistulas. Surg Clin N Am 76:1009–1018, 1996
12. MacFadyen BV, Dudrick SJ, Ruberg RL: Management of gastrointestinal fistulas with parenteral hyperalimentation. Surgery 74:100–105, 1973
13. Himal HS, Allard JR, Nadeau JE, et al: The importance of adequate nutrition in closure of small intestinal fistulas. Br J Surg 61:724–726, 1974
14. Deitel M: Nutritional management of external gastrointestinal fistulas. Can J Surg 19:505–511, 1976
15. Thomas RJS, Rosalion A: The use of parenteral nutrition in the management of external gastrointestinal tract fistulae. Aust N Z J Surg 48:535–539, 1978
16. Reber HA, Roberts C, Way LW, et al: Management of external gastrointestinal fistulas. Ann Surg 188:460–467, 1978
17. Sheldon GF, Gardiner BN, Way LW, et al: Management of gastrointestinal fistulas. Surg Gynecol Obstet 133:385–389, 1971
18. Torres AJ, Landa JI, Moreno-Azcoita M, et al: Somatostatin in the management of gastrointestinal fistulas. A multicenter trial. Arch Surg 127:97–100, 1992
19. Hodin RA, Matthews JB: Small intestine. IN Surgery: Basic Science and Clinical Evidence. Norton JA, Bollinger RR, Chang AE, et al (eds). Springer-Verlag, New York, 2001, pp. 617–646
20. Hamilton RF, Davis WC, Stephenson DV, et al: Effects of parenteral hyperalimentation on upper gastrointestinal tract secretions. Arch Surg 102:348–352, 1971
21. Garden OJ, Dykes EH, Carter DC: Surgical and nutritional management of postoperative duodenal fistulas. Dig Dis Sci 33:30–35, 1988
22. Rocchio MA, Mochar C-J, Hass KF, et al: Use of chemically defined diets in the management of patient with high output gastrointestinal cutaneous fistulas. Am J Surg 127:148–156, 1984
23. Wolfe B, Keltner RM, Willman VL: Intestinal fistula output in regular, elemental, and intravenous alimentation. Am J Surg 124:803–806, 1972
24. Oakley JR, Steiger E, Lavery IC, et al: Catastrophic enterocutaneous fistulae. The role of home hyperalimentation. Cleve Clin Quart 46:133–136, 1979

RENAL DISEASE

Background

Renal failure patients experience a variety of clinical and metabolic abnormalities that can affect their nutrition status. The degree of nutritional impairment is dependent on the concurrent stress, degree and duration (chronic or acute) of renal impairment, and the treatment modality. In chronic renal failure (CRF), altered taste sensation, anorexia, nausea, and unpalatable diets all lead to decreased nutrient intake. CRF has also been associated with a state of chronic inflammation that promotes catabolism and anorexia.[1] In acute renal failure (ARF), hypermetabolism is present, protein breakdown is accelerated, and protein synthesis is impaired.[2] Renal replacement therapy (RRT) further aggravates protein nutriture by inducing losses of protein, amino acids and albumin. Other metabolic abnormalities include altered glucose utilization[3] and impaired lipid metabolism.[4] These metabolic abnormalities result in negative nitrogen balance and abnormalities in serum amino acid, glucose and triglyceride levels during nutrition support. As a result, protein-calorie malnutrition (PCM) is a frequent complication in renal failure patients.[5] The presence of PCM in patients with CRF and end-stage renal disease (ESRD) remains one of the strongest predictors of morbidity and mortality in this cohort.[6]

Evidence

PCM is often identified in renal patients by laboratory testing.[7] Visceral protein measurements are not well suited for assessment in renal patients. However, individuals with low serum albumin levels and a serum prealbumin level <30 mg/dL are at risk for PCM.[8,9] Serum albumin is also a predictor of mortality in renal failure. The relative risk of death is five times greater when serum albumin is low (below 3 to 3.4 g/dL).[10]

Dietary protein restriction offers several theoretic benefits for patients with progressive CRF. Motivated, closely monitored patients with CRF not on dialysis placed on low protein diets (0.6 g/kg per day) and very low protein diets (0.3 g/kg per day) supplemented with essential amino acids have been shown to be capable of maintaining their nutritional status.[11] The modification of diet in a major renal disease (MDRD) study showed no improvement resulting from protein restriction in CRF patients except for those with advanced CRF. It should be noted that patients with diabetes mellitus were excluded from the MDRD study and may have benefited from protein restriction.[12] At present, the conventional recommendation for protein intake in CRF is 0.6 to 0.8 g/kg per day.[13]

Loss of amino acids (approximately 10 to 12 g per hemodialysis therapy) occurs with high efficiency dialysis.[14] Protein losses during peritoneal dialysis can be even higher, often accounting for up to 15 g of protein losses during episodes of peritonitis.[15] Hence, intake of 1.2 g/kg per day of protein for maintenance hemodialysis patients and 1.2 to 1.3 g/kg per day for patients receiving chronic ambulatory peritoneal dialysis (CAPD) is recommended.[16] In ARF patients undergoing continuous hemofiltration, control of azotemia is

possible while providing more than 1 g/kg per day of protein. There continues to be controversy whether increased protein intakes are associated with increasing urea nitrogen appearance (UNA). However, Macias et al showed that ARF patients who received 1 g/kg per day or greater of protein achieved positive nitrogen balance and had lower UNA. Conversely, patients receiving nutrition at levels less than 1 g/kg per day of protein had significantly greater nitrogen deficits.[17]

An early clinical study of PN in patients with ARF showed improved survival in patients receiving small doses of essential amino acids plus dextrose, when compared with dextrose alone.[18] However, a subsequent prospective, randomized, controlled trial comparing essential amino acid administration to a balanced mixture of general amino acids (essential and nonessential amino acids) demonstrated no difference in the formulations' effect on mortality, nitrogen balance, or BUN.[19] Further data suggest that there may be an increased complication rate with development of hyperammonemia and metabolic encephalopathy when only essential amino acids are used for longer than 2 to 3 weeks.[20] In renal failure patients, nonessential amino acids including, arginine, ornithine, and citrulline should be supplied to enable detoxification of ammonia via the Krebs urea cycle.[20] As such, caution should be used when very low protein diets (0.3 to 0.5 g essential amino acids per day) are prescribed for nonhypermetabolic ARF patients.

It is generally believed that negative nitrogen balance in hypermetabolic patients cannot be reversed solely with SNS. However, the results from Macias et al[17] suggest that achievement of positive nitrogen balance in patients with ARF requires between 1.5 and 1.8 g protein/kg per day. Although such levels of protein support have also been associated with increasing protein catabolic rates, the magnitude of the increase can be diminished by providing adequate energy substrates (25 to 35 kcal/kg per day).

Special Considerations

Intradialytic parenteral nutrition (IDPN) has been used as a supplement to protein and calorie intake for malnourished patients receiving maintenance hemodialysis. Disadvantages of this modality are that it can only supplement nutrition provided by other means, it is expensive, and it does not improve the patient's oral intake. As such, IDPN should be reserved for patients who cannot meet their nutrient needs orally and who are not candidates for EN or PN because of gastrointestinal intolerance, venous access problems, or other reasons.[13]

Supplementation of water-soluble vitamins (thiamine, riboflavin, pyridoxine, cyanobalamin, folic acid, biotin, niacin, pantothenic acid, and ascorbic acid) should be provided to patients receiving dialysis due to intradialytic losses. Caution should be exercised with supplementation of vitamin A (Retinol) as hypervitaminosis A is often noted in patients with ESRD.

Patients with advanced renal failure (GFR < 25 mL/min/1.73 m^2) have disordered bone metabolism and are at significant risk for renal osteodystrophy. Phosphorus restriction, calcium supplementation, and consideration of dihydroxy-vitamin-D_3 supplementation is recommended.[21]

Practice Guidelines *Renal Disease*

1. Renal failure patients are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Well-monitored patients with advanced chronic renal insufficiency but not on dialysis should receive diets restricted to 0.6 to 0.8 g of protein/kg per day. (A)
3. Patients with CRF on hemodialysis or peritoneal dialysis should receive 1.2 to 1.3 g of protein/kg per day. (B)
4. Patients undergoing continuous hemofiltration should receive at least 1.0 g of protein/kg per day. (B)
5. Patients with ARF receiving SNS should be given a balanced mixture of both essential and nonessential amino acids. (A)
6. Patients with ARF who are severely malnourished or hypercatabolic should receive 1.5 to 1.8 g of protein/kg per day. (B)
7. Intradialytic parenteral nutrition should only be considered in situations of gut failure or other unusual circumstances where EN and PN are not feasible. (C)
8. Water-soluble vitamin supplementation is required for patients treated with dialysis. (A)
9. Vitamin A status should be carefully monitored in patients with CRF. (A)

REFERENCES

1. Docci D, Bilancioni R, Baldrati L, et al: Elevated acute phase reactants in hemodialysis patients. Clin Nephrol 34:88–91, 1990
2. Druml W: Protein metabolism in acute renal failure. Miner Electrolyte Metab 24:47–54, 1998
3. Riella MC: Nutrition in acute renal failure. Renal Failure 19:237–252, 1997
4. Druml W, Fischer M, Sertl S, et al: Fat elimination in acute renal failure: long-chain vs medium-chain triglycerides. Am J Clin Nutr 55:468–472, 1992
5. Ahmed KR, Kopple JD: Nutrition in maintenance hemodialysis patients. IN Nutritional Management of Renal Disease. Kopple JD (ed). Baltimore, Williams & Wilkins, 1996, pp 563–560
6. Barrett BJ, Parfrey PF, Morgan J, et al: Prediction of early death in end-stage renal disease patients starting dialysis. Am J Kidney Dis 29:214–222, 1997
7. Brivet FG, Kleinknecht DJ, Loirat P, at al: Acute renal failure in intensive care units—causes, outcome, and prognostic factors of hospital mortality; a prospective, multicenter study. French Study Group on Acute Renal Failure. Crit Care Med 24:192–198, 1996
8. Kaysen GA, Rathore V, Shearer GC, et al: Mechanisms of hypoalbuminemia in hemodialysis patients. Kidney Int 48:510–516, 1995
9. Sreedhara R, Avram MM, Blanco M, et al: Prealbumin is the best nutritional predictor of survival in hemodialysis and peritoneal dialysis. Am J Kidney Dis 28:937–942, 1996
10. Lowrie EG, Lew NL: Death risk in hemodialysis patients: the predictive value of commonly measured variables and an evaluation of death rate differences between facilities. Am J Kidney Dis 15:458–482, 1990
11. Kasiske BL, Lakatua JD, Ma JZ, et al: A meta-analysis of the

effects of dietary protein restriction on the rate of decline in renal function. Am J Kidney Dis 31:954–961, 1998
12. Levey AS, Adler S, Caggiula AW, et al: Effects of dietary protein restriction on the progression of advanced renal disease in the modification of diet in renal disease study. Am J Kidney Dis 27:652–663, 1996
13. K/DOQI, National Kidney Foundation: Clinical practice guidelines for nutrition in chronic renal failure. Am J Kidney Dis 35(Suppl 2):S1–S140, 2000
14. Ikizler TA, Flakoll PJ, Parker RA, et al: Amino acid and albumin losses during hemodialysis. Kidney Int 46:830–837, 1994
15. Blumenkrantz MJ, Gahl GM, Kopple JD, et al: Protein losses during peritoneal dialysis. Kidney Int 19:593–602, 1981
16. Ambler C, Kopple J: Nutrition support for patients with renal failure. IN A.S.P.E.N. Nutrition Support Practice Manual. Klein S (ed). American Society for Parenteral and Enteral Nutrition, Silver Spring, MD, 1998, pp 16.1–16.12
17. Macias WL, Alaka KJ, Murphy MH, et al: Impact of the nutritional regimen on protein catabolism and nitrogen balance in patients with acute renal failure. JPEN 20:56–62, 1996
18. Abel RM, Beck CH, Abbott WM, et al: Improved survival from acute renal failure after treatment with intravenous L-amino acids and glucose. N Engl J Med 288:695–699, 1973
19. Mirtallo JM, Schneider PJ, Mavko K, et al: A comparison of essential and general amino acid infusions in the nutrition support of patients with compromised renal function. JPEN 6:109–113, 1982
20. Nakasaki H, Katayama T, Yokoyama S, et al: Complication of parenteral nutrition composed of essential amino acids and histidine in adults with renal failure. JPEN 17:86–90, 1993
21. Maroni BJ: Nutrition in renal disease. IN Primer on Kidney Diseases, 2nd ed. Greenberg A (ed). Academy Press, San Diego, 1998, pp 440–447

NEUROLOGIC IMPAIRMENT

Background

Neurologic impairment may occur acutely as a result of traumatic brain injury (TBI), cerebral vascular accident (CVA), or infection or may occur as a result of chronic, degenerative processes.

Acute neurologic injury, such as severe TBI (described as a Glascow Coma Scale < 8), can result in a complex cascade of metabolic, physiologic, and functional alterations.[1] Nutrition assessment must take into consideration the significant hypermetabolism, hypercatabolism, and nitrogen wasting followed by rapid lean body mass wasting and visceral protein depletion seen with TBI.[2,3] Nonsedated patients with TBI have mean resting metabolic expenditures 140% to 200% above predicted.[4] This may be attributed, in part, to the cytokine response, counter-regulatory hormones released postinsult, and/or steroid therapy.[2,4] Brain death and the use of barbiturates or neuromuscular blockers decrease energy expenditure.[2] Predictive equations have been inconsistent in determining caloric needs; research supports the routine use of indirect calorimetry in this population.[1]

Nitrogen losses mimic that of patients with 20% to 40% body surface area burns with an average nitrogen excretion of 20 g/d during the acute injury phase.[4] Steroid therapy may further exacerbate nitrogen losses; the degree is dependent on dose and duration of therapy. Increased exogenous protein administration in the early injury phase cannot replete the losses, which peak approximately 7 to 10 days postinjury.[2] Despite adequate nutrition support, restoration of nitrogen balance is often not realized until 2 to 3 weeks postinjury.[4]

Metabolic homeostasis is further altered as evidenced by marked hyperglycemia, altered gastrointestinal function, and depressed immune status markers. The degree of hyperglycemia is linked to the severity of injury and poorer clinical outcome; however, more research is needed to determine if prevention of hyperglycemia actually improves patient outcome.[5] Delayed gastric emptying can be an impediment to early gut feeding. Although the exact mechanism is unknown, increased intracranial pressure, cytokines, and pharmacologic agents may play a role.[6] Small bowel feedings with concurrent stomach decompression and prokinetic agents may promote tolerance of EN. Zinc losses, due to the acute-phase response, are also seen in head injury; hypozincemia, and increased urinary zinc excretion can depress immune status, which may impair or slow neurological recovery.[2] Zinc supplementation may be beneficial in head-injured patients.[3]

Unlike patients with TBI, spinal cord–injured patients are hypometabolic, depending on the severity of injury, with energy expenditure approximately 94% of predicted by the Harris-Benedict equation. Decreased resting energy expenditure is correlated with the degree of lean body mass loss.[7] It is common for patients to experience an approximate 10% weight loss in the immediate postinjury phase.[3] Predictive equations must be used with caution as overfeeding may occur in an attempt to reverse foreseeable negative nitrogen balance.[7] Serial indirect calorimetry measurements are the most accurate predictors of fluctuating metabolic requirements.[7] These patients are also plagued with gastrointestinal and metabolic complications, which may result in nutritional compromise over time. These include gastritis, ileus, hypercalcemia and hypercalciura due to immobilization, osteoporosis, neurogenic bowel and bladder (often associated with fecal impaction and urinary tract infections), development of pressure ulcers, anemia, and hypoalbuminemia.[3]

Degenerative neurological diseases (eg, Parkinson's disease, multiple sclerosis, amylotrophic lateral sclerosis) as well as CVA differ in that most of the metabolic and physiologic changes occur in the chronic stage of disease instead of the acute phase. CVAs are strongly associated with dysphagia, although a large percentage of patients recover swallowing function over time.[8] Screening for dysphagia, before the initiation of an oral feeding regimen, has been shown to decrease length of stay and incidence of aspiration pneumonia in patients with a CVA.[9] Patients with progressive Parkinson's disease are plagued with gastrointestinal symptoms such as anorexia, dysphagia, excessive salivation, drooling, constipation and delayed gastric emptying.[3] Persistent weight loss and dysphagia are hallmark symptoms of amylotrophic lateral sclerosis and may result in the need for long-term nutrition support, preferably, EN via a percutaneous endoscopic gastrostomy tube.[10]

Despite the unique nuances of neurologic diseases, feeding challenges are a prevalent cause of malnutrition. Impaired oral feeding may result in the need for nutrition support due to dysphagia, risk of aspiration due to an inability to protect the

airway, respiratory muscle weakness, gastroparesis or gastrointestinal reflux, and/or impaired appetite control centers in the brain.[11] Nutrition assessment must be individualized to address the distinct problems.

Evidence

Early nutrition support is important in the acutely injured neurologically impaired patient. Studies support early initiation of SNS, ideally, within 48 hours.[12] Early administration of SNS has been shown to be predictive of a lower risk of infections and has trended toward improved survival and reduced disability.[12] EN initiated within 72 hours of a CVA is associated with a decreased length of stay.[13] More studies are needed to confirm these relationships. PN can be initiated early in the postinjury phase, whereas impaired gastric emptying occasionally delays the initiation of EN via the gastric route.[14,15] Achievement of nutritional requirements may be delayed with EN for 10 to 14 days.[5] Although some studies suggest a trend toward improved outcomes with PN versus EN as assessed by survival and incidence of septic complications, this finding is not universal and may merely reflect the ability to administer target quantities of nutrients earlier with PN in some patients.[14–16]

Several studies support the use of small bowel feeding as a means to promote more timely, adequate, and well-tolerated EN.[17,18] These studies suggest improved nitrogen retention, reduced incidence of infections, and decreased days in the intensive care unit.[17,18] Establishing and maintaining placement of nasoenteric feeding tubes remains a clinical challenge.[17] Other studies have succeeded with gastric feeding and show no differences in feeding tolerance or rates of aspiration.[19,20] Taylor and colleagues were able to administer full nutritional requirements day 1 postinjury via the gastric or intestinal routes.[20]

EN remains the preferred method of SNS for neurologically impaired patients because of relative ease of use and lower cost. However, adjunct or exclusive PN should be administered to achieve nutrition goals if gastrointestinal function is impaired or aspiration is problematic.[5,21]

Practice Guidelines *Neurologic Impairment*

1. Patients with neurologic impairment are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. SNS should be initiated early in patients with moderate or severe TBI. (B)
3. When SNS is required, EN is preferred if it is tolerated. (C)
4. PN should be administered to patients with TBI if SNS is indicated and EN does not meet the nutritional requirements. (C)
5. Indirect calorimetry should be utilized, if available, to accurately determine nutrient requirements in patients with TBI and CVAs. (B)
6. Swallowing function should be evaluated to determine the safety of oral feedings and risk of aspiration before the initiation of an oral diet. (B)

REFERENCES

1. Sunderland PM, Heilbrun MP: Estimating energy expenditure in traumatic brain injury: comparison of indirect calorimetry with predictive formulas. Neurosurgery 31:246–253, 1992
2. Young B, Ott L, Phillips R, et al: Metabolic management of the patient with head injury. Neurosurg Clin N Am 2:301–320, 1991
3. Varella L, Jastremski CA: Neurological impairment. IN The Science and Practice of Nutrition Support, A Case Based Core Curriculum. Gottschlich M (ed). Kendell/Hunt Publishing Company, Dubuque, IA, 2001
4. Clifton GL, Robertson CS, Grossman RG, et al: The metabolic response to severe head injury. J Neurosurg 60:687–696, 1984
5. Wilson RF, Tyburski JG: Metabolic responses and nutritional therapy in patients with severe head injuries. J Head Trauma Rehabil 13:11–27, 1998
6. Weekes E, Elia M: Observations on the patterns of 24-hour energy expenditure changes in body composition and gastric emptying in head-injured patients receiving nasogastric tube feeding. JPEN 20:31–37, 1996
7. Rodriguez DJ, Benzel EC, Clevenger FW: The metabolic response to spinal cord injury. Spinal Cord 35:599–604, 1997
8. Dray TG, Hillel AD, Miller RM: Dysphagia caused by neurological deficits. Oryngol Clin N Am 31:507–524, 1998
9. Odderson IR, Keaton JC, McKenna BS: Swallow management in patients on an acute stroke pathway: quality is cost effective. Arch Phys Med Rehabil 76:1130–1133, 1995
10. Mazzini L, Corra T, Zacala M, et al: Percutaneous endoscopic gastrostomy and enteral nutrition in amyotrophic lateral sclerosis. J Neurol 242:695–698, 1995
11. Groher ME: Dysphagia Diagnosis and Management, 3rd ed. Butterworth-Heinemann, Boston, 1997
12. Yanagawa T, Bunn F, Roberts I, et al: Nutritional support for head-injured patients (Cochrane Review). IN The Cochrane Library, Update Software, Oxford, 2001, pp 1–20
13. Nyswonger GD, Helmchen RH: Early enteral nutrition and length of stay in stroke patients. J Neurosci Nurs 24:220–223, 1992
14. Rapp RP, Young B, Twyman D, et al: The favorable effect of early parenteral feeding on survival in head-injured patients. J Neurosurg 58:906–911, 1987
15. Young B, Ott L, Twyman D, et al: The effect of nutritional support on outcome from severe head injury. J Neurosurg 67:668–676, 1983
16. Klein S, Kinney J, Jeejeebhoy K, et al: Nutrition support in clinical practice: Review of published data and recommendations for future research directions. JPEN 21:133–156, 1997
17. Ott L, Annis K, Hatton J, et al: Postpyloric enteral feeding costs for patients with severe head injury: blind placement, endoscopy, and PEG/J versus TPN. J Neurotrauma 16:233–242, 1999
18. Grahm TW, Zadrozny DB, Harrington T: The benefits of early jejunal hyperalimentation in the head-injured patient. Neurosurgery 25:729–735, 1989
19. Klodell CT, Carroll M, Carrillo EH, et al: Routine intragastric feeding following traumatic brain injury is safe and well tolerated. Am J Surg 179:168–171, 2000
20. Taylor SJ, Fettes SB, Jewkes C, et al: Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. Crit Care Med 27:2525–2531, 1999
21. Twyman D: Nutritional management of the critically ill neurologic patient. Crit Care Clin 1:39–49, 1997

CANCER

Background

Nutrition status has an important effect on quality of life and sense of well-being in cancer patients. Malnutrition and weight loss often contribute to the death of cancer patients.[1]

Cancer cachexia is a syndrome characterized by progressive, involuntary weight loss. Clinical features include host tissue wasting, anorexia, skeletal muscle atrophy, anergy, fatigue, anemia, and hypoalbuminemia. Causes of cancer cachexia include anorexia, mechanical factors in the gastrointestinal tract related to tumor, side effects of surgery, chemotherapy, and/or radiation therapy, alterations in intermediary and energy metabolism, and changes in the host cytokine and hormonal millieu. The cancer cachexia syndrome (CCS), which is observed in approximately 50% of cancer patients,[2] involves a heterogeneous medley of physiologic and metabolic derangements resulting in potentially life-threatening malnutrition.[3] Although often seen in patients with advanced malignancies, CCS may be present in the early stages of tumor growth.

Weight loss in cancer patients is of prognostic significance. For any given tumor type, survival is shorter in patients who experience pretreatment weight loss.[2] Furthermore, CCS is a problematic cause of symptom distress in cancer patients.[4,5] Early recognition and intervention to prevent worsening of CCS may afford the best opportunity to prevent its debilitating consequences.[4]

Nutrition assessment of cancer patients is accomplished by taking a nutrition history and conducting a complete physical exam guided by the subjective global assessment or a modified version.[6,7] Diagnosis, stage of cancer, weight loss history, and changes in diet are especially informative in cancer patients. Serum albumin may also be helpful, as it has been shown to be of prognostic significance.[8] Despite the important role of malnutrition in the pathogenesis of cancer, nutrition care is often overlooked in this patient population.[8]

Evidence

Pharmacologic interventions play only a limited role in overcoming the anorexia and metabolic derangements seen in CCS. Research has focused on the use of specialized nutrition support (SNS), bypassing oral intake to overcome CCS related anorexia.

Numerous studies, as summarized by Boseki, have looked at the effect of SNS on nutritional parameters in cancer patients.[9] Parenteral nutrition (TPN) consistently causes weight gain, increases body fat, and improves nitrogen balance. The effect of TPN on lean body mass is minimal. The effects of enteral nutrition (EN) on body composition are less consistent; EN usually causes weight gain and improves nitrogen balance. Neither EN nor TPN, when administered for 7 to 49 days, have demonstrably beneficial effects on serum proteins. Specialized nutrition support has less of an effect on nutritional indices in cancer patients than in noncancer patients.[9,10] Enthusiasm for the use of SNS in cancer patients has historically been tempered by concern that provision of nutrients may stimulate tumor growth and metastasis. There are few relevant clinical studies.[11–13] Absent any overt effects, it is reasonable to ignore these theoretical considerations when contemplating the use of SNS in patients.

Extensive data are available concerning the use of SNS in cancer patients and have been summarized elsewhere.[14,15]

Routine use of SNS in patients undergoing major cancer operations does not improve surgical outcomes when either morbidity or mortality are used as endpoints. Preoperative SNS may be beneficial in moderately or severely malnourished patients if administered for 7 to 14 days preoperatively. In this situation, the potential benefits of nutrition support must be weighed against the potential risks of the SNS itself and of delaying the operation.[14,15]

There is no benefit to the routine use of SNS as an adjunct to chemotherapy.[16] Chemotherapy toxicity is not reduced; tumor responses and patient survival are not improved. Because of an increased risk of infection associated with the use of TPN, routine adjunctive use in patients receiving chemotherapy is actually deleterious. Specialized nutrition support is appropriate in patients receiving active anticancer treatment who are malnourished and who will be unable to absorb adequate nutrients for a prolonged period of time.

There are few clinical trials investigating the routine use of SNS as an adjunct to radiation therapy in cancer patients.[17] There is no clearly defined role for routine EN, TPN, or oral supplements during head and neck, abdominal, or pelvic irradiation.

Special Considerations

Some nutrients have specific biologic effects on tumor and host. Use of specific substances for effects beyond their nutritional role may be referred to as nutritional pharmacology. Four nutrients have been the subject of recent research: glutamine; arginine; nucleic acids; and essential fatty acids.[15] There are no clinical trial data to support the use of these substrates individually in cancer patients, with the possible exception of the use of glutamine in patients undergoing allogeneic bone marrow transplantation.[18,19] Clinical trials have investigated nutritional pharmacologic interventions in perioperative cancer patients using a mixture of "immune enhancing" substrates in an enteral formula containing supplemental arginine, RNA, and n-3 fatty acids. Biomarkers such as immune status and nitrogen balance may be favorably affected by these specific nutrients, but the effect on clinical endpoints is inconclusive. Currently, there is no proven role for combined specific nutrient supplementation in the care of cancer patients.[15]

The palliative use of SNS in cancer patients is rarely appropriate, although this issue remains controversial and is emotionally charged. In carefully selected patients, however, home TPN may lengthen survival and improve quality of life.[20–22] If patients are to benefit from this complex, intrusive, and expensive therapy they (1) must be physically and emotionally capable of participating in their own care; (2) should have an estimated life expectancy of greater than 40 to 60

days; (3) require strong social and financial support at home, including a dedicated in home lay care provider; and (4) fail trials of less invasive medical therapies.[23] Those patients with a life expectancy of less than 40 days may be palliated with home intravenous fluid therapy, although this is also controversial.[20,24]

Practice Guidelines
Cancer

1. Patients with cancer are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. SNS should not be used routinely in patients undergoing major cancer operations. (A)
3. Preoperative SNS may be beneficial in moderately or severely malnourished patients if administered for 7 to 14 days preoperatively, but the potential benefits of nutrition support must be weighed against the potential risks of the SNS itself and of delaying the operation. (A)
4. SNS should not be used routinely as an adjunct to chemotherapy. (A)
5. SNS should not be used routinely in patients undergoing head and neck, abdominal, or pelvic irradiation. (B)
6. SNS is appropriate in patients receiving active anticancer treatment who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period of time. (C)
7. The palliative use of SNS in terminally ill cancer patients is rarely indicated. (B)

REFERENCES

1. Inagaki J, Rodriguez V, Bodey GP: Causes of death in cancer patients. Cancer 33:568–573, 1974
2. DeWys WD, Begg D, Lavin PT, et al: Prognostic effect of weight loss prior to chemotherapy in cancer patients. Am J Med 69:491–497, 1980
3. Kern KA, Norton JA: Cancer cachexia. JPEN 12:286–298, 1988
4. Ottery FD: Supportive nutrition to prevent cachexia and improve quality of life. Semin Oncol 22(Suppl 13):98–111, 1995
5. Puccio M, Nathanson L: The cancer cachexia syndrome. Semin Oncol 24:277–287, 1997
6. Detsky AS, McLaughlin JR, Baker JP, et al: What is subjective global assessment of nutritional status? JPEN 11:8–13, 1987
7. Ottery FD: Definition of standardized nutritional assessment and interventional pathways in oncology. Nutrition 12:S15–S, 19, 1996
8. Delmore G: Assessment of nutritional status in cancer patients: Widely neglected? Support Care Cancer 5:376–380, 1997
9. Bozzetti F: Effects of artificial nutrition on the nutritional status of cancer patients. JPEN 13:406–420, 1989
10. Goldstein AS, Elwun DH, Askanazi J: Functional and metabolic changes during feeding in gastrointestinal cancer. J Am Coll Nutr 8:530–536, 1989
11. Baron PL, Lawrence W, Chan WMY, et al: Effects of parenteral nutrition on cell cycle kinetics of head and neck cancer. Arch Surg 121:1282–1286, 1986
12. Frank JL, Lawrence W Jr, Banks WL Jr, et al: Modulation of cell cycle kinetics in human cancer with total parenteral nutrition. Cancer 69:1858–1864, 1992
13. Franchi F, Rossi-Fanelli F, Seminara P, et al: Cell kinetics of gastrointestinal tumors after different nutritional regimens. A preliminary report. J Clin Gastroenterol 13:313–315, 1991
14. Klein S, Koretz RL: Nutrition support in patients with cancer: What do the data really show? Nutr Clin Pract 9:91–100, 1994
15. August DA: Nutritional care of cancer patients. IN Surgery: Scientific Basis and Current Practice. Norton JA (ed). Springer Verlag, New York, 2001, pp 1841–1861
16. Anonymous: Parenteral nutrition in patients receiving cancer chemotherapy. American College of Physicians. Ann Intern Med 110:734–736, 1989
17. Klein S, Kinney J, Jeejeebhoy K, et al: Nutrition support in clinical practice: Review of published data and recommendations for future research directions. JPEN 21:133–156, 1997
18. Szeluga DJ, Stuart RK, Brookmeyer R, et al: Nutritional support of bone marrow transplant recipients: A prospective randomized clinical trial comparing total parenteral nutrition to an enteral feeding program. Cancer Res 47:3309–3316, 1987
19. Schloerb PR, Amare M: Total parenteral nutrition with glutamine in bone marrow transplantation and other clinical applications (a randomized, double-blind study). JPEN 17:407–413, 1993
20. August DA, Thorn D, Fisher RL, et al: Home parenteral nutrition for patients with inoperable malignant bowel obstruction. JPEN 15:323–327, 1991
21. King LA, Carson LF, Konstantinides RN, et al: Outcome assessment of home parenteral nutrition in patients with gynecologic malignancies: What have we learned in a decade of experience? Gynecologic Oncol 51:377–382, 1993
22. Cozzaglio L, Balzola F, Cosentino F, et al: Outcome of cancer patients receiving home parenteral nutrition. JPEN 21:339–342, 1997
23. Baines M, Oliver DJ, Carter RI: Medical management of intestinal obstruction in patients with advanced malignant disease: A clinical and pathological study. Lancet 2:990–993, 1985
24. Welk T: Clinical and ethical considerations of fluid and electrolyte management in the terminally ill client. J Intravenous Nursing 22:43–47, 1999

CANCER: HEMATOPOETIC CELL TRANSPLANTATION

Background

Hematopoetic cell transplantation (HCT) refers to an array of therapies whose short- and long-term outcomes are affected by diagnosis, disease stage, transplant type (autologous, family related allogeneic, unrelated allogeneic), degree of donor histocompatibility, preparative regimen (myeloablative vs nonmyeloablative), stem cell source (bone marrow, peripheral blood, placental cord blood), age, prior therapy, and nutritional status.[1,2] Conventional HCT applies high-dose chemotherapy with or without irradiation to eradicate tumor in patients with malignancy. In allograft recipients, the patient's own immune system is also ablated to prevent graft rejection. Such marrow ablative regimens are among the most intensive therapies used in oncology. Lower intensity cytoreduction may also be used to establish a mixed chimera, with preservation of host T-cell–mediated immunity.[3] Gastrointestinal tract or liver complications are almost always the dose-limiting toxicities for these therapies.[4] The disruption of the mucosal barrier contributes to the pathogenesis of infection and fevers of unknown origin in the period of neutropenia that lasts 2 to 6 weeks. Patients experience a prolonged period of minimal oral intake, often lasting well beyond stem cell engraftment owing to the delayed effects of cytoreductive therapy on appetite, taste, salivary function, gastric emptying, and intestinal function.[5]

Autologous HCT is associated with low transplant-related mortality, but less favorable cure rates than

allogeneic HCT, which benefits from a graft-versus-tumor effect.[1] Recipients of allografts, however, suffer high transplant-related mortality as a result of donor T-lymphocyte–mediated graft-versus-host disease (GVHD). Acute GVHD occurs in the first few months post transplant and targets the skin, liver and gastrointestinal tract. A chronic form resembling collagen-like immune disorders may develop several months to years post transplant and involve single or multiple organs (skin, liver, oral mucosa, eyes, muscolskeletal system, lung, esophagus, and vagina). Moderate to severe GVHD and the multidrug regimens used in its prevention and treatment result in profound and prolonged immunosuppression. Despite advances in management, GVHD remains a significant problem because of the expanding use of unrelated and partially histocompatible related donors. Patients frequently have elevated nutrient requirements, altered carbohydrate, lipid and protein metabolism, experience difficulty eating for a variety of reasons dependent on organ involvement, and require modified diets, oral supplements, or SNS to prevent malnutrition.[4,6]

Significantly higher mortality occurs in underweight patients undergoing HCT, even amongst those with only mildly deficits.[2,7] Obesity also appears to have a negative influence on outcome.[7–9] The role, if any, for pretransplant intervention, has not been investigated.

Evidence

Mixing types of transplant, a variety of diagnoses, and other variables known to be associated with different short- and long-term outcomes have weakened clinical trials of nutrition support in HCT. TPN may improve long-term survival in allogeneic HCT patients,[10] but no randomized trials of sufficient size have been carried out in autologous HCT to establish its efficacy. A few small trials failed to demonstrate a benefit of TPN compared with no nutrition support[11] or an aggressive enteral feeding program,[12] but these studies were not large enough to rule out Type II errors. Another approach has been to establish the characteristics of HCT patients who require TPN. By setting standard criteria for weight loss and number of days with minimal oral intake, TPN is used with increasing frequency for patients with TBI versus chemotherapy only, allogeneic versus autolgous donors, and histoincompatible versus histocompatible donors.[13] Increased incidence of infections,[10–12] appetite suppression and delayed refeeding posttransplant,[14] inability to maintain lean body mass,[4] and hepatobiliary complications are all associated with the provision of TPN in HCT.

Early peri-transplant enteral tube feeding after conventional conditioning regimens is associated with a high rate of failure based on the limited published experience.[12,15] The challenges of establishing a safe enteral route after marrow ablative preparative regimens are formidable owing to bleeding, the risk of aspiration pneumonia, sinusitis, diarrhea, ileus and/or abdominal pain, delayed gastric emptying, and vomiting. Once a well-functioning white cell and platelet graft is established and oral and gastrointestinal tissues have healed, tube feeding is feasible as a transition step from TPN to oral diet or when nutrition support is indicated for late complications such as GVHD.[16]

Special Considerations

Two randomized, double-blind trials examined the benefits of intravenous glutamine and found mixed results in terms of clinical infection[17,18]; the relevance of these data with current antimicrobial regimens is unclear. The shorter length of hospital stay observed in glutamine-treated patients in both these trials is confounded by mixed patient types, failure to analyze as intent to treat, and lack of objective criteria for hospital discharge. Neither intravenous nor oral glutamine has reduced severity of oral mucositis or dependence on TPN[17–21] with the exception of a subset of autologous patients in one trial.[22] In this same trial glutamine appeared to worsen mucositis in recipients of allogeneic HCT.[22] Studies with sufficient power to assess any effect of glutamine on relapse, survival, and incidence, and severity of GVHD have not been reported.

Practice Guidelines *Cancer: Hematopoetic Cell Transplantation*

1. All patients undergoing conventional HCT with myeloablative conditioning regimens are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. When PN is used, it should be discontinued as soon as conditioning-related toxicities have resolved after stem cell engraftment. (A)
3. When gastrointestinal function returns post engraftment, EN should be used in patients in whom oral intake is inadequate to meet nutritional requirements. (B)
4. Pharmacologic doses of glutamine should not be used in patients undergoing HCT. (A)
5. Patients should receive dietary counseling regarding high risk foods and safe food handling during the period of immunocompromise. (B)
6. SNS is appropriate for patients undergoing HCT who develop moderate to severe GVHD accompanied by poor oral intake. (C)

REFERENCES

1. Thomas ED, Blume KG, Forman SJ (eds). Hematopoietic Cell Transplantation, 2nd ed. Blackwell Science, Malden, MA, 1999
2. Deeg HJ, Seidel K, Bruemmer B, et al: Impact of patient weight on non-relapse mortality after marrow transplantation. Bone Marrow Transplant 15:461–468, 1995
3. McSweeney PA, Storb R: Hematology, 2nd ed. Mixed chimerism. Preclinical studies and clinical applications. Biol Blood Marrow Transplant 5:192–203, 1999
4. Bensinger WI, Buckner CD: Preparative regimens. IN Hematopoietic Cell Transplantation, 2nd ed. Thomas ED, Blume KG, Forman SJ (eds). Blackwell Science, Malden, MA, 1999, pp 123–134
5. Aker SN, Lenssen P: Nutritional support in hematological malignancies. IN Hemotology: Basic Principles and Practice, 3rd ed.

Hoffman R, Benz EJ, Shattil SJ, et al (eds). Churchill Livingstone, New York, 2000, pp 1501–1514
6. Lenssen P, Sherry ME, Stern J, et al: Prevalence of nutrition-related problems among long-term survivors of allogeneic marrow transplantation. J Am Diet Assoc 90:835–842, 1990
7. Dickson TM, Kusnierz-Glaz CR, Blume KG, et al: Impact of admission body weight and chemotherapy dose adjustment on the outcome of autologous bone marrow transplantation. Biol Blood Marrow Transplant 5:290–305, 1999
8. Morton AJ, Gooley T, Hansen JA, et al: Association between pretransplant interferon-alpha and outcome after unrelated donor marrow transplantation for chronic myelogenous leukemia in chronic phase. Blood 92:394–401, 1998
9. Fleming DR, Rayens MK, Garrison J: Impact of obesity on allogeneic stem cell transplant patients: A matched case-controlled study. Am J Med 102:265–268, 1997
10. Weisdorf SA, Lysne J, Wind D, et al: Positive effect of prophylactic total parenteral nutrition on long-term outcome of bone marrow transplantation. Transplantation 43:833–838, 1987
11. Lough M, Watkins R, Campbell M, et al: Parenteral nutrition in bone marrow transplantation. Clin Nutr 9:97–101, 1990
12. Szeluga DJ, Stuart RK, Brookmeyer R, et al: Nutritional support of bone marrow transplant recipients: A prospective, randomized clinical trial comparing total parenteral nutrition to an enteral feeding program. Cancer Res 47:3309–3316, 1987
13. Iestra JA, Fibbe WE, Zwinderman AH, et al: Parenteral nutrition following intensive cytotoxic therapy: an exploratory study on the need for parenteral nutrition after various treatment approaches for haematological malignancies. Bone Marrow Transplant 23:933–939, 1999
14. Charuhas PM, Fosberg KL, Bruemmer B, et al: A double-blind randomized trial comparing outpatient parenteral nutrition with intravenous hydration: Effect on resumption of oral intake after marrow transplantation. JPEN 21:157–161, 1997
15. Lenssen P, Bruemmer B, Aker SN, et al: Nutrient support in hematopoietic cell transplantation. JPEN 25:219–228, 2001
16. Roberts SR, Miller JE: Success using PEG tubes in marrow transplant recipients. Nutr Clin Pract 13:74–78, 1998
17. Ziegler TR, Young LS, Benfell K, et al: Clinical and metabolic efficiency of glutamine-supplemented parenteral nutrition after bone marrow transplantation: A randomized, double-blind, controlled study. Ann Intern Med 116:821–828, 1992
18. Schloerb PR, Amare M: Total parenteral nutrition with glutamine in bone marrow transplantation and other clinical applications (a randomized, double-blind study). JPEN 17:407–413, 1993
19. Jebb SA, Marcus R, Elia M: A pilot study of oral glutamine supplementation in patients receiving bone marrow transplants. Clin Nutr 14:162–165, 1995
20. Schloerb PR, Skikne BS: Oral and parenteral glutamine in bone marrow transplantation: A randomized, double-blind study. JPEN 23:117–122, 1999
21. Dickson TMC, Wong RM, Negrin RS, et al: Effect of oral glutamine supplementation during bone marrow transplantation. JPEN 24:61–66, 2000
22. Anderson PM, Ramsay NKC, Shu XO, et al: Effect of low-dose oral glutamine on painful stomatitis during bone marrow transplantation. Bone Marrow Transplant 22:339, 1998

HIV/ACQUIRED IMMUNO-DEFICIENCY SYNDROME

Background

Nutrition plays a pivotal role in the course, quality of life, and outcomes of patients with the acquired immunodeficiency syndrome (AIDS). Protein-calorie malnutrition is common in HIV-infected patients. The advent of highly active antiretroviral therapy (HAART) has markedly reduced the incidence of malnutrition. However, an emerging syndrome of subcutaneous fat depletion and visceral fat accumulation has been recognized and is associated with a variety of metabolic abnormalities, including hyperlipidemia and insulin resistance.

AIDS wasting syndrome (AWS) is defined by the CDC as an involuntary weight loss greater than 10% of baseline body weight plus either chronic diarrhea (at least two loose stools per day for 30 days or more) or chronic weakness and documented fever (for 30 days or more, intermittent or constant) in the absence of concurrent illness or any condition other than HIV infection that could explain the findings.[1]

This definition is based on total weight rather than body composition and does not take into consideration the rate at which weight loss occurs. Disproportionate loss of lean body mass (LBM) has been correlated with an increased risk of adverse outcomes.[2] Significant loss of LBM may occur with total body weight loss less than 10% baseline and may herald the onset of infection. Loss of LBM may occur early in the course of HIV disease.[3] A sexual dimorphism in the patterns of wasting may exist with women losing more fat early on due to higher baseline fat stores, whereas LBM loss that occurs later in the course of AWS seems to be comparable in both genders.[4] Men with higher fat stores seem to lose more fat and less LBM compared with other men with lower fat stores.[5]

The causes of AWS are multifactorial and relate to food intake, nutrient absorption in the gut, and metabolic alterations in energy expenditure.

Decreased food intake is multifactorial in etiology. Oral and esophageal abnormalities, altered smell and taste sensation, and depression all contribute to the development of food aversion and anorexia. In addition, secondary anorexia occurs due to infection and release of pro-inflammatory cytokines. Malabsorption also affects food intake. Social isolation and decline in socioeconomic status often result in reduced access to proper nutrition.

AIDS patients are susceptible to infection with a variety of small bowel pathogens resulting in enteropathy and malabsorption. Even with aggressive work-up, a specific cause of diarrhea is not identified in a substantial number of patients. The pathogenesis of malabsorption is multifactorial and includes primary enterocyte injury with partial villous atrophy and crypt hyperplasia, ileal dysfunction with bile salt wasting and fat malabsorption, and oxidative enteropathy. The consequences of malabsorption include decreased appetite, and "enterogastrone" effects including dry mouth, decreased gastric acid secretion, decreased rate of gastric emptying, and slowed intestinal transit.[6]

Metabolic dysfunction in AWS is similar to other conditions associated with cachexia such as cancer and COPD. When increased protein turnover is present, resting energy expenditure is raised, but total energy expenditure is not. Plasma pro-inflammatory cytokines (interleukin-1, interleukin-6, tumor necrosis Factor alpha) are increased and regulatory cytokines such as interleukin-12 are decreased.[7] These findings are not uniform. Evidence suggests that decreased energy intake rather than elevated energy expenditure, is the prime determinant of weight loss in AWS.[8] Hypogonadism is also a contributor to loss of muscle mass. The prevalence of hypogonadism in AWS patients is high and the important anabolic effects of testosterone are uncontested.

The severity of AWS is of prognostic importance irrespective of the underlying cause of wasting and immune status. Body composition studies have shown that LBM loss, decline in quality of life and total body weight depletion occur predictably as patients near death.[2] This pattern is similar to previous reports of starvation with or without associated infections. Nutrition assessment in AIDS is similar to other entities and should include a detailed nutrition history (including current, usual, and ideal body weights), a complete physical examination, assessment of LBM using anthropometric tools, routine laboratory markers, and (when available) either bioelectrical impedance analysis (BIA) or dual energy X-ray absorptiometry (DEXA).[9]

Evidence

It seems logical that early intervention to prevent LBM depletion and successful repletion of lost metabolically active tissue would improve outcomes and enhance quality of life in patients with AIDS. There are few supportive data.

Before the introduction of HAART, an estimated two thirds of all HIV patients satisfied CDC criteria for AWS.[10] Although the prevalence of AWS has significantly declined, numerous reports suggest that malnutrition is still common. The use, compliance, and response to HAART is variable and the impact on body cell mass is uncertain. Although it is not clear what the numbers are 4 years into the HAART era, the impact on reduction of infections and improvement of immune function and survival is undeniable. The restoration of total body weight may, however, be mainly related to a gain in fat and some reports have suggested persistent body cell mass loss.[10]

A randomized, controlled study has shown that nutrition counseling in combination with caloric supplements may have a beneficial effect on fat free mass and may retard protein catabolism in AIDS patients.[11] Therapeutic interventions specifically targeting wasting include appetite stimulants (eg, dronabinol, megestrol acetate), cytokine inhibitors (eg, thalidomide, cyproheptadine, ketotifen, pentoxifylline, fish oil, *N*-acetylcysteine), and anabolic agents (eg, testosterone, nandrolone, oxandrolone, recombinant human growth hormone). A randomized, placebo-controlled study showed that megestrol in doses of 400 to 800 mg/d promotes appetite and weight gain, but with a predominance of fat gain. Concerning side effects include a diabetogenic effect as well as Cushingoid symptoms and potential for adrenal insufficiency if discontinued precipitously.[12] Short-term dronabinol use in doses of 2.5 mg twice a day has not been demonstrated to increase lean body mass, and effect on total body weight is minimal. A positive effect on appetite has been observed in a placebo-controlled study, although food intake was not measured.[13] Dronabinol was associated with significant CNS side effects.

In a randomized, placebo-controlled trial, treatment with recombinant human growth hormone (rhGH) at doses of 0.1 mg/kg subcutaneously for 12 weeks resulted in a significant and sustained increase in weight that was accompanied by an even greater increase in LBM and a decrease in fat, plus improvement in treadmill work output.[14] Concerning issues include the development of hyperglycemia and diabetes with long-term use. Long-term rhGH therapy is considerably more expensive than other therapies.

Thalidomide, a drug known for its anti-inflammatory properties, has shown benefit in increasing weight. In one double blind placebo-controlled study using thalidomide at 100 or 200 mg orally for 8 weeks, over one-half of the weight gain was fat-free mass.[15] Longer courses and higher doses may be limited by drug side effects. Access to thalidomide is strictly controlled to avoid potential teratogenic effects.

The value of testosterone in the treatment of AWS remains under scrutiny, with placebo-controlled studies showing sustained increases in LBM at doses of 300 mg IM every 3 weeks in hypogonadal men.[16] Some encouraging results were found in women with AWS who had transdermal testosterone administered in a pilot study.[17] Treatment was well tolerated.

Resistance training has been evaluated as a safe alternative to pharmacologic therapy. A short-term course of high-intensity progressive resistance training has been shown to increase lean body mass in HIV-infected patients, including a few AWS patients. Resistance training in one observational study looking at eugonadal men with AWS increased LBM without the adverse effects on metabolic variables of anabolic therapies.[18]

The combination of pharmacological doses of nandrolone decanoate with progressive resistance training in one randomized, open-label study, yielded significant gains in total weight, lean body mass, body cell mass, muscle size, and strength when compared with anabolic therapy alone.[19] Interestingly, the combination of testosterone and resistance training in hypogonadal men did not show any additive effects compared with each intervention alone in one randomized, placebo-controlled study.[20]

Special Considerations

In a double-blind, randomized, placebo-controlled study, the combination of three nutrients, consisting of beta-hydroxy-beta-methylbutyrate (HMB), L-glutamine (Gln) and L-arginine (Arg), was shown to slow the course of lean tissue loss in patients with AWS.[21] The combination of L-glutamine (40 g/d) and antioxidants increased weight and body cell mass in another placebo-controlled study.[22] In the setting of malabsorption, semi-elemental diets were shown to result in weight and LBM gain in a randomized, open-label study.[23]

PN has been evaluated in both home and inpatient settings. Although central venous access clearly results in an increased risk for bloodstream infections, a transient impact on weight and LBM has been shown in certain studies.[24] No clear effect on survival was demonstrated. PN is also markedly more expensive than other modes of feeding.

Few studies have looked at the outcomes of EN in AWS. Transient increases in total body weight have been demonstrated in small, randomized studies, at

the expense of a higher rate of procedure-related complications.[25] The effect on survival remains controversial, although extensive data from other illnesses associated with wasting has shown no survival benefit in the absence of treatment of the underlying illness.

Few studies have evaluated the outcomes of surgery as a function of nutrition status in AIDS patients. Expert opinion is that HIV infection is not a significant, independent risk factor for major surgical procedures and the risk of major surgery in this population is not unlike that for other immunocompromised or malnourished patients.[26]

An alarming observation in the HAART era has been the development of HIV-associated lipodystrophy. Reported prevalence rates vary considerably, due at least in part to the lack of a case definition, the imprecision of self-report and physician perceptions, and varying durations of follow-up. The morphologic manifestations of lipodystrophy differ by sex and race. The various body composition and metabolic complications are multifactorial in their etiologies. Initial analyses suggest there is little or no short-term increase in cardiac risk, but do not settle the question of long-term risk.

Practice Guidelines *HIV/Acquired Immuno-Deficiency Syndrome*

1. Patients with HIV are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Nutrition assessment of patients with HIV should include quantitative measurement of LBM using DEXA or BIA. (B)
3. Patients with AWS should receive specific AWS directed therapy, including anabolic agents and/or resistance training, testosterone in hypogonadal men, and appetite stimulants for those with decreased appetite. (A)
4. SNS has a very limited role in AWS and should be reserved for patients receiving active, disease directed treatment who are unable to meet their nutrient requirements by oral feeding (B)

REFERENCES

1. Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. Morbid Mortal Weekly Rep 36:3–15, 1987
2. Kotler DP, Tierney AR, Wang J, et al: Magnitude of body-cell-mass depletion and the timing of death from wasting in AIDS. Am J Clin Nutr 50(3):444–447, 1989
3. Ott M, Lembcke B, Fischer H: Early changes of body composition in human immunodeficiency virus-infected patients: tetrapolar body impedance analysis indicates significant malnutrition. Am J Clin Nutr 57(1):15–19, 1993
4. Kotler DP, Thea DM, Heo M: Relative influences of sex, race, environment, and HIV infection on body composition in adults. Am J Clin Nutr 69(3):432–439, 1999
5. Mulligan K, Tai VW, Schambelan M: Cross-sectional and longitudinal evaluation of body composition in men with HIV infection. J Acquir Immune Defic Syndr Hum Retrovirol 15(1):43–48, 1997
6. Kotler DP: Human immunodeficiency virus-related wasting: malabsorption syndromes. Semin Oncol 25(2 Suppl 6):70–75, 1998
7. Baronzio G, Zambelli A, Comi D, et al: Proinflammatory and regulatory cytokine levels in AIDS cachexia. In Vivo 13(6):499–502, 1999
8. Macallan DC, Noble C, Baldwin C: Energy expenditure and wasting in human immunodeficiency virus infection. N Engl J Med 333(2):83–88, 1995
9. Suttmann U, Ockenga J, Selberg O: Incidence and prognostic value of malnutrition and wasting in human immunodeficiency virus-infected outpatients. J Acquir Immune Defic Syndr Hum Retrovirol 8(3):239–246, 1995
10. Corcoran C, Grinspoon S: Treatments for wasting in patients with the acquired immunodeficiency syndrome. N Engl J Med 340(22):1740–1750, 1999
11. Schwenk A, Steuck H, Kremer G: Oral supplements as adjunctive treatment to nutritional counseling in malnourished HIV-infected patients: randomized controlled trial. Clin Nutr 18(6): 371–374, 1999
12. Von Roenn JH, Armstrong D, Kotler DP: Megestrol acetate in patients with AIDS-related cachexia. Ann Intern Med 121(6): 393–399, 1994
13. Beal JE, Olson R, Laubenstein L: Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. J Pain Symptom Manage 10(2):89–97, 1995
14. Schambelan M, Mulligan K, Grunfeld C: Recombinant human growth hormone in patients with HIV-associated wasting. A randomized, placebo-controlled trial. Serostim Study Group. Ann Intern Med 125(11):873–882, 1996
15. Kaplan G, Thomas S, Fierer DS: Thalidomide for the treatment of AIDS-associated wasting. AIDS Res Hum Retroviruses 16(14): 1345–1355, 2000
16. Grinspoon S, Corcoran C, Anderson E: Sustained anabolic effects of long-term androgen administration in men with AIDS wasting. Clin Infect Dis 28(3):634–636, 1999
17. Miller K, Corcoran C, Armstrong C: Transdermal testosterone administration in women with acquired immunodeficiency syndrome wasting: a pilot study. J Clin Endocrinol Metab 83(8): 2717–225, 1998
18. Roubenoff R, McDermott A, Weiss L: Short-term progressive resistance training increases strength and lean body mass in adults infected with human immunodeficiency virus. AIDS 13(2):231–239, 1999
19. Sattler FR, Jaque SV, Schroeder ET: Effects of pharmacological doses of nandrolone decanoate and progressive resistance training in immunodeficient patients infected with human immunodeficiency virus. J Clin Endocrinol Metab 84(4):1268–1276, 1999
20. Bhasin S, Storer TW, Javanbakht M: Testosterone replacement and resistance exercise in HIV-infected men with weight loss and low testosterone levels. JAMA 9;283(6):763–770, 2000
21. Clark RH, Feleke G, Din M: Nutritional treatment for acquired immunodeficiency virus-associated wasting using beta-hydroxy beta-methylbutyrate, glutamine, and arginine: a randomized, double-blind, placebo-controlled study. JPEN 24(3):133–139, 2000
22. Shabert JK, Winslow C, Lacey JM: Glutamine-antioxidant supplementation increases body cell mass in AIDS patients with weight loss: a randomized, double-blind controlled trial. Nutrition 15(11–12):860–864, 1999
23. Kotler DP, Fogleman L, Tierney AR: Comparison of total parenteral nutrition and an oral, semielemental diet on body composition, physical function, and nutrition-related costs in patients with malabsorption due to acquired immunodeficiency syndrome. JPEN 22(3):120–126, 1998
24. Melchior JC, Chastang C, Gelas P: Efficacy of 2-month total parenteral nutrition in AIDS patients: A controlled randomized prospective trial. The French Multicenter Total Parenteral Nutrition Cooperative Group Study. AIDS 10(4):379–384, 1996
25. Cappell MS, Godil A: A multicenter case-controlled study of percutaneous endoscopic gastrostomy in HIV-seropositive patients. Am J Gastroenterol. 88(12):2059–2066, 1993
26. Harris HW, Schecter WP: Surgical risk assessment and management in patients with HIV disease. Gastroenterol Clin N Am 26(2):377–391, 1997

CRITICAL CARE: BURNS

Background

The stress response to burn injury is associated with a spectrum of hormonal, metabolic, immunologic, and nutrition abnormalities that are generally commensurate with the depth and size of the burn.[1–6] Recovery from burns has been classified into (1) a shock or resuscitation phase, (2) the acute catabolic phase, and (3) the adaptive anabolic phase. Particularly relevant to nutrition support is the loss of heat, water, protein, and micronutrients through open wound, along with systemic manifestations of increased energy expenditure and accelerated protein degradation. Complex endocrine and cytokine alterations likely contribute to postburn hypermetabolism and hypercatabolism, although other effectors play a role as well.[3–5]

The destructive consequences of prolonged, untreated catabolism in the burn patient have long been documented.[1,2,7,8] Clinically, patients who withstand the ravages of postburn hypermetabolism and catabolism become debilitated with weight loss[1–3,7–10] and erosion of lean body mass.[11,12] Children are especially vulnerable because they are still growing. A large burn can retard linear growth and decrease growth velocity for several years.[9,13,14] Parameters such as weight,[3] caloric balance,[15,16] serum transferrin,[17,18] and prealbumin[19–20] are correlated with risk of infection and delayed wound healing, which are complications of malnutrition.

Evidence

SNS is a significant positive effector of outcome and should receive priority consideration postburn. An aggressive nutrition approach is required to address burn-induced hypermetabolism, enhance nitrogen retention, and maximize conditions conducive to anabolism, immunocompetence, and healing.

Assessment of nutrition status (with an emphasis on energy and protein needs) is required on admission, and ongoing reassessment should occur until the patient is no longer at risk.[4,5] Nutritional requirements may be determined either by direct measurement or estimated using generally accepted tools.[4–6] In either case, interpretation of nutrition parameters must include recognition of relevant limitations.[5,21]

It is undisputed that energy[1–3,5–8,11,15,22–24] and protein needs[4,5,25,26] are heightened postburn and that adequate, but not excessive, calories should be provided.[4–6,23] Nevertheless, there is no consensus regarding an optimal method for defining macronutrient goals. At least 30 mathematical equations have been developed for estimating the energy needs of burn patients, incorporating various demographic data such as weight, body surface area, and body surface area burned.[4–6,24,27–29] The validity and reliability of such formulae have been questioned by many.[22,29,31] When feasible, indirect calorimetry is recommended to assess and reassess caloric needs.[4,5,23,24] A factor of 20% to 30% above the measured energy expenditure is commonly recommended to account for increased caloric demands from physical therapy along with the stresses of wound care.[4,22,32]

A number of clinical investigations document increased protein needs postburn.[25–27] The classic study by Alexander and colleagues showed that severely burned children receiving 20% to 23% of total calories from protein (calorie to nitrogen ratio of 110:1) had better immune function, higher survival rates, fewer bacteremic days, and fewer days on systemic antibiotics compared with a control group receiving only 17% of total calories as protein (calorie to nitrogen ratio of 150:1).[25]

Nutrition support of the burn patient is best accomplished enterally. Not uncommonly, a high-calorie, high-protein oral diet is sufficient to maintain small burns (<20% surface area) not complicated by facial injury, inhalation injury, psychological difficulties, or preburn malnutrition. Patients with larger surface area burns generally have difficulty consuming sufficient calories and protein by mouth. Consequently, EN should be initiated as soon as practical, preferably within the first 24 hours postburn.[4,6,33–37] Burn patients are normally tube-fed nasogastrically[36,37] or nasoenterically.[16,35,38,39] Burn severity generally dictates which enteral route is indicated. Gastric ileus, which limits use of the stomach for EN, is common and often resurfaces during operative procedures, septic episodes, major dressing changes or other complicating events. It is therefore standard procedure in many burn units to routinely use transpyloric feeding methods in an effort to negate the necessity for tube feeding interruptions.[5,16,28,35,38,39]

PN is associated with complications (intestinal dysmotility, hepatic steatosis, septic morbidity, and catheter-related infection). In several prospective trials, Herndon and associates have demonstrated that PN was associated with increased mortality in severely burned patients.[40,41] Hence, the use of PN is reserved for those patients where gastrointestinal support is anticipated to be impossible for a prolonged period.[42,43]

Special Considerations

Pharmacologic nutritional modulation of metabolism, prostaglandins, and cytokines and the adjunctive role of anabolic agents such as hormones and growth factors represent potential modalities for further enhancing wound healing and immunocompetence postburn. Among the specific nutrients most frequently used in the pharmacologic support of burn patients are arginine, glutamine, omega-3 fatty acids, zinc, and vitamins A and C. Although the results of preliminary clinical trials involving arginine,[44] glutamine[45] and omega-3 fatty acids[44] look promising, considerable controversy remains.[38,39] Even less well understood are the requirements and pharmacologic effects of specific micronutrients,[46,47] although supplementation with a number of vitamins and trace elements has become standard practice.[6,28,48–53]

The combination of various nutrient modulators into purported "immune enhancing" formulations has been evaluated with dubious results. Burn patients receiving the Shriners' diet (eg, high protein, low fat and linoleic acid, and fortified with omega-3 fatty acids, arginine, cysteine, histidine, vitamins A and C, and

zinc) experienced fewer wound and general infections along with a shortened length of hospital stay.[44] On the other hand, Saffle et al[39] found no advantage of an immune enhancing substrate (containing omega-3 fatty acids, nucleotides, and arginine) when compared with a simple high-protein enteral formula. Additional studies are required to determine the efficacy of pharmacologic nutrient enrichment.

Practice Guidelines *Critical Care: Burns*

1. Patients with second or third degree burns are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Adequate calories must be provided to address the hypermetabolism associated with acute burn injury. (A)
3. When possible, the energy requirements of burn patients should be measured using indirect calorimetry. (B)
4. Severely burned patients require increased intake of protein until significant wound healing is achieved. (A)
5. There is no current role for the routine use of specific nutrients and anabolic agents (eg, arginine, glutamine, omega-3 fatty acids, vitamins, trace minerals, antioxidants, growth hormone, oxandrolone, etc) in burn patients. (B)
6. EN should be used in preference to PN in burn patients requiring SNS. (A)
7. EN should be initiated as soon as possible in patients with moderate/severe burns. (A)
8. PN should be reserved for patients who require SNS and in whom EN is contraindicated or is unlikely to meet nutritional requirements within 4 to 5 days. (B)

REFERENCES

1. Wilmore DW: Nutrition and metabolism following thermal injury. Clin Plast Surg 1:603–606, 1974
2. Wilmore DW, Curreri PW, Spitzer KW, et al: Supranormal dietary intake in thermally injured hypermetabolic patients. Surg Gynecol Obstet 132:881–886, 1971
3. Wilmore DW, Kinney JM: Panel Report on nutritional support of patients with trauma or infection. Am J Clin Nutr 34:1213–1222, 1981
4. Mayes T, Gottschlich MM: Burns and wound healing. IN The Science and Practice of Nutrition Support. A Case-Based Core Curriculum. Gottschlich MM (ed). Kendall Hunt Publishing Co., Dubuque, IN, 2001, pp 391–420
5. Mayes T, Gottschlich MM. Burns. IN Contemporary Nutrition Support Practice. Matarese L, Gottschlich M (eds). WB Saunders Co, Philadelphia, PA, 1998, pp 590–610
6. Peck M: American Burn Association Clinical Guidelines. Initial nutrition support of burn patients. J Burn Care Rehabil 22:595–665, 2001
7. Gump FE, Kinney JM: Energy balance and weight loss in burned patients. Arch Surg 103:442–448, 1971
8. Guber EV, Zimina EP: Variations of energy metabolism in burns. Fed Proc 23:441–443, 1964
9. Childs C, Hall T, Davenport PJ, et al: Failure of TPN supplementation to improve liver function, immunity and mortality in thermally injured patients. J Trauma 27:195–204, 1987
10. Newsome TW, Mason AD, Pruitt BA: Weight loss following thermal injury. Ann Surg 179:215–217, 1973
11. Gore DC, Rutan RL, Hildreth MA, et al: Comparison of resting energy expenditures and caloric intake in children with severe burns. J Burn Care Rehabil 11:400–404, 1990
12. Bessy PQ, Jiang ZM, Johnson DJ, et al: Post-traumatic skeletal muscle proteolysis: the role of the ormonal environment. World J Surg 13:465–470, 1989
13. Prelack K, Petras L, Antoon A, et al: Measures of height and weight in children recovering from severe burn injury. J Burn Care Rehabil 18:S171, 1997
14. Rutan RL, Herndon DN: Growth delay in postburn pediatric patients. Arch Surg 125:392–395, 1990
15. Mancusi-Ungaro HR, Van Way CW, McCool C: Caloric and nitrogen balances as predictors of nutritional outcome in patients with burns. J Burn Care Rehabil 13:695–702, 1992
16. Jenkins M, Gottschlich MM, Mayes T, et al: Enteral feeding during operative procedures. J Burn Care Rehabil 15:199–205, 1994
17. Jensen TG, Long JM, Dudrich SJ, et al: Nutritional assessment indications of postburn complications. J Am Diet Assoc 85:68–72, 1985
18. Ogle CK, Alexander JW: The relationship of bacteremia to levels of transferrin, albumin and total serum protein in burn patients. Burns 8:32–38, 1981
19. Gottschlich MM, Baumer T, Jenkins M, et al: The prognostic value of nutritional and inflammatory indices in patients with burns. J Burn Care Rehabil 13:105–113, 1992
20. Morath MA, Miller SF, Finley RK, et al: Interpretation of nutritional parameters in burn patients. J Burn Care Rehabil 4:361–366, 1984
21. Cynober L, Prugnaud O, Lioret N, et al: Serum transthyretin levels in patients with burn injury. Surgery 109:640–644, 1991
22. Saffle JR, Medina E, Raymond J, et al: Use of indirect calorimetry in the nutritional management of burned patients. J Trauma 25:32–39, 1985
23. Saffle JR, Larson CM, Sullivan J: A randomized trail of indirect calorimetry-based feedings in thermal injury. J Trauma 30:776–782, 1990
24. Curreri PW, Richmond D, Marvin J, et al: Dietary requirements of patients with major burns. J Am Diet Assoc 65:415–417, 1974
25. Alexander JW, MacMillan BC, Stinnett JP, et al: Beneficial effects of aggressive protein feeding in severely burned children. Ann Surg 192:505–517, 1980
26. Matsuda T, Kagan RJ, Hanumadass M, et al: The importance of burn wound size in determining the optimal calorie: nitrogen ratio. Surgery 94:562–568, 1983
27. Cunningham JJ, Lydon MK, Russell WE: Calorie and protein provision for recovery from severe burns in infants and young children. Am J Clin Nutr 51:553–557, 1990
28. Williamson J: Actual burn nutrition care practices. A national survey (part II). J Burn Care Rehabil 10:185–194, 1989
29. Mayes T, Gottschlich MM, Khoury J, et al: Evaluation of predicted and measured energy requirements in burned children. J Am Diet Assoc 96:24–29, 1996
30. Hildreth MA, Herndon DN, Parks DH, et al: Evaluation of a caloric requirement formula in burned children treated with early excision. J Trauma 27:188–189, 1987
31. Turner WW, Ireton CS, Hunt JL, et al: Predicting energy expenditure in burned patients. J Trauma 25:11–16, 1985
32. Goran MI, Peters EJ, Herndon DN, et al: Total energy expenditure in burned children using the doubly labeled water technique. Am J Physiol 259:E576–E585, 1990
33. Taylor SJ: Early enhanced enteral nutrition in burned patients is associated with fewer infective complications and shorter hospital stay. J Hum Nutr Dietet 12:85–91, 1999
34. Gottschlich MM, Warden GD, Michel M, et al: Diarrhea in tube-fed burn patients: incidence, etiology, nutritional impact and prevention. JPEN 12:338–345, 1988
35. Jenkins M, Gottschlich MM, Alexander JW, et al: Effect of immediate enteral feeding on the hypermetabolic response following severe burn injury. JPEN 13:12, 1989
36. McDonald WS, Sharp CW, Deitch EA: Immediate enteral feeding in burn patients is safe and effective. Ann Surg 213:177–183, 1991

37. Raff T, Hartmann B, Germann G: Early intragastric feeding of seriously burned and long-term ventilated patients: a review of 55 patients. Burns 23:19–25, 1997
38. Garrel DR, Razi M, Lariviere F, et al: Improved clinical status and length of care with low fat nutrition support in burn patients. JPEN 19:482–491, 1995
39. Saffle JR, Wiebke G, Jennings K, et al: Randomized trial of immune-enhancing enteral nutrition in burn patients. J Trauma 42:73–802, 1997
40. Herndon DN, Stein MD, Rutan TC, et al: Failure of TPN supplementation to improve liver function, immunity and mortality in thermally injured patients. J Trauma 27:195–204, 1987
41. Herndon DN, Barrow RE, Stein MD, et al: Increased mortality with intravenous supplemental feeding in severely burned patients. J Burn Care Rehabil 10:309–313, 1989
42. Gottschlich MM, Warden GD: Parenteral nutrition in the burned patient. IN Total Parenteral Nutrition. Fischer JE (ed). Little, Brown and Co, Boston, 1991, pp 279–298
43. Goodwin CW: Parenteral nutrition in thermal injuries. IN Clinical Nutrition: Parenteral Nutrition. Rombeau JL, Caldwell MD (eds). WB Saunders Co, Philadelphia, 1993, pp 566–584
44. Gottschlich MM, Jenkins M, Warden GD, et al: Differential effects of three enteral dietary regimens on selected outcome variables in burn patients. JPEN 14:225–236, 1990
45. Ogle CK, Ogle JD, Mao JX, et al: Effect of glutamine on phagocytosis and bacterial killing by normal and pediatric burn patient neutrophils. JPEN 18:128–133, 1994
46. Berger MM, Spertini F, Spertini F, et al: Trace element supplementation modulates pulmonary infection rates after major burns: a double-blind, placebo-controlled study. Am J Clin Nutr 68:365–371, 1998
47. Rock CL, Dechert DE, Khilnani R, et al: Carotenoids and antioxidant vitamins in patients after burn injury. J Burn Care Rehabil 18:269–278, 1997
48. Gottschlich MM, Warden GD: Vitamin supplementation in the patient with burns. J Burn Care Rehabil 11:275–279, 1990
49. Manning AJ, Meyer N, Klein GL: Vitamin and trace element homeostasis following burn injury. IN Total Burn Care. Herndon DN (ed). WB Saunders Co, Philadelphia, PA, 1996, pp 251–258
50. Gamlier Z, DeBiasse MA, Demling RJ: Essential microminerals and their response to burn injury. J Burn Care Rehabil 17:264–272, 1996
51. King N, Goodwin CW: Use of vitamin supplements for burned patients: a national survey. J Am Diet Assoc 84:923–925, 1984
52. Shippee RL, Wilson SW, King N: Trace mineral supplementation of burn patients: a national survey. J Am Diet Assoc 87:300–303, 1987

CRITICAL CARE: CRITICAL ILLNESS

Background

Critical illness refers to a wide spectrum of life-threatening medical or surgical conditions usually requiring intensive care unit (ICU) level care. Most critically ill patients exhibit at least severe single organ system dysfunction necessitating active therapeutic support. Sepsis or the systemic inflammatory response syndrome (SIRS) is present in a substantial number of cases. Sepsis is the systemic response to infection and is thought to result from the activation of a series of endogenous mediators, including classical hormones, cytokines, coagulation factors, eicosanoids, and others.[1–4] The systemic inflammatory response syndrome is clinically indistinguishable from the septic syndrome, thought to result from the same endogenous mediators, and can occur in patients with severe pancreatitis, hemorrhage, burns, ischemia, and other severe noninfectious diseases.[1]

The most prominent metabolic alterations characterizing sepsis and SIRS include hypermetabolism, hyperglycemia with insulin resistance, accelerated lipolysis, and net protein catabolism.[3,5,6] The combined impact of these metabolic alterations, bed rest, and lack of nutritional intake can lead to rapid and severe depletion of lean body mass. Nutrition support cannot fully prevent or reverse the metabolic alterations and disruptions in body composition associated with critical illness.[5,7] Nutrition support in these patients is supportive (as opposed to therapeutic) in that it can slow the rate of net protein catabolism.[5,7]

It has been proposed that atrophy of the gastrointestinal tract resulting from disuse contributes to morbidity and mortality in critically ill patients by facilitating or permitting the translocation of enteric bacteria or their metabolic products into the circulation.[8] However, a clear path of evidence linking fasting, gut atrophy, bacterial translocation, and the development of sepsis or SIRS in humans has not been established.[9,10]

A corollary of the gut atrophy-bacterial translocation hypothesis is that, by virtue of its intravenous delivery, PN leads to gut atrophy, and therefore increases the risk of bacterial translocation. Such a connection has not been confirmed to date.[10–12] Moreover, several reports have documented abnormal intestinal structure and function in patients receiving EN, thus bringing into question the putative "protective" effect of enteral feedings.[11,13] In addition, in some studies EN is no better than PN in preventing the development of multisystem organ failure in septic patients,[14] nor does it prevent increases in gastrointestinal permeability (a measure frequently used as a surrogate for bacterial translocation) after upper gastrointestinal surgery.[15,16]

Edema and nonspecific changes in plasma protein concentrations frequently hamper nutrition assessment during critical illness. Premorbid nutrition status, severity of disease, and clinically sound predictions of future clinical course should help identify those patients at both ends of the spectrum of nutrition risk.

Multiple investigators have examined the alterations in energy expenditure associated with critical illness, most frequently in septic and posttrauma patients.[5,17–21] These and other studies have documented substantial increases in resting energy expenditure during critical illness and the inaccuracy of predictive equations in the assessment of energy expenditure in these subjects.[22–24] Recent publications demonstrate increased non-resting energy expenditure (ie, activity) after the first week of critical illness.[19] Total energy expenditure in septic patients was 25 ± 5 kcal/kg per day during the first week of illness and closely correlated with the measured resting energy expenditure rate. Energy expenditure increased to 47 ± 6 kcal/kg per day during the second week of illness and was markedly higher than the measured resting expenditure.[19] It remains to be determined if feeding at rates greater than 25 to 30 kcal/kg per day is of benefit to these patients. It appears, in addition, that provision of 1 g/kg per day protein suffices to minimize loss of body protein during the initial 2 weeks of critical illness.[25] There is little information regarding requirements for minerals, trace elements and vitamins during critical illness.[26,27] Although low serum concentrations of some antioxidants have been documented,[2,8]

there is no information regarding requirements, bioavailability, or efficacy of replacement in the critically ill patient.

Evidence

It is not known how long critically ill patients can survive without food. It appears obvious that denying nutrition support will, over an unknown but finite period of time aggravate pre-existing nutritional deficits or establish malnutrition as a co-morbidity in critically ill patients. If results from patients recovering from major surgery can be cautiously extrapolated to other critically ill patients, morbidity and mortality increase significantly after 2 weeks of glucose infusion (at rates of 250 to 300 g/d) when compared with nutritionally complete PN.[29] Most importantly, initiating PN after 2 weeks of glucose infusion does not improve outcome.[29] It appears reasonable to recommend that some form of SNS be started after 5 to 10 days of fasting in patients who are likely to remain unable to eat for an additional week or more.

A meta-analysis was conducted of studies comparing PN to "standard care" (intravenous dextrose plus oral diet when tolerated) in a heterogeneous group of well-nourished and malnourished critically ill patients. Twenty-six clinical trials met the criteria for inclusion in the meta-analysis. However, only three of these trials did not involve elective surgical patients. Of the three, one addressed patients with acute neurologic injury, one subjects with pancreatitis, and the remaining study involved major burns. The meta-analysis showed no effect of therapy on mortality and a modest decrease in complications in patients receiving PN only in studies that required that patients be malnourished at time of enrollment.[30] There is no comparable analysis of the efficacy of EN in comparison to "standard therapy."

EN has emerged as the preferred manner of nutrition support in patients requiring SNS. Rationales for this preference have included its lower cost and presumed increased safety over PN. Although often repeated, these perceived advantages have been challenged.[11,16] Studies of patients after major trauma in which PN was compared with a variety of EN protocols using standard polymeric diets, elemental diets, or diets supplemented with a variety of specific nutrients including glutamine, branched-chain amino acids, omega-3 fatty acids, arginine, and nucleotides, generally report improvements in some measures of outcome (ie, infectious complications) in the enterally fed patients.[31–33] These findings are supported by the results of a recent meta-analysis that pooled the results of 22 randomized trials of the use of immune-enhancing EN formulas (containing some combination of arginine, glutamine, nucleotides, and omega-3 fatty acids) in critically ill and perioperative patients.[34] Immune-enhancing EN appears to effect a modest reduction in infectious complications, especially in perioperative patients, but has no apparent effect on mortality. A recent report on the use of EN in a specific group of critically ill patients (those suffering from severe head trauma) well illustrates the problems found in practice with the use of enteral feedings.[55] In this study, only 53% of patients were able to tolerate sufficient enteral support to avoid the need for supplemental PN, caloric intake through the enteral route averaged only 77 ± 2% of prescription, most patients required more than one feeding tube insertion (mean of 2.2 ± 0.2 tubes per patient), 11% evidenced severe gastrointestinal symptoms, and 14% of the patients suffered aspiration pneumonia. This study is the only one to report on the cost of the surgical, endoscopic, or radiologic placement of postpyloric feeding tubes. In this regard, there appears to be no advantage in delivering feedings beyond the pylorus (nasoduodenal tubes, feeding jejunostomies) in reducing the risk of aspiration.[35]

Special Considerations

The effects of supplementing enteral or parenteral diets with a variety of nutrients at pharmacologic doses has been explored in multiple trials, mostly including trauma and surgical patients. Studies have investigated the effects of supplemental branched-chained amino acids, glutamine, arginine, omega-3 fatty acids, RNA, and others. For the most part, studies have used diets supplemented with more than one of these nutrients, thus making assessment of efficacy of specific supplements impossible. A recent meta-analysis suggests these so-called immuno-enhancing formulas may reduce the incidence of infectious complications in critically ill patients but do not alter mortality. In some subgroups, mortality may actually be increased.[34]

A recent review of the use of supplemental branched-chain amino acids in critically ill patients failed to identify specific benefit from these compounds.[36] One study investigated the use of glutamine supplementation during PN in critically ill patients and reported improved survival at 6 months in the supplemented group.[37] These findings were not duplicated when glutamine was supplemented enterally.[38] A randomized trial comparing glutamine-supplemented enteral feedings to isocaloric, isonitrogenous, nonsupplemented feeds in severe trauma documented reductions in the incidence of pneumonia, bacteremia, and sepsis in patients receiving the supplemented diets.[39] Oral supplementation with glutamine at high doses (30 g/d) had no effects on several outcome measures after bone marrow transplantation when compared with placebo.[40]

Recent meta-analyses of trials of "immune enhancing" enteral diets containing supplemental arginine, glutamine, branched-chain amino acids, omega-3 fatty acids, RNA, and trace elements in critical illness concluded that the use of the aforementioned diets reduced the risk of infection, ventilator days, and hospital length of stay without influencing mortality.[41,42] These results have not been confirmed by others.[43] One study documented increased mortality in patients receiving "immune enhancing" diets.[44]

A recent study provided evidence for improved outcome in acute respiratory distress syndrome patients fed low carbohydrate diets supplemented with specific fatty acids (eicosapentanoid acid and gamma-linolenic

acid) and antioxidants.[45] The specific role of the different supplemented nutrients was not established.

Practice Guidelines
Critical Care: Critical Illness

1. Patients with critical illnesses are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. SNS should be initiated when it is anticipated that critically ill patients will be unable to meet their nutrient needs orally for a period of 5–10 days. (B)
3. EN is the preferred route of feeding in critically ill patients requiring SNS. (B)
4. PN should be reserved for those patients requiring SNS in whom EN is not possible. (C)

REFERENCES

1. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 20:864–874, 1992
2. Vrees MD Albina JE: Metabolic response to illness and its mediators. IN Clinical Nutrition: Parenteral Nutrition, Rombeau JL, Rolandelli RH (eds). WB Saunders, Philadelphia, 2000, pp 21–34
3. Plank, LD Hill, GL: Sequential metabolic changes following induction of systemic inflammatory response in patients with severe sepsis or major blunt trauma. World J Surg 24:630–638, 2000
4. Hill AG: Initiators and propagators of the metabolic response to injury. World J Surg 24:624–629, 2000
5. Shaw JHF, Wolfe RR: An integrated analysis of glucose, fat, and protein metabolism in severely traumatized patients. Studies in the basal state and the response to total parenteral nutrition. Ann Surg 209:63–72, 1987
6. Wolfe RR Martini WZ: Changes in intermediary metabolism in severe surgical illness. World J Surg 24:639–647, 2000
7. Streat SJ, Beddoe AH, Hill GL: Aggressive nutritional support does not prevent protein loss despite fat gain in septic intensive care patients. J Trauma 27:262–266, 1987
8. Wilmore DW, Smith RJ, O'Dwyer ST, et al: The gut: A central organ after surgical stress. Surgery 104:917–923, 1988
9. Klein S, Alpers DH, Grand RJ, et al: Advances in nutrition and gastroenterology: Summary of the 1997 A.S.P.E.N. Research Workshop. JPEN 22:3–13, 1998
10. Lipman TO: Bacterial translocation and enteral nutrition in humans: An outsider looks in. JPEN 19:156–165, 1995
11. Lipman TO: Grains or veins: Is enteral nutrition really better than parenteral nutrition? A look at the evidence. JPEN 22:167–182, 1998
12. Sedman PC, MacFie J,' Sagar P, et al: The prevalence of gut translocation in humans. Gastroenterology 107:643–649, 1994
13. Cummins A, Chu G, Faust L, et al: Malabsorption and villous atrophy in patients receiving enteral feeding. JPEN 19:193–198, 1995
14. Cerra FB, McPerson JP, Konstantinides FN, et al: Enteral nutrition does not prevent multiple organ failure syndrome (MOFS) after sepsis. Surgery 104:727–733, 1988
15. Brooks AD, Hochwald SN, Heslin MJ, et al: Intestinal permeability after early postoperative enteral nutrition in patients with upper gastrointestinal malignancy. JPEN 23:75–79, 1999
16. Reynolds JV, Kanwar S, Welsh FKS, et al: Does the route of feeding modify gut barrier function and clinical outcome in patients after major upper gastrointestinal surgery? JPEN 21:196–201, 1997
17. Moriyama S, Okamoto K, Tabira Y, et al: Evaluation of oxygen consumption and resting energy expenditure in critically ill patients with systemic inflammatory response syndrome. Crit Care Med 27:2133–2136, 1999
18. Monk DN, Plank LD, Franch-Arca G, et al: Sequential changes in the metabolic response in critically injured patients during the first 25 days after blunt trauma. Ann Surg 223:395–405, 1996
19. Uehara M, Plank LD, Hill GL: Components of energy expenditure in patients with severe sepsis and major trauma: A basis for clinical care. Crit Care Med 27:1295–1302, 1999
20. Koea JB, Wolfe RR, Shaw JHF: Total energy expenditure during total parenteral nutrition: Ambulatory patients at home versus patients with sepsis in surgical intensive care. Surgery 118:54–62, 1995
21. Khorram-Sefat R, Behrendt W, Heiden A, et al: Long-term measurements of energy expenditure in severe burn injury. World J Surg 23:115–122, 1999
22. Epstein CD, Peerless JR, Martin JE, et al: Comparison of methods of measurements of oxygen consumption in mechanically ventilated patients with multiple trauma: The Fick method versus indirect calorimetry. Crit Care Med 28:1363–1369, 2000
23. Weissman C, Kemper M, Askanazi J, et al: Resting metabolic rate of the critically ill patient: measured versus predicted. Anesthesiology 64:673–679, 1986
24. Weissman C, Kemper M, Damask MC, et al: Effect of routine intensive care interactions on metabolic rate. Chest 86:815–818, 1984
25. Ishibashi N, Plank LD, Sando K, et al: Optimal protein requirements during the first 2 weeks after the onset of critical illness. Crit Care Med 26:1529–1535, 1998
26. Story DA, Ronco C, Bellomo R: Trace element and vitamin concentrations and losses in critically ill patients treated with continuous venovenous hemofiltration. Crit Care Med 27:220–223, 1999
27. Elia M: Changing concepts of nutrient requirements in disease: implications for artificial nutritional support. Lancet 345:1279–1284, 1995
28. Schorah CJ, Downing C, Piripitsi A, et al: Total vitamin C, ascorbic acid, and dehydroascorbic acid concentrations in plasma of critically ill patients. Am J Clin Nutr 63:760–765, 1996
29. Sandström R, Drott C, Hyltander A, et al: The effect of postoperative intravenous feeding (TPN) on outcome following major surgery evaluated in a randomized study. Ann Surg 217:185–195, 1993
30. Heyland DK, MacDonald S, Keefe L, et al: Total parenteral nutrition in the critically ill patient. A meta-analysis. JAMA 280:2013–2019, 1998
31. Heyland DK: Nutritional support in the critically ill patient. A critical review of the evidence. Critical Care Clin 14:423–440, 1998
32. Moore FA, Moore EE, Kudsk KA, et al: Clinical benefits of an immune-enhancing diet for early postinjury enteral feeding. J Trauma 37:607–615, 1994
33. Moore FA, Moore EE, Jones TN, et al: TEN versus TPN following major abdominal trauma-reduced septic morbidity. J Trauma 29:916–923, 1989
34. Heyland DK, Novak F, Drover JW, et al: Should immunonutrition become routine in critically ill patients? A systematic review of the evidence. JAMA 286:944–953, 2001
35. Ott L, Annis K, Hatton J, et al: Postpyloric enteral feeding costs for patients with severe head injury: Blind placement, endoscopy, and PEG/J versus TPN. J Neurotrauma 16:233–242, 1999
36. Klein S, Kinney J, Jeejeebhoy K, et al: Nutrition support in clinical practice: Review of published data and recommendations for future research directions. JPEN 21:133–156, 1997
37. Griffiths RD, Jones C, Palmer TEA: Six-month outcome of critically ill patients given glutamine-supplemented parenteral nutrition. Nutrition 13:295–302, 1997
38. Jones C, Palmer TEA, Griffiths RD: Randomized clinical outcome study of critically ill patients given glutamine-supplemented enteral nutrition. Nutrition 15:108–115, 1999
39. Houdijk APJ, Rijnsburger ER, Jansen J, et al: Randomised trial of glutamine-enriched enteral nutrition on infectious morbidity in patients with multiple trauma. Lancet 352:772–776, 1998

40. Dickson TMC, Wong RM, Negrin RS, et al: Effect of oral glutamine supplementation during bone marrow transplantation. JPEN 24:61–66, 2000
41. Beale RJ, Bryg DJ, Bihari DJ: Immunonutrition in the critically ill: A systematic review of clinical outcome. Crit Care Med 27:2799–2805, 1999
42. Heys SD, Walker LG, Smith I, et al: Enteral nutritional supplementation with key nutrients in patients with critical illness and cancer. A meta-analysis of randomized controlled clinical trials. Ann Surg 229:467–477, 1999
43. Heslin MJ, Latkany L, Leung D, et al: A prospective, randomized trial of early enteral feeding after resection of upper gastrointestinal malignancy. Ann of Surg 226:567–580, 1997
44. Bower RH, Cerra FB, Bershadsky B, et al: Early enteral administration of a formula (Impact®) supplemented with arginine, nucleotides, and fish oil in intensive care unit patients: Results of a multicenter, prospective, randomized, clinical trial. Crit Care Med 23:436–449, 1995
45. Gadek JE, DeMichele SJ, Karlstad MD, et al: Effect of enteral feeding with eicosapentaenoic acid, g-linolenic acid, and antioxidants in patients with acute respiratory distress syndrome. Crit Care Med 27:1409–1420, 1999

HYPEREMESIS GRAVIDARUM

Background

Nausea and vomiting occur commonly within the first trimester of pregnancy, generally without detrimental effect on mother and fetus. Nausea and vomiting affects 50 to 90% of women in early pregnancy. Known as "morning sickness" the symptoms generally begin between the 4th and 7th week and peak by the 12th week of pregnancy. Weight loss and nutritional deficiencies are uncommon in this situation and nutritional intervention is not necessary.[1] Hyperemesis gravidarum (HG) is a severe form of nausea and vomiting that occurs in up to 1% of pregnancies. It is manifested by persistent vomiting that occurs for the first time before the 20th week of gestation, weight loss greater than 5% of prepregnancy weight, fluid and electrolyte alterations, acid–base disturbances, and ketonuria.[2] HG can have deleterious effects on mother and fetus. The etiology of HG remains unclear but may be associated with elevated levels of gestational hormones, gastrointestinal dysfunction, or thyroid abnormalities. When conventional management using antiemetic therapy, intravenous therapy, and oral nutrient modification are unsuccessful in achieving adequate weight gain, patients with HG become candidates for SNS.

Evidence

Patients who are unable to attain appropriate weight gain despite conservative measures of diet modification, intravenous hydration, and antiemetic therapy are candidates for EN or PN. Hsu et al[3] reported effective relief of intractable nausea and vomiting by provision of EN using an 8-F nasogastric tube in seven patients with HG. In a study of 30 patients, Gulley et al[4] described better control of nausea and vomiting with small-bore nasogastric tube feeding than they obtained with traditional measures using intravenous hydration and antiemetic therapy. PN is indicated in cases of HG when enteral feeding cannot be tolerated. PN is safe and effective in this setting.[2]

Special Considerations

The initiation of SNS in patients with significant malnutrition may result in refeeding syndrome. Refeeding syndrome is a serious metabolic derangement manifested by hypophosphatomeia, hypokalemia, hypomagnesemia, and edema in response to reinitiating nutrient intake in malnourished individuals.[5,6] Women with HG resulting in malnutrition should be considered at risk for developing refeeding syndrome.

Decreased thiamine levels, frequently seen in patients with HG,[7] increases the risk for Wernicke's encephalopathy, a potentially fatal neurologic syndrome.[8–10] Thiamine supplementation should be considered with initiation of dextrose-containing fluids in patients with HG.

Practice Guidelines *Hyperemesis Gravidarum*

1. Pregnant women are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. SNS is indicated in women with hyperemesis gravidarum who are unable to achieve appropriate weight gain despite the use of noninvasive therapies. (B)
3. When SNS is indicated, EN should be initiated as a slow, continuous, isotonic EN infusion to minimize nausea and vomiting and establish adequate calorie intake. (B)
4. PN should be used to treat hyperemesis gravidarum when EN is not tolerated. (B)
5. When SNS is started in malnourished women with hyperemesis gravidarum, thiamin supplementation and careful monitoring for signs of development of refeeding syndrome should be instituted. (B)

REFERENCES

1. Gadsby R, Barnie-Achdead AM, Jagger C: A prospective study of nausea and vomiting during pregnancy. Br J Gen Pract 43:245–248, 1993
2. Wagner BA, Worthington P, Russo-Stieglitz KE, et al: Nutritional management of hyperemesis gravidarum. Nutr Clin Pract 15:65–76, 2000
3. Hsu JJ, Clark-Glena R, Nelson DK, et al: Nasogastric enteral feeding in the management of hyperemesis gravidarum. Obstet Gynecol 88(3):343–346, 1996
4. Gulley RM, Pleog NV, Gulley J: Treatment of hyperemesis gravidarum with nasogastric feeding. Nutr Clin Pract 8(1):33–35, 1993
5. Solomon SM, Kirby DF: The refeeding syndrome: a review. JPEN 14(1):90–97, 1990
6. Havala T, Shronts E: Managing the complications associated with refeeding. Nutr Clin Pract 5:23–29, 1990
7. Van Stuijevenberg ME, Schabort I, Labadarios D, et al: The nutritional status and treatment of patients with hyperemesis gravidarum. Am J Obstet Gynecol 172(5):1585–1591, 1995
8. Omer SM, al Kawi MZ, al Watban J, et al: Acute Wernicke's encephalopathy associated with hyperemesis gravidarum: magnetic resonance imaging findings. J Neuroimag 5(4):252–253, 1995
9. Lavin PJ, Smith D, Kori SH, et al: Wernicke's encephalopathy: a predictable complication of hyperemesis gravidarum. Obstet Gynecol 63(suppl):13S–15S, 1983

10. Wood P, Murray A, Sinha B, et al: Wernicke's encephalopathy induced by hyperemesis gravidarum: Case reports. Br J Obstet Gynecol 90:583–586, 1983

PSYCHIATRIC DISORDERS: EATING DISORDERS

Background

Eating disorders involve a complex blend of physiological disruption, behavioral dysfunction, and environmental susceptibility. Of the three eating disorders listed in the Diagnostic and Statistical Manual-IV (anorexia nervosa, bulimia nervosa, and binge eating disorder), the diagnostic standards for anorexia nervosa are the only ones that include measurable malnutrition (weight 85% of ideal).[1]

Although the incidence of malnutrition in anorexia nervosa is 100%, its presentation can vary. Some of the more common medical complications include arrhythmias, bradycardia, hypercholesterolemia, amenorrhea, muscle loss, reduced gastrointestinal motility, constipation, impaired kidney function, immune system dysfunction, hypothermia, and impaired taste.[2]

Malnutrition is also associated with numerous neuroendocrine aberrations. For example, compromised nutrition status has been associated with increased physical activity, alterations in appetite, and impaired memory and learning ability.[3–5] Normal feeding behavior is dependent on a nervous system that can engage activities that support this goal. It is important to improve nutrition status in an expedient fashion so that neuroendocrine-based behaviors related to malnutrition do not impair the individual's ability to respond to behavioral psychotherapy.

In many cases, an additional psychiatric diagnosis exists in conjunction with the eating disorder (eg, depression, anxiety disorder, obsessive-compulsive disorder), and recovery may depend on response to psychoactive medications. Evidence suggests that these drugs are not as active in malnourished patients.[6] Nutrition support can be an important component of eating disorder treatment, as it can accelerate the individual's response to therapeutic interventions.

It is not uncommon for an individual to experience a hypermetabolic period when treatment is initiated. This calorie level can be 10 times what the person was eating before seeking treatment; introduced into a malnourished gastrointestinal tract, it can create severe bloating, cramping and constipation. Complicating this scenario is the malnourished patient that may interpret these changes not as short-term issues but as weight gain that needs to be acted upon. The anxiety that these early refeeding events creates, compounded with an already fragile state, can create a spiral that is difficult to break. Nutrition support can reduce total caloric volume as well as total oral food volume and help to ease the discomfort of early refeeding.

Evidence

Because prolonged malnutrition related to eating disorders may permanently alter brain structure,[7] early recognition and intervention are important for improving the long-term outcome of treatment. These interventions may not be easily initiated, because a person with anorexia nervosa typically presents as bright, well-versed in nutrition, and desirous of making dietary changes to enhance nutrition status. She may honestly believe that she can, and will, eat more tomorrow.

It is important to recognize that the biobehavioral disruptions that malnutrition has caused may make it impossible for the individual to carry intent through to actual behaviors. In addition, the perfectionistic tendencies typical of anorexia nervosa create a perception on the part of the patient that nutrition support is a punitive measure or an indication of treatment failure. Much energy may be devoted to bargaining, delaying the use of this treatment option, and focusing on anything but the task at hand—restoring adequate nutrition status. The proactive practitioner needs to develop the ability to recognize early in treatment when a patient is likely to be able to implement desired behavior changes and when it is appropriate to use nutrition support without a prolonged waiting period.

It is important that the interdisciplinary treatment team develop standard criteria and procedures for the use of SNS. A decision tree with strict deadlines may be helpful to keep the team focused on what is best for the patient's recovery and to limit their susceptibility to patient bargaining and treatment delays. A unified front is important, as the dissenting practitioner who even nonverbally communicates disagreement with the team decision is likely to be targeted by the patient as the one who can change the team decision and who can dilute the effectiveness of the team as a whole.

Nutrition assessment in anorexia should include total weight, but should be complemented with other anthropometric measures that are not as sensitive to manipulation by the patient and that are reflective of long-term nutrition trends (eg, percentage body fat, midarm muscle circumference). It is important to note that many of the standard nutrition assessment measurements used in other medical diagnoses are often normal in anorexia nervosa. Typical findings in malnourished patients with anorexia nervosa include severe weight loss (20% to 30% or more of usual body weight), constipation, cold intolerance, fatigue, yellow skin secondary to hypercarotinemia, knuckle scarring and enamel erosion secondary to self-inducement of vomiting, hirsutism, iron deficiency anemia, hypokalemia, and hyponatremia.[8] Visceral protein measurements that have been found to be helpful include C-3 complement level, serum ferritin, serum iron, and transferrin saturation.[9]

Although the purpose of nutrition support is to restore body mass and optimal function, the long-term goal of treatment in anorexia nervosa is to restore normal, orally based food behaviors. Unless there is a complicating medical condition that precludes oral intake, nutrition support in anorexia nervosa should always be an adjunct to, not a replacement for, oral nutrition therapy. Occasionally, a patient becomes dependent on nutrition support as it provides a means of avoiding contact with food. This behavior should be discouraged. Joining peers at mealtime and developing comfort with food by sitting at a table with friends or

family is an important step toward recovery and should not be eliminated because nutrition support is part of the treatment plan.

Indications for SNS in patients with anorexia nervosa include severe malnutrition (greater than 30% recent weight loss or current weight less than 65% of ideal body weight) in patients who are unable or unwilling to ingest adequate nutrition. EN is generally sufficient, with only rare patients requiring PN. These patients are at high risk for developing refeeding syndrome. SNS should be initiated at no more than 70% of predicted resting energy expenditure. Monitoring for possibly fatal manifestations of refeeding syndrome should include initial frequent monitoring of serum electrolytes, calcium, magnesium, phosphate, and acid-base status. The short-term goal of SNS should be to safely restore the patient's nutrition status to a level compatible with stable health (greater than 80% of ideal body weight).[8]

Special Considerations

In anorexia nervosa, nutrition support is as much a psychological treatment as it is a medical one. If the patient's unique perception and response style is not taken into account in the nutrition support treatment plan, the feeding is likely to be sabotaged.

An individual whose intentional behaviors have brought her weight to a level where nutrition support is necessary has been engaged in her eating disorder for a significant period of time. During that time, she has experienced the frustration of family members, friends, and caregivers who were unable to help her regain her health. It is not uncommon for loved ones, in a moment of frustration, to threaten a tube feeding as punishment for not complying with the recommended course of treatment. When nutrition support actually becomes a necessity, it can be perceived by the individual as a personal failure. It is important that when such an intervention is decided upon, that time is provided in therapy to process those feelings and to facilitate a perspective of nutrition support as a positive, nurturing decision.

Sexual abuse is common in eating disorders.[10] For the individual who has been a victim of abuse, especially oral sexual abuse, the sensations experienced during placement of the tube feeding may provoke memories that are frightening and retraumatizing. It is important to prepare the individual for the procedure by discussing what to expect. Personnel performing tube placement also need to be aware of the patient's psychological presentation. Verbal and physical language should be gentle.

Practice Guidelines
Psychiatric Disorders: Eating Disorders

1. All patients with anorexia nervosa are malnourished and should undergo formal nutrition assessment with development of a nutrition care plan. (B)
2. SNS should be initiated in patients with anorexia nervosa with severe malnutrition (greater than 30% recent weight loss or current weight less than 65% of ideal body weight) who are unable or unwilling to ingest adequate nutrition. (B)
3. Upon initiation of SNS in patients with anorexia nervosa, frequent fluid, electrolyte, and acid–base monitoring must be undertaken to avoid sequelae of the refeeding syndrome. (A)

REFERENCES

1. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. American Psychiatric Association, Washington, DC, 1994
2. Alexander T: Medical Complications in Eating Disorders. IN Eating Disorders: Putting It All Together. Woolsey M (ed). American Dietetic Association, Chicago, 2000
3. Wyrwicka W: Anorexia nervosa as a case of complex instrumental conditioning. Exp Neurol 83(3):579–599, 1984
4. Jiang JC, Gietzen DW: Anorectic response to amino acid imbalance: a selective serotonin3 effect? Pharmacol Biochem Behav 47(1):59–63, 1994
5. Castro CA, Tracy M, Rudy JW: Early-life undernutrition impairs the development of the learning and short-term memory processes mediating performance in a conditional-spatial discrimination task. Behav Brain Res 32(3):255–264, 1989
6. Walsh BT, Devlin MJ. The pharmacologic treatment of eating disorders. Psychiatr Clin N Am 15(1):149–160, 1992
7. Lambe EK, Katzman DK, Mikulis DJ, et al: Cerebral gray matter volume deficits after weight recovery from anorexia nervosa. Arch Gen Psychiatry 54(6):537–542, 1997
8. Russell M, Cromer M, Grant J. Complications of enteral nutrition therapy. IN The Science and Practice of Nutrition Support. Gottschlich MM (ed). Kendall/Hunt, Dubuque, IA, 2001:189–209
9. Keddy D, Lyon TJ: Assessing Nutritional Status. Eating Disorders Rev 9(5): 5–7, 1998
10. Kratina K: Sexual Abuse, Dissociative Disorders and the Eating Disorders: Nutrition Therapy as a Healing Tool. IN Eating Disorders: Putting It All Together. Woolsey M (ed). American Dietetic Association, Chicago, 2000

PERIOPERATIVE NUTRITION SUPPORT

Background

Malnourished patients undergoing surgical procedures are at increased risk for postoperative morbidity and mortality when compared with well-nourished patients.[1] However, it is difficult to definitively demonstrate a causal relationship between malnutrition and surgical outcome. Malnutrition may, in many cases, serve as a surrogate marker of severity of disease.

Evidence

Multiple prospective trials have looked at the efficacy of SNS given in the preoperative and postoperative periods to prevent complications and effect outcome.[2,3] The trials that have been done however, are difficult to compare due in part to variability in (1) the definitions of and incidence of malnutrition and other comorbidities; (2) the route of admission and duration of nutrition support; (3) the amount and composition of the nutrition support; and (4) the incidence of nutrition support–related complications.

In most of the prospective, randomized, controlled trials (PRCT) performed, preoperative PN has been shown to decrease the incidence of postoperative complications by an absolute rate of approximately 10%.[2,3] Most patients in these studies had gastrointestinal cancer and were categorized as moderately malnourished. The benefits were seen mostly in patients who were severely malnourished.[4] Improvements in patient selection and avoidance of overfeeding and hyperglyce-

mia may allow these moderate benefits to be achieved in other patient populations. The use of preoperative EN has been compared with an ad libitum oral diet, mostly in patients who had cancer.[5,6] The overall incidence of postoperative complications was lower in the EN fed patients.

The routine use of early postoperative PN has been studied in multiple PRCTs. Many of the patients in these studies were moderately malnourished. The absolute rate of complications in these studies was approximately 10% higher in the PN-fed groups.[2] Four PRCTs have compared the use of early postoperative EN with routine postoperative diet advancement. Most of these patients had gastrointestinal tract cancers. There were no obvious differences between the groups in operative morbidity or mortality.[2] Postoperative EN has been compared with PN as well. Generally, the incidence of complications was higher in the PN groups.[7–9]

The use of "immune-enhancing" EN, specifically, enteral diets supplemented with L-arginine, ω-3 fatty acids, and ribonucleic acids has been studied in postoperative gastrointestinal cancer patients and in critical illness. Biomarkers such as immune status and nitrogen balance may be favorably affected by these specific nutrients. A recent meta-analysis that included nine randomized trials that studied the use of perioperative immune-enhancing EN in elective surgical patients suggested a favorable impact on the rate of post-operative infectious complications and on length of hospital stay.[10] Oral supplements have been used in the postoperative period, and one PRCT showed a significant decrease in complications in the supplemented group.[11]

Practice Guidelines
Perioperative Nutrition Support

1. Preoperative SNS should be administered to moderately or severely malnourished patients undergoing major gastrointestinal surgery for 7 to 14 days if the operation can be safely postponed. (A)
2. PN should not routinely be given in the immediate postoperative period to patients undergoing major gastrointestinal procedures. (A)
3. Postoperative SNS should be administered to patients whom it is anticipated will be unable to meet their nutrient needs orally for a period of 7 to 10 days. (B)

REFERENCES

1. Mullen GL, Buzby GP, Waldman MT, et al: Prediction of operative morbidity and mortality by preoperative nutritional assessment. Surg Forum 30:80–82, 1979
2. Klein S, Kinney J, Jeejeebhoy K, et al: Nutrition support in clinical practice: Review of published data and recommendations for future research directions. JPEN 21:133–157, 1997
3. Torosian MJ: Perioperative nutrition support for patients undergoing gastrointestinal surgery: Critical analysis and recommendations. World J Surgery 23:565–569, 1999
4. VA TPN Cooperative Study: Perioperative total parenteral nutrition in surgical patients. N Engl J. Med 325:525–532, 1991
5. Von Meyenfeldt M, Meijerink W, Rouflart M, et al: Perioperative nutritional support: Randomized clinical trial. Clin Nutr 11:180–186, 1992
6. Shukla HS, Rao PR, Banu N, et al: Enteral hyperalimentation in malnourished surgical patients. Indian J Med Res 80:339–346, 1984
7. Baigrie RJ, Devitt PG, Watkins S: Enteral versus parenteral nutrition after esophagogastric surgery; a prospective randomized comparison. Aust NZ J Surg 66:668–670, 1996
8. Reynolds JV, Kanwar S, Welsh FKS, et al: Does the route of feeding modify gut barrier function and clinical outcome in patients after major upper gastrointestinal surgery? JPEN 21:196–201, 1997
9. Braga M, Gianotti L, Vignoli A, et al: Artificial nutrition after major abdominal surgery: Impact of route of administration and composition of the diet. Crit Care Med 26(1):24–30, 1998
10. Heyland DK, Novak F, Drover JW, et al: Should immunonutrition become routine in crtically ill patients? A systematic review of the evidence. JAMA 286:944–953, 2001
11. Kiele AM, Barry MJ, Emery PW, et al: Two phase randomized controlled clinical trial of prospective oral dietary supplements in surgical patients. Gut 40(3):343–349, 1997

Section XII: Administration of Specialized Nutrition Support—Issues Unique to Pediatrics

INDICATIONS, TYPES, AND ROUTES OF ADMINISTRATION: ENTERAL NUTRITION

Indications

Background. The most common indication for EN in the Neonatal Intensive Care Unit (NICU) is immaturity. The ability to suck, swallow, and breathe in a well-coordinated fashion occurs at approximately 32 to 34 weeks gestational age. Infants less mature than this are tube-fed.[1] Preterm or term infants who are too sick to nipple-feed or who are mechanically ventilated are tube-fed. Infants whose nutrient and/or calorie needs cannot be met by oral feeding may benefit from EN. Conditions under which enteral feeding may be considered include chronic lung disease, cystic fibrosis, congenital heart disease, alimentary tract disease or dysfunction, renal disease, hypermetabolic states, severe trauma, and neurologic disease, among others.[1]

Human milk is considered the ideal food for healthy and most sick infants.[1,2] If the infant is too sick, immature, or weak to directly breastfeed, milk can be pumped and fed to the baby by tube. Protocols exist for collecting, storing, and feeding pumped human milk.[3] Generally, donor milk (from a mother other than the infant's own) is not used because human milk may be a vehicle for transmission of infectious diseases including HIV-1.

If human milk is not available or indicated, iron-fortified infant formula is recommended for the first year of life.[1] Standards for nutrient content of infant formulas have been established by the American Academy of Pediatrics (AAP) and the Infant Formula Act.[1] Clinical trials demonstrating weight gain, normal serum chemical indices, and normal nutrient balance in healthy infants must precede the marketing of new infant formulas in the United States. Although most infants can be successfully fed with human milk or standard cow milk–based formula, a variety of formulas for different indications is available (see Table I).

The AAP recommends that all formulas fed to infants be fortified with iron at 10 to 12 mg/L (greater than 6.7 mg/100 kcal).[1] Iron is important for normal mental and motor development. Low-iron formulas remain on the US market, partly because iron is perceived to cause gastrointestinal and behavioral problems. Preventing iron-deficiency is paramount because children who were treated for iron deficiency in infancy continue to have developmental and learning problems at age 10.[4]

Soy formulas are both milk-free and lactose-free. Soy protein, glucose polymers (and sometimes sucrose), and vegetable oils are the energy-providing nutrients in soy formulas. Indications and contraindications for use of soy formulas have recently been reviewed by the AAP1 and are shown in Table I.

Casein hydrolysate formulas contain extensively hydrolyzed protein. They generally do not elicit an immunologic response in infants with allergies to intact cow milk or soy protein. Casein hydrolysates are also recommended for infants with significant malabsorption secondary to gastrointestinal or hepatobiliary disease.[1] These formulas are lactose-free and may contain medium-chain triglycerides to facilitate fat absorption.

Special considerations are required to meet the nutritional needs of preterm infants. Milk of mothers who deliver preterm is higher in protein and electrolytes and more suited to the preterm infant's needs than is the milk of mothers who deliver at term. Even preterm human milk, however, is suboptimal in nutrient content to meet the needs of small preterm infants.[1] Commercial human milk fortifiers have been developed to supplement nutrient intake. Special formulas are available for preterm infants not receiving human milk. In-hospital preterm formula differs qualitatively (in blends of carbohydrates and fats) and quantitatively (in higher amounts of many nutrients) from term formula. Preterm discharge formulas have a nutrient content intermediate to that of an in-hospital preterm formula and a standard term formula.

Human milk and infant formulas are 20 calories per fluid ounce (cal/fl oz) at standard dilution. Feedings are generally started at 20 cal/fl oz since no clear benefit to starting with dilute formula has been shown. Tube-fed infants who are fluid-sensitive may benefit from concentrated feedings at 24 to 30 cal/fl oz.[5] The increased renal solute load and osmolality in concentrated formulas must be considered. Caloric supplements may be used with or instead of formula concentration as the individual case warrants.[6]

Additional detailed information about infant formulas is published elsewhere[7] and is available directly from the manufacturers.

Evidence. Although breastfeeding is recommended in

TABLE I
Enteral feeding products for infants

Product category/description	Indication/usage	Contraindications/cautions
Human milk	Healthy and sick term infants For preterm infants when fortified	Many inborn errors of metabolism; maternal infection with milk-transmitted organisms; maternal ingestion of certain medications
Cow milk-based formulas, iron-fortified	Healthy term infants	Cow-milk protein intolerance; lactose intolerance; clinical conditions for which special products are more appropriate
Cow milk-based, lactose-free formulas	Lactase deficiency/lactose intolerance	Cow milk protein intolerance; galactosemia (enough galactose remains)
Cow milk-based, low mineral/electrolyte formula	Hypocalcemia/hyperphosphatemia Renal disease	Cow milk protein intolerance Note: This is a low-iron formula; iron should be supplied from other sources
Cow milk-based, high (86%) MCT (medium-chain triglyceride) formula	Severe fat malabsorption Chylothorax	Note: Monitor for signs of essential fatty acid deficiency if used for prolonged periods.
Cow milk-based follow-up formula	Older infants who are eating solid foods	Note: No advantage over breastfeeding or standard infant formula for the first year of life. (AAP)
Soy-based formula (milk-free, lactose-free)	Galactosemia; hereditary or transient lactase deficiency; documented IgE-mediated allergy to cow milk; vegetarian-based diet	Birth weight < 1800 g Prevention of colic or allergy Cow milk protein-induced enterocolitis or enteropathy
Soy-based formula with fiber	Diarrhea	Constipation
Casein-hydrolysate formulas	Allergies; intact protein sensitivity	Note: Infants with severe cow milk protein allergies may react to whey-protein hydrolysate formula
Amino acid-based formulas	Malabsorption (due to gastrointestinal or hepatobiliary disease)	
Human milk fortifiers (HMF)	Preterm/LBW infants	Note: Fortifiers are low iron; additional iron should be supplied from other sources
Preterm formulas	Preterm/LBW infants	
Preterm discharge formulas	Former preterm/LBW infants from hospital discharge through 9 months of age	
Amino acid-modified + other special formulas	Inborn errors of metabolism	Incomplete sources of nutrition Note: must be managed by a team accustomed to managing inborn errors of metabolism

most situations, a large prospective, randomized controlled trial (PRCT) concluded that the use of infant formula for infants whose mothers are HIV-1 positive helps prevent infant infections and is associated with improved HIV-1–free survival.[8]

Commercial cow milk–based infant formulas have been tested extensively in controlled and field conditions; they meet the nutrient needs of infants when used as the sole source of nutrition for the first 6 months of life and as the primary source of nutrition for the second 6 months.[1]

In three PRCTs, no difference in gastrointestinal intolerance or behavioral abnormalities was seen in infants on iron-fortified formulas compared with those on low-iron formulas.[9]

Soy formulas have been shown to promote growth and bone mineralization in healthy, term infants similar to that seen in br^ast-fed and cow milk–based formula-fed infants.[1,10]

Infants who are allergic to intact proteins do not react on double-blind, placebo-controlled challenge to casein hydrolysate formulas.[11] Infants who are exquisitely allergic to intact or even hydrolyzed proteins show symptom resolution and normal growth on amino acid–based formulas.[12]

PRCTs have shown that multinutrient fortification of human milk improves growth in preterm infants.[13,14] Preterm formulas promote growth and bone mineralization at an intrauterine rate.[1] In controlled trials, preterm infants had improved developmental outcomes when fed fortified human milk or preterm formula as opposed to term formula during the neonatal period.[15,16] When controlled for other variables, these effects of early nutrition persist up to age 8 years.[17] Thus, choice of early nourishment for preterms is of long-term importance.

After hospital discharge, use of preterm discharge formulas (as opposed to term formulas) results in improved growth and bone mineralization in former preterm infants.[18,19] The AAP recommends use of preterm discharge formulas for former preterm infants to the age of 9 months.[1]

Routes of Enteral Nutrition

Background. Infants who are greater than 32 to 34 weeks gestational age and free from respiratory disease are generally nipple fed. Enteral feeding (by nasogastric or orogastric tube) is most commonly used in the NICU for infants who are preterm (less than 32 to 34 weeks gestational age), weak, or critically ill.

Transpyloric feedings may be used for infants who have delayed gastric emptying.[20] Continuous feedings are used when the gastric reservoir function and the regulatory function of the pylorus are bypassed with transpyloric tube placement.

A gastrostomy tube should be considered for infants who will be unable to orally feed for 2 to 3 months.[1,20] Infants with either neurological problems precluding nipple feedings or anatomical alimentary tract malfor-

mations above the level of the stomach are good candidates for gastrostomy feedings.

Evidence. Tubes may either be left indwelling for up to 3 days or removed and replaced for each feeding without affecting the infant's weight gain or cardiorespiratory status.[21]

In PRCTs, gastrointestinal (GI) priming (eg, tube feeding 20 mL/kg per day for 10 days) is associated with enhanced gut motility[22,23] and better mineral retention[23] in comparison with enteral starvation after preterm birth. Necrotizing entercolitis (NEC) rates are not increased with GI priming, even when an umbilical arterial catheter is in place.[24] Several retrospective studies have shown that NEC rates are higher in at-risk infants whose feedings are advanced at a rate greater than 20 mL/kg per day.[1] Increasing at a rate of 20 mL/kg per day allows the infant to reach approximately 150 mL/kg per day (and approximately 100 Cal/kg per day at 20 Cal/fl oz) in 1 week of progressive feeding advancement. Feedings can then be adjusted as fluid, calorie, and nutrient needs dictate.

Two PRCTs in preterm infants have shown that both continuous and bolus feeding methods result in similar outcomes of growth, macronutrient retention, length of hospitalization, and days to reach full feedings.[25,26] A third, large PRCT showed improved feeding tolerance (less gastric residual volume) with bolus feedings.[23] In practice, continuous feedings may be better tolerated than bolus feedings by infants with malabsorption problems. However, the continuous feeding method is associated with reduced nutrient delivery when compared with the bolus feeding method.[1]

Practice Guidelines *Indications, Types, and Routes of Administration: Enteral Nutrition*

1. Preterm and ill newborns are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Infants who are greater than 32 to 34 weeks gestational age and free from respiratory disease should be nipple-fed. (B)
3. EN should be administered to infants through a nasogastric or orogastric tube that can either be left in for up to 3 days or placed before and removed after each feeding. (A)
4. Human milk or iron-fortified, cow milk–based infant formula should be used for most term infants. (B)
5. Fortified human milk or preterm formula should be used for preterm infants. (B)
6. Feedings for sick or preterm infants should be started within the first few days of life at 20 Cal/fl oz and at 20 mL/kg per day and advanced at 20 mL/kg per day according to the infant's clinical condition. (B)
7. A gastrostomy should be considered for infants who will require tube feeding for longer than 2 to 3 months. (C)
8. Infants with nasogastric, orogastric, or gastrostomy tubes may be fed by either bolus or continuous method. (A)

REFERENCES

1. American Academy of Pediatrics Committee on Nutrition: Pediatric Nutrition Handbook, 4th ed. AAP, Elk Grove Village, IL, 1998
2. Position of the American Dietetic Association: Promotion of breast-feeding. J Am Dietet Assoc 97:662–666, 1997
3. Hurst NM, Myatt A, Schanler RJ: Growth and development of a hospital-based lactation program and mother's own milk bank. JOGNN 27:503–510, 1998
4. Lozoff B, Jimenez E, Hagen J, et al: Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. Pediatrics 105(4):e51, 2000
5. Davis A: Indications and techniques for enteral feeds. IN Pediatric Enteral Nutrition. Baker SB, Baker RD Jr, Davis A (eds). Chapman & Hall, New York, 1994
6. Davis A, Baker SB: The use of modular nutrients in pediatrics. JPEN 20:228–236, 1996
7. Sapsford AL: Human milk and enteral nutrition products. IN Nutritional Care for High-Risk Newborns. Groh-Wargo S, Thompson M, Cox JH (eds). Precept Press, Chicago, IL, 2000
8. Nduati R, John G, Mbori-Hgacha D, et al: Effect of breastfeeding and formula feeding on transmission of HIV-1. A randomized clinical trial. JAMA 283:1167–1174, 2000
9. American Academy of Pediatrics Committee on Nutrition: Iron fortification of infant formulas. Pediatrics 104:119–123, 1999
10. Lasekan JB, Ostrom KM, Jacobs JR, et al: Growth of newborn, term infants fed soy formulas for 1 year. Clin Pediatr 38:563–571, 1999
11. Sampson HA, Bernhisel-Broadbent J, Yang E, et al: Safety of casein hydrolysate formula in children with cow milk allergy. J Pediatr 118:520–525, 1991
12. Hill DJ, Heine RG, Cameron DJS, et al: The natural history of intolerance to soy and extensively hydrolyzed formula in infants with multiple food protein intolerance. J Pediatr 135:118–121, 1999
13. Wauben IP, Atkinson SA, Grad TL, et al: Moderate nutrient supplementation of mother's milk for preterm infants supports adequate bone mass and short-term growth: A randomized, controlled trial. Am J Clin Nutr 67:465–472, 1998
14. Barrett Reis B, Hall RT, Schanler RJ, et al: Enhanced growth of preterm infants fed a new powdered human milk fortifier: A randomized controlled trial. Pediatrics 106:581, 2000
15. Lucas A, Morley R, Cole TJ, et al: Early diet in preterm babies and developmental status at 18 months. Lancet 335:1477–1481, 1990
16. Lucas A, Morley R, Cole TJ, et al: A randomised multicentre study of human milk versus formula and later development in preterm infants. Arch Dis Child 70:F141–F146, 1994
17. Lucas A, Morley R, Cole TJ: Randomised trial of early diet in preterm babies and later intelligence quotient. Br Med J 317: 1481–1487, 1998
18. Lucas A, Bishop NJ, King FJ, et al: Randomised trial of nutrition for preterm infants after discharge. Arch Dis Child 67:324–327, 1992
19. Bishop NJ, King FJ, Lucas A: Increased bone mineral content of preterm infants fed with a nutrient enriched formula after discharge from hospital. Arch Dis Child 68:573–578, 1993
20. Wessel JJ: Feeding methodologies. IN Nutritional Care for High-Risk Newborns. Groh-Wargo S, Thompson M, Cox JH (eds). Precept Press, Chicago, IL 2000, pp 321–340
21. Symington A, Ballantyne M, Pinelli J, et al: Indwelling versus intermittent feeding tubes in premature neonates. JOGNN 24:321–326, 1995
22. McClure RJ, Newell SJ: Randomised controlled trial of trophic feeding and gut motility. Arch Dis Child Fetal Neonatal Ed 80:F54–F58, 1999
23. Schanler RJ, Shulman RJ, Lau C, et al: Feeding strategies for premature infants: Randomized trial of gastrointestinal priming and tube-feeding method. Pediatrics 103:434–439, 1999
24. Davey AM, Wagner CL, Cox C, et al: Feeding premature infants while low umbilical artery catheters are in place: A prospective, randomized trial. J Pediatr 124:795–799, 1994

25. Silvestre MAA, Morbach CA, Brans YW, et al: A prospective randomized trial comparing continuous versus intermittent feeding methods in very low birth weight neonates. J Pediatr 128:748–752, 1996
26. Akintorin SM, Kamat M, Pildes RS, et al: A prospective randomized trial of feeding methods in very low birth weight infants. Pediatrics 100(4):e4, 1997

INDICATIONS, TYPES, AND ROUTES OF ADMINISTRATION: PARENTERAL NUTRITION

Background

PN is indicated in infants and children who are unable to tolerate adequate enteral feedings to sustain their nutritional requirements. This may occur in children who suffer from chronic malnutrition (failure to thrive) or who are at high risk for developing malnutrition as a result of acute medical illness or prolonged post-operative recovery. This commonly includes (1) premature infants, due to immaturity of their gastrointestinal tracts, (2) infants/children in whom prolonged starvation is anticipated, ie, necrotizing enterocolitis, pancreatitis, graft-versus-host disease or postoperatively, and (3) pediatric patients with inadequate intestinal nutrient absorption (short-bowel syndrome, intestinal pseudoobstruction, postchemotherapy, etc). The maximum period of tolerable undernutrition depends on the patient's age, baseline nutrition status, and underlying medical conditions.

The therapeutic goal of PN in children is both to maintain nutrition status and to achieve balanced somatic growth. Various components in PN may induce major metabolic disturbances, end organ dysfunction, and drug interactions that mandate periodic monitoring, and meticulous surveillance.[1]

The administration of PN requires the placement of an appropriate venous access device to safely deliver the hyperosmotic fluid. Peripheral infusion of parenteral formulations is limited to dextrose concentrations of less than 12.5%.[1] Because supraphysiologic fluid volumes would be necessary to meet the high caloric demand of infants and children using these concentrations, peripheral parenteral nutrition (PPN) is rarely indicated. PPN is useful only for partial nutrition supplementation or as bridge therapy for patients awaiting central access. Consequently, full PN support in children typically requires central venous access. This may pose significant technical challenges and complications in the pediatric population. Moreover, the care and maintenance of these indwelling venous catheters is associated with infectious and mechanical complications that may create significant morbidities and, rarely, mortality.[2,3]

In preparing and planning for a patient to receive PN, the goals should be clearly stated by determining the patient's (1) nutritional requirements, (2) baseline metabolic parameters, (3) anticipated PN duration, (4) accessibility of central veins, (5) the most appropriate device for placement, and (6) the complications of therapy. Despite the obvious benefits of PN, numerous complications (metabolic, infectious, and mechanical) may arise as a result of PN use. Consequently, the multiple risks of PN should be weighed against the benefits of nutrition support prior to the initiation of therapy in each individual patient. Moreover, a systematic schedule of metabolic monitoring is mandated.[4]

Evidence

The optimal time for initiating PN is dependent on the child's baseline nutrition status, disease acuity, and age.[1,3] Strong evidence exists that many hospitalized pediatric patients are undernourished. Seminal work by Koop reported that 18% to 40% of hospitalized pediatric surgical patients suffer acute protein calorie malnutrition.[5] Periera et al[6] demonstrated that premature infants have energy stores that last 4 to 12 days. They reported that depletion of nutritional stores may occur as early as 4 days in high-risk infants. Therefore, PN may be indicated within 48 hours of surgery in premature infants or children with significant premorbid nutrition risk factors.[6] Because of their more replete energy reserves, older children usually do not require PN unless undernutrition is anticipated to extend beyond 7 days.[1] Several studies reviewed by Levy et al cite improved outcomes in patients whose SNS was started early in the setting of acute illness.[7] Numerous studies reviewed by Leonberg et al confirm the ability of long-term PN with regard to maintaining growth and weight gain.[8]

Catheter selection is based on patient factors and the anticipated duration of PN therapy. Two principle categories of devices are available for achieving venous access: temporary (percutaneous) or permanent (tunneled or implantable). Temporary percutaneous catheters may be used when PN duration will be less than 3 weeks, whereas tunneled devices should be used for longer periods of therapy.[2] Placement of an implantable subcutaneous titanium or plastic port is also an option. Several prospective, nonrandomized studies have demonstrated a lower rate of catheter sepsis when subcutaneous ports are used.[9,10] However, these devices have not been used widely in young children requiring chronic PN because they require a needle stick for each port access.[2] Several studies are ongoing to delineate the incidence of complications according to the type of venous access device used.[11]

The principal factor influencing the selection of the route of venous access is the caloric requirement. The poor tolerance of peripheral veins of hyperosmotic solutions limits their utility to supply adequate calories. Gazitua et al demonstrated a 100% incidence of peripheral phlebitis with infusion of PN solutions of >600 mOsm (a typical infusion of 10% dextrose with electrolytes is almost 1000 mOsm).[12,13] Either percutaneous venipuncture or a venous cutdown approach must be used to obtain central access. The route of access is dependent on the patient's size, medical status, available venous access sites, and indicated catheter type. Venous cutdown procedures are favored in small patients (premature infants) and patients with coagulopathies. This approach essentially eliminates the insertion risks of pneumothorax and hemothorax.[14] The distal end of the vessel is usually ligated using the cutdown approach, preventing its use for future access.

Percutaneous venipuncture is often the easiest means of achieving central venous access. Excellent technical reviews are available on the subject.[15] Alternative sites are necessary for those patients who present with multiple sites of central venous thrombosis. Liberal use of duplex ultrasonography or magnetic resonance imaging to assess venous patency should be used in these patients. Alternative access sites include the azygous, inferior epigastric, and intercostals veins. As a final resort, a translumbar catheterization of the inferior vena cava may achieve reliable access for PN.[3]

Improvements in design over the last two decades have led to the development of small caliber catheters ranging in size from 2F to 4F. PICC lines (peripherally inserted central venous catheter) are becoming a common route of PN administration.[2,3] They have recently gained popularity because of their ease of bedside insertion and good patient tolerance. Numerous prospective, nonrandomized studies have reported a decreased incidence of major morbidity relative to surgically placed central venous catheters. Long-term morbidities such as risk of catheter-related sepsis and thrombosis are similar to surgically placed lines.[16] The compelling data from these studies and clinical experiences have made PICC lines the catheter of choice for many hospitalized children requiring extended venous access.[17] There are no studies in the current literature on the risks or benefits of these catheters for long-term outpatient PN therapy.

Special Considerations

Four major categories of complications exist: (1) mechanical or technical; (2) infectious; (3) metabolic; and (4) nutritional. Mechanical or technical complications are those problems related to catheter placement, ie, pneumothorax, hemothorax, cardiac tamponade, or equipment malfunction. Catheter thrombosis is a significant problem with a rate ranging from 0% to 50% of all central lines. This may lead to partial catheter malfunction, infection, or loss.[2,3] Several reviews report an association between catheter thrombosis and infection.[18–20] A potential early sign of catheter thrombosis is progressively sluggish or absent blood return on catheter aspiration. Thrombolytic agents are effective dissolving catheter thrombi. There are no standardized protocols for catheter thromblysis, based on a multicenter prospective randomized control studies.[21,22]

Catheter-related infections are the most common complications associated with central venous access for PN. The incidence may approach 60% in long-term devices.[1,17–19,22] The diagnosis of catheter infection and sepsis requires a high index of suspicion (ie, fever, erythema at catheter site, vague constitutional symptoms). Critical evidence-based assessments of therapies and clinical outcomes have been plagued by the lack of consistently accepted diagnostic criteria and classifications. Recently published guidelines by the Centers for Disease Control (CDC) for prevention of catheter-related infections have standardized the nomenclature. Localized infections are defined as erythema, tenderness, induration, or purulence that occurs at the exit-site or along the tunnel. Pocket infections occur only with implantable ports. Systemic infections, formerly called catheter sepsis or bacteremia, are defined as a positive culture of the catheter tip or a positive pathogen isolated from both blood drawn through the catheter and peripherally.[23]

Staphylococcus epidermidis, Staphylococcus aureus, and other skin flora are the most common pathogens isolated in patients with systemic infections. Enterococcus and enteric flora are the next most frequently isolated organisms. Although less common, Candida is an important pathogen because of its virulence and resistance to treatment.[2]

Therapy for catheter infections is dependent on the type of infection and pathogen. Exit site infections are often cleared with topical measures and systemic antibiotics, whereas tunnel and pocket infections usually require catheter removal.[24–26] Although the "gold standard" therapy for systemic catheter-related infections is line removal, many lines may be effectively treated without catheter removal.[2] Widmer reported that patient factors such as immunocompetence and the virulence of the pathogen determine the efficacy of antibiotic therapy.[27] When signs of systemic infection are present, early initiation of empiric intravenous antibiotic therapy is crucial to ensure catheter salvage. Blood cultures should be obtained both centrally and peripherally prior to the initiation of intravenous antibiotics.[23]

Treatment protocols vary widely, and there are no randomized, prospective studies stratifying pediatric patients by important risk factors like age, disease, acuity, or pathogen to support the appropriate antibiotic selection or length of therapy.[2,3]

Existing studies support the institution of antistaphylococcal therapy given through the catheter for community-acquired infections.[3,23,28,29] Antibiotic treatment is governed by the sensitivities of the blood cultures. Therapy is then continued for at least a 10-day period. The recent increased incidence of methicillin-resistant coagulase-negative staphylococcal infections in hospitalized or chronically ill patients warrants the institution of empiric vancomycin therapy as the initial coverage in these compromised patients.[2,3] Neonates, short-bowel patients, and hospitalized children should receive additional coverage for Gram-negative organisms. Repeat blood cultures at the end of treatment are indicated to confirm microbial clearance. Deterioration of clinical status during antibiotic therapy or failed catheter sterilization by treatment are indications for catheter removal. Infections with *S. aureus*, Gram-negative bacteria, and Candida may be especially virulent and lethal. Candida, though uncommon, should be considered with low-grade infections and when the child has received multiple antibiotics. The treatment for Candida line sepsis is removal, along with a complete course of antifungal therapy.[4,30]

Various materials, caps, valves and coatings have been proposed to decrease rates of catheter infection. Silver-chelated cuffs and antibiotic/antiseptic-impregnated catheters are two recent technological developments that show great promise. These catheters decrease infection rates in randomized, controlled

studies, but the effect is short-lived.[2] Despite numerous studies on silver chelated cuffed catheters, the literature supporting their use is limited.[31,32]

Use of a valve-tipped catheter has been advocated to reduce thrombotic complications, however, in a prospective trial in pediatric oncology patients, no benefit was shown to support the use of these catheters.[33]

Practice Guidelines *Indications, Types, and Routes of Administration: Parenteral Nutrition*

1. Pediatric patients unable to meet their nutrient requirements orally or with EN should receive PN. (B)
2. PN should be initiated within 1 day of birth in neonates and within 5 to 7 days in pediatric patients unable to meet their nutrient requirements orally or with EN. (C)
3. Catheter exit site infections should be treated topically and with systemic antibiotics. (B)
4. Tunnel infections should be treated with catheter removal. (B)
5. Systemic catheter-related infections should be initially treated with at least a 10-day course of intravenous antibiotics given through the catheter, adjusting the antibiotics according to the sensitivities of the blood cultures. (B)
6. Clinical deterioration, persistent infection or Candida sepsis should be treated with prompt catheter removal. (B)

REFERENCES

1. Acra SA, Rollins C: Principles and guidelines for parenteral nutrition in children. Pediatric Ann 28:2, 113–120, 1999
2. Krzywda, EA, Andris DA, Edmiston CE: Catheter infections: Diagnosis, etiology, treatment and prevention, Nutr Clin Pract 14:1781999
3. Chung DH, Ziegler MM: Central venous catheter access. Nutrition 14:119–123, 1998
4. Meadows, N: Monitoring and complications of parenteral nutrition. Nutrition 14:806–808, 1998
5. Cooper A, Jakobowski D, Spiker J, et al: Nutrition assessment: An integral part of the preoperative pediatric surgical evaluation. J Pediatr Surg 16:554, 1982
6. Pereira GR, Zeigler MM: Nutritional care of the surgical neonate. Clin Perinatol 16:233, 1989
7. Levy JS, Winter RW, Heird WC: Total parenteral nutrition in pediatric patients. Pediatr Rev 2:99, 1980
8. Leonberg BL, Chuang E, Eicher P, et al: Long term growth and development in children after home parenteral nutrition. J Pediatr 132:461, 1998
9. La Quaglia MP, Lucan A, Thaler HT, et al: A prospective analysis of vascular access device-related infections in children. J Pediatr Surg 27:840, 1992
10. Miller K, Buchanan GR, Zappa S, et al: Implantable venous access devices in children with hemophilia: A report of low infection rates. J Pediatr 132(6):934–938, 1998
11. Orr ME: Vascular access device selection for parenteral nutrition. Nutr Clin Pract 14:172, 1999
12. Gazitua R, Wilbon K, Bistrian BR, et al: Factors determining peripheral vein tolerance to amino acid infusions. Arch Surg 114:897, 1979
13. Shizgal HM, Knowles JB. Peripheral amino acids. IN Parenteral Nurtrition, 2nd ed. Fischer JE (ed). Little Brown and Company, Boston, 1991:389
14. Chathas MK, Paton JB, Fisher DE: Percutaneous central venous catheterization: Three years experience in a neonatal intensive care unit. Am J Dis Child 144:1246, 1990
15. Cobb LM, Vinocur CD, Wagner CW, et al: The central venous anatomy in infants. Surg Gynecol Obstet 165:230, 1987
16. Alhimyary A, Fernandez C, Picard M, et al: Safety and efficacy of total parenteral nutrition delivered via a peripherally inserted central venous catheter. Nutr Clin Pract 11:199, 1996
17. Wiener ES: Catheter sepsis: The central venous line Achilles' heel. Semin Pediatr Surg 4:207, 1995
18. Decker MD, Edwards KM: Central venous catheter infections. Pediatr Clin N Am 35:579, 1988
19. Mansfield PF, Hohn DC, Fornage BD, et al: Complications and failures of subclavian-vein catheterization. N Engl J Med 331: 1735, 1994
20. Atkinson JB, Chamberlin K, Boody BA: A prospective randomized trial: Urokinase as an adjuvant in the treatment of proven Hickman catheter sepsis. J Pediatr Surg 33:714, 1988
21. Kellerman S, Chan J, Jarvis W: Use of urokinase in pediatric hematology/oncology patients. Am J Infect Control 26:502, 1998
22. Tobiasky R, Lui K, Dalton DM, et al: Complications of Central Venous access Devices in children with and without Cancer. J Pediatr Child Health 33:509–514, 1997
23. Hospital Infection Control Advisory Committee, Centers for Disease Control and Prevention: Guidelines for prevention of intravascular-device related infections. Infect Control Hosp Epidemiol 17:438, 1996
24. Groeger JS, Lucas AB, Thaler HT, et al: Infectious morbidity associated with long-term use of venous access devices in patients with cancer. Ann Intern Med 119:1168–1174, 1993
25. Hiemenz J, Skelton J, Pizzo PA: Perspective on the management of catheter-related Infections in cancer patients. Pediatr Surg 22:702–707, 1987
26. Whitman E: Complications associated with the use of central venous access devices. Curr Probl Surg 33:313–378, 1996
27. Widmer AF: Intravenous-related infections. IN Prevention and Control of Nosocomial Infections. Wenzel RP (ed). Williams & Wilkins, Philadelphia, 1997, p 771
28. Buchanan AL, Moukarzel A, Goodson B, et al: Catheter related infections associated with home parenteral infections and predictive factors of catheter removal in their treatment. JPEN 18:297, 1994
29. Newman K, Tenney J, Reed W: Infectious and non-infectious complications of Hickman catheters. Microbiol Rev A345:156, 1987
30. Lecciones JA, Lee JW, Navano EE, et al: Vascular catheter associated fungemia: Analysis of 155 episodes. Clin Infect Dis 14:875, 1992
31. Pasquale MD, Campbell JM, Magnant CM: Groshong versus Hickman catheters. Surg Gynecol Obstet 172:408, 1992
32. Beekman SE, Henderson DK. Unfinished business: assessing the efficacy of extraluminal silver ions on the prevention of microbial colonization and catheter-associated infection. Crit Care Med 27:456–458, 1999
33. Warner BW, Haygood MM, Davies SL, Hennies GA: A randomized, prospective trial of standard Hickman compared with Groshong central venous catheters in pediatric oncology patients. J Am Coll Surgeons 183:140, 1996

COMPLICATIONS UNIQUE TO NEONATES: ENTERAL NUTRITION

Background

EN in the neonate can be associated with a variety of technical, gastrointestinal, developmental, and metabolic complications.

Sick neonates (who cannot nipple-feed) are generally fed using nasogastric or orogastric tubes. Tubes are usually inserted by nurses who check tube placement by auscultation and by pH of the fluid aspirated from the tube. Tube malposition can result in delivery of

nutrients either upstream or downstream from the intended site of infusion (leading to aspiration or dumping). Nasogastric tubes may cause nasal congestion or erosion.

Gastrostomy tubes may be used for long-term tube feeding in neonates. A common complication with gastrostomy tubes is migration of the tube.[1] Feeding tubes may also be occluded by crushed medications. Feeding pump malfunction can be associated with over- or under-delivery of feeding substrate.

A serious complication of enteral feedings in neonates (particularly preterms) is neonatal necrotizing enterocolitis (NEC). Gastrointestinal complications of EN in the neonate include emesis, abdominal distension, and diarrhea. Although occurrence of these symptoms may be a harbinger for NEC, they are frequently signs of less severe feeding intolerance. Emesis and/or abdominal distension may be an indication of obstruction, intolerance of the rate of feeding or impaired gastric emptying.

Diarrhea can be related to hyperosmolality of the feeding, rate of delivery of the feeding, malabsorption, contaminated feedings, and/or gastrointestinal tract infections.

Long-term tube feeding without nipple feeding can result in oral aversion. Early and frequent oral stimulation is necessary to avoid this complication.[1]

Although less frequent with EN than with PN, metabolic complications may occur. Fluid and/or electrolyte abnormalities, glucose abnormalities, nutrient deficiencies, and/or metabolic bone disease (in preterms) are occasionally seen. In severely malnourished infants, overzealous nutritional rehabilitation may be hazardous. Refeeding may result in hyperglycemia, hypokalemia, hypophosphatemia, and hypomagnesemia.

Evidence

Use of a small, properly anchored soft tube reduces the risks of nasal congestion or erosion. The risk of gastric or intestinal perforation (by stiff, nonpliable tubes) is reduced by use of tubes made of polyurethane or silicone rubber, rather than polyvinyl chloride.[1]

Gastrostomy tube migration can be minimized by firmly attaching the tube and placing a mark on the tube to facilitate detection of migration.[1] Tube occlusion by medications is avoided in neonates by use of liquid medications. Tube flushing also reduces the risk of occlusion. In neonates, tubes should be flushed with 1 mL of air instead of water to avoid fluid overload.[2] Smaller volume, continuous feedings in neonates are generally infused by intravenous pumps, which are more accurate than enteral pumps.

If gastrointestinal obstruction is ruled out, prokinetic drugs may be helpful in treating abdominal distension and/or emesis.[3] Diarrhea can be minimized with correct formula selection, concentration, and preparation, and with review of medications.[4] Diarrhea may be managed by decreasing the feeding rate.[3] Fiber has not been shown to be efficacious in the treatment of diarrhea in infants less than 6 months of age.[5] However, soy formula with fiber has been shown to reduce the duration of loose stools in older infants with moderate-to-severe diarrhea[6] and with antibiotic-induced diarrhea.[7]

Careful handling of commercially sterile, ready-to-feed bottled formulas using aspectic techinque, reduces the risk of formula contamination.[8] Non–ready-to-feed enteral formulas for infants should be prepared using aseptic technique in a designated hospital formula room (or separate formula preparation area).[9] Individual formula portions that are removed from floor stock (or refrigeration) and opened should be used within 4 hours or discarded,[9] although commercially sterile products may be hung in a closed delivery system for 8 to 12 hours.[4] Hospital-prepared tube feedings or human milk should not be hung for more than 4 hours.[4] Disposable enteral delivery equipment (tubing, fasteners, etc) should be changed every 24 hours and should not be reused.[4]

Non-nutritive sucking (sucking on a pacifier while being tube-fed) facilitates transition from tube to bottle feeding in preterm infants and is associated with a decrease in length of hospital stay.[10] Preterm infants are more likely to breastfeed if they receive supplemental feedings by nasogastric tube rather than by bottle.[11]

Practice Guidelines *Complications Unique to Neonates: Enteral Nutrition*

1. Feeding tube position should be verified before feeding is initiated. (C)
2. When administered by feeding tube, medications should be given in liquid form. (C)
3. Enteral feedings (including human milk) should be handled and stored using aseptic technique. (B)
4. Nonnutritive sucking during tube feeding should be encouraged. (A)

REFERENCES

1. American Academy of Pediatrics, Committee on Nutrition: Pediatric Nutrition Handbook, 4th ed. AAP, Elk Grove Village, IL, 1998
2. Armstrong VL: Teaching pediatric tube feeding to caregivers. Ross Products Division, Columbus, OH, 1999, p 30
3. Marchand V, Baker SB, Baker RD: Enteral nutrition in the pediatric population. Gastrointest Endoscop Clin N Amer 8:669–702, 1998
4. Davis A: Indications and techniques for enteral feeds. IN Pediatric Enteral Nutrition. Baker SB, Baker RD, Davis A (eds). Chapman & Hall, New York, 1994, pp 67–94
5. Vanderhoof JA, Murray ND, Paule CL, et al: Use of soy fiber in acute diarrhea in infants and toddlers. Clin Pediatr 36:135–139, 1997
6. Brown KH, Perez F, Peerson JM, et al: Effect of dietary fiber (soy polysaccharide) on the severity, duration and nutritional outcome of acute, watery diarrhea in children. Pediatrics 92:241–247, 1993
7. Burks AW, Vanderhoof JA, Mehra S, et al: Randomized clinical trial of soy formula with and without fiber in antibiotic induced diarrhea. J Pediatr 139:578, 2001
8. Patchell CJ, Anderton A, Holden C, et al: Reducing bacterial contamination of enteral feeds. Arch Dis Child 78:166–168, 1998
9. American Dietetic Association: Preparation of Formula for Infants: Guidelines for Health Care Facilities. ADA, Chicago, IL, 1991, pp 1–100
10. Pinelli J, Symington A: Non-nutritive sucking for promoting

physiologic stability and nutrition in preterm infants (Cochrane Review). IN The Cochrane Library, Issue 1, 2000. Oxford: Update Software
11. Kliethermes PA, Cross ML, Lanese MG, et al: Transitioning preterm infants with nasogastric tube supplementation: Increased likelihood of breastfeeding. JOGNN 28:264–273, 1998

COMPLICATIONS UNIQUE TO NEONATES: PARENTERAL—FLUID AND ELECTROLYTES

Background

PN significantly contributes to the patients' daily fluid intake. Electrolyte imbalances in patients receiving PN are generally related to the PN, underlying clinical conditions, and drug therapy. Changes in intake, losses, redistribution, and physiologic and pathophysiologic regulatory mechanisms affect electrolyte homeostasis.[1,2] The treatment of electrolyte disorders relies on the identification of the etiology and is guided by the acuity and the presence or absence of symptoms. PN solutions should not be used primarily to manage fluid and electrolyte abnormalities, but adjustments in PN solutions can avoid and/or ameliorate potential complications.

Evidence

Premature infants lose sodium in the urine because of the immaturity of the sodium reabsorptive capacity of the kidneys and with diuretic therapy. Hyponatremia, due to water retention, is managed by free water restriction and gentle diuresis.[3,4] Hyponatremia in infants may lead to poor tissue growth and adverse developmental outcomes. Normalizing sodium intake promotes cell growth and weight gain.[5,6] A general goal should be a urine sodium concentration greater than 10 mEq/L. Hypernatremia denotes free water deficit and is corrected with free water and sodium restriction. Sodium concentrations in PN can be adjusted to a maximum of 154 mEq/L or the equivalent of normal saline.

Hypokalemia is more common than hyperkalemia in hospitalized patients.[7] Hyperkalemia is frequent in very low birth weight infants[8] and is usually the result of reduced renal clearance (renal failure, potassium-sparing diuretics), impaired renal drug excretion (trimethoprim-sulfamethoxazole), excessive potassium load (hemolysis, blood transfusions), redistribution (metabolic acidosis), or protein catabolism.[9] To avoid toxicity, potassium concentrations in PN solutions as well as in other intravenous admixtures should be carefully watched. Although rare patients may require more potassium, potassium concentration in PN solutions is usually limited to 80 mEq/L.

Hypomagnesemia is usually associated with severe diarrhea, medications (diuretics, aminoglycosides, Amphotericin B) or maternal diabetes.[10,11] Hypermagnesemia may be seen in infants born to pre-eclamptic mothers treated with magnesium sulfate and usually resolves within 48 to 72 hours.[12,13] Hypermagnesemia also occurs in the setting of impaired renal function.[14] Serum calcium concentrations are higher, and serum parathyroid hormone concentrations lower in hypermagnesemic neonates, perhaps because of suppression of neonatal parathyroid function.

Hypocalcemia may be due to hypoalbuminemia, hypoparathyroidism, vitamin D deficiency, hyperphosphatemia, or medication-induced urinary calcium excretion (diuretics, corticosteroids).[1,22] Two studies, including a randomized controlled trial, show that hypocalcemia may result from hypercalciuria secondary to amino acid intake from PN. In this situation, serum phosphate concentrations rise significantly.[15,16] Pelegano et al[17] studied the effect of PN calcium-to-phosphate ratio (in mg) in very low birth weight infants. Calcium retention was higher with a 2:1 ratio, whereas phosphate retention was higher with a 1.7: 1 or 1.3:1 ratio. In two studies, supplementation of phosphate in neonates with hypophosphatemia resulted in decreased calciuria and increased calcium retention.[18,19] Vielisis et al[20] showed that a phosphate dose of 1.34 mM/kg per day (40 mg/kg per day) is necessary to normalize serum phosphate concentrations in critically ill neonates without inducing phosphaturia. Metastatic calcification may occur when the serum Ca/P product exceeds 60 to 70 mg^2/dL^2.[21] Based on these studies, it appears that a 1.7:1 calcium-to-phosphate ratio in PN allows for the highest absolute retention of both minerals and simulates the in utero accretion of calcium and phosphate.

Practice Guidelines *Complications Unique to Neonates: Parenteral—Fluid and Electrolytes*

1. Hyponatremia in premature infants should be corrected by increasing sodium intake in order to promote tissue growth and weight gain. (A)
2. Calcium and phosphate concentrations should be optimized in PN solutions to promote maximum bone mineral retention. (A)

REFERENCES

1. Schultz NJ, Chitwood-Dagner KK: Body electrolyte homeostasis. IN Pharmacotherapy: A Pathophysiologic Approach. Dipiro JT, Talbert RL, Yee GC, et al (eds). Appleton & Lange, Stamford, 1997, pp 1105–1137
2. Dunham B, Marcuard S, Khazanie PG, et al: The solubility of calcium and phosphorus in neonatal total parenteral nutrition solutions. JPEN 15:608–611, 1991
3. Modi N: Hyponatraemia in the newborn. Arch Dis Child 78:F81–F84, 1988
4. Maguire D, Doyle P: Sodium balance in very-low-birth-weight infants. Crit Care Nurse 14:61–66, 1994
5. Haycock GB: The influence of sodium on growth in infancy. Pediatr Nephrol 7:871–875, 1993
6. Bower TR, Pringle KC, Soper RT: Sodium deficit causing decreased weigh gain and metabolic acidosis in infants with ileostomy. J Pediatr Surg 23:567–572, 1988
7. Weiner ID, Wingo CS: Hypokalemia-consequences, causes, and correction. J Am Soc Nephrol 8:1179–1188, 1997
8. Shaffer SG, Kilbride HW, Hayen LK, et al: Hyperkalemia in very low birth weight infants. J Pediatr 121:275–279, 1992
9. Fukuda Y, Kojima T, Ono A, et al: Factors causing hyperkalemia in premature infants. Am J Perinatol 6:76–79, 1989
10. Ahsan SK, al-Swoyan S, Hanif M, et al: Hypomagnesemia and clinical implications in children and neonates. Indian J Med Sci 52:541–547, 1998
11. Weintrob N, Karp M, Hod M, et al: Short- and long-range complications in offspring of diabetic mothers. J Diabetes Complications 10:294–301, 1996
12. McGuiness GA, Weinstein MM, Cruikshank DP, et al: Effects of

magnesium sulfate treatment on perinatal calcium metabolism. II. Obstet Gynecol 56:595–600, 1980
13. Donovan EF, Tsang RC, Steichen JJ, et al: Neonatal hypermagnesemia: Effect on parathyroid hormone and calcium homeostasis. J Pediatr 96:305–310, 1980
14. Nadler JL, Rude RK: Disorders of magnesium metabolism. Endocrinol Metab Clin N Am 24:623–641, 1995
15. Bengoa JM, Sitrin MD, Wood RJ, et al: Amino acid-induced hypercalciuria in patients on total parenteral nutrition. Am J Clin Nutr 38:264–269, 1983
16. Prestridge LL, Schanler RJ, Shulman RJ, et al: Effect of parenteral calcium and phosphorus therapy on mineral retention and bone mineral content in very low birth weight infants. J Pediatr 122:761–768, 1993
17. Pelegano JF, Rowe JC, Carey DE, et al: Effect of calcium/phosphorus ratio on mineral retention in parenterally fed premature infants. J Pediatr Gastroenterol Nutr 12:351–355, 1991
18. Chessex P, Pineault M, Zebiche H, et al: Calciuria in parenterally fed preterm infants: Role of phosphorus intake. J Pediatr 5:794–796, 1985
19. Cary DE, Goetz CA, Horak E, et al: Phosphorus wasting during phosphorus supplementation of human milk feedings in preterm infants. J Pediatr 5:790–793, 1985
20. Vileisis RA: Effect of phosphorus intake in total parenteral nutrition infusates in premature neonates. J Pediatr 110:586–589, 1987
21. Gertner JM: Disorders of calcium and phosphorus homeostasis. Pediatr Clin N Am 37:1441–1465, 1990

COMPLICATIONS UNIQUE TO NEONATES: HYPERGLYCEMIA AND HYPOGLYCEMIA

Background

Premature infants are at increased risk for hyperglycemia possibly due to saturation of insulin receptors or the immaturity of hepatic and pancreatic response.[1,2] Hyperglycemia may also be the result of sepsis, surgery, or respiratory distress and may lead to derangements in fluid and electrolyte status.[3,4] Hyperglycemia in the neonate is defined as plasma glucose concentration greater than 150 mg/dL or whole blood glucose concentrations greater than 125 mg/dL. Hypoglycemia is defined as blood glucose concentrations less than 40 mg/dL.[2] In patients receiving PN, hypoglycemia may be caused by sudden cessation of the PN infusion.

Evidence

Premature, low-gestational-age, and low-birth-weight infants are more likely to develop hyperglycemia.[3,4] The incidence of hyperglycemia in has been reported between 43 and 86% in premature infants and increases with increasing prematurity.[4,5] It is also seen more frequently in patients requiring mechanical ventilation.[6] Hyperglycemia was found in 43% of premature infants receiving dextrose infusions at a mean rate of 4.7 to 4.9 mg/kg per minute (range, 3 to 7 mg/kg per minute).[4,7] In very premature infants, hyperglycemia will almost invariably occur as the infusion rate increases beyond 8 mg/kg per minute.[8] Because this rate of dextrose infusion is insufficient to allow full caloric delivery, insulin may needed for additional carbohydrate administration.

Continuous insulin infusion (0.01–0.1 unit/kg per hour) has been shown to be safe and effective in managing hyperglycemia in the neonate.[9,10] Glucose concentrations should be monitored at least every 2 hours, aiming for blood glucose concentrations between 100 and 150 mg/dL. Collins et al,[11] in a prospective randomized trial, evaluated the administration of insulin by continuous infusion for an average of 14 days in 24 extremely low birth weight infants. They showed improved glucose tolerance, greater protein and calorie intake, and greater weight gain in the insulin-treated group compared with the control group.

Hypoglycemia develops rapidly in neonates if feedings are delayed or interrupted, because of the immaturity of homeostatic mechanisms. Additionally, infants receiving PN may have high levels of insulin that suppresses ketogenesis; this may linger after abrupt discontinuation of PN.[12,13] Bendorf et al[14] showed in a controlled trial that acute discontinuation of PN lead to a greater incidence of hypoglycemia in young infants. Older children (more than 2 years of age),[15] however, were not affected by abrupt discontinuation of PN. It is recommended that PN be tapered over 1 to 2 hours in infants before discontinuation to avoid reactive hypoglycemia. Although there is no established time period, significant hypoglycemia can be seen as early as 15 to 30 minutes after stopping PN; this should guide the timing of initial blood glucose sampling for monitoring these children.[15] Blood glucose concentrations should be checked within 15 to 60 minutes after discontinuation of PN.

Practice Guidelines
Complications Unique to Neonates: Hyperglycemia and Hypoglycemia

1. Dextrose infusion rates in infants should not exceed 10 to 14 mg/kg per minute. (A)
2. Insulin administration by continuous infusion is safe and effective in controlling parenteral nutrition–associated hyperglycemia in infants. (A)
3. PN should be tapered off over 1 to 2 hours before discontinuation in infants under age 2. (B)

REFERENCES

1. Pollak A, Cowett RM, Schwartz R, et al: Glucose disposal in low-birth-weight infants during steady-state hyperglycemia: effects of exogenous insulin administration. Pediatrics 61:546–549, 1978
2. Farrag HM, Cowett RM: Glucose homeostasis in the micropremie. Clin Perinatol 27:1–22, 2000
3. Stonestreet BS, Rubin L, Pollak A, et al: Renal functions of low birth infants with hyperglycemia and glucosuria produced by glucose infusions. Pediatrics 66:561–567, 1976
4. Zarif M, Pildes RS, Vidyasagar D: Insulin and growth-hormone responses in neonatal hyperglycemia. Diabetes 25:428–433, 1976
6. Dweck HS, Cassady G: Glucose intolerance in infants of very low birth weight. I. Incidence of hyperglycemia in infants of birth weights 1,100 grams or less. Pediatrics 53:189–195, 1974
7. Binder N, Raschko PK, Benda GI, et al: Insulin infusion with parenteral nutrition in extremely low birth weight infants with hyperglycemia. J Pediatr 114:273–280, 1989
8. Jones MO, Pierro A, Hammond P, et al: Glucose utilization in the surgical newborn infant receiving total parenteral nutrition. J Pediatr Surg 28:1121–1124, 1993
9. Heron P, Bourchier D: Insulin infusions in infants of birthweight less than 1250 g and with glucose intolerance. Aust Pediatr J 24:362–365, 1988

10. Kanarek KS, Santeiro ML, Malone JI: Continuous infusion of insulin in hyperglycemic low-birth weight infants receiving parenteral nutrition with and without lipids. JPEN 15:417–420, 1991
11. Collins JW Jr, Hoppe M, Brown K, et al: A controlled trial of insulin infusion and parenteral nutrition in extremely low birth weight infants with glucose intolerance. J Pediatr 118:921–927, 1991
12. Cornblath M, Hawdon JM, Williams AF, et al: Controversies regarding the definition of neonatal hypoglycemia: suggested operational thresholds. Pediatrics 105:1141–1145, 2000
13. Dudrick SJ, Macfadyen BV Jr, Van Buren CT, et al. Parenteral hyperalimentation. Metabolic problems and solutions. Ann Surg 176:259–264, 1972
14. Bendorf K, Friesen CA, Roberts CC: Glucose response to discontinuation of parenteral nutrition in patients less than 3 years of age. JPEN 20:120–122, 1996
15. Werlin SL, Wyatt D, Camitta B: Effect of abrupt discontinuation of high glucose infusion rates during parenteral nutrition. J Pediatr 124:441–444, 1994

COMPLICATIONS UNIQUE TO NEONATES: HYPERTRIGLYCERIDEMIA

Background

PN-associated hypertriglyceridemia is usually due to uncontrolled hyperglycemia[1] or the administration of excessive amounts of lipid emulsion.[2] Reduced lipid clearance occurs with prematurity, low birth weight, and sepsis.[3]

Evidence

Overfeeding of carbohydrates leads to hyperglycemia and hypertriglyceridemia.[1] If hypertriglyceridemia and hyperglycemia coexist, an attempt should be made first to achieve normoglycemia. Lipid clearance in premature infants is less than half that of mature infants, most likely because of limited lipoprotein lipase activity.[4] In a prospective study that examined the tolerance of 10% lipid emulsions in 262 infants, a significant correlation was found between low birth weight and high serum triglyceride concentrations.[5] Two studies in low-birth-weight infants reported that sepsis impairs lipid utilization.[6,7] Increasing the lipid emulsion dose from 2 to 3 g/kg per day increased serum triglyceride and fatty acid concentrations in septic infants more than in nonseptic infants. Lipid dose in premature septic infants may need to be reduced.[8] Hypertriglyceridemia may also be seen in acute illness.[8] Haumont et al reported that the higher phospholipid content found in 10% lipid emulsions in comparison to 20% lipid emulsions is associated with accumulation of cholesterol, triglycerides, and phospholipids in low-birth-weight infants and can be corrected by reverting back to 20% emulsions.[6,9–11] A slower rate of lipid emulsion infusion has also been shown to result in less elevation of serum triglyceride levels.[12,13] Lipids can be safely administered on the first day of life (at a rate of 1 g/kg per day).[14,15] The American Academy of Pediatrics recommends limiting lipid infusion rates to less than 0.25 g/kg per hour in low-birth-weight infants, while not exceeding 3 g/kg per day.[16] Lipoprotein lipase (LPL) and hepatic lipases are needed for lipid clearance.[4,17] Heparin can increase LPL levels and lipolytic activity, stabilizing triglyceride levels.[18,19] Unless heparin administration is contraindicated, adding heparin at a dose of 1 unit/mL of neonatal PN solution improves lipid emulsion clearance.

Premature infants have low carnitine reserves. Low carnitine levels can also be seen in full-term neonates receiving long-term PN.[20,21] Carnitine supplementation may increase lipid clearance,[22,23] but low plasma carnitine concentrations do not necessarily correlate with elevated serum triglyceride concentrations.[24] It has been shown that fatty acid oxidation and improved triglyceride levels are seen in premature infants receiving supplemental intravenous carnitine who are also receiving lipid emulsions.[25] Although studies are somewhat inconclusive, the administration of L-carnitine (at a dose of 10 mg/kg per day) seems to enhance fatty acid oxidation, especially in carnitine-deficient infants. L-carnitine may be useful in infants with hypertriglyceridemia when other etiologies have been ruled out. Guidelines on monitoring for hypertriglyceridemia are predominately empiric.

Practice Guidelines
Complications Unique to Neonates: Hypertriglyceridemia

1. Lipid emulsion infusions in infants should begin at 0.5 to 1 g/kg per day and advance at rate of 0.5 g/kg per day to a maximum of 3 g/kg per day. (A)
2. Lipid emulsion infusion rates should be reduced in premature or septic infants and serum triglyceride concentrations should be monitored. (B)
3. If serum triglyceride concentrations exceed 200 mg/dL in the neonate, lipid emulsion infusion should be suspended and then restarted at a rate of 0.5 to 1 g/kg per day. (B)
4. Intravenous heparin, at a dose of 1 unit/mL of PN fluids, should be given to enhance the clearance of lipid emulsions. (B)
5. A trial of carnitine supplementation should be given to premature infants with unexplained hypertriglyceridemia. (B)
6. Infants should receive 20% lipid emulsion to improve clearance of triglycerides and phospholipids. (B)

REFERENCES

1. Aarsland A, Chinkes D, Wolfe RR: Hepatic and whole-body fat synthesis in humans during carbohydrate overfeeding. Am J Clin Nutr 65:1774–1782, 1997
2. Andrew F, Chan G, Schiff D: Lipid metabolism in the neonate. I. The effects of Intralipid infusion on plasma triglyceride and free fatty acid concentrations in the neonate. J Pediatr 88:273–278, 1976
3. Haumont D, Deckelbaum RJ, Richelle M, et al: Plasma lipid and plasma lipoprotein concentrations in low birth weight infants given parenteral nutrition with twenty or ten percent lipid emulsion. J Pediatr 115:787–793, 1989
4. Dhanireddy R, Hamosh M, Sivasubramanian KN, et al: Postheparin lipolytic activity and Intralipid clearance in very low-birth-weight infants. J Pediatr 98:617–622, 1981
5. De Leeuw R, Kok K, De Vries IJ, et al: Tolerance of intravenously administered lipid in newborns. Acta Poediatr Scand 74:52–56, 1985
6. Park W, Paust H, Schroder H: Lipid infusion in premature infants suffering from sepsis. JPEN 8:290–292, 1984

7. Park W, Paust H, Brosicke H, et al: Impaired fat utilization in parenterally fed low-birth-weight infants suffering from sepsis. JPEN 10:627–630, 1986
8. Dahlstrom KA, Goulet OJ, Roberts RL, et al: Lipid tolerance in children receiving long-term parenteral nutrition: A biochemical an immunological study. J Pediatr 113:985–990, 1988
9. Haumont D, Richelle M, Deckelbaum RJ, et al: Effect of liposomal content of lipid emulsions on plasma lipid concentrations in low birth weight infants receiving parenteral nutrition. J Pediatr 121:759–763, 1992
10. Carpentier YA: Intravascular metabolism of fat emulsions. Clin Nutr 8:115–125, 1989
11. Griffin E, Breckenridge WC, Kuksis MH, et al: Appearance and characterization of lipoprotein X during continuous Intralipid infusion in the neonate. J Clin Invest 64:1703–1712, 1979
12. Kao LC, Cheng MH, Warburton D: Triglycerides, free fatty acids, free fatty acid/albumin molar ratio, and cholesterol levels in serum of neonates receiving long-term lipid infusions: Controlled trials of continuous and intermittent regimens. J Pediatr 104: 429–435, 1984
13. Brans WY, Andrew DS, Carrillo DW, et al: Tolerance of fat emulsions in very-low-birth-weight neonates. Am J Dis Child 142:145–152, 1988
14. Gilbertson N, Kovar IZ, Cox DJ, et al: Introduction of intravenous lipid administration on the first day of life in the very low birth weight neonate. J Pediatr 119:615–623, 1991
15. Wells DH, Ferlauto JJ, Forbes DJ, et al: Lipid tolerance in the very low birth weight infant on intravenous and enteral feedings. JPEN 13:263–267, 1989
17. American Academy of Pediatrics, Committee on Nutrition: Nutritional needs of low-birth weight infants. Pediatrics 75:976–986, 1985
18. Zaidan H, Dhanireddy R, Hamosh M, et al: The effect of continuous heparin administration on Intralipid clearing in very low birth weight infants. J Pediatr 101:599–602, 1982
19. Spear ML, Stahl GE, Hamosh M, et al: Effect of heparin dose and infusion rate on lipid clearance and bilirubin binding in premature infants receiving intravenous fat emulsions. J Pediatr 112: 94–98, 1988
20. Schmidt-Sommerfeld E, Penn D, Wolf H: Carnitine deficiency in premature infants receiving total parenteral nutrition: Effect of L-carnitine supplementation. J Pediatr 931–935, 1983
21. Tibboel D, Delemarre FMC, Przyrembel H, et al: Carnitine deficiency in surgical neonates receiving total parenteral nutrition. J Pediatr Surg 25:418–421, 1990
22. Larson LE, Olegard R, Ljung ML, et al: Parenteral nutrition in preterm neonates with and without carnitine supplementation. Acta Anaesthesiol Scand 34:501–505, 1990
23. Smith RB, Sachan DS, Plattsmier J, et al: Plasma carnitine alterations in premature infants receiving various nutritional regimens. JPEN 12:37–42, 1988
24. Helms RA, Mauer EC, Hay WW Jr et al. Effect of intravenous L-carnitine on growth parameters and fat metabolism during parenteral nutrition in neonates. JPEN 14:448–453, 1990
25. Bonner CM, DeBrie KL, Hug G, et al: Effects of parenteral L-carnitine supplementation on fat metabolism and nutrition in premature infants. J Pediatr 126:287–292, 1995

COMPLICATIONS UNIQUE TO NEONATES: HEPATOBILIARY

Background

PN-associated cholestasis (PNAC) is the most common and life-threatening long-term complication of PN in children.[1–3] About 30% to 60% of children develop PN-associated hepatic dysfunction during long-term PN.[4] The mean time to onset of PNAC was reported to be 42 days.[2,5] Factors that correlate with PNAC include prematurity, low birth weight,[6] overfeeding, lack of enteral feeding,[7,8] long duration of PN,[8–10] recurrent sepsis,[6,11] and short-bowel syndrome.[10,12] Although several markers indicate PNAC, elevated serum conjugated bilirubin concentration is one of the best established parameters.[3,13,14]

Evidence

Reestablishing enteral feedings may lead to a regression of jaundice and normalization of liver function tests (LFTs).[15,16] The etiology of PNAC is unknown. PNAC may be due to the build-up and toxic effects of elevated serum and bile levels of lithocholic acid,[17,18] or a reduction of gastrointestinal hormones blood levels, including cholecystokinin.[7,19] Other potential etiologies include amino acid profile changes with PN,[20] bacterial overgrowth,[8] and bowel dysfunction due to decreased bowel length.[10] PNAC is more commonly seen in children with recurrent sepsis.[6,11,22,23] Treatment or avoidance of sepsis may reduce the risk of PNAC.[24,25]

Providing a balanced energy source by altering the carbohydrates-to-fat ratio may improve LFTs and reduced PN-associated hepatic complications.[22,26] Although overfeeding should be avoided,[25,29] there is no convincing evidence that lipid emulsions at normal doses induce cholestasis.[27] Limiting lipid emulsion dose in children to a rate of no more than 3 g/kg per day is recommended to avoid hepatic steatosis.[28]

Although animal studies have shown that PN-associated liver toxicity may be mediated by one or more amino acids, particularly methionine, convincing human data are lacking.[29,30]

No definitive preventive measure is known. Three studies have shown ursodeoxycholic acid (UDCA) to be safe. It can reduce serum bilirubin levels and, in some studies, normalize of transaminase levels.[31–33] These were retrospective, noncontrolled studies. UDCA is only available for oral administration and has limited usage in neonates who cannot absorb oral medications. Intravenous administration of CCK-octapeptide has been reported to have some benefit in reducing conjugated bilirubin in some patients with PNAC.[34,35] CCK-octapeptide has also been shown to lead to lower conjugated bilirubin levels if given prophylactically to long-term PN infants.[36] These studies were all either retrospective or nonrandomized trials. Antibiotics such as metronidazole and oral gentamicin have been used to prevent bacterial overgrowth. Neonates who received oral gentamicin showed no significant rise in peak or mean direct serum bilirubin concentrations, compared with a significantly higher mean and peak direct serum bilirubin concentrations in neonates who did not receive oral gentamicin.[37] Two other studies showed evidence of a benefit of intravenous metronidazole on PNAC.[38,39] Although phenobarbital has been used to treat PNAC,[40,41] other studies have shown it to worsen the course of PNAC.[42,43] Taurine supplementation in premature infants has shown to improve bile flow and bile acid excretion.[44] Levels of taurine are low in premature infants and those with short-bowel syndrome.[45] Cooke et al[46] evaluated the role of taurine deficiency in the pathogenesis of PNAC in 20 premature infants. Taurine at a dose of 10.8 mg/kg/d for 10 days did not alter hepatocellular function. Forchielli et al[47] compared the effects of two different taurine-sup-

plemented amino acid formulations on PNAC in infants less than 1 year of age. The overall incidence of cholestasis was 43%, but PNAC was judged by the authors as the cause in only 21.4% of infants. The effects of taurine supplementation on reversing or protecting against PNAC are inconclusive. Carnitine is not a routine constituent of PN formulas and carnitine deficiency in PN patients has been suggested as a predisposing factor to liver dysfunction. Two case reports of adults with hepatocyte fatty infiltration showed improvement in LFTs and normalized bilirubin concentrations with carnitine supplementation.[48,49] Another report in four adults showed no change in liver morphology with carnitine,[50] and declines in carnitine levels probably have little adverse effect.[51] Cyclic infusion of PN over less than 24 hours allows hepatic rest by reducing continuous and compulsive liver overloading and may reduce PNAC.[52] Although studies have failed to demonstrate a statistically significant reduction in cholestasis, levels of bilirubin have been observed to fall with conversion to a cyclic regimen.[52]

Practice Guidelines
Complications Unique to Neonates: Hepatobiliary

1. Avoidance of overfeeding, early initiation of enteral nutrition, and prevention and aggressive treatment of sepsis should be used to minimize the incidence of PN associated cholestasis. (B)
2. Administration of ursodeoxycholic acid or cholecystokinin should be considered if EN cannot be given. (B)
3. PN should be administered using a cyclic regimen when possible if long-term use is anticipated. (C)

REFERENCES

1. Rodgers BM, Hollenbeck JI, Donnelly WH, et al: Intrahepatic cholestasis with parenteral alimentation. Am J Surg 131:149–155, 1976
2. Hodes JE, Grosfeld JL, Weber TR, et al: Hepatic failure in infants on total parenteral nutrition (TPN): Clinical and histopathologic observations. J Pediatr Surg 17:463–468, 1982
3. Benjamin DR: Hepatobiliary dysfunction in infants and children associated with long-term total parenteral nutrition. A clinicopathologic study. Am J Clin Pathol 76:276–283, 1981
4. Suita S, Ikeda K, Nagasaki A, et al: Follow-up studies of children treated with a long-term intravenous nutrition (IVN) during the neonatal period. J Pediatr Surg 17:37–42, 1982
5. Beale E, Nelson R, Bucciarelli R, et al: Intrahepatic cholestasis associated with parenteral nutrition in premature infants. Pediatrics 64:342–347, 1979
6. Beath S, Davies P, Papadpoulou A, et al: Parenteral nutrition-related cholestasis in postsurgical neonates: Multivariate analysis of risk factors. J Pediatr Surg 31:604–606, 1996
7. Lucas A, Bloom R, Aynsley-Green A: Metabolic and endocrine consequences of depriving preterm infants of enteral nutrition. Acta Pediatr Scand 72:245–249, 1983
8. Colomb V, Goulet O, Rambaud C, et al: Long-term parenteral nutrition in children: liver and gallbladder disease. Trans Proc 24:1054–1055, 1992
9. Drongowski RA, Coran AG: An analysis of factors contributing to the development of total parenteral nutrition-induced cholestasis. JPEN 13:586–589, 1989
10. Cavicchi M, Beau P, Crenn P, et al: Prevalence of liver disease and contributing factors in patients receiving home parenteral nutrition for permanent intestinal failure. Ann Intern Med 132: 525–532, 2000
11. Manginello FP, Javitt NB: Parenteral nutrition and neonatal cholestasis. J Pediatr 94:296–298, 1979
12. Ito Y, Shils ME: Liver dysfunction associated with long-term total parenteral nutrition in patients with massive bowel resection. JPEN 15:271–276, 1991
13. Black DD, Whitington PF, Korones SD: The effect of short-term total parenteral nutrition on hepatic function in the human neonate: A prospective randomized study demonstrating alteration of hepatic canalicular function. J Pediatr 99:445–449, 1981
14. Beath SV, Needham SJ, Kelly DA, et al: Clinical features and prognosis of children assessed for isolated small bowel or combined small bowel and liver transplantation. J Pediatr Surg 32:459–461, 1997
15. Pereira GR, Sherman MS, DiGiacomo J, et al: Hyperalimentation-induced cholestasis: increased incidence and severity in premature infants. Am J Dis Chil 135:842–845, 1981
16. Barbier J, Gineste D, Kraimps JL, et al: Complications hepatobiliaires de la nutrition parenterale totale. Chirurgie 118:47–54, 1992
17. Fouin-Fortunet H, Le Quernec L, Erlinger S, et al: Hepatic alterations during total parenteral nutrition in patients with inflammatory bowel disease: A possible consequence of lithocholate toxicity. Gastroenterology 82:932–937, 1982
18. Farrell MK, Balistreri WF, Suchy FJ: Serum-sulfated lithocholate as an indicator of cholestasis during parenteral nutrition in infants and children. JPEN 6:30–33, 1982
19. Jawaheer G, Pierro A, Lloyd DA, et al: Gall bladder contractility in neonates: Effects of parenteral and enteral feeding. Arch Dis Child 72:F200–F202, 1995
20. Brown MR, Thunberg BG, Golub L, et al: Decreased cholestasis with enteral instead of intravenous protein in the very-low-birth infant. J Pediatr Gastroenterol Nutr 9:21–27, 1989
21. Simmons MG, Georgeson KE, Figueroa R, et al: Liver failure in parenteral nutrition-dependent children with short bowel syndrome. Trans Proc 28:2701, 1996
22. Buchmiller CE, Kleiman-Wexler RL, Ephgrave KS, et al: Liver dysfunction and energy source: Results of a randomized clinical trial. JPEN 17:301–306, 1993
23. Clark PJ, Bail MJ, Kettlewell MG: Liver associated tests in patients receiving parenteral nutrition. JPEN 15:54–59, 1991
24. Beau P, Barrioz T, Ingrand P: Total parenteral nutrition-related cholestatic hepatopathy, is it an infectious disease? Gastroenterol Clin Biol 18:63–67, 1994
25. Messing B, Colombel JF, Heresbach D, et al: Chronic cholestasis and macronutrient excess in patients treated with prolonged parenteral nutrition. Nutrition 8:30–35, 1992
26. Meguid MM, Akahoshi MP, Jeffers S, et al: Amelioration of metabolic complications of conventional total parenteral nutrition. Arch Surg 119:1294–1298, 1984
27. Wagner WH, Lowry AC, Silberman H: Similar liver function abnormalities occur in patients receiving glucose-based and lipid-based parenteral nutrition. Am J Gastroenterol 78:199–202, 1983
28. Reif S, Tano M, Oliverio R, et al: Total parenteral nutrition-induced steatosis: reversal by parenteral lipid infusions. JPEN 15:102–104, 1991
29. Vileisis RA, Inwood RJ, Hunt CE: Prospective controlled study of parenteral nutrition-associated cholestatic jaundice: Effect of protein intake. J Pediatr 96:893–897, 1980
30. Moss RL, Haynes AL, Pastuszyn A, et al: Methionine infusion reproduces liver injury of parenteral nutrition cholestasis. Pediatr Res 45:664–668, 1999
31. Levine A, Maayan A, Shamir R, et al: Parenteral nutrition-associated cholestasis in preterm neonates: Evaluation of ursodeoxycholic acid treatment. J Pediatr Endocrinol Metab 12:549–553, 1999
32. Spagnuolo MI, Iorio R, Vegnente A et al: Ursodeoxycholic acid for the treatment of cholestasis in children on long-term total parenteral nutrition: A pilot study. Gastroenterology 111:716–719, 1996
33. Narkewicz MR, Smith D, Gregory C, et al: Effect of ursodeoxycholic acid therapy on hepatic function in children with intrahepatic cholestatic liver disease. J Pediatr Gastroenterol Nutr 26:49–55, 1998

34. Rintala RJ, Lindahl H, Pohjavuori M: Total parenteral nutrition-associated cholestasis in surgical neonates may be reversed by intravenous cholecystokinin: A preliminary report. J Pediatr Surg 30:827–830, 1995
35. Teitelbaum DH, Han-Markey T, Schumacher RE: Treatment of parenteral nutrition associated cholestasis with cholecystokinin-octapeptide. J Ped Surg 30:1082–1085, 1995
36. Teitelbaum DH, Han-Markey T, Drongowski R, et al: Use of cholecystokinin to prevent the development of parenteral nutrition-associated cholestasis. JPEN 20:100–103, 1997
37. Kaufman SS, Loseke CA, Lupo JV, et al: Influence of bacterial overgrowth and intestinal inflammation on duration of parenteral nutrition in children with short bowel syndrome. J Pediatr 131:356–361, 1997
38. Spurr SG, Grylack LJ, Mehta NR: Hyperalimentation-associated neonatal cholestasis: Effect of oral gentamicin. JPEN 13:633–636, 1989
39. Kubota A, Okada A, Imura K, et al: The effect of metronidazole on TPN-associated liver dysfunction in neonates. J Pediatr Surg 6:618–621, 1990
40. Capron JP, Gineston JL, Herve MA, et al: Metronidazole in prevention of cholestasis associated with total parenteral nutrition. Lancet 1:446–447, 1983
41. South M, King A, Chir B: Parenteral nutrition-associated cholestasis: recovery following phenobarbitone. JPEN 11:208–209, 1987
42. Gleghorn EE, Merritt RJ, Subramanian N, et al: Phenobarbital does not prevent total parenteral nutrition-associated cholestasis in noninfected neonates. JPEN 10:282–283, 1986
43. Nemeth A, Wikstrom SA, Strandvik B: Phenobarbital can aggravate a cholestatic bile acid pattern in infants with obstructive cholangiopathy. J Pediatr Gastroenterol Nutr 10:290–297, 1990
44. Okamoto E, Rassin DK, Zucker CL, et al: Role of taurine in feeding the low-birth-weight infant. J Pediatr 104:936–940, 1984
45. Cooper A, Betts JM, Pereira GR, et al: Taurine deficiency in the severe hepatic dysfunction complicating total parenteral nutrition. J Pediatr Surg 19:462–465, 1984
46. Cooke RJ, Whitington PF, Kelts D: Effect of taurine supplementation on hepatic function during short-term parenteral nutrition in the preterm infant. J Pediatr Gastroenterol Nutr 3:234–238, 1984
47. Forchielli NL, Gura KM, Sandler R, et al: Aminosyn PF or Trophamine: Which provides more protection from cholestasis associated with total parenteral nutrition? J Pediatr Gastroenterol Nutr 21:374–382, 1995
48. Palombo JD, Schnure F, Bistrian BR, et al: Improvement of liver function tests by administration of L-carnitine to a carnitine-deficient patient receiving home parenteral nutrition: A case report. JPEN 11:88–92, 1987
49. Worthley LI, Fishlock RC, Snoswell AM: Carnitine deficiency with hyperbilirubinemia, generalized skeletal muscle weakness and reactive hypoglycemia in a patient on long-term total parenteral nutrition: treatment with intravenous L-carnitine. JPEN 7:176–180, 1983
50. Bowyer BA, Miles JM, Haymond MW, et al: L-carnitine therapy in home parenteral nutrition patients with abnormal liver tests and low plasma carnitine concentrations. Gastroenterology 94:434–438, 1988
51. Moukarzel AA, Dahlstrom KA, Buchman AL, et al: Carnitine status of children receiving long-term total parenteral nutrition: a longitudinal prospective study. J Pediatr 120:759–762, 1992
52. Collier S, Crough J, Hendricks, et al. Use of parenteral nutrition in infants less than 6 months of age. Nutr Clin Pract 9:65–68, 1994

COMPLICATIONS UNIQUE TO NEONATES: METABOLIC BONE DISEASE

Background

Metabolic bone disease (MBD) has been reported in infants and premature neonates receiving PN.[1,2] The incidence of MBD is unknown, but it is common in patients receiving long-term PN.[3,4] Biochemical evidence of MBD may include hypercalciuria, hypercalcemia, hyperphosphatemia, elevated serum alkaline phosphatase, low-normal plasma parathyroid hormone, and normal 25-hydroxyvitamin D and low 1,25 hydroxyvitamin D plasma concentrations.[4,5] The etiology of bone demineralization or inadequate bone matrix mineralization is multifactorial and often associated with calcium, phosphorus, and vitamin D deficiencies.[6,7] Aluminum accumulation in bones[8] and excessive vitamin D may also contribute.[9]

Evidence

Hypocalcemia in MBD patients may be due to decreased calcium intake or increased urinary calcium elimination. Because of solubility limitations, calcium and phosphate in neonatal PN are generally inadequate to meet the needs for optimal bone growth. There are few clinical trials investigating MBD in infants and children and most data are derived from studies in adult patients.

Investigators have shown that very low birth weight infants who received high calcium (1.68 mM/dL) and phosphate (2 mM/dL) in their daily PN had greater calcium and phosphate retention and greater bone mineral content.[7,10,11] Hypocalcemia due to hypercalciuria has been consistently reported in patients receiving PN. Factors known to promote hypercalciuria include increased calcium intake, decreased phosphate supplementation, excessive amino acid infusion, chronic metabolic acidosis, and cyclic PN infusion. A reduction in calciuria and bone pain can be achieved by reducing calcium intake and altering the calcium-to-phosphate ratio from 1:1.5 to 1:2.[12] Several studies have correlated amino acid intake with hypercalciuria.[5,13,14] Chronic metabolic acidosis from excessive amounts of amino acids or from D-lactic acidosis can lead to MBD by direct loss of bone involving buffering bone systems or impaired vitamin D metabolism.[15,16]

Two studies comparing cycled versus noncycled administration of PN showed that cycling increases bone mineral loss.[14,17] In one of these studies, measurement of bone mass by photon absorbtiometry showed reduced vertebral bone mass but not wrist bone mass in long-term (55.2 ± 8.7 months) PN patients.

Small amounts of aluminum are present in calcium and phosphate salts, vitamins, heparin, and trace element solutions.[18] Aluminum in PN solutions may result in a decreased rate of bone formation.[18,19] Koo et al[20] found that aluminum accumulated at the mineralization front of bones in premature infants. Measurement of serum aluminum concentration can help determine the role of aluminum excess when MBD is suspected in long-term PN patients. Aluminum toxicity may be a particular problem in young infants whose kidneys cannot adequately excrete aluminum compared with older children. The FDA has recommended restriction of aluminum contamination in large volume parenterals to a maximum of 25 μg/L. Patients who have elevated aluminun levels should have parenteral sources of aluminum investigated.[21]

Underlying conditions and concurrent medications may also be responsible or predispose to MBD. These

are especially prevelant in patients with malabsorption, glucocorticoid administration, and antineoplastic agents.[19,21]

Several reports of improvement of MBD after vitamin D removal from PN suggest a possible role of vitamin D in the development of MBD.[9,22] If this is attempted, it is advised that patients have their plasma PTH and 25-hydroxyvitamin D and 1,25 hydroxyvitamin D concentrations measured. If PTH and 1,25 hydroxyvitamin D concentrations are low and 25 hydroxyvitamin D concentrations are normal, then vitamin D should be withdrawn from the PN solution.

Practice Guidelines
Complications Unique to Neonates: Metabolic Bone Disease

1. Calcium and phosphate should be provided in adequate amounts to assure optimal bone mineralization in long-term PN patients. (A)
2. Serum aluminum concentrations should be measured whenever unexplained MBD is present in long-term PN patients. (B)
3. In patients with low PTH and 1,25 hydroxyvitamin D concentrations and normal 25 hydroxyvitamin D concentration with MBD, vitamin D should be removed from the PN solution. (B)

REFERENCES

1. The TS, Kollee LA, Boon JM, et al: Rickets in a preterm infant during intravenous alimentation. Acta Pediatr Scand 72:769–71, 1993
2. Kien CL, Browning C, Jona J, et al: Rickets in premature infants receiving parenteral nutrition: A case report and review of the literature. JPEN 6:152–156, 1982
3. Shike M, Harrison JE, Sturtridge WC, et al: Metabolic bone disease in patients receiving long-term total parenteral nutrition. Ann Intern Med 92:343–350, 1980
4. Shike M, Shils ME, Heller A. et al: Bone disease in prolonged parenteral nutrition: Osteopenia without mineralization defect. Am J Clin Nutr 44:89–98, 1986
5. De Vernejoul MC, Messing B, Modrowski D, et al: Multifactorial low remodeling bone disease during cyclic total parenteral nutrition. J Clin Endocrinol Metab 60:109, 1985
6. Leape LL, Valaes T: Rickets in low birth weight infants receiving total parenteral nutrition. J Pediatr Surg 11:665–674, 1976
7. Prestridge LL, Schanler RJ, Shulman R, et al: Effect of parenteral calcium and phosphorus on mineral retention and bone mineral content in very low birth weight infants. J Pediatr 122:761–768, 1993
8. Vargas JH, Klein GL, Ament ME, et al: Metabolic bone disease of total parenteral nutrition: Course after changing from casein to amino acids in parenteral solutions with reduced aluminum content. Am J Clin Nutr 48:1070–1078, 1988
9. Shike M, Sturtridge WC, Tam CS, et al: A possible role for vitamin D in the genesis of parenteral nutrition-induced metabolic bone disease. Ann Intern Med 95:560–568, 1981
10. Wood RJ, Sitrin MD, Cusson GJ, et al: Reduction of total parenteral nutrition-induced urinary calcium loss by increasing the phosphorus in the total parenteral nutrition prescription. JPEN 10:188–190, 1986
11. Sloan GM, White DE, Brennan MF: Calcium and phosphorus metabolism during total parenteral nutrition. Ann Surg 197: 1–6, 1983
12. Larchet M, Garabedian M, Bourdeau A et al: Calcium metabolism in children during long-term total parenteral nutrition: The influence of calcium, phosphorus, and vitamin D intakes. J Pediatr Gastroenterol Nutr 13:367–375, 1991
13. Bengoa JM, Sitrin MD, Wood RJ, et al: Amino acid-induced hypercalciuria in patients on total parenteral nutrition. Am J Clin Nutr 38:264–269, 1983
14. Lipkin EW, Ott SM, Chesnut CH, et al: Mineral loss in the parenteral nutrition patient. Am J Clin Nutr 47:515–523, 1988
15. Cunningham J, Fraher LJ, Clemens TL, et al: Chronic acidosis with metabolic bone disease. Am J Med 73:199–204, 1982
16. Karton MA, Rettmer R, Lipkin EW, et al: D-Lactate and metabolic bone disease in patients receiving long-term parenteral nutrition. JPEN 13:132–135, 1989
17. Wood RJ, Bengoa JM, Sitrin MD, et al: Calciuric effect of cyclic versus continuous total parenteral nutrition. Am J Clin Nutr 41:614–619, 1985
18. Koo WWK, Kaplan LA, Horn J, et al: Aluminum on parenteral nutrition solution-sources and possible alternatives. JPEN 10:591–595, 1986
19. Klein GL: Metabolic bone disease of total parenteral nutrition. Nutrition 14:149–152, 1998
20. Koo WWK, Kaplan LA, Bendon R, et al: Response to aluminum in parenteral nutrition during infancy. J Pediatr 109:883–887, 1986
21. Seidner DL, Licata A: Parenteral nutrition associated metabolic bone disease: Pathophysiology, evaluation, and treatment. Nutr Clin Pract 15:163–170, 2000
22. Verhage AH, Cheong WK, Allard JP, et al: Increase in lumbar spine bone mineral content in patients on long-term parenteral nutrition without vitamin D supplementation. JPEN 19:431–436, 1995

Section XIII: Specific Guidelines for Disease—Pediatrics

NECROTIZING ENTEROCOLITIS

Background

Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergency in the neonatal population.[1] It is characterized by abdominal distention and tenderness, pneumatosis intestinalis, bloody stools, gangrenous or perforated bowel, sepsis, and shock.[2] The primary risk factor for NEC is prematurity because approximately 90% of all cases occur in this population.[3] Other risk factors associated with this disease include aggressive enteral feedings, infectious agents, and hypoxic-ischemic insults.

Evidence

Through retrospective chart review and a case control study, rapid advancement of EN has been associated with development of NEC.[4] NEC is associated with feeding volume increments greater than 35 cc/kg per day. Recently, a prospective randomized trial examined slow (15 cc/kg per day) *versus* fast (35 cc/kg per day) increments in enteral feeding in 185 formula-fed infants with birth weights ranging from 501 to 1500 g.[5] This study showed that the incidence of NEC was not significantly different between the two groups. Of note, the fast group did reach goal feedings and regained their birth weight sooner than the slow group, but at discharge there were no significant age differences between the groups.

Infection is a necessary component of NEC; various studies support this assertion. Gram-negative rods, such as *Klebsiella, Escherichia coli,* or *Enterobacter,* are frequently isolated from infants with NEC.[6] Human milk feeding has been shown to decrease the incidence of NEC, perhaps because of the immune-enhancing effects of breast milk, which contains immunoglobulins, lysozyme, macrophages, and PAF acetyl hydrolase.[7]

Clinical and physiologic evidence support the role of hypoxic and/or ischemic injury as a secondary, rather than primary, contributing factor to NEC.[2] Bacterial toxins could initiate endothelial disruption in infants' immature vasculature, resulting in vascular compromise.[8] A recent study examining postnatal hemodynamic blood flow in very low birth weight infants concluded that early feedings do not significantly influence postnatal splanchnic blood flow in the first week of life.[9] One infant in the study experienced NEC, but his blood flow velocity did not differ from the other 19 study subjects. Once NEC develops, enteral feedings should be stopped and PN initiated.

Practice Guidelines
Necrotizing Enterocolitis

1. Newborns with NEC are at nutrition risk and should undergo formal nutrition assessment with development of a nutrition care plan. (B)
2. The rate of advancement of EN feeding increments should be kept to less than 35 cc/kg per day to decrease the risk of NEC. (B)
3. Fresh human milk feeding should be encouraged in neonates. (B)
4. PN should be initiated in infants when NEC is diagnosed. (B)

REFERENCES

1. Neu J, Weiss MD: Necrotizing enterocolitis: Pathophysiology and prevention. JPEN 23:S13–S17, 1999
2. Neu J: Necrotizing enterolcolitis: The search for a unifying pathogenic theory leading to prevention. Pediatr Clin N Am 43:409–432, 1996
3. Israel EJ: Neonatal necrotizing enterolcolitis, a disease of the immature intestinal mucosal barrier. Acta Paediatr Suppl 396: 27–32, 1994
4. McKeown RE, Marsh TD, Amaranth W, et al: Role of delayed feeding and of feeding increments in necrotizing enterocolitis. J Pediatr 121:764–770, 1992
5. Rayyis SF, Ambalavana N, Wright L, et al: Randomized trial of "slow" versus "fast" feed advancements on the incidence of necrotizing enterocolitis in very low birth weight infants. J Pediatr 134:293–297, 1999
6. Bell MJ, Shackelford RD, Feigin J, et al: Epidemiologic and bacteriologic evaluation of neonatal necrotizing enterocolitis. J Pediatr Surg 14:1–4, 1979
7. Lucas A, Cole TJ: Breast milk and neonatal necrotizing enterocolitis. Lancet 336:1519–1523, 1990
8. Nowicki PT, Nankervis CA: The role of the circulation in the pathogenesis of necrotizing enterocolitis. Clin Perinatol 21:219–234, 1994
9. Yanowitz T, Yao A, Pettigrew KD, et al: Postnatal hemodynamic changes in very-low birthweight infants. J Appl Physiol 87:370–380, 1999

SHORT BOWEL SYNDROME

Background

Short bowel syndrome (SBS) has been defined as the anatomic or functional absence of more than 50% of the normal small intestine.[1] This is a good working defini-

tion because SBS cannot strictly be defined by anatomy. Accurate measurement of remaining bowel is difficult, and absorption of nutrients may not correlate with bowel length if the remaining bowel is damaged. There is typically an attempt at the time of intestinal resection to save as much bowel as possible; however, some of the salvaged bowel may not function normally.[2] In an animal model, intestinal surgery and anastomosis without resection has a significant affect on gut growth, maturation, and disaccharidase activity.[3]

Intestinal loss and injury can result from necrotizing enterocolitis, mid-gut volvulus, abdominal wall defects, intestinal atresias, vascular infarct, cloacal extrophy, long-segment Hirschsprung's disease, or trauma.[1,4] The injury may not only be reflected in abnormal absorption, but also in altered motility. Premature infants who undergo bowel resection may have more potential than term infants for intestinal growth. The mean length of small bowel is 142 ± 22 cm in infants 19 to 27 weeks gestational age, 217 ± 24 cm in infants between 27 and 35 weeks gestational age, and 304 ± 44 cm in infants 35 weeks gestational age and older.[5]

Infants and children with SBS have less surface area for absorption of nutrients and decreased transit time. Malabsorption of nutrients results in excessive fluid and electrolyte losses from stool output. The nutrients malabsorbed will depend on the area of the bowel resected or damaged. Reviews suggest that infants without an ileocecal valve are dependent on PN longer those with an intact valve.[6–9]

PN is used for the initial management of SBS. This use of replacement fluids may be necessary as well if fluid and electrolyte losses are high. Urine electrolytes are more helpful in determining total body sodium status than serum electrolytes. Urine electrolytes will reflect total body status if renal function is normal. Urinary changes in sodium excretion will occur before any change is noted in serum sodium concentration. Sodium-depleted infants do not grow normally.[10–13] Sodium can be added to PN or EN formulations and urine electrolytes monitored to titrate the amount of supplementation needed. Zinc losses from ileostomy fluid may be 12 mg/L and 17 mg/L from diarrhea.[14,15] These losses should be considered when developing the nutrition care plan.

Hypersecretion can be seen in infants and children after a major intestinal resection and the start of enteral feedings.[16] An H_2 blocker can be added to PN to treat the associated gastric acid hypersecretion.[17,18]

Bacterial overgrowth may occur as a result of poor motility and dilated bowel. Stasis of intestinal contents leads to bacterial overgrowth, which can alter absorption and cause increased stooling.[19] The ^{13}C-xylose breath test has been used to diagnose overgrowth.[20] For infants prone to overgrowth, routine scheduled antibiotic treatment may be useful. D-Lactic acidosis has been reported in children with bacterial overgrowth, causing metabolic acidosis, drowsiness, and confusion.[21,22] This diagnosis should be considered in a child with SBS who presents with metabolic acidosis, high serum anion gap, normal lactate level, and without urinary ketones.[23] It may result from a combination of factors including carbohydrate malabsorption with increased delivery of nutrients to the colon, high carbohydrate intake, colonic flora of the type that produce D-lactic acid, decreased colonic motility, and impaired D-lactate metabolism.[23]

The optimal formula for feeding infants and children with SBS is not known. Elemental amino acid based formulas are suggested by some clinicians and have been shown to be well tolerated.[24,25]

There is no agreement on the amount of stool output that should be accepted. Usually, limits should be imposed on feeding once the stool output exceeds 45 ml/kg per day. However, a higher volume of stool output may be acceptable.[26] Careful fluid and electrolyte management is essential as dehydration can occur rapidly.

Long-term survival of infants and children with SBS depends on the ability of the intestine to adapt and the remaining intestine to increase its absorptive capacity.[27] Many agents have been promoted as supporting gut adaptation; hopefully, clinical trials in infants and children will be forthcoming.

Evidence

PN is used to manage SBS until bowel adaptation and gut growth is sufficient to permit normal growth with EN or oral nutrition.[18] Because of the life-saving necessity to administer PN acutely in patients with SBS, most of the studies on nutrition management strategies for SBS involve retrospective chart review articles or cohort analyses. Most pediatric centers do not have sufficient numbers of these patients to perform clinical trials. Cross-over designs for intestinal adaptation may encounter difficulties because of the lingering effect of one treatment on another. It is difficult to match patients exactly, as gestational age and length of time from initial resection may affect adaptation. Multicenter trials appear to be the best way to conduct nutrition research for infants and children with SBS.[28] The use of a coordinated interdisciplinary team for the management of SBS has been shown to be useful in maintaining growth and decreasing dependence on PN.[28]

Optimal timing of the initiation of EN has not been established. A controlled trial of 11 infants with intestinal disease showed improved absorption of nutrients (fat, nitrogen, calcium, zinc, and copper) as well as improved weight gain with the use of continuous versus intermittent administration of EN.[29] Hydrolyzed formulas may also be better tolerated by some patients.[24] There is no agreement on the type of formula or breast milk to be used to treat SBS in neonates and infants. There has been a prospective, randomized, cross-over design study of two protein hydrolysate formulas given by continuous infusion. Energy absorption was the same with both formulas, but differences in the amount of malabsorbed carbohydrate existed. The authors suggested use of a hydrolysate formula with a lower percentage of carbohydrate and a higher percentage of fat.[30]

Many nutrients and factors have been discussed as possible pro-adaptation agents. Until clinical trials on

pediatric patients occur, recommendations cannot be made concerning their use.

Practice Guidelines
Short Bowel Syndrome

1. Children with SBS are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. PN should be initiated as soon as possible postoperatively in patients with SBS. (B)
3. Continuous gastric feedings should be used initially in children with SBS receiving EN. (B)
4. Patients must be monitored for macronutrient and micronutrient deficiencies. (C)
5. A coordinated interdisciplinary team approach should be involved with the management of SBS patients. (B)

REFERENCES

1. Ziegler MM: Short bowel syndrome in infancy: Etiology and management. Clin Perinatol 13:167 ,1986
2. Taylor SF, Sokol RJ: Infants with short bowel syndrome. IN Neonatal Nutrition and Metabolism. Hay WW (ed). Mosby, St Louis, 1991, p 437
3. Stringel G, Uuay R, Guertin L: The effect of intestinal anastomosis on gut growth and maturation. J Pediatr Surg 24:1086, 1989
4. Georgeson KE, Breaux CW Jr: Outcome and intestinal adaptation in neonatal short bowel syndrome. J Pediatr Surg 27:344–348, 1992
5. Touloukian RJ, Smith GJ: Normal intestinal length in preterm infants. J Pediatr Surg 18:720, 1983
6. Georgeson KE, Breaux CW Jr: Outcome and intestinal adaptation in neonatal short-bowel syndrome. J Pediatr Surg 27:344, 1992
7. Goulet OJ, Revillon Y, Jan D, et al: Neonatal short bowel syndrome. J Pediatr 119:18, 1991
8. Ladd AP, Rescoria FR, West KW, et al: Long term follow-up after bowel resection for necrotizing enterocolitis: Factors affecting outcome. J Pediatr Surg 33:967, 1998
9. Chaet MS, Farrell MK, Ziegler MM, et al: Intensive nutrition support an remedial surgical intervention for extreme short bowel syndrome. J Pediatr Gastroenterol Nutr 19:295, 1994
10. Mews CF: Topics in neonatal nutrition. Early ileostomy closure to prevent chronic salt and water losses in infants. J Perinatol 12:297, 1992
11. Sacher P, Hirsign T, Gressler J, et al: The importance of oral sodium replacement in ileostomy patients. Prog Pediatr Surg 24:226, 1989
12. Bower TR, Pringle KC, Soper RT, et al: Sodium deficit causing decreased weight gain and metabolic acidosis in infants with ileostomy. J Pediatr Surg 23:567, 1988
13. Schwarz KB, Tennberg JL, Bell MJ, et al: Sodium needs of infants and children with ileostomy. J Pediatr 102:509, 1983
14. Shulman RJ: Zinc and copper balance studies in infants receiving TPN. Am J Clin Nutr 49:879, 1989
15. Solomons NW, Ruz M: Essential and beneficial trace elements in pediatric parenteral nutrition. IN Pediatric Enteral Nutrition. Baker RD Jr, Baker SS, Davis AM (eds). Chapman & Hall, New York, 1997, p 181
16. Hyman PE, Everett SL, Harada T: Gastric acid hypersecretion in short bowel syndrome in infants: Association with extent of resection and enteral feeding. J Pediatr Gastroenterol Nutr 5:191–197, 1986
17. Hyman PE, Garvey TQ III, Harada T: Effect of ranitidine on gastric acid hypersecretion in an infant with short bowel syndrome. J Pediatr Gastroenterol Nutr 4:316–319, 1985
18. Redel CA, Schulman RJ: Gastrointestinal disorders. IN Pediatric Enteral Nutrition. Baker RD Jr, Baker SS, Davis AM (eds). Chapman & Hall, New York, 1997, p 315
19. Kaufman SS, Loseke CA, Lupo JV, et al: Influence of bacterial overgrowth and intestinal inflammation on duration of parenteral nutrition in children with short bowel syndrome. J Pediatr 131:356, 1997
20. Dellert SF, Nowicki MJ, Farrell MK, et al: The ^{13}C-xylose breath test for the diagnosis of small bowel bacterial overgrowth in children. J Pediatr Gastroenterol 25:153, 1997
21. Perlmutter DH, Boyle JT, Campos JM, et al: D-lactic acidosis in children: An unusual metabolic complication of small bowel resection. J Pediatr 102:234, 1983
22. Gurevitch J, Sela B, Jonas A, et al: D-lactic acidosis: A treatable encephalopathy in pediatric patients. Acta Paediatrica 82:11, 1993
23. Uribarri J, Oh MS, Carroll HJ: D-Lactic acidosis. A review of clinical presentation, biochemical features, and pathophysiological mechanisms. Medicine. 77:73–82, 1998
24. Bines J, Francis D, Hill D: Reducing parenteral requirement in children with short bowel syndrome: Impact of an amino acid based complete infant formula. J Pediatr Gastroenterol Nutr 26:123–128, 1998
25. Vanderhoof JA, Matya SM: Enteral and parenteral nutrition in patients with short bowel syndrome. Eur J Surg 9:214–219, 1999
26. Alkalay AL, Fleisher DR, Pomerance JJ, et al: Management of premature infants with extensive bowel resection with high volume enteral infusates. Israel J Med Sci 31:298, 1995
27. Piena-Spoel M, Shaman-Koendjibharie M, Yamanouchi T, et al: "Gut-feeling" or evidence based approaches in the evaluation and treatment of human short bowel syndrome. Pediatr Surg Int 16:155–164, 2000
28. Koehler AN, Yaworski JA, Gardner M, et al: Coordinated interdisciplinary management of pediatric intestinal failure: A 2 year review. J Pediatr Surg 35:380–385, 2000
29. Parker P, Stroop S, Greene H: A controlled comparison of continuous versus intermittent feeding in the treatment of infants with intestinal disease. J Pediatr 1981, 99:360–364, 1981
30. Galeano NF, Lepage G, Leroy C, et al: Comparison of two special infant formulas designed for the treatment of protracted diarrhea. J Pediatr Gastroenterol Nutr 7:76–83, 1998

LIVER DISEASE

Background

Nutrition management of the infant and child with liver disease depends on the type of liver disease. Nutrition disturbances are uncommon in acute liver disease, but common and often severe in chronic liver disease. The nutritional abnormalities that accompany liver disease in children, and in the management have been reviewed in detail by several authors.[1–3]

In acute liver disease, weight loss may occur because of vomiting and anorexia, but malnutrition is uncommon. In chronic liver diseases of childhood, there are multiple causes of malnutrition, including (1) decreased intake secondary to nausea, vomiting, anorexia, ascites, and depression; (2) impaired nutrient digestion and absorption secondary to bile salt deficiency and pancreatic insufficiency that accompanies some liver diseases; and (3) increased energy requirements secondary to hypermetabolism and infection.[4] Adults with chronic liver disease exhibit accelerated protein breakdown and inefficient protein synthesis[5]; whether or not these phenomena occur in children with chronic liver disease is unknown.

Nutrition assessment in infants and children with chronic liver disease is important but problematic. Useful parameters include height, upper extremity anthropometrics, subjective assessment, and 24-hour

dietary recall. A decrease in height-for-age percentile has been shown to be a useful indicator of the duration of malnutrition in children with chronic liver disease.[6] Body weight can be misleading because of the contribution of hepatosplenomegaly, ascites, and edema, which can mask underlying weight loss.[7] Lower extremity anthropometrics can be erroneous because of edema.

Because the plasma proteins conventionally used in nutrition assessment (eg, albumin, prealbumin, transferrin) are synthesized by the liver, their concentration can be depressed by liver failure and/or malnutrition. In fact, in adults it has been shown that the plasma concentration of these proteins correlates more with the severity of liver injury rather than with the degree of malnutrition as assessed by anthropometric methods.[8] Nitrogen balance studies done in adults with chronic liver disease are difficult to interpret because decreased hepatic urea synthesis leads to underestimation of urinary nitrogen losses[9]; presumably, such studies would also be problematic in children, as would the use of immune parameters as an index of nutrition status.[10]

Although plasma concentrations of vitamins are often used to assess nutrition status, there are several drugs given to children with chronic liver disease that affect the blood concentrations of some vitamins. For example, bile-acid binding resins such as colestipol and cholestyramine may interfere with the absorption of the fat-soluble vitamins A, D, E, and K. Diphenylhydantoin and phenobarbital increase hepatic metabolism of vitamin D, thereby lowering the plasma concentration of 25-hydroxy-cholecalciferol.

Evidence

Protein metabolism is impaired in children with biliary atresia, the most common indication for liver transplantation in the pediatric age group.[4] Typically, in healthy infants, about 4% to 9% of overall energy expenditure is due to protein oxidation.[11] In contrast, in children with biliary atresia, 17% of overall energy expenditure is due to protein oxidation, and nitrogen balance is near zero.[4] In patients with chronic liver disease, plasma concentrations of the aromatic amino acids are elevated, and those of the branched-chain amino acids depressed.[12] Pierro et al[4] have shown that resting energy expenditure was about 29% higher than expected in infants with biliary atresia and that only 35% of the metabolizable energy intake was retained for growth in these children. As measured by the respiratory quotient, infants with biliary atresia probably metabolize carbohydrate predominantly, as opposed to adults with chronic liver disease, in whom carbohydrate metabolism is decreased.[13]

Infants with biliary atresia exhibit deficiencies of long-chain polyunsaturated fatty acids,[14] which are improved but not entirely reversed 1 year after liver transplantation.[15] Dietary interventions to prevent/treat these deficiencies have yet to be developed. However, administration of medium-chain triglyceride supplements to infants and children with biliary atresia has been shown to improve growth and decrease steatorrhea.[16] It should be noted that medium-chain triglycerides do not contain essential fatty acids, and thus long-chain fatty acids must also be administered. Poor absorption of fat soluble vitamins is common, and vitamin supplementation is an important part of the management of these children.

Although vitamin A is malabsorbed in the presence of cholestasis, plasma retinol concentrations may be misleading. Mourey et al[17] have suggested that the molar ratio of retinol to retinol-binding protein may be better than plasma retinol in assessing the vitamin A status of children with liver disease. According to Heubi et al,[18] 25-OH vitamin D3 is better absorbed by cholestatic children than vitamin D_2, and thus is the supplement of choice for such children. Sokol et al[19] have demonstrated that vitamin E–deficiency induced neuropathy is common in children with chronic cholestasis and is preventable by administration of D-α-tocopherol polyethylene glycol-1000 succinate, the form of vitamin E that is best absorbed by children with chronic cholestasis. Vitamin K deficiency is a preventable cause of coagulopathy in infants with chronic cholestasis[20]; oral supplements may suffice, although parenteral vitamin K may be necessary. The specific amounts of fat-soluble vitamin supplementation recommended for oral and parenteral administration as well as the method of monitoring have been detailed in a recent review article.[21]

Although decreased intake and malabsorption secondary to enteropathy may predispose children with chronic liver disease to deficiencies of the water-soluble vitamins, there are no data to support this postulate. Adults with chronic liver disease are prone to develop deficiency of zinc and/or selenium, but similar data in children are not available. In theory, children with liver disease are at risk for iron deficiency because of recurrent variceal hemorrhage and for calcium deficiency because of vitamin D deficiency. However, calcium absorption in these children is normal.[22]

Special Considerations

In the setting of acute liver failure, despite the risk of hyperammonemia, it is important not to overrestrict protein, because endogenous ammoniagenesis can result from catabolism of body proteins. Infants should be given 1.0 to 1.5 g protein/kg per day and children and teenagers 0.5 to 1.0 g protein/kg per day dry weight. Glucose infusions should provide 6 to 8 mg/kg per minute of glucose to prevent hypoglycemia. There is some evidence that hepatic encephalopathy in adults can be improved by administration of oral or intravenous branched-chain amino acid supplements[23]; similar studies in children are lacking. Because hypokalemia can exacerbate renal ammoniagenesis, attention should be given to providing sufficient potassium to avoid this problem.

Moukarzel et al[24] have shown that pretransplant nutrition status in children with end-stage liver disease correlates significantly with the outcome of orthotopic liver transplantation. Children with a pathologic height z score had a higher incidence of posttransplantation infections and surgical complications, and a

higher mortality rate. Chin et al[25] have shown that administration of branched-chain amino acid–rich nutritional supplements to children with chronic liver disease awaiting liver transplantation increases weight, height, total body potassium, mid-upper arm circumference, and subscapular skin-fold thickness and reduces the need for albumin infusions. In an uncontrolled trial, Guimber et al[26] demonstrated that children with end-stage liver disease who fail EN can increase weight when given PN. In the presence of hyperaldosteronism, which so often accompanies end-stage liver disease, dietary sodium restriction may be necessary as may potassium supplementation. Although there are no randomized, controlled trials that demonstrate efficacy, PN in the immediate postoperative period may facilitate ventilator weaning, reduce risk of infection, and improve wound repair.[27] A cholesterol-lowering drug may be necessary to treat the chronic hyperlipidemic effects of cyclosporine.

There are a number of rare inborn errors of metabolism that cause liver disease, each of which may require specific dietary supplementation. One of the more common of these disorders is galactosemia, in which dietary management consists of removing milk and milk products from the diet. Hereditary fructose intolerance is treated by strict elimination of fructose from the diet. In Wilson's disease, the mainstay of treatment is administration of copper-chelating agents such as penicillamine; restriction of high-copper foods such as shellfish, liver, nuts, seeds, and chocolate also is important. Dietary management of hereditary tyrosinemia is focused on restriction of phenylalanine, tyrosine, and methionine.

Practice Guidelines
Liver Disease

1. Children with liver disease are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. In patients with chronic cholestatic liver disease, intake of vitamins A, D, E, and K should be supplemented. (B)
3. Medium-chain triglycerides should be given to children with chronic liver disease to promote growth. (B)
4. Preoperative and postoperative SNS may be beneficial for malnourished children with end-stage chronic liver disease undergoing liver transplantation. (B)

REFERENCES

1. Novy MA, Schwarz KB: Nutritional considerations and management of the child with liver disease. Nutrition 13:177–184, 1997
2. Protheroe SM: Feeding the child with chronic liver disease. Nutrition 14:796–800, 1998
3. Kaufman SE, Murray ND, Wood RP, et al: Nutritional support for the infant with extrahepatic biliary atresia. J Pediatr 110(5): 679, 1987
4. Pierro A, Koletzko B, Carnielli V, et al: Resting energy expenditure is increased in infants and children with extrahepatic biliary atresia. J Pediatr Surg 24;534, 1989
5. McCullough AJ, Tavill AS: Disordered energy and protein metabolism in liver disease. Semin Liver Dis 11;265, 1991
6. Goulet OJ, deGoyet DV, Otte JB, et al: Preoperative nutritional evaluation and support for liver transplantation in children. Transplant Proc 4:3249, 1987
7. Sokol RJ, Stall C: Anthropometric evaluation of children with chronic liver disease. Am J Clin Nutr 52:203, 1990
8. Merli M, Romiti A, Riggio O, et al: Optimal nutritional indexes in chronic liver disease. JPEN 11:130S, 1987
9. Dolz C, Raurich JM, Ibanez J, et al: Ascites increases the resting energy expenditure in liver cirrhosis. Gastroenterology 100:738, 1991
10. O'Keefe SJ, Carraher TE, El-Zayadi AR, et al: Malnutrition and immuno-incompetence in patients with liver disease. Lancet 2:615, 1980
11. Pierro A, Carnielli V, Riller RM, et al: Metabolism of intravenous fat emulsion in the surgical newborn. J Pediatr Surg 24;[1]95, 1989
12. Rosen HM, Yoshimura N, Hodgman BA, et al: Plasma amino acid patterns in hepatic encephalopathy of differing etiology. Gastroenterology 72:483–87, 1977
13. Schneeweiss B, Graninger W, Ferenci P, et al: Energy metabolism in patients with acute and chronic liver disease. Hepatology 11:387, 1990
14. Gourley GR, Farrell PM, Odell BG: Essential fatty acid deficiency after hepatic portoenterostomy for biliary atresia. Am J Clin Nutr 36:1194–1199, 1982
15. Lapillonne A, Hakme C, Mamoux V, et al: Effects of liver transplantation on long-chain polyunsaturated fatty acid status in infants with biliary atresia. JPGN 30:528–532, 2000
16. Cohen MI, Gartner LM: The use of medium chain triglycerides in the management of biliary atresia. J Pediatr 79(3):379, 1971
17. Mourey MS, Siegenthaler G, Amadee-Manesme O: Regulation of metabolism of retinol-binding protein by vitamin A status in children with biliary atresia. Am J Clin Nutr 51:638, 1990
18. Heubi JE, Hollis BW, Specker B, et al: Bone disease in chronic childhood cholestasis. I. Vitamin D absorption and metabolism. Hepatology 9:252–264, 1989
19. Sokol RJ, Guggenheim MA, Iannaccone ST, et al: Improved neurologic function following long-term correction of vitamin E deficiency in children with chronic cholestasis. N Engl J Med 313:1580, 1985
20. Yanofsky RA, Jackson VG, Lilly JR, et al: The multiple coagulopathies of biliary atresia. Am J Hematol 16:171, 1984
21. Ramaccioni V, Soriano HE, Arumugam R, et al: Nutritional aspects of chronic liver disease and liver transplantation in children. JPGN 30:361–367, 2000
22. Bucuvalas JC, Heubi JE, Specker BL, et al: Calcium absorption in bone disease associated with chronic cholestasis during childhood. Hepatology 12:1200, 1990
23. Cerra RB, Cheung NK, Fisher JE, et al: Disease-specific amino acid infusion (F080) in hepatic encephalopathy: A prospective, randomized, double-blind, controlled trial. JPEN 9:288, 1985
24. Mourkarzel AA, Najm I, Vargas J, et al: Effects of nutritional status on the outcome of orthotopic liver transplantation in pediatric patients. Transplant Proc 22,4:1560–63, 1990
25. Chin SE, Shepherd RW, Thomas BJ, et al: Nutritional support in children with end-stage liver disease: a randomized crossover trial of a branched-chain amino acid supplement. Am J Clin Nutr 56:158–163, 1992
26. Guimber D, Michaud L, Ategbo S, et al: Experience of parenteral nutrition for nutritional rescue in children with severe liver disease following failure of enteral nutrition. Pediatr Transplantation 3:139–145, 1999
27. ESPEN guidelines for nutrition in liver disease and transplantation: Consensus guidelines. Clin Nutr 16:43, 1997

INFLAMMATORY BOWEL DISEASE

Background

Inflammatory bowel disease is actually a continuum of diseases characterized by contiguous inflammation of the rectum and colon (ulcerative colitis) on one end of the spectrum and by patchy inflammation, which can occur anywhere in the gastrointestinal tract (Crohn's

disease) on the other end of the spectrum. The etiology is not clearly defined. Both EN and PN have been used to treat malnutrition and to replace specific nutrient deficiencies patients with either ulcerative colitis or Crohn's disease.

Crohn's disease most commonly starts in the distal ileum. Growth failure is often present and may be the sole manifestation.[1] The most common cause of growth failure in Crohn's disease is energy deficiency secondary to poor oral intake.[2,3] This decline in intake may be a learned response because of associated abdominal pain and diarrhea often caused by food. Proinflammatory cytokines may also induce anorexia.[4] Other contributing factors may include malabsorption, increased energy expenditure, and losses in the stool. Hypoalbuminemia and micronutrient deficiencies are also common.[3] The hypoalbuminemia is due primarily to inflammation and an associated protein-losing enteropathy.[3] In severe Crohn's disease, prednisone is generally prescribed. However, it is difficult to regulate the steroid dose to both minimize disease activity while optimizing growth. Importantly, although steroids have a role in the decrease of linear growth rate, the overall level of disease activity has a greater impact.[5] Excessive doses of prednisone may compromise linear growth by modulating growth hormone (GH)/insulin-like growth factor-1 (IGF-1) axis. Glucocorticoids inhibit GH release, interfere with GH-binding, and suppress IGF-1 activity.[6]

Evidence

EN support can improve weight gain and linear growth, particularly in adolescents with compromised growth.[2,7–9] Adjunctive night-time feedings given one out of every fourth month resulted in prolonged disease remission in eight patients.[2] A larger study showed that long-term supplementation with enteral feedings each night prolonged remission when used in conjunction with an otherwise unrestricted diet.[8] Others have shown that peptide-based supplemental feedings also improve disease activity and the sense of well-being. A more recent study has shown that in children with Crohn's disease and growth failure, the use of night-time feeds was associated with catch-up growth.[9] These effects are postulated to be derived from normalization of nutrition status and repletion of lean tissue mass.[10] Although primary EN therapy contributes to the maintenance of remission,[8,11] some studies have suggested that EN alone induces remission, in the absence of other medical treatments.[12–14] However, meta-analyses, which include studies of pediatric patients, performed by two different groups, showed that steroids are more effective than EN in achieving remission.[15,16] Much of this work has been criticized in that many of the studies assessed efficacy based on subjective parameters; because steroids induce a feeling of well-being, this may influence the perceived efficacy of steroid therapy over EN.[17] More recent studies also suggest that newly diagnosed patients respond to EN better than patients who have recurrent disease.[18] EN may provide essential small intestinal nutrients(ie, glutamine) and/or may modify the production of inflammatory mediators.[4]

Several studies in adults have shown no role for SNS in inducing or maintaining remission in patients with ulcerative colitis. No studies are available in children. Clearly, SNS is appropriate in patients unable to maintain normal nutrition status with oral intake alone.

Special Considerations

Several nutrient deficiencies may occur in patients with inflammatory bowel disease. In a study of 162 children with inflammatory bowel disease, bone mineral density was significantly lower than in controls[19]; no effective treatments are known at this time. Bone density was lowest in pubertal or prepubertal girls with Crohn's disease. The degree of bone density loss was correlated with corticosteroid dose. Zinc deficiency has also been described in patients with inflammatory bowel disease.[20] This deficiency is secondary to malabsorption, and is predominately seen in patients who are already malnourished.

Practice Guidelines *Inflammatory Bowel Disease*

1. Children with inflammatory bowel disease are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. EN should be given to children with IBD and growth retardation to help induce a growth spurt. (A)
3. EN should be used as an adjunct to medical therapy in patients with IBD who are unable to maintain their nutrition status with oral intake. (B)
4. PN should be used in children with IBD who are unable to maintain normal growth and development on EN or a standard diet. (B)

REFERENCES

1. Kanof ME, Lake AM, Bayless TM: Decreased height velocity in children and adolescents before the diagnosis of Crohn's Disease. Gastroenterology 95:1523–1527, 1988
2. Belli DC, Seidman E, Bouthillier L, et al: Chronic intermittent elemental diet improves growth in children with Crohn's disease. Gastroenterology 94:603–610, 1988
3. Seidman EG, LeLeiko N, Ament M, et al: Nutritional issues in pediatric inflammatory bowel disease. Symposium report. J Pediatr Gastroenterol Nutr 12:424–438, 1991
4. Ruemmele FM, Roy CC, Leby E, et al: Nutrition as primary therapy in pediatric Crohn's disease: Fact or fantasy. J Pediatr 136:285–291, 2000
5. Motil KJ, Grand RJ, Davis-Kraft L, et al: Growth failure in children with inflammatory bowel disease: A prospective study. Gastroenterology 105:681–691, 1993
6. Allen DB: Growth and growth disorders. Endocrinol Metabol Clin 25:699–717, 1996
7. Morin CL, Roulet M, Roy CC, et al: Continuous elemental enteral alimentation children with Crohn's disease and growth failure. Gastroenterology 79:1205–1210, 1980
8. Kirschner BS, Klich JR, Kalman SS, et al: Reversal of growth retardation in Crohn's disease with therapy emphasizing oral nutritional restitution. Gastroenterology 80:10–15, 1981
9. Wilchanski M, Sherman P, Pencharz P, et al: Supplementary enteral nutrition maintains remission in pediatric Crohn's disease. Gut 38:543–554, 1996
10. Khoshoo V, Reifen R, Neuman MG, et al: Effect of low-and

high-fat, peptide-based diets on body composition and disease activity in adolescents with active Crohn's disease. JPEN 20:401–405, 1996
11. Polk DB, Hattner JA, Kerner JA: Improved growth and disease activity after intermittent administration of a defined formula diet in children with Crohn's disease. JPEN 16:499–504, 1992
12. Sanderson IR, Udeen S, Davies PS, et al: Remission induced by an elemental diet in small bowel Crohn's disease. Arch Dis Child 62:123–127, 1987
13. Ruuska T, Savilahti E, Maki M, et al: Exclusive whole protein enteral diet versus prednisolone in the treatment of acute Crohn's disease in children. J Pediatr Gastroenterol Nutr 19:175–180, 1994
14. Fujimura Y, Honda K, Sato I, et al: Remarkable improvement of growth and developmental retardation in Crohn's disease by parenteral and enteral nutrition therapy. Intern Med 31:39–43, 1992
15. Griffiths AM, Ohlsson A, Sherman PM, et al: Meta-analysis of enteral nutrition as a primary treatment of active Crohn's disease. Gastroenterology 108:1056–1067, 1995
16. Fernandez-Banares F, Cabre E, Esteve-Comas M, et al: How effective is enteral nutrition in inducing clinical remission in active Crohn's disease? A meta-analysis of the randomized clinical trials. JPEN 19:356–364, 1995
17. Perman JA, Beattie RM, Bentsen BS, et al: Concepts in pediatric gastroenterology and nutrition, Part IV: Childhood Crohn's disease and the efficacy of enteral diets. Nutrition 14:345–350, 1998
18. Seidman E: Nutritional therapy for Crohn's disease: Lessons from the Ste-Justine hospital experience. Inflamm Bowel Dis 49–53, 1997
19. Gokhale R, Favis MJ, Karrison T, et al: Bone mineral density assessment in children with inflammatory bowel disease. Gastroenterology 114(5):902–911, 1998
20. Valberg LS, Flanagan PR, Kertesz A, et al: Zinc absorption in inflammatory bowel disease. Dig Dis Sci 31(7):724–731, 1986

GASTROINTESTINAL PSEUDO-OBSTRUCTION

Background

Pseudo-obstruction is a term that describes a functional obstruction of the intestinal tract in the absence of mechanical obstruction. Pseudo-obstruction is characterized by dysmotility, which results in abdominal distention, nausea, vomiting, and variable degrees of malabsorption.[1] Primary pseudo-obstruction is caused by an abnormality of either the gastrointestinal visceral smooth muscle or its innervation.[2] Diseases include familial and sporadic visceromyopathies and visceral neuropathies. Secondary causes include endocrine diseases (diabetes, hypothyroidism, hypoparathyroidism), drugs, radiation, and connective tissue diseases. Intestinal pseudo-obstructive disorders are diagnosed manometrically.[3] The potential use of EN depends on which segment(s) of the gastrointestinal tract are affected. Prolonged obstructive episodes can result in acute or chronic calorie deficits. Prokinetic agents are useful in some patients.[4]

Evidence

There is a recent long-term follow-up of 44 patients with intestinal pseudo-obstruction.[3] In this study, 20 (45%) were surviving on enteral feedings alone. However, 14 (32%) had died and another 10 (23%) were PN-dependent because of recurrent episodes of obstruction. Sixty-four percent of the infants who died had PN-related complications.[3] Treatment may include placement of a decompressing gastrostomy or small bowel stoma. Symptoms may be improved using a decompressing stoma when the dysmotile segment is distal to the stoma.[3] Jejunal tube feedings, in children who were unable to tolerate gastrostomy tube feedings were tolerated and successful in maintaining nutrition status in 11 of 18 children.[4] The best predictor of jejunal tube feeding tolerance was preservation of a migrating motor complex in either the duodenum or the jejunum.[4] Appropriate treatment of bacterial overgrowth may protect the liver. Shortened intestinal length and urinary tract involvement were poor prognostic factors.[3]

Practice Guidelines *Gastrointestinal Psuedo-Obstruction*

1. Children with intestinal pseudo-obstruction are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Continuous EN in combination with a stoma placed above an isolated dysmotile segment should be considered in patients with pseudo-obstruction unable to tolerate oral feedings. (B)
3. Jejunal-tube feeding should be attempted in children with gastrointestinal pseudo-obstruction who have an intact intestinal migrating motor complex in either the duodenum or the jejunum. (B)

REFERENCES

1. Vargas JH, Sachs P, Ament ME: Chronic intestinal pseudo-obstruction syndrome in pediatrics. Results of a national survey by members of the North American Society of Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr 7:323–332, 1988
2. Rudolph CD, Hyman PE, Altshculer SM, et al: Diagnosis and treatment of chronic intestinal pseudo-obstruction in children: Report of consensus workshop. J Pediatr Gastroenterol Nutr 24:108–112, 1997
3. Heneyke S, Smith VV, Spitz L, et al: Chronic intestinal pseudo-obstruction: Treatment and long-term follow-up of 44 patients. Arch Dis Child 81:21–27, 1999
4. DiLorenzo C, Flores AF, Buie T, et al: Intestinal motility and jejunal feeding in children with chronic intestinal pseudo-obstruction. Gastroenterology 108:1379–1385, 1995

INTRACTABLE DIARRHEA OF INFANCY

Background

The term "intractable diarrhea of infancy" refers to infants less than 3 months of age who develop diarrhea that lasts for more than 2 weeks. Their underlying diagnoses may include cystic fibrosis, Hirschsprung's disease, protein intolerance, and disaccharidase deficiency.[1,2] However, frequently the etiology is unclear. These infants will most likely require SNS to maintain appropriate weight gain and growth. Data in this area are limited. Some of the data offered below were obtained from infants beyond this age group and is also extrapolated from studies in acute care settings.

Evidence

Continuous enteral feedings may improve nutrient tolerance and nutrient balance compared to bolus feedings of the same composition.[4] However, exclusive EN may be impossible because of malaborption of fats or carbohydrates.[1] Infants who have signs of carbohydrate malabsorption on elemental or semi-elemental formulas may be unable to digest long-chain carbohydrates.[5] Diet may be advanced more effectively by gradually adding fructose to a carbohydrate-free formula.[5] There are a few small, controlled studies that assess the efficacy of different formulas. Casein and whey hydrolysates were shown to be equally effective in one study.[6] In another prospective study of 10 patients, an elemental formula improved malnutrition and supported catch-up growth over 3 years.[7] A high proportion of MCTs in the diet may improve tolerance. More recent studies have critically examined the issues of other constituents in the hopes of decreasing the duration of diarrhea and stool volumes. Importantly, most investigators feel that normal dietary feeding through an acute diarrheal episode is acceptable.[8] The World Health Organization (WHO) found that many infants will improve with normal feedings (65%). However, a significant number need to be transitioned to a specialized diet.[9] Additionally, although breast feeding is the preferred method of feeding, full-strength cows milk appears to be quite adequate in the setting of acute diarrhea.[10,11] Children who fail cows milk will need to be transitioned to a specialized diet. Use of a lactose-free, soy-based product appears to be benificial.[12,13] Supplementation of the diet with fiber may reduce the duration of liquid stool excretion.[14]

Because EN alone may be insufficient to overcome malabsorption, PN may be used as an additional energy source along with EN. However, in one study, PN in the absence of EN delayed recovery and prolonged hospitalization in 8 of 13 patients who had severe chronic diarrhea.[3]

Practice Guidelines
Intractable Diarrhea of Infancy

1. Infants with intractable diarrhea are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Continuous EN should be given to children with intractable diarrhea unable to maintain normal nutrition status with oral intake. (B)
3. PN should be given to children with intractable diarrhea unable to maintain normal nutrition status with oral intake and EN. (B)
4. A high-fat, high-MCT containing EN formulation should be given to children with intractable diarrhea who are carbohydrate intolerant. (C)

REFERENCES

1. Kleinman RE, Galeano NF, Ghishan F, et al: Nutritional management of chronic diarrhea and/or malabsorption. J Pediatr Gastroenterol Nutr 9:407–415, 1989
2. Lo CW, Walker WA: Chronic protracted diarrhea of infancy: A nutritional disease. Pediatrics 72:786–800, 1983
3. Orenstein SR: Enteral versus parenteral therapy for intractable diarrhea of infancy: A prospective, randomized trial. J Pediatr 109:277–286, 1986
4. Parker P, Stroop S, Greene H: A controlled comparison of continuous versus intermittent feeding in the treatment of infants with intestinal disease. J Peds 99:360–364, 1981
5. Clark JH, Bullock L, Fitzgerald JF: Dietary fructose in the management of intractable diarrhea of infancy. J Pediatr Gastroenterol Nutr 5:81–86, 1986
6. Galeano NF, Lepage G, Leroy C, et al: Comparison of two special infant formulas designed for the treatment of protracted diarrhea. J Pediatr Gastroenterol Nutr 7:76–83, 1988
7. Paerregaard A, Hjelt K, Christiansen L, et al: Postenteritis enteropathy in infancy. A prospective study of 10 patients, with special relevance to growth pattern, long-term outcome, and incidence. Acta Pediatr Scand 79:1045–1051, 1990
8. Margolis PA. Litteer T, Hare N, et al: Effects of unrestricted diet on mild infantile diarrhea. A practice-based study. Am J Dis Child 144(2): 162–164, 1990
9. Anonymous: Evaluation of an algorithm for the treatment of persistent diarrhoea: A multicentre study. International Working Group on Persistent Diarrhoea. Bull WHO 74(5): 479–489, 1996
10. Wan C, Phillips MR, Dibley MJ, et al: Randomised trial of different rates of feeding in acute diarrhoea. Arch Dis Child 81(6): 487–491, 1999
11. Chew F, Penna FJ, Peret Filho LA, et al: Is dilution of cows' milk formula necessary for dietary management of acute diarrhoea in infants aged less than 6 months? Lancet 341(8839):194–197, 1993
12. Fayad IM, Hashem M, Hussein A, et al: Comparison of soy-based formulas with lactose and with sucrose in the treatment of acute diarrhea in infants. Arch Pediatr Adoles Med 153(7):675–680, 1999
13. Santosham M, Brown KH: Oral rehydration therapy and dietary therapy for acute childhood diarrhea. Pediatr Rev 8:273–278, 1987
14. Brown KH, Perez F, Peerson JM, et al: Effect of dietary fiber (soy polysaccharide) on the severity, duration, and nutritional outcome of acute, watery diarrhea in children. Pediatrics 92(2):241–247, 1993

PULMONARY: BRONCHOPULMONARY DYSPLASIA

Background

Bronchopulmonary dysplasia (BPD) is a chronic lung disease defined by the abnormal development of the lungs and air passages exacerbated by the effects of mechanical ventilation. It occurs predominantly in premature infants. Criteria for diagnosis of this disease vary, but it is generally agreed that the need for supplemental oxygen beyond day 28 of life and signs of chronic chest x-ray changes defines BPD. Symptom management, growth, nutrition, and psychosocial development are all vital areas of infant care in patients with BPD.

Evidence

Growth standards for premature infants are based on in utero growth curves. To approximate these growth patterns, energy needs have been estimated to be 120 to 130 kcal/kg in this population.[1] Growth failure in BPD patients results from increased metabolic expenditure, inadequate caloric intake, or a combination of both.[2] The increased metabolic demand may necessitate provision of even greater amounts of energy (130 to 160 kcal/kg per day) as infants with

BPD go from the neonatal phase to a convalescence phase.[3] Infants fed a protein- and mineral-enriched formula versus a standard isocaloric formula experienced catch-up growth in the first month of corrected gestational age.[4] However, complete catch up growth was not attained even at 3 months corrected age and multiple factors, including dexamethasone treatment, may play a growth inhibitory role. Socioeconomic status and illness after hospital discharge are also associated with growth failure in BPD patients.[5] Comprehensive nutrition counseling, ensuring adequate intake and parental support and education after hospital discharge may benefit these patients.

Short- and long-term steroid use in children may impair growth.[6] Preterm infants treated with dexamethasone show delayed linear growth up to 6 months corrected age.[7] Lower levels of serum growth factors, including insulin growth factor 1 and its binding protein, are also associated with steroid administration and impaired physical growth in this population.[8]

Vitamin A deficiency has been associated with BPD. In a pilot study to determine appropriate supplemental doses to achieve a normal, full term-infant serum vitamin A level, preterm infants were given various enteral and intramuscular vitamin A supplements.[9] Intramuscular vitamin A supplementation of 5000 IU three times per week was needed before serum levels were normalized.[10,11] A meta-analysis of five studies in which neonates were either randomized or quasirandomized to vitamin A versus placebo did not demonstrate any effect on mortality. However, there was a trend toward more rapid weaning from oxygen dependence in neonates receiving vitamin A. The use of vitamin A must be weighed with potential risks of repeated intramuscular injections. For some patients, oral supplementation may be appropriate.

Practice Guidelines
Bronchopulmonary Dysplasia

1. Children with BPD are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Infants with BPD should be provided as much as 130 kcal/kg per day to promote growth. (B)

REFERENCES

1. Oh W: Nutritional management of infants with bronchopulmonary dysplasia. IN Bronchopulmonary Dysplasia and Related Chronic Respiratory Disorders. Farrell PM, Taussig LM (eds). Ross Laboratories, Columbus, OH, 1986, pp 96–104
2. Kurzner SI, Garg M, Bautista DB, et al: Growth failure in infants with bronchopulmonary dysplasia: Nutrition and elevated resting metabolic expenditure. Pediatrics 81:379–84, 1988
3. Cox JH: Bronchopulmonary dysplasia. IN Nutritional Care for High-Risk Newborns. Groh-Wargo S, Thompson M, Cox J (eds). Precept Press, Chicago, 1994
4. Brunton JA, Saigal S, Atkinson SA: Growth and body composition in infants with bronchopulmonary dysplasia up to 3 months corrected age: A randomized trial of a high-energy nutrient-enriched formula fed after hospital discharge. J Pediatr 133: 340–345, 1998
5. Johnson DB, Cheney C, Monsen ER: Nutrition and feeding in infants with bronchopulmonary dysplasia after initial hospital discharge: Risk factors for growth failure. J Am Diet Assoc 98:649–656, 1998
6. Laron Z, Pertzolan A: The comparative effect of 6-fluoroprednisolone, 6-methylprednisolone, and hydrocortisone on linear growth of children with congenital adrenal virilism and Addison's disease. J Pediatr 73:774–783, 1968
7. Weiler HA, Paes B, Shah JK, et al: Longitudinal assessment of growth and bone mineral accretion in prematurely born infants treated for chronic lung disease with dexamethasone. J Early Hum Dev 47:271–286, 1997
8. Skinner AM, Battin M, Solimano A, et al: Growth and growth factors in premature infants receiving dexamethasone for bronchopulmonary dysplasia. Am J Perinatol 14:539–546, 1997
9. Kennedy KA, Stoll BJ, Ehrenkranz RA, et al: Vitamin A to prevent bronchopulmonary dysplasia in very-low-birth-weight infants: Has the dose been too low? Early Hum Dev 49:19–31, 1997
10. Atkinson SA, Abrams SA: Symposium: Pediatric pulmonary insufficiency: Nutritional strategies for prevention and treatment-special nutritional needs of infants for prevention of and recovery from bronchopulmonary dysplasia. J Nutr 131:9335–9345, 2001
11. Darlow BA, Graham PJ: Vitamin A supplementation for preventing morbidity and mortality in very low birthweight infants. Cochrane Database Syst Rev 2000 [computer file] (2) ICD00501, 2001

PULMONARY: EXTRACORPOREAL MEMBRANE OXYGENATION

Background

Extracorporeal membrane oxygenation (ECMO) involves the use of a modified heart-lung machine with a membrane oxygenator.[1] This technology has been used successfully in the neonates to treat respiratory failure. Persistent pulmonary hypertension (PPHN), congenital diaphragmatic hernia, congenital heart diseases, and meconium aspiration are some of the disease states treated with this short-term therapy. ECMO is also used to treat pediatric and adult respiratory failure.

Evidence

PN is commonly begun as soon as possible in the neonatal patient. The newborn infant has limited body reserves; therefore, prolonged starvation is dangerous. The ECMO circuit may be used to administer PN.[2] Fluid management in these patients is often challenging because of the underlying lung disease. The PN is often concentrated to maximize caloric delivery and minimize infusion volume.

Recent work, using stable isotope methodology, looked at energy expenditure in nine parenterally fed neonates on ECMO, and post-ECMO therapy.[3] Energy expenditure was similar while on ECMO and post-ECMO treatment (88.6 kcal/kg per day *versus* 84.3 kcal/kg per day) and ECMO did not provide a "metabolic rest."

Nitrogen balance and protein metabolism has also been studied in this population. Earlier work examining various intravenous nitrogen and calorie feeding regimens in 11 newborns on ECMO determined that nonprotein calories greater than 60 kcal/kg per day and protein intake greater than 1.5 g/kg per day were

necessary to achieve positive nitrogen balance.[4] Protein intake greater than 2.5 g/kg per day promoted maximum positive balance. Recently, nitrogen balance in 12 neonates on ECMO was studied using isotope methodology.[5] Increasing total caloric delivery from 60 to 113 kcal/kg per day did not change protein catabolism, but CO_2 production was increased.

EN in the neonatal ECMO patient is rarely performed because of concerns of risk of necrotizing enterocolitis and hypoxia. There is little evidence to support this statement. Enteral feedings have been performed in two limited studies. EN was introduced to seven patients on ECMO, six with meconium aspiration syndrome and one with PPHN.[6] Using the sugar absorption test, which measures urinary excretion of inert markers, intestinal permeability and absorption of neutral molecules did not differ between groups fed parenterally or enterally. These authors note that intestinal integrity is compromised in ECMO neonates but feeding them enterally did not exacerbate that condition. Successful EN in thirteen pediatric-aged patients has been documented in a retrospective review.[7]

Practice Guidelines
Extracorporeal Membrane Oxygenation

1. Children on ECMO are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. PN, using the ECMO circuit for access, should be initiated as soon as hemodynamic stability is attained. (B)
3. PN should be administered to ECMO patients to deliver 60 to 90 kcal/kg per day and a maximum of 2.5 g/kg per day protein. (B)
4. EN should be attempted when the ECMO patient is clinically stable. (C)

REFERENCES

1. Cilley RE, Wesley JR, Zwischenberger JB, et al: Gas exchange measurements in neonates treated with extracorporeal membrane oxygenation. J Pediatr Surg 23(4):306–311, 1988
2. Brown RL, Wessel J, Warner BW: Nutrition considerations in the neonatal extracorporeal life support patient. Nutr Clin Pract 9:22–27, 1994
3. Keshen TH, Miller RG, Jahoor F, et al: Stable isotopic quantitation of protein metabolism and energy expenditure in neonates on- and post-extracorporeal life support. J Pediatr Surg 32(7): 958–963, 1997
4. Weber TR, Shah M, Stephens C, et al: Nitrogen balance in patients treated with extracorporeal membrane oxygenation. J Pediatr Surg 28(7):906–908, 1993
5. Shew SB, Keshen TH, Jahoor F, et al: The determinants of protein catabolism in neonates on extracorporeal membrane oxygenation. J Pediatr Surg 34(7):1086–1090, 1999
6. Piena M, Albers MJIJ, VanHaard PMM, et al: Introduction of enteral feeding in neonates on extracorporeal membrane oxygenation after evaluation of intestinal permeability changes. J Pediatr Surg 33(1):30–34, 1998
7. Pettignano R, Heard M, Davis R, et al: Total enteral nutrition versus total parenteral nutrition during pediatric extracorporeal membrane oxygenation. Crit Care Med 26(2):358–363, 1998

CHRONIC RENAL FAILURE

Background

Nutrition plays a critical role in the treatment of children with chronic renal failure. Nutrition management depends upon the type and stage of the kidney disease, whether the child is on dialysis, and the method of dialysis. Nutrition status has an important effect on growth velocity, brain growth, and overall development. This is particularly true in early childhood. Growth impairment occurs more often and is more severe in children with congenital renal anomalies or with onset of renal failure before age 2 years.[1] Chronic metabolic acidosis, azotemia, chronic malnutrition, and anorexia contribute to compromised growth and nutritional deficits.[2] Protein-calorie malnutrition (PCM) is a major risk factor for morbidity and mortality in these patients.[3] Causes of PCM include (1) inadequate dietary intake, (2) dialytic losses of protein, amino acids, vitamins, and other essential nutrients, (3) inadequate dialysis, (4) hormonal and metabolic disturbances, and (5) catabolic diseases associated with uremia, especially infections.[2] Elevated uremic toxins that cause inflammation and ulceration of the gastrointestinal mucosa may cause gastritis, esophagitis, nausea, vomiting, diarrhea, and anorexia.[4] Factors that contribute to growth retardation include acidosis, Vitamin D deficiency, bone disease, and possible disturbances in growth hormone and insulin-like growth factor-1.[5]

Renal osteodystrophy is a major concern for infants and children with chronic renal failure because of their altered calcium and phosphate homeostasis. Plasma concentrations of 1,25 dihydroxy Vitamin D_3 have been found to be significantly reduced when the glomerular filtration rate (GFR) is below 50% of normal.[6] Chronic acidosis alters the normal accretion of hydroxyapatite into bone matrix, resulting in the loss of bone mineral and an increase in urinary calcium excretion. These factors contribute to the development of renal osteodystrophy.[7]

Nutrition assessment in children with renal failure should include growth parameters such as mid-arm circumference, triceps skinfold thickness, head circumference (in 3 year olds or less), weight or estimated dry weight, and standard deviation score for height (SDS or Z score).[8]

Evidence

Because of the lack of controlled studies in the pediatric population, recommendations are frequently extrapolated from adult scientific trials.[9] Research has focused on the use of enteral supplements and tube feedings to improve energy and protein intake when growth failure occurs or is threatened. It is well documented that energy intake in this population is suboptimal. Numerous studies have shown that growth failure occurs in infants with renal failure who have caloric intakes less than 70% of the RDA.[10]

Feeding disorders, such as gastroesophageal reflux, may be present in more than 70% of infants with chronic renal failure; suggesting that organic factors may contribute significantly to inadequate nutrient

intake.[11] Provision of tube feedings within the first few months of life in children with congenital renal failure can allow them to achieve normal growth rates and meet energy requirements.[1] The benefits of tube feedings must be weighed against their potential adverse consequences. Severe eating difficulties such as the inability to chew and swallow, and food refusal are found in children when chronic nasogastric feedings are started before 1 year of age.[12] Catch-up growth can be achieved when caloric supplementation greater than the recommended dietary allowance (RDA) for age is initiated with glucose polymers. Weight gain in these children includes proportional increases in both body fat and lean body mass.[4]

Chronic intravascular depletion caused by severe polyuria and polydipsia has been hypothesized to contribute to growth failure in children with obstructive uropathy or renal dysplasia. A very high intake of dilute formula (at 180 to 240 mL/kg per 24 hours) with sodium supplementation (2 to 4 mEq/100 mL of formula) promotes intravascular volume repletion, catch-up growth, and maintenance of growth velocity.[13] In contrast, children with oliguria often require fluid restriction and calorically dense formulas to simultaneously maintain fluid balance and meet calorie needs. An increased mortality rate has been shown in newborns receiving formula densities of greater than 50 kcal/30 mL.[9]

Protein restriction to limit excessive filtration and subsequent deterioration of renal function has been suggested in children. However, the benefits are unproven, and restriction may not be compatible with normal growth.[14] Children requiring peritoneal dialysis suffer from significant protein losses through the dialysate effluent, which can contribute to PCM.[15] Aggressive nutrition support via nasogastric or gastrostomy feedings may be required. Children less than 6 years old on continuously cycled peritoneal dialysis (CCPD) were found to have greater peritoneal protein losses than older children.[16] The trend toward obesity in aggressively fed infants and young children may be a consequence of tube feeding. Excessive calorie intake, plus dialysate glucose resorption in infants with enhanced peritoneal membrane permeability may be partially responsible.[15,16]

Nutrition support in acute renal failure requiring continuous renal replacement therapies (CRRT) such as continuous veno-venous hemofiltration (CVVH) or continuous veno-venous hemodiafiltration (CVVHD) often requires SNS to meet the demands of the catabolic state.[17] Indirect calorimetry may be helpful to measuring energy expenditure; overfeeding is contraindicated in this patient population.[18] Negative nitrogen balance occurs in patients despite the delivery of standard PN containing 1.5 g/kg per day of protein and calorie intake of 20% to 30% above resting energy expenditure.[17] No significant differences in amino acid losses were measured between CVVH and CVVHD modalities.[17]

Special Considerations

A 3-month trial of oral nutrition supplementation in both hemodialysis and peritoneal dialysis patients showed improvement in serum albumin, weight gain, and anthropometric measurements. The cost of preventing and/or treating malnutrition with supplements appears significantly less than the cost of hospitalization for patients with end-stage renal disease (ESRD) and superimposed malnutrition.[19]

Children with polyuric renal disease who were prescribed a high-volume, low-concentration formula with sodium supplementation were able to maintain normal growth velocity without the use of growth hormone and to postpone initiation of dialysis despite a creatinine clearance <10 mL/min. This specific nutrition therapy may be advantageous when dialysis is not easily available and growth hormone cannot be used because of cost.[13]

Data on vitamin status in ESRD patients are controversial. Water-soluble vitamin deficiencies have been studied in chronic dialysis patients. Causes include inadequate dietary intake, losses during dialysis, and altered vitamin metabolism.[3] Dietary vitamin intake provided by infant formula plus a daily water-soluble vitamin supplement was associated with normal or greater than normal vitamin levels in infants on chronic peritoneal dialysis. Vitamin A levels were elevated despite the absence of vitamin A in the oral vitamin supplement.[20] Vitamin A and its potential toxicity in chronic renal failure patients receiving PN remains controversial. Infants and young children may have low stores and need vitamin A for appropriate development.[9] Levels of vitamin A must be monitored in patients with chronic renal failure, and if they become elevated, supplementation should be stopped.

Homocysteine, carnitine, and glutamine are three nutrients currently under study. Elevated blood homocysteine levels may be used in the future to detect "subclinical" vitamin B deficiency and suggest subsequent treatment.[21] There are insufficient data to support the routine use of L-carnitine in chronic dialysis patients; however, it may help treat erythropoeitin-resistant anemia.[8] Patients with chronic renal failure are at risk for metabolic bone disease. There are no published guidelines. In general, treatment of metabolic bone disease is indicated when the intact PTH levels are above 240 pg/mL. If phosphate restriction or binders do not lower the iPTH <220 pg/mL, then Vitamin D replacement therapy is recommended. Dosage is dependent on serum calcium, serum phosphorus, alkaline phosphatase, and PTH. Hypercalcemia should be avoided.

A recent study on children undergoing peritoneal dialysis noted the following age-appropriate diet guidelines[22]: 102 kcal/kg and 2 to 2.5 g protein/kg for ages 1 to 3 years; 90 kcal/kg and 2 to 2.5 g protein/kg for ages 4 to 6 years; 70 kcal/kg and 2 to 2.5 g protein/kg for ages 7 to 10 years; and 40 to 55 kcal/kg and 1.5 g protein/kg for ages 11 to 18 years.

Nonurea nitrogen excretion in children receiving PD was significantly greater than previous reported, and it varied with age and with growth hormone therapy. Children with residual renal function excreted more nitrogen, which may have reflected a higher protein intake. Although urea nitrogen excretion in dialysate and urine can be

used to predict dialysate and protein needs in pediatric patients, it is clinically impractical.

Practice Guidelines
Chronic Renal Failure

1. Children with chronic renal failure are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Oral supplements or SNS should be given to infants and children with renal failure who are not growing normally. (B)
3. Supplemental fluid and sodium should be given to children with polyuric, salt wasting renal disease. (B)
4. Energy intakes for children with chronic renal failure and for those treated with maintenance hemodialysis, or peritoneal dialysis, should be at the RDA level for chronological age, and modified depending upon the child's response. (C)
5. Vitamin A levels should be monitored closely in children with renal failure. (C)
6. SNS should be given to patients with acute renal failure receiving continuous renal replacement therapies to promote positive nitrogen balance and meet energy needs. (B)

REFERENCES

1. Reed E, Roy L, Gaskin K, et al: Nutrition intervention and growth in children with chronic renal failure. J Renal Nutr 8:122–126, 1998
2. Massie M, Niimi K, Yang W, et al: Nutrition assessment of children with chronic renal insufficiency. J Renal Nutr 2:2–12, 1992
3. Pereira A, Hamani N, Nogueira, et al: Oral vitamin intake of children receiving long-term dialysis. J Renal Nutr 10:24–29, 2000
4. Lancaster L: Renal failure: Pathophysiology, assessment and intervention. Part II. Nephrol Nurse 30–38, 1983
5. Kurtin P, Shapiro A: Effect of defined caloric supplementation on growth of children with renal disease. J Renal Nutr 2:13–17, 1992
6. Weiss R: Management of chronic renal failure. Pediatr Ann 17:584–589, 1988
7. Sedman A, Friedman A, Boineau F, et al: Nutritional management of the child with mild to moderate chronic renal failure. J Pediatr 129:S13–S18, 1996
8. NKF-DOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure. Am J Kidney Dis 35:S105–S108, S112–S121, 2000
9. Spinozzi N, Nelson P: Nutrition support in the newborn intensive care unit. J Renal Nutr 6:188–197, 1996
10. Yiu V, Harmon W, Spinozzi N, et al: High calorie nutrition for infants with chronic renal disease. J Renal Nutr 6:203–206, 1996
11. Ruley E, Bock G, Kerzner B, et al: Feeding disorders and gastroesophageal reflux in infants with chronic renal failure. Pediatr Nephrol 3:424–442, 1989
12. Strologo L, Principato F, Sinibaldi D, et al: Feeding dysfunction in infants with severe chronic renal failure after long-term nasogastric tubefeeding. Pediatr Nephrol 11:84–86, 1997
13. Sedman AS, Parekh RS, DeVee JL, et al: Cost effective management of children with polyuric renal failure [abstract A0763]. J Am Soc Nephrol 7:1398, 1996
14. Raymond N, Dwyer J, Nevins P, et al: An approach to protein restriction in children with renal insufficiency. Pediatr Nephrol 4:145–151, 1990
15. Quan A, Baum M: Protein losses in children on continuous cycler peritoneal dialysis. Pediatr Nephrol 10:728–731, 1996
16. Schaefer F, Klaus G, Mehls O, et al: Peritoneal transport properties and dialysis dose affect growth and nutritional status in children on chronic peritoneal dialysis. J Am Soc Nephrol 10:1786–1792, 1999
17. Maxvold N, Smoyer W, Custer J, et al: Amino acid loss and nitrogen balance in critically-ill children with acute renal failure: A prospective comparison between classic hemofiltration vs hemofiltration with dialysis. Crit Care Med 28:1161–1165, 2000
18. Monson P, Mehta R: Nutritional considerations in continuous renal replacement therapies. Semin Dialysis 9:152–160, 1996
19. Fedje L, Moore L: A role for oral nutrition supplements in the malnutrition of renal disease. J Renal Nutr 6:198–202, 1996
20. Warady B, Kriley M, Alon U, et al: Vitamin status of infants receiving long-term peritoneal dialysis. Pediatr Nephrol 8:354–356, 1994
21. Makoff R, Dwyer J, Rocco M: Folic acid, pyridoxine, cobalamin, and homocysteine and their relationship to cardiovascular disease in end-stage renal disease. J Renal Nutr 6:2–11, 1996
22. Mendley SR, Majkowski NL: Urea and nitrogen excretion in pediatric peritoneal dialysis patients. Kidney Int 58:2564–2570, 2000

CENTRAL NERVOUS SYSTEM DISORDERS

Background

According to a position statement of the American Dietetic Association, "all children with special health needs should have access to nutrition services provided within a system of interdisciplinary services that is preventive, family centered, community based, and culturally competent."[1] Neurologically impaired describes those children with special needs, chronic conditions, and developmental delay that affect growth and development.[1] A large percentage of this population has at least one nutrition-based problem that can complicate their overall condition.[2–4]

Growth failure is a common problem in neurologically impaired children. Measurement of mid-upper arm circumference and triceps skinfold thickness may be useful in assessing adiposity and identifying reduced muscle mass.[2] Children with severe disabilities often fall below the 10th and 25th percentile on the NCHS growth chart. Children who exhibit growth two standard deviations or more below the norm should be monitored carefully.[5] Weight for height above the 50th percentile may represent excess adipose tissue. In some neurologically impaired children, muscle mass may be low so they may be obese even though weight plots are within the norm for age or height.[4] Children with histories of malnutrition and poor growth should be monitored every 6 months after weight goals have been achieved.[6]

Damage to the developing central nervous system may result in significant dysfunction in the gastrointestinal tract and may be reflected in impaired oral-motor function, rumination, gastroesophageal reflux, delayed gastric emptying, and constipation. Additionally, a variety of drugs may lead to nutrition deficits.[3,7,8] All of these factors can contribute to feeding difficulties. When oral intake does not keep up with growth demands, EN may be indicated.[4,9] Selectively, a fundoplication may need to be performed along with the gastrostomy to prevent GER.[10,11] Oral feeding skills should be maintained if at all possible during the period of EN.[1] PN may be indicated in cases of malabsorption, aspiration, or chronic intractable vomiting when small-bowel feedings are not possible.[10] Feeding

and swallowing difficulties can result in decreased nutrient intake. Intervention strategies include assistance with swallowing, texture modification, increased energy density nutrition supplements, and alternative routes of feeding.[3,5–7,10]

Evidence

Children with developmental disabilities may experience deficiencies of calcium, iron, thiamin, vitamin C, folic acid, vitamin A, riboflavin, and thiamine.[3,4,7] Dietary reference intakes (DRI) based on ideal weight for height or other reference charts should be used to estimate nutrition needs.[2] Equations have been proposed that calculate energy needs based on activity levels and muscle tone.[3,5] Motor dysfunction and stature can also be used to refine estimates of energy needs. For children 5 to 11 years old, energy needs may be estimated at 13.9 kcal/cm with mild to moderate motor dysfunction or 11.1 kcal/cm for severe dysfunction.[7] Athetotic forms of cerebral palsy (CP) require additional caloric intake, perhaps up to as much as 6000 kcal/d.[3] It is suggested that nomograms be used to determine energy needs of disabled children;[6] appropriate growth charts are available for those with Trisomy 21, Turners, Prader-Willi, and Williams Syndromes, and spastic quadriplegia.[2,5,6] Many severely impaired children remain below the 5th percentile for height and weight. Upper arm length may be less compromised than lower leg length and can be used to follow linear growth.[4] Triceps skinfold using cutoff values less than the 10th percentile for age, and gender has been shown to identify malnourished children and screen for depleted fat stores in children with CP.[12] Children with spastic quadriplegia cerebral palsy (SQCP) with low fat stores measured by triceps skinfold have a lower resting energy expenditure (REE) adjusted for fat-free mass than children with adequate fat stores. Total energy expenditure (TEE) and the ratio of TEE to resting energy expenditure (REE) is lower for the SQCP group than a control group. Well nourished SQCP children have a lower TEE:REE ratio than poorly nourished SQCP children. Improved linear growth and weight gain is seen in children who have the shortest duration of time between onset of the neurologic disorder and institution of nutrition therapy.[2] It appears that nutrition-related growth failure and abnormal REE in these neurologically impaired children is related to inadequate energy intake.[13–15] Infants who are small for gestational age and do not exhibit catch-up growth in head circumferecne are at particular risk for developmental delay.[2]

Studies have shown improved weight gain and TSF thickness with EN.[15] Undernutrition causes growth failure in patients with disabilities.[15] Tube feeding of the special needs population has been shown to have a positive influence on the lives of the children and families including weight gain, ease of feeding after tube placement, decrease of feeding time, decrease in aspiration, and resolution of reflux with concomitant fundoplication procedure. There is a trend toward improved weight/height ratio in children less than 4 years of age with gastrostomy placement and a weight gain in those older than 12 years.[2,4,6] Although a variety of complications may occur with tube feedings, in one extensive review, there was no mortality associated with surgical placement of the tube.[16] It has been shown that endoscopic gastrostomy is a safe procedure for children.[13] Enteral feeding results in a trend toward normalized weight/height ratio for children with CP younger than 4 years and significant weight gain in those older than 12 years.[17] There is a statistically significant difference in mortality rates between tube-fed and non–tube-fed children. EN of neurologically impaired children who have a tracheostomy reduces mortality.[11]

Fractures related to osteoporosis are a problem in severely disabled children. Activity and nutrition factors are the major determinants of bone-mineral density. Risk factors for low bone-mineral density include lack of ambulation, use of anticonvulsant medications, low calcium intake (<500 mg/d), low calorie and nutrient intake, low body-mass index, and reduced skinfold thickness.[18,19]

There is an increase in postoperative complications in patients with CP who have a serum albumin level below 3.5 g/dL or a total lymphocyte count less than 1500 cells/mm^3.[20] Although not proven, it is suggested by these authors that aggressive measures should be used to improve the nutrition status before surgery.[21]

It has been shown that whey-based formulas can decrease gastric emptying time compared with a casein-based formulas in children with spastic quadriplegia, developmental delay, scoliosis, and profound mental retardation. Whey-based formulas may improve nutrition status and decrease the risk of aspiration pneumonia.[21] Soy polysaccharide fiber has been shown to improve bowel function in nonambulatory, profoundly disabled youths.[22]

Pulse oximetry has been used to monitor hemoglobin saturation during oral feeding in children with multiple disabilities and should be considered for all children with severe dysphagia and multiple disabilities. The finding of hypoxemia can help support the decision to use gastrostomy tube feedings.[10] Respiratory inductance plethysmograph and nasal airflow measurement by thermistors are also accurate, noninvasive methods of monitoring cardiopulmonary adaptation during oral feedings. Positioning patients in the left lateral decubitus position may provide temporary relief in impaired children who have recurrent gastric distention and vomiting. Complete resolution of the distension and/or vomiting does not occur, however, until after adequate weight gain.[21]

Practice Guidelines
Central Nervous System Disorders

1. Children with neurologic impairment children are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Protein and energy needs should be targeted according to the neurologically impaired child's

estimated energy needs modified by their level of disability and current nutritional deficits. (B)

3. SNS should be initiated in children with neurologic impairment in cases of failure to thrive as determined by growth charts and disease-specific nomograms. (B)

REFERENCES

1. Position of The American Dietetic Association: Nutrition services for children with special health needs. J Am Diet Assoc 95:809–812, 1995
2. Bonnema S: Neurological Compromise. IN Nutrition Manual for At-Risk Infants and Toddlers. Cox J (ed). Precept Press, Chicago, 1997, pp 113–133
3. Tilton ACH, Miller MD: Nutritional support of the developmentally disabled child. IN Textbook of Pediatric Nutrition. Suskind RM, Lewinger-Suskind L (ed). Raven Press, New York, 1993, pp 485–491
4. Motil K: Enteral nutrition in the neurologically impaired child. IN Pediatric Enteral Nutrition. Baker S, Baker R, Davis A (eds). Chapman & Hall, New York, 1994, pp 217–237
5. Krick J, Murphy P, Savidge S: Physical handicap/nutritional management of cerebral palsy. IN Encyclopedia of Human Nutrition. Sandler M, Strain JJ, Cabalero B, et al (eds). Academic Press, London, 1998, pp 1531–1539
6. Amundson J, et al: Early identification and treatment necessary to prevent malnutrition in children and adolescents with severe disabilities. J Am Diet Assoc 94:880–883, 1994
7. Bandini L, Ekvall SW, Patterson, et al: Neurological disorders. IN Pediatric Nutrition in Chronic Diseases and Developmental Disabilities. Ekvall S (ed). Oxford University Press, New York, 1993, pp 89–161
8. Cloud H: Developmental disabilities: IN Handbook of Pediatric Nutrition, 2nd ed. Samour PQ, Helm KK, Lang CE (eds). Aspen Publications, Gaithersburg MD, 1999, pp 293–314
9. Young C: Nutrition. IN Pediatric Swallowing and Feeding, Arvedson JC, Brodsky L (eds). Singular Publishing Group, San Diego, 1993, pp 157–208
10. Rogers BT, et al: Hypoxemia during oral feeding of children with severe cerebral palsy. Dev Med Child Neurol 35:3–10, 1993
11. Strauss D, Kastner T, Ashwal S, et al: Tube feeding and mortality in children with severe disabilities and mental retardation. Pediatrics 99:358–362, 1997
12. Samson-Fang LJ, Stevenson RD: Identification of malnutrition in children with cerebral palsy: poor performance of weight-for-height centiles. Dev Med Child Neurol 42:162–8, 2000
13. Stallings VA, Cronk C, Zemel B, et al: Body composition in children with spastic quadriplegic cerebral palsy. J Pediatr 126: 833–839, 1995
14. Stallings VA, Cronk C, Davies J, et al: Energy expenditure of children and adolescents with severe disabilities: a cerebral palsy model. Am J Clin Nutr 64: 627–634, 1996
15. Isaacs JS, Georgeson K, Cloud H, et al: Weight gain and triceps skinfold fat mass after gastrostomy placement in children with developmental disabilities. J Am Diet Assoc 94:849–854, 1994
16. Smith S, Camfield C, Camfield P: Living with cerebral palsy and tube feeding: A population-based follow-up study. J Pediatr 135: 307–310, 1999
17. Brant CQ, Stanich P, Ferrari AP: Improvement of children's nutritional status after enteral feeding by PEG: An interim report. Gastrointest Endosc 50:183–188, 1999
18. Henderson R, Lin P, Greene W: Bone-mineral density in children and adolescents who have spastic cerebral palsy. J Bone Joint Surg Am 77-A:1671–1681, 1995
19. Baer M, Kozlowski B, Blyler E, et al: Vitamin D, calcium, and bone status in children with development delay in relation to anticonvulsant use and ambulatory status. Am J Clin Nutr 65:1042–1051, 1997
20. Jevsevar D, Karlin L: The relationship between preoperative nutrition status and complications after an operation for scoliosis in patients who have cerebral palsy. J Bone Joint Surg Am 75-A:880–884, 1993
21. Fried M, Khoshoo V, Secker D, et al: Decrease in gastric emptying time and episodes of regurgitation in children with spastic quadriplegia fed a whey-based formula. J Pediatr 120:569–572, 1992
22. Liebl BH, Fisher MH, VanCakar SC, et al: Dietary fiber and long-term large bowel response in enterally nourished nonambulatory profoundly retarded youth. JPEN 14:371–375, 1990

CANCER AND BONE MARROW TRANSPLANTATION

Background

Treatment for childhood cancer is typically intensive, nearly always involving surgery and/or combination chemotherapy to eradicate the malignancy. Radiation therapy may also be required. Side effects of these treatments include anorexia, altered taste acuity, catabolism, immunosuppression, and gastrointestinal problems such as nausea, mucositis, gastric stasis, malabsorption, and diarrhea.[1–3] The incidence of malnutrition among newly ill pediatric patients appears to be the same whether the diagnosis is malignant or benign illness[4,5]; however, poor nutrition status at diagnosis of malignancy has been found to correlate with decreased survival.[4] Further, when a child begins treatment for malignancy, food intake often decreases and the risk for protein-calorie malnutrition (PCM) increases.[5,6] Malnourished children experience more treatment delays and have a higher infection rate, which may adversely affect outcome.[7] SNS has been shown to improve quality of life in some situations by increasing the child's sense of well-being and ability to play.[8]

Nutrition assessment of children with cancer should be done at the start of treatment and periodically thereafter. This should include a standard pediatric age appropriate assessment including a diet history, a weight history, a physical examination, and attention to psychosocial factors such as interest in food, irritability, and energy level.[9] A comprehensive nutrition care plan should be developed, including goals for prevention or reversal of PCM and support for the child's normal growth.[1,5] Nutrition counseling should aim to enable parents/caregivers to cope with appetite changes, early satiety, and other problems that can arise after treatment is begun.[5] Appetite stimulants such as megestrol acetate may be considered, although their use in children with cancer has not been adequately studied. Criteria for the initiation of nutrition intervention were recommended by the American Academy of Pediatrics task force on the special nutrition needs of children with malignancies. These recommendations should be followed by all clinicians who care for pediatric oncology patients.[1] During cancer treatment, ongoing nutrition assessment can be accomplished effectively using weight changes and weight-for-height-measurements, and standardized subjective assessment of oral intake.[9–11]

Evidence

Nutrition assessment is an important element of the care of children with cancer. It has been shown that

poor oral intake is the best predictor of the need for SNS.[12]

The intent of SNS should be the prevention or reversal of PCM.[13] Decisions regarding the use of EN or PN will depend on the clinical setting. PN via a central venous catheter appears more effective in reversing pre-existing PCM during intensive cancer therapy than peripheral parenteral nutrition (PPN) or oral therapy.[14] The use of PN must be tempered with the potential for complications. A meta-analysis of published controlled studies concluded that the use of PN is associated with an increased infection rate in children who have a central venous catheter in place for cancer therapy.[15]

EN has been shown to be successful at reversing PCM during intensive chemotherapy, especially when administered via a feeding protocol.[16,17]

Gastrostomy tube (GT) placement is becoming more common to provide EN. GT feeding has been shown to be effective at reversing PCM, with relatively minor complications.[18–20] There is some evidence that the appetite stimulant megestrol acetate may be effective in the treatment of chemotherapy-induced anorexia; however, adrenal insufficiency is a potential side effect.[21] EN, whether via nasogastric tube or GT, is less expensive than PN.[18,22]

Home EN may be less stressful for the patient and family than home PN.[23] Using the gut whenever possible during and after treatment may enhance patients' ability to consume adequate amounts of food. The use of PN after discharge after bone marrow transplantation delays return to normal oral intake.[24]

Special Considerations

Pediatric patients undergoing bone marrow transplantation are very likely to require SNS for at least part of the transplant hospitalization. Although PN has been the standard nutrition support therapy, EN may be appropriate under certain circumstances.[25]

Trials of nutritional pharmacology (high doses of specialized nutrients) have yielded conflicting results. Recent studies using the amino acid glutamine during bone marrow transplantation have not shown statistically significant benefit, although trends suggest further research is warranted.[26,27] A recent controlled study has shown that low-dose glutamine can reduce the incidence of painful stomatitis.[28] The use of pharmacologic doses of nutrients should be limited to controlled trials until the data clearly indicate presence or absence of benefit.

Alternative or complementary nutrition treatments are of unproven efficacy.[29] When the caregiver of a child with cancer intends to give alternative nutritional therapy products to the child, the product(s) should be evaluated for their potential to harm and the findings communicated to the family. When children are terminally ill from their disease, nutrition cannot change the outcome. The burden of using SNS must be weighed against the benefits. In terminally ill children, SNS should be used only if it will improve the patient's quality of life.[30]

Practice Guidelines
Cancer and Bone Marrow Transplantation

1. Children with cancer are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. SNS and dietary interventions should be undertaken to promote normal growth and development and to provide for energy requirements in those cancer patients who cannot meet their needs orally. (B)
3. Palliative administration of SNS in terminally ill children with cancer is rarely indicated. (B)

REFERENCES

1. Mauer AM, Burgess JB, Donaldson SS, et al: Special nutritional needs of children with malignancies: A review. JPEN 14:315–324, 1990
2. Pencharz PB: Aggressive oral, enteral or parenteral nutrition: Prescriptive decisions in children with cancer. Int J Cancer Suppl 11:73–75, 1998
3. Andrassy RJ, Chwals WJ: Nutritional support of the pediatric oncology patient. Nutrition 14:124–129, 1998
4. Donaldson SS, Wesley MN, DeWys WD, et al: A study of the nutritional status of pediatric cancer patients. Am J Dis Child 135:1107–1112, 1981
5. Carter P, Carr D, Van Eys J, et al: Energy and nutrient intake of children with cancer. J Am Diet Assoc 82:610–615, 1983
6. Skolin I, Axelsson K, Ghannad P, et al: Nutrient intakes and weight development in children during chemotherapy for malignant disease. Oral Oncol 33:364–368, 1997
7. Rickard KA, Detamore CM, Coates TD, et al: Effect of nutrition staging on treatment delays and outcome in stage IV neuroblastoma. Cancer 52:587–598, 1983
8. VanEys J: Benefits of nutritional intervention on nutritional status, quality of life and survival. Int J Cancer Suppl 11:66–68, 1998
9. Hammill PV, Drizd TA, Johnson CL, et al: Physical growth: National Center for Health Statistics percentiles. Am J Clin Nutr 32:607–6629, 1979
10. Motil KJ: Sensitive measures of nutritional status in children in hospital and in the field. Int J Cancer Suppl 11:2–9, 1998
11. Attard-Montaldo SP, Hadley J, Kingston JE, et al: Ongoing assessment of nutritional status in children with malignant disease. Pediatr Hematol Oncol 15:393–403, 1998
12. Tyc VL, Vallelunga L, Mahoney S, et al: Nutritional and treatment-related characteristics of pediatric oncology patients referred or not referred for nutritional support. Med Pediatr Oncol 25:379–388, 1995
13. Klein S, Koretz R: Nutrition support in patients with cancer: what do the data really show? Nutr Clin Pract 9:91–100, 1994
14. Rickard KA, Godshall BJ, Loghmani ES, et al: Integration of nutrition support into oncologic treatment protocols for high and low nutritional risk children with Wilm's tumor. A prospective randomized study. Cancer 64:491–509, 1989
15. Christensen ML, Hancock ML, Gattuso J, et al: Parenteral nutrition associated with increased infection in children with cancer. Cancer 72:2732–2738, 1993
16. Den Broeder E, Lippens RJ, van't Hof MA, et al: Effects of naso-gastric tube feeding on the nutritional status of children with cancer. Eur J Clin Nutr 52:494–500, 1998
17. Pietsch JB, Ford C, Whitlock JA: Nasogastric tube feedings in children with high-risk cancer: a pilot study. J Pediatr Hematol Oncol 21:111–114, 1999
18. Aquino VM, Smyrl CB, Hagg R, et al: Enteral nutritional support by gastrostomy tube in children with cancer. J Pediatr 127:58–62, 1995
19. Mathew P, Bowman L, Williams R, et al: Complications and

effectiveness of gastrostomy feeding in pediatric cancer patients. J Pediatr Hematol Oncol 18:81–85, 1996
20. Barron MA, Duncan DS, Green GJ, et al: Efficacy and safety of radiologically placed gastrostomy tubes in paediatric haematology/oncology patients. Med Pediatr Oncol 34:177–182, 2000
21. Aconza C, Castro L, Crespo D, et al: Megestrol acetate therapy for anorexia and weight loss in children with malignant solid tumours. Aliment Pharmacol Ther 10:577–586, 1996
22. Lipman TO: Grains or veins: Is enteral nutrition really better than parenteral nutrition? A look at the evidence. JPEN 22:167–182, 1998
23. Padilla GV, Grant MM: Psychosocial aspects of artificial feeding. Cancer 55(Suppl 1):301–304, 1985
24. Charuhas PM, Fosberg KL, Bruemmer B, et al: A double-blind randomized trial comparing outpatient parenteral nutrition with hydration: effect on resumption of oral intake after marrow transplantation. JPEN 21:157–161, 1997
25. Szeluga DJ, Stuart RK, Brookmeyer R, et al: Nutritional support of bone marrow transplant recipients: a prospective, randomized clinical trial comparing total parenteral nutrition to an enteral feeding program. Cancer Res 47:3309–3316, 1987
26. Dickson TM, Wong RM, Negrin RS, et al: Effect of oral glutamine supplementation during bone marrow transplantation. JPEN 24:61–66, 2000
27. Schloerb PR, Skikne BS: Oral and parenteral glutamine in bone marrow transplantation: A randomized study. JPEN 23:117–122, 1999
28. Anderson PM,. Ramsay NK, Shu XO, et al: Effect of low-dose oral glutamine on painful stomatitis during bone marrow transplantation. Bone Marrow Transplantation. 22(4): 339–344, 1998
29. Weitzman S: Alternative nutritional cancer therapies. Int J Cancer Suppl 11:69–72, 1998
30. Torelli GF, Campos AD, Meguid MM: Use of TPN in terminally ill cancer patients. Nutrition 15:665–667, 1999

CRITICAL CARE—PEDIATRICS

Background

Alterations in the energy requirements of pediatric patients due to the response to an acute metabolic stress can be quite dramatic, even in contrast to the stressed, hypermetabolic adult. Growth velocity during early infancy is higher than at any other time during childhood and is exceeded only by intrauterine growth rates.[1] These additional growth requirements must be met in critically ill pediatric patient.

Acute injury markedly alters energy needs. First, acute injury induces a catabolic response that is proportional to the magnitude, nature, and duration of the injury. Increased serum counter-regulatory hormone concentrations induce insulin and growth hormone resistance,[2] resulting in the catabolism of endogenous stores of protein, carbohydrate, and fat to provide essential substrate intermediates and energy necessary to support the ongoing metabolic stress response. During this catabolic response, somatic growth can not occur, and, therefore, the caloric allotment for growth, which is substantial in infancy, should *not* be administered. Second, children treated in the intensive care setting are frequently sedated, and their activity level is markedly reduced; this may reduce energy needs. Third, the intensive care environment is temperature-controlled and insensible energy losses are substantially reduced. This is especially true for children who are mechanically ventilated because, in addition to reduced energy needs for the work of breathing, these patients are ventilated with heated, humidified air. This can reduce insensible losses by one third. To account for these alterations in energy metabolism, measured energy expenditure values or basal energy requirements should be provided. The significance of this therapeutic strategy is to avoid the provision of calories and/or nutritional substrates in excess of the energy required to maintain the metabolic homeostasis of the injury response. Overfeeding has deleterious consequences.[1] It increases ventilatory work by increasing CO_2 production.[4] This can prolong the need for mechanical ventilation.[3,4] Overfeeding may also impair liver function by inducing steatosis and cholestasis, ,and increase the risk of infection secondary to hyperglycemia.

Nutrition assessment of critically ill pediatric patients can be quantitatively accomplished by measuring (1) the visceral (or constitutive) protein pool; (2) the acute-phase protein pool; (3) nitrogen balance; and (4) energy expenditure.[1] Prealbumin is readily measured in most hospitals and is a good marker for the visceral protein pool.[5] Albumin, which has a large pool and much longer half-life, should not be used because it is not indicative of the immediate nutrition status and may be skewed by changes in fluid status. Within 12 to 24 hours of initiation of stress, serum acute-phase protein levels rise because of hepatic reprioritization of protein synthesis in response to injury.[5] The rise is proportional to the severity of injury. Some hospitals are capable of measuring C-reactive protein (CRP) as an index of the acute-phase response. When measured serially (once a day during the acute response period), serum prealbumin and CRP are inversely related (ie, serum prealbumin levels decrease and CRP levels increase with the magnitude proportional to injury severity and then return to normal as the acute injury response resolves). Decreases in serum CRP values to less than 2 mg/dL have been associated with the return of anabolic metabolism[6] and are followed by increases in serum prealbumin levels. Energy expenditure can be measured at bedside using indirect calorimetry.[1] Although a variety of predictive equations have been proposed,[7] clinical and patient variability (especially in the infant population) makes these estimates problematic.[8,9] Direct measurement of energy use in individual patients achieves greater accuracy and can help avoid overfeeding. In addition, actual serial measurements show changes in respiratory quotient, which help to identify resumption of anabolic metabolism after injury.[1,6]

Evidence

To avoid overfeeding children during acute metabolic stress, energy expenditure should be measured. Energy delivery should not exceed measured values. When the respiratory quotient decreases to 1.0 in infants up to 1 year of age, calorie intake may be advanced slowly to meet predicted energy requirements for age and weight. In the absence of indirect calorimetry, published basal energy requirements based on age, weight, and gender offer reasonable guidelines for basal energy requirements.[10] During metabolic stress, for infants up to 2 years of age, micronutrient substrates should be provided as follows: pro-

tein (2.5 to 3.0 g/kg per day), carbohydrate (8.5 to 10 g/kg per day), and fat (1gm/kg per day). From 2 to 11 years of age, protein should be decreased to 2.0 g/kg per day and carbohydrate to 5 g/kg per day. Above 12 years of age, protein should be reduced to 1.5 to 2.0 g/kg per day and fat to 0.5 g/kg per day. A study of critically ill children less than 2 years of age in a pediatric intensive care setting showed that actual measured energy expenditure values average about 50% of what the predicted energy requirement would be for those children if they were healthy and normally active.[3]

Decrease of serum CRP values to less than 2 mg/dL and rising prealbumin values may be used as guidelines for advancing SNS to normal predicted levels based on age and weight.[1,6] Decrease in total urinary nitrogen may also be used as an indicator of the resumption of normal (versus stressed) metabolism. Increasing serum prealbumin concentrations are associated with increased energy intake after the acute metabolic stress has resolved,[11] and can be useful to assess the adequacy of energy delivery during the post-stress recovery period. EN is preferred to PN whenever possible. The visceral protein response is significantly greater and occurs earlier with EN versus PN after severe injury.[12] In severely injured infants and children, a soft, transpyloric feeding tube can provide safe enteral access for early postinjury support (particularly in premature infants with delayed gastric emptying).[13] A number of studies have demonstrated a significant benefit of EN over PN in appropriately matched, critically ill adults.[14–16] Few data, however, are available in the pediatric age group.

Special Considerations

The supplemental use of growth hormone in severely burned pediatric patients has been shown to offer significant benefit by accelerating wound healing and reducing hospital stay[17,18] and has been associated with significantly greater and earlier increases in the visceral protein pool response.[19]

Monitoring the acute metabolic response to injury may be advantageous. Stratification of injury severity can be accomplished by monitoring either acute-phase protein pool changes[1] or energy expenditure.[20] The development of postinjury sepsis can be detected by serial monitoring of acute-phase protein pool changes.[21] EN intolerance can also be useful for this purpose in severely burned children.[22] Both acute-phase and visceral protein pool injury-induced changes have been shown to predict mortality in critically ill infants.[23]

Practice Guidelines *Critical Care—Pediatrics*

1. Children with critical illnesses are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Energy expenditure should be measured serially to determine the energy needs of critically ill children. (B)
3. If indirect calorimetry is not feasible, energy should be provided to critically ill children based on published formulas or nomograms to avoid overfeeding. (B)
4. When SNS is indicated in critically ill children, EN is preferable to PN whenever feasible. (B)

REFERENCES

1. Chwals WJ: Pediatric enteral and parenteral surgical nutrition. IN Grenvik, Ayres, Holbrook, et al (eds.), Textbook of Critical Care, 4th ed. WB Saunders, Philadelphia, 2000
2. Rowe MI, Chwals WJ: The neonate as a patient. IN O'Neill JA, Rowe MI, Fonkalsrud EW, et al (eds.), Pediatric Surgery, 5th ed. Mosby-Year Book, St Louis, MO, 1997
3. Chwals WJ, Lally KP, Woolley MM, et al: Measured energy expenditure in critically ill infants and young children. J Surg Res 1988, 44:467
4. Letton RW, Chwals WJ, Jamie A, et al: Neonatal lipid utilization increases with injury severity: Recombinant human growth hormone versus placebo. J Pediatr Surg 31:1068–1072, 1996
5. Dickson PW, Bannister D, Schreiber G: Minor burns lead to major changes in synthesis rates of plasma proteins in the liver. J Trauma 27:283–286, 1987
6. Letton RW, Chwals WJ, Jamie A, et al: Early postoperative alterations in infant energy utilization increases the risk of overfeeding. J Pediatr Surg 30(7):988–992, 1995
7. White MS, Shepherd RW, McEniery JA: Energy expenditure in 100 ventilated, critically ill children: Improving the accuracy of predictive equations. Crit Care Med 28:2307–2312, 2000
8. McClave SA, Lowen CC, Kleber MJ, et al: Are patients fed appropriately according to their caloric requirements? JPEN 22(6):375–381, 1998
9. Mayes T, Gottschlich MM, Khoury J, et al: Evaluation of predicted and measured energy requirements in burned children. J Am Diet Assoc 96(1):24–29, 1996
10. Talbot FB: Basal metabolism standards for children. Am J Dis Child 55:455–459, 1938
11. Chwals WJ, Fernandez ME, Charles BJ, et al: Serum visceral protein levels reflect protein-calorie repletion in neonates recovering from major surgery. J Pediatr Surg 27(3):317–321, 1992
12. Kudsk KA, Minard G, Wojtysiak SL, et al: Visceral protein response to enteral versus parenteral nutrition and sepsis in patients with trauma. Surgery 116(3):516–523, 1994
13. Lucas A, Bloom SR, Aynsley-Green A: Gut hormones and minimal enteral feeding. Acta Paediatr Scand 75:719–723, 1986
14. Moore FA, Feliciano DV, Andrassy RJ, et al: Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. Ann Surg 216(2): 172–183, 1992
15. Kudsk KA, Croce MA, Fabian TC, et al: Enteral versus parenteral feeding. Effects on septic morbidity after blunt and penetrating abdominal trauma. Ann Surg 215(5):503–511; discussion 511–513, 1992
16. Kudsk KA, Minard G, Croce MA, et al: A randomized trial of isonitrogenous enteral diets after severe trauma. An immune-enhancing diet reduces septic complications. Ann Surg 224(4): 531–5340; discussion 540–543, 1996
17. Herndon DN, Barrow RE, Kunkel KR, et al: Effects of recombinant human growth hormone on donor-site healing in severely burned children. Ann Surg 212(4):424–429; discussion 430–431, 1990
18. Gilpin DA, Barrow RE, Rutan RL, et al: Recombinant human growth hormone accelerates wound healing in children with large cutaneous burns. Ann Surg 220(1):19–24, 1994
19. Jeschke MG, Barrow RE, Herndon DN: Recombinant human growth hormone treatment in pediatric burn patients and its role during the hepatic acute phase response. Crit Care Med 28:1578–1584, 2000
20. Chwals WJ, Letton RW, Jamie A, et al: Stratification of injury severity using energy expenditure response in surgical infants. J Pediatr Surg 30:1161, 1995
21. Chwals WJ, Fernandez ME, Jamie AC, et al: Detection of postoperative sepsis in infants using metabolic stress monitoring. Arch Surg 129:437–442, 1994

22. Wolf SE, Jeschke MG, Rose JK, et al: An indicator of sepsis-associated mortality in burned children. Arch Surg 132:1310–1314, 1997
23. Chwals WJ, Fernandez MD, Jamie AC, et al: Relationship of metabolic indices to postoperative mortality in surgical infants. J Pediatr Surg 28:819–822, 1993

CYSTIC FIBROSIS

Background

Cystic Fibrosis (CF) is an autosomal recessive genetic syndrome characterized by viscid exocrine gland secretions that may obstruct the bronchi, pancreatic and bile ducts, and the intestines. CF currently affects approximately 30,000 children and adults in the United States.[1] One in 31 Americans is a carrier of the abnormal gene. The major cause of death in patients with CF is pulmonary insufficiency leading to respiratory failure. Nutrition status has been found to strongly correlate with pulmonary status and to affect recovery from illness.[2] Median survival is 32.3 years based on data from the Cystic Fibrosis Foundation Patient Registry 1998.[3]

The relationship between nutrition status and long term survival in patients with CF is well documented.[4] Factors that affect nutrition status include pancreatic insufficiency, maldigestion/malabsorption of fat and fat-soluble vitamins, and loss of bile salts and bile acids associated with steatorrhea, and bulky stools. In addition, patients who have undergone intestinal resection secondary to bowel obstruction resulting from meconium ileus may have reduced absorptive capabilities.[4] Chronic pulmonary infections and deteriorating pulmonary function are associated with anorexia and increased energy requirements that can lead to malnutrition. Two additional factors that contribute to poor nutrition status in CF patients are cystic fibrosis–related diabetes (CFRD) and cholestatic liver disease.

Nutrition assessment in CF patients is accomplished by first determining energy requirements, taking into account the effects of dietary intake, activity, pulmonary status, extent of malabsorption (pancreatic sufficient or insufficient), and hypermetabolism. Laboratory measurements suggested at time of diagnosis and yearly include electrolyte and acid–base parameters, complete blood count, serum albumin, and plasma or serum retinal and alpha tocopherol levels.[4] Careful, consistent monitoring of growth parameters (height, weight, weight-for-height, and head circumference) is also essential.

Evidence

Children with CF have augmented energy needs during periods of growth, such as infancy and adolescence.[5] Energy requirements remain high in advanced lung disease. To offset these energy needs, 120 to 150% of Recommended Daily Allowance (RDA) for energy is encouraged.[3] However, recent studies have shown that CF children often do not achieve this level of energy intake.[3] Energy intake should also increase during pregnancy and CFRD.[6]

A meta-analysis of nutrition intervention and management addressed four types of medical interventions: oral supplementation, EN, PN, and behavioral modification.[3] The CF Foundation Clinical Practice Guidelines suggest that nutrition management be guided by "a graded response that is appropriate for the needs of each patient."[4] These guidelines describe a tiered approach. All CF patients should receive nutrition instruction, dietary counseling, pancreatic enzyme replacement, and vitamin supplementation. For those patients at risk of developing energy imbalance (eg, frequent pulmonary infections or periods of rapid growth), further education and monitoring are important. Additionally, these patients may need calorically dense feedings and behavioral assessment and counseling. For those patients with a weight to height index of 85% to 90% of ideal weight, oral supplements should be given. For those patients with a weight-to-height index consistently less than 85% of ideal body weight, EN should be initiated. There is no compelling evidence to support the use of any specialized formula, although supplements should be nutritionally balanced with respect to micronutrients.[4] Finally, for those children with a weight-to-height index of less than 75% of ideal weight, continuous EN or PN should be initiated. With continuous drip tube feedings, pancreatic enzyme supplements are required for digestion. It is generally recommended that patients take enzymes at the start of bedtime tube feedings, although this can be altered to allow for individual tolerances. PN is usually indicated for short-term therapy with specific problems such as short-gut syndrome, pancreatitis, severe gastroenteritis, and postoperative management in patients who have had major surgical procedures.[4] PN may be required for lung transplant candidates and individuals who refuse EN.[4]

Special Considerations

Growth rates and energy requirements are highest during the first 2 years of life.[4] Pancreatic enzyme replacement therapy should be initiated with each feeding in the presence of maldigestion/malabsorption.[7] Enzymes should be given with all types of milk products including human breast milk and predigested formulas. Predigested formulas are used for CF infants who have short gut syndrome or cholestasis.[7] CF infants fed human breast milk can sustain normal growth while on pancreatic enzyme replacement. Special attention should be given to their caloric needs and potential metabolic complications such as hypoproteinemia and hyponatremic alkalosis.[4,7,8] Nutrition and electrolyte status and growth velocity should be monitored at 1- to 3-month intervals.[4] Because of the low sodium content of breast milk, supplemental sodium chloride, especially during summer months, may be indicated. An appropriate/safe dosage is 2 to 4 mEq/kg per day.[4]

The increasing life expectancy of patients with CF allows the development of additional medical complications such as CFRD and osteoporosis. Up to 75% of CF adults have some form of glucose intolerance, and 15% have frank CFRD.[6]

CFRD has features of both Type 1 and Type II diabetes, but is a separate, unique condition. Causes of

CFRD include pancreatic scarring due to thickened excretions, insulin resistance due to chronic infections, and elevated cortisol levels. CFRD can be intermittent; in such cases, insulin is needed during infections and with steroid treatment. In chronic CFRD, insulin is required at all times. The goal of CFRD therapy is to maintain blood glucose in a range as close to normal as possible.[6] With CFRD, patients are instructed to continue a high-calorie, high-protein, high-fat, high-salt diet to maintain body weight. Individuals with CF should understand the effect of carbohydrates on blood glucose levels as well as how to balance food, insulin, and physical activity to maintain near normal blood glucose levels.

Osteoporosis and fractures are a recognized problem in both children and adults with CF.[9] Several studies have documented diminished bone mineralization in adults with CF. There is also concern over skeletal growth and development in children with CF.[10] Possible risk factors for low bone density include small body size, low weight-for-height, decreased physical activity, use of corticosteroids, delayed skeletal or sexual maturation, gonadal dysfunction, and severity of illness.[11] Current treatment options include increased calcium and vitamin D intake, weight-bearing physical activity, and use of bisphosphonates, calcitonin, and/or estrogens.[12] Further studies must be conducted to identify the etiology of osteoporosis in CF patients and to determine the best prevention and treatment methods.[13]

Because of malabsorption, the fat soluble vitamins A, D, E, and K may become depleted in patients with CF. Fat soluble vitamin serum levels should be monitored annually. CF patients with pancreatic insufficiency should receive a water miscible vitamin designed specifically for CF.

Practice Guidelines
Cystic Fibrosis

1. Patients with CF are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. CF patients with exocrine pancreatic insufficiency require enzyme replacement therapy and a water miscible multivitamin specifically designed for CF. (C)
3. Vitamins A, D, E and K serum levels should be monitored annually in CF patinets. (B)
4. A weight-height index greater than 90% of ideal should be maintained during periods of rapid growth (infancy and adolescence), pulmonary insufficiency, or infection in CF patients. (C)
5. CF children with a weight-for-height index less than 85% should have dietary intake monitored and undergo behavioral assessment and counseling. (B)
6. SNS should be initiated in children with CF with a weight-for-height index less than 90%. (A)

REFERENCES

1. Facts about Cystic Fibrosis. Cystic Fibrosis Foundation, Revised January 24, 2000, http: //www.cff.org/facts.htm
2. Jelalian E, Stark LJ, Reynolds L, Seifer R: Nutrition intervention for weight gain in cystic fibrosis: A meta analysis. J Pediatr 486–492, 1998
3. Cystic Fibrosis Foundation, Patient Registry: Annual Data Report. Cystic Fibrosis Foundation, September 1999, pp 1 and 19, 1998
4. Clinical Practice Guidelines for Cystic Fibrosis: Cystic Fibrosis Foundation 1997, Appendix IV, Volume I, Section V
5. Luder E: Achieving Optimal Nutrition for People with Cystic Fibrosis Home Line. June 1997 Edition. http://www.cff/org/homeline199706.htm
6. Hardin D, Brunzell C, Schissel K, et al: Managing Cystic Fibrosis Related Diabetes (CFRD) An Instruction Guide for Patients and Families. Cystic Fibrosis Foundation, 1999
7. Ramsey B, Farrell P, Pencharz P, and the Consensus Committee. Nutritional Assessment and Management in Cystic Fibrosis: A Consensus Report. Am J Clin Nutr 55:108–116, 1992
8. Durie PR, Pencharz PB: Nutrition. Br Med Bull 48(4):823–847, 1992
9. Donovan Jr DS, Papadopoulas A, Staron RB, et al: Bone mass and vitamin D deficiency in adults with advanced cystic fibrosis lung disease. Am J Respir Crit Care Med 157:1892–1899, 1998
10. Henderson RC, Madsen CD: Bone mineral content and body composition in children and young adults with cystic fibrosis. Pediatr Pulmonol 27:80–84, 1999
11. Bhudhikanok GS, Wang M-C, Marcus R, et al: Bone acquisition and loss in children and adults with cystic fibrosis: A longitudinal study. J Pediatr 133:18–27, 1998
12. Zemel B: Clinical Assessment of Bone Health in Children and Young Adults. The Children's Hospital of Philadelphia. Thirteenth Annual North American Cystic Fibrosis Conference, 1999
13. Lambert JP: Osteoporosis: A new challenge in cystic fibrosis. Pharmacotherapy 20:34–51, 2000

INBORN ERRORS OF METABOLISM

Background

Nutritional therapy is often the primary, or even only, treatment for children with inborn errors or metabolism and requires an in-depth understanding of the metabolic processes involved. Depending on the particular inborn error, inadequate or inappropriate nutrition can result in mental retardation, growth failure, and metabolic/neurologic crises.[1] Goals of nutrition support in children with inborn errors of metabolism include optimizing growth and development and minimizing any metabolic complications. Examples of nutritional therapy for these disorders include the following:

1. Restricting substrates in patients with blocked metabolic pathways to prevent accumulation of toxic precursors such as phenylalanine (phenylketonuria), galactose (galatosomia), and leucine (maple syrup urine disease);
2. Facilitating alternative metabolic pathways to decrease accumulated toxic precursors in blocked reaction sequences (eg, glycine therapy in patients with isovaleric acidemia);
3. Supplying products of blocked primary pathways [eg, arginine in patients with urea cycle disorders, tyrosine in phenylketonuria (PKU), and glucose in glycogen storage disease type I];
4. Supplementing conditionally essential nutrients (eg, carnitine in patients with organic acidemias);

5. Stabilizing altered enzyme proteins (eg, thiamine to increase enzyme activity in patients with maple syrup urine disease);
6. Replacing deficient cofactors (eg, vitamin B-12 therapy in patients with methylmalonic aciduria and vitamin B-6 in homocystinuria);
7. Inducing enzyme production (eg, glucose to affect gene transcription in patients with type I tyrosinemia);
8. Supplementing nutrients that are inadequately absorbed or not released from their apoenzyme (eg, biotin in patients with biotinidase deficiency).
9. Avoidance of fasting in disorders in which catabolism results in toxicity from metabolic breakdown products or in lack of energy supply because of inability to utilize the energy of fatty acid oxidation [eg, medium chain acylCoA dehydrogenase deficiency (MCAD)].

Evidence

The use of SNS in children with inborn errors of metabolism, including the use of specialized formulations, must be individualized for the specific patient and for the specific inborn error of metabolism.[1,2] Chemically defined formulations have been developed for many of the inborn errors of metabolism, including phenylketonuria, homocystinuria, maple syrup urine disease, propionic acidemia, methylmalonic acidemia, histidinemia, hyperlysinemia, tyrosinemia, and the urea cycle disorders. Protocols have been developed for each of these inborn errors of metabolism to optimize nutrition support.[2] With most of the inborn errors of metabolism, short-term studies clearly demonstrate improvement with nutrition intervention (eg, in patients with methylmalonic and propionic acidemia, type I glycogen storage disease, maple syrup urine disease, and phenylketonuria).[3–6] However, because of the small number of children diagnosed with each of these conditions, data from prospective long-term studies demonstrating the effect of nutrition support are not conclusive, except in the case of phenylketonuria.[7–9] Studies in the United States showed that IQ in children with PKU, diagnosed by newborn screening programs and treated within the first 4 weeks of life with a phenylalanine-restricted diet, was within 5 to 10 points of their unaffected siblings. This compared with an IQ of about 40 to 50 in untreated children. In the United Kingdom, the Medical Research Council showed that outcome in PKU was closely related to degree of dietary compliance throughout childhood. The international collaborative project on maternal PKU demonstrated that the severe mental retardation, microcephaly, and congenital heart disease that occurred in more than 90% of infants born to mothers with PKU untreated by diet during pregnancy could be nearly completely prevented by good dietary control established before pregnancy.

In most of these conditions, abnormal concentrations of metabolites can severely affect neurologic function. Fasting even for a brief period may lead to potentially life-threatening metabolic decompensation due to an inability to mobilize substrate (eg, glycogen storage disease type I), a deficiency of energy production (eg, disorders of fatty acid oxidation), or a breakdown of protein or fat leading to accumulation of toxic metabolites.[10] Disorders of fatty acid oxidation and transport result in an inability to mobilize fatty acids for energy metabolism.[11,12] Symptoms occur when the carbohydrate stores of glycogen in liver are exhausted and the body begins to depend on fat for energy. When transportor-oxidation of fatty acids cannot go to completion, hypoglycemia results. If untreated, death may occur. In some disorders, myopathy and cardiomyopathy develop. Fever, anorexia, nausea and vomiting, which accompany typical intercurrent illnesses in infants and small children, or major metabolic stresses such as trauma or surgery, worsen the catabolic state and the rapidity of decompensation. Toxic concentrations of substrate also decrease appetite and result in nausea and vomiting. In many of these disorders, acute nutrition intervention, including the provision of adequate glucose and/or fat calories to prevent catabolism, may be essential to prevent neurologic injury or death. The provision of protein is far more complex[6,13] and usually not necessary for short-term treatment, although PN can be safely used by experienced metabolic specialists.[14]

Practice Guidelines *Inborn Errors of Metabolism*

1. Children with inborn errors of metabolism are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Adequate nutritional intake in infants and children with inborn errors of metabolism should be assured to support normal growth and minimize neurologic impairment. (B)
3. Many children with inborn errors of metabolism should eat only small amounts of normal foods and often need to rely upon special formulations (medical foods) for most of their needs for calories, protein, trace minerals, and vitamins. (B)
4. Infants and children with inborn errors of metabolism require frequent monitoring of their condition, with appropriate changes in diet to achieve adequate growth and minimize metabolic complications. (B)
5. SNS is required in children with inborn errors of metabolism to maintain growth development and metabolic homeostasis; special attention should be focused on the particular metabolic pathway that is abnormal to assure appropriate, disease specific formula modification. (B)
6. Aggressive nutritional intervention should be used in children with inborn errors of metabolism at times of catabolic stress to prevent, metabolic decompensation, severe neurologic complications and death. (B)

REFERENCES

1. Seashore M, Wappner R: Genetics in Primary Care and Clinical Medicine. Appleton Lange, Englewood Cliffs, NJ, 1996, Chapters 13–15
2. Acosta PB, Ryan AS: Functions of dietitians providing nutrition support to patients with inherited metabolic disorders. J Am Diet Assoc 97:783–786; quiz 787–788, 824 (IV), 1997
3. Winter S, Buist N: Clinical treatment guide to inborn errors of metabolism 1998. J Rare Dis 4:19–46 (IV), 1998
4. Cockburn F, Clark BJ: Recommendations for protein and amino acid intake in phenylketonuric patients. Eur J Pediatr 155: S125–S129 (IV), 1996
5. van der Meer SB, Poggi F, Spada M, et al: Clinical outcome and long-term management of 17 patients with propionic acidaemia. Eur J Pediatr 155:205–210 (III), 1996
6. Parsons HG, Carter RJ, Unrath M, et al: Evaluation of branched-chain amino acid intake in children with maple syrup urine disease and methylmalonic aciduria. J Inherit Metab Dis 13:125–136 (III), 1990
7. Smith I, Beasley M: Intelligence and behaviour in children with early treated phenylketonuria. A report from the MRC/DHSS phenylketonuria register. Eur J Clin Nutr 43:1–5. (IIA), 1989
8. Koch R, Azen C, Friedman EG, et al: Paired comparisons between early treated PKU children and their matched sibling controls on intelligence and school achievement test results at eight years of age. J Inherit Metab Dis 7:86–90 (IIA), 1984
9. Koch R, Levy HL, Matalon R, et al: The international collaborative study of maternal phenylketonuria: status report 1994. Acta Paediatr Suppl 407:111–119 (IIA), 1994
10. Morris AA, Leonard JV: Early recognition of metabolic decompensation. Arch Dis Child 76:555–556 (III), 1997
11. Brivet M, Boutron A, Slama A, et al: Defects in activation and transport of fatty acids. J Inherit Metab Dis 22:428–441 (III), 1999
12. Cederbaum SD: SIDS and disorders of fatty acid oxidation: where do we go from here? J Pediatr 132:913–914 (IV), 1998
13. Acosta PB, Yannicelli S: Protein intake affects phenylalanine requirements and growth of infants with phenylketonuria. Acta Paediatr Suppl 1994, 407:66–67. (IIA)
14. Koga Y, Iwanaga T, Yoshida I, et al: Maple syrup urine disease: Nutritional management by intravenous hyperalimentation and uneventful course after surgical repair of dislocation of the hip. J Inherit Metab Dis 21:177–178 (III), 1998

SOLID ORGAN TRANSPLANTATION

Background

Malnutrition and growth failure from end-stage organ diseases predisposes pretransplant pediatric patients to increased morbidity and mortality. Organ transplantation is an effective and often necessary treatment for children with end-stage liver, kidney, or cardiac diseases. Liver and kidney are the most common pediatric solid organ transplants performed.[1,2] End-stage organ disease often precludes the ability to consume, metabolize, and adequately utilize nutrients to maintain adipose tissue and lean body mass.

Nutrient requirements for these infants and pediatric patients are much higher then normal because of increased energy expenditure, need for repletion, and (in some instances) malabsorption.

The primary goal of nutrition care for pediatric patient posttransplantation is to provide appropriate nutrition support to reestablish normal growth and development. The ultimate objectives are complete rehabilitation and improved quality of life.[3]

During the acute posttransplant period, patients are catabolic. There are increased nitrogen losses secondary to preexisting malnutrition, surgical stresses and the use of corticosteroids.[4] PN may be required for a short period of time after transplant until bowel function is reestablished, or if complications develop. Aggressive nutrition support in the immediate postoperative period improves immune function parameters, promotes wound healing, promotes positive nitrogen balance, facilitates weaning from ventilatory support, and shortens intensive care unit length of stay.[2,4] PN can be weaned as the postoperative ileus resolves and oral feedings are instituted. Supplemental EN may be necessary for some infants and young children to complement oral intake and to provide adequate calories and protein for repletion. Nocturnal feedings, the preferred method of supplementation, allow ambulation and development of appetite during daytime hours. Nocturnal supplementation also helps to normalize eating behaviors with family and peers.[5,6]

Poor nutrition status, catch-up growth requirements, postoperative medications, and surgical or medical complications must all be taken into account during the posttransplant phase in an effort to achieve nutrition goals. For infants and young children, energy requirements are generally estimated at 100 to 130 kcal/kg per day with 2.5 to 3.0 g/kg per day of protein. Older children generally require 70 to 90 kcal/kg per day with 2.0 to 2.5 g/kg per day of protein. Needs must be adjusted frequently based on clinical status and graft function.[2,4]

Evidence

Although growth retardation is reported in pediatric patients both before and after transplantation, some improvements have been seen with changes in immunosuppressive protocols, early weaning of corticosteroids, and careful monitoring of nutrition support.

A study of 119 children after liver transplant reported linear growth improvement in most patients, with the onset of catch-up growth between 6 and 24 months after transplantation.[1] Further, a study examining the outcomes of children with or without malnutrition showed significantly improved 1-year survival rates in those patients who were identified as being well nourished.[5] This was true whether the child had undergone a liver transplant or remained on a waiting list.

Impaired growth has been reported in 79% of prepubertal cardiac transplant recipients who received daily prednisone for 1 or more years, yet normal range weight and height is achieved by 5 years in 88% of children receiving heart transplants in infancy.[1]

The North American Pediatric Renal Transplant Cooperative Study concluded that 75% of pediatric patients postrenal transplant have persistent growth retardation. Of various factors that could predict growth posttransplant, only age at transplant and the original height deficit are significant. Children with preexisting growth retardation who are over the age of 6 years at transplant are unlikely to exhibit catch-up growth after kidney transplant.[1,7] Although improvements in linear growth have been seen after pediatric liver and heart transplants, growth retardation remains problematic after renal transplantation.

Children with congenital chronic renal failure (CRF) are at highest risk for growth retardation. During

infancy and early childhood, malnutrition and electrolyte imbalances are the main contributors to reduced growth. During puberty, hormonal disturbances are responsible for growth impairment. In infancy, loss of growth potential can be prevented by adequate nutrition. However, later in life, catch-up growth can not be induced by nutrition intervention or dialysis. Renal transplantation allows for catch-up growth in a small percentage of patients. Administration of corticosteroids on an alternate day schedule can improve growth in some but not all patients. Treatment with recombinant human growth hormone (rhGH) has been shown to improve growth velocity and growth in all stages of renal disease and after transplantation. rhGH is able to antagonize several of the side effects of long-term glucocorticoid administration posttransplant, such as growth failure, protein wasting, and osteoporosis, without significant side effects. The improvement of growth is most marked in the prepubertal patients and during the first year of rhGH treatment.[8]

An optimal quality of life with restoration of normal growth and development is a primary goal of pediatric transplant. Linear growth is of critical importance to the emotional well-being and reintegration of transplant recipients into normal childhood activities. Body image may be affected by changes in appearance caused by medications, poor growth, and surgical scars. Adolescents are at highest psychosocial risk. These issues can lead to risk taking behavior, which may evolve into medication noncompliance, poor medical follow-up, and drug or alcohol abuse. Noncompliance is a major cause of late rejection episodes in adolescents. Once suspected, intervention to resolve noncompliance should be initiated to meet the psychosocial needs of the adolescent.[1]

Special Considerations

Posttransplant complications that most significantly affect nutrition management include organ rejection, infection, fever, wound complications, and renal insufficiency.

Chronic illness and anorexia can alter a child's eating habits. Because some children have been exclusively fed formula, they may have difficulty accepting different solid foods because of taste and texture sensitivities. Taste aversions can occur because of the oral administration of multiple medications and changes in formula types.[4] Another factor specific to pediatric transplantation that can negatively influence feeding habits and nutrition status is oral aversion secondary to intubations and preoperative enteral feedings. Subsequently, some chronically ill children may experience developmental and feeding difficulties.[2]

Growth retardation is reported in children both before and after transplantation. More recently, trends in growth have improved because of careful monitoring of nutritional status, aggressive uses of SNS, and early reduction of corticosteroid dose. Compromises in graft function and multiple operative interventions because of postoperative complications can also contribute to poor linear growth. Graft rejection negatively affects growth because of pulsed corticosteroid administration, the primary treatment for acute rejection. This increase in steroids can also lead to exacerbation of nutrition drug—nutrient interaction. Dietary modifications to treat the side effects caused by immunosuppressive medications may be required, such as sodium restriction for hypertension or ascites, carbohydrate restriction for hyperglycemia, and vitamin and mineral supplementation.[1,2]

Excessive weight gain may occur after solid organ transplantation secondary to increased appetite from corticosteroids and the freedom of an unrestricted diet. Hyperlipidemia, seen more commonly in renal transplantation, hypertension, hyperglycemia, and osteoporosis can also occur from the use of steroids and other immunosuppressive drugs.[2,6]

Bone disease is a common risk in transplant patients. Pretransplant bone demineralization in conjunction with high-dose steroids causes calcium depletion through decreased intestinal absorption and increased bone reabsorption. Detailed diet histories can provide insight into the actual calcium intakes of these patients. Many of these children have poor intakes of dairy products because of previous diet restrictions or intolerance. Calcium supplementation may be helpful in some cases of mild disease. Careful monitoring of serum electrolytes and mineral levels along with periodic bone density studies during the follow-up period can provide information needed to consider drug therapy to treat bone disease.[2]

Management of immunosuppression depends on nutrition status. In a study of pediatric patients after renal transplantation, those who were malnourished before their transplant had lower cyclosporine levels compared with those with normal nutrition.[9]

Practice Guidelines *Solid Organ Transplantation*

1. Children awaiting solid organ transplants or who have received solid organ transplants are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Nutrition support in patients awaiting solid organ transplantation should be used to maximize nutrition status before surgery. (C)
3. After transplantation, patients should receive regular nutrition monitoring and counseling. (C)

REFERENCES

1. Kosmach B, Webber S, Reyes J: Care of the pediatric solid organ transplant recipient. Pediatr Clin N Am 45:1395–1418, 1998
2. Parkman-Williams C: Nutritional management following kidney or liver transplant. Pediatric Manual of Clinical Dietetics. American Dietetic Association, 299–308, 1998
3. Becht MB, Pedersen S, Ryckman F, Balistreri W: Growth and nutritional management of pediatric patients following orthotopic liver transplant. Gastroenterol Clin N Am 22:367–380, 1993
4. Kelly DA: Nutritional factors affecting growth before and after liver transplantation. Pediatr Transplant 1:80–84, 1997
5. Shepard RW: Pre and postoperative nutritional care in liver transplantation in children. J Gastroenterol Hepatol 11:S7–S10, 1996

6. Hasse JM: Solid organ transplantation. IN Matarese L, Gottschlich M (eds). Contemporary Nutrition Support Practice—A Clinical Guide. WB Saunders, Philadelphia, 40:547–560, 1998
7. Tejani A, Sullivan K: Long-term follow-up of growth in children post-transplantation. Kidney Int Suppl 43:S56–S58, 1993
8. Mehls O, Blum WF, Schaefer F, Tonschoff B, Scharer K: Growth Failure in Renal Disease. Baillieres Clin Endocrinol Metab 6:665–685, 1992
9. Lares-Asseff I, Zaltzman S, Perez Guille MG, et al: Pharmacokinetics of cyclosporine as a function of energy-protein deficiency in children with chronic renal failure. J Clin Pharm 37:179–185, 1997

EATING DISORDERS

Background

Nutrition support is an important component of the treatment of infants and children with eating disorders.[1–3] Children presenting with serious eating problems may be affected by both physical illnesses and environmental stresses. Common physical illnesses associated with eating disorders include gastroesophageal reflux,[4–7] cancer,[8] and prolonged periods without eating due to endotracheal intubation[9] or other medical treatment. Also at risk are infants with congenital cardiac disease, a history of prematurity, and with physical disabilities, developmental delay, and chronic illness. Oromotor dysfunction may cause disordered eating. These children usually have hypotonia and drooling or tongue protrusion. Children with spastic cerebral palsy may also have oromotor problems.[10]

Infants and children may develop anorexia in situations of chaos and stress, including periods of anxiety or depression or a disordered parent-child relationship.[11–14] Additionally, emotional disturbances can present as feeding problems in infancy.[15] Rarely, an infant eating disorder can develop in conjunction with Munchausen syndrome by proxy or factitious food allergies. Some infants and children develop conditioned aversions to some or all foods. An aversion could be to a taste, a texture, or a combination of tastes and textures. These children may have gagging, wretching, or vomiting as part of their symptom complex. In the most severe cases the thought of food, or eating, or an activity associated with eating (such as sitting in the high chair) can stimulate vomiting.

One of the most common mistakes made in the evaluation of infants and children with feeding disorders is emphasis on nutrition to the exclusion of eating behavior and mechanics. It is important to separately evaluate the child's nutrition status, the child's physical ability to eat, and the child's psychological state related to eating. Therefore, the assessment should include a nutrition evaluation, a medical evaluation, and a feeding evaluation with particular emphasis on the neurological exam. The feeding evaluation should include assessment of mechanical functions of eating and the psychological conditions associated with eating. Older children may be evaluated as outpatients. Breast- or bottle-fed babies are often more easily evaluated in a clinical setting.

Nutrition treatment options for children with eating disorders depend on their degree of malnutrition and its duration.[16] Children with severe undernutrition (less than 70% of median body weight for height) present a life threatening acute problem; nutrition support takes precedence in the treatment priorities. The risk for serious complications of malnutrition is increased with decreasing age.[17] A nasogastric tube affords the best short-term access for EN.[18] Nasogastric tubes can be safely used for a few months, if necessary.[19] Placement of a nasogastric tube can exacerbate a feeding problem caused by psychological, behavioral, or environmental issues.[17] Immediate nutrition rehabilitation may give the child more energy for feeding. In addition, this treatment reduces the parent's anxiety about the child starving. Potential refeeding complications should be monitored if tube feedings are initiated. Rarely, long-term nutrition support by tube feeding may be needed for children with eating disorders. In this case, a gastrostomy tube should be placed. Many children further decrease their oral intake after tube feedings have been started, and this option should be considered only when other options have failed and undernutrition becomes health or life threatening. These children should receive behavioral therapy with the goal of eventual weaning from gastrostomy tube feeding.[20] A nutritionally complete formula should be used to nourish the child. As the child increases oral intake, the gastrostomy tube feeding should be decreased accordingly. There is rarely a role for PN in children with eating disorders. A common complication of tube feeding in children with eating disorders is conditioned retching, gagging, or vomiting at the time of tube feeding. A calm reaction by the parents and pleasant feeding routine are helpful.

Children with mild-to-moderate undernutrition (more than 70% of median body weight for height) can usually be nutritionally rehabilitated using high calorie foods without tube feeding. The use of high calorie formulas and the addition of high fat foods to the child's diet may be adequate for increasing the child's caloric intake.[21] An organized schedule of meals for school age children is effective.[22,23] Limitation of nonnutritious foods, drinks, and continuous snacking (grazing) is also helpful. Many children with eating disorders do not have normal hunger-satiety experiences. Therefore, the use of hunger as a motivator for eating may not be helpful.[24,25]

Behavioral therapy is an important component to the treatment of children with mild-to-moderate undernutrition. In some cases, children with eating disorders require partial or complete care away from their families, such as in therapeutic day care or foster placement. Inpatient treatment programs are available for refractory eating.

EN should provide 1.5 to 2.0 times maintenance calories for children with moderate-to-severe malnutrition.[26] When the child reaches an acceptable weight-for-height, the amount of EN should be decreased to maintenance calories (including the child's oral intake). Children with mild malnutrition, who require tube feeding, should be started on maintenance calories.

Circadian rhythms should be considered when planning tube feedings for children who may regain their ability to eat orally. The desire to eat is linked to

physiologic cues stemming from the body's normal diurnal experience of the timing of eating.[27–29] Children who are maintained on night time drip-feedings will often experience the desire for feeding because they are going to bed. This creates an inconvenient conflict for families trying to optimize oral feeding. The choice of formula for children with eating disorders is based on caloric density, cost, and availability.[30,31] Formulas with fiber may be helpful to avoid constipation for children more than 1 year of age.

Monitoring of height, weight, and head circumference should be done monthly when children are started on tube feedings.

Evidence

There has been little research on clinical decision-making concerning nutrition support in children with eating disorders. There is a need for well-designed studies to compare the outcomes of patients treated with SNS and oral therapy compared with patients treated with behaviorally only. It is important that comparison groups have similar degrees of malnutrition and of behavioral dysfunction.[7] There is also very little research on the outcomes of behavioral treatment for children with eating disorders.

Practice Guidelines *Eating Disorders*

1. Children with eating disorders are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Infants and children with eating disorders should receive an oromotor assessment by an occupational therapist, speech therapist, nurse, or physician with training in pediatric oromotor dysfunction. (B)
3. Infants and children with eating disorders should receive a behavioral feeding assessment by an infant mental health specialist, psychologist, social worker, nurse, or physician with training in the behavioral aspects of infant and child feeding. (B)
4. Infants and children with eating disorders and severe malnutrition (less than 70% ideal weight for height) should receive high-calorie supplemental nutrition, using SNS if necessary. (B)
5. Infants and children requiring nasogastric tube feedings for more than 2 months should be evaluated for gastrostomy tube placement. (B)
6. Infants and children requiring tube feedings for eating disorders should receive the minimum supplemental support necessary to maintain growth and development. (B)
7. A therapeutic plan for rehabilitation of oral feeding should be developed for children with feeding disorders who require feeding via nasogastric or gastrostomy feeding tubes. (C)

REFERENCES

1. Linscheid TR: Eating problems in children. IN Handbook of Clinical Child Psychology, 2nd ed. Walter CE, Roberts MC (eds). John Wiley & Sons, New York, 1992, pp 451–473
2. Linscheid TR, Budd KS, Rasnake LK: Pediatric feeding disorders. IN Handbook of Pediatric Psychology, 2nd ed. Roberts MC (ed). Guildford Press, New York, 1995, pp 501–515
3. Christophersen ER, Hall CL: Eating patterns and associated problems encountered in normal children. Issues Compr Pediatr Nurs 3:1–16, 1978
4. Hart JJ: Pediatric gastroesophageal reflux. Am Fam Physician 54:2463–2472, 1996
5. Hillemeier AC: Gastroesophageal reflux: Diagnostic and therapeutic approaches. Pediatr Clin N Am 43:197–212, 1996
6. Hyman, PE: Gastroesophageal reflux: One reason why baby won't eat. J Pediatr 125:S103–S109, 1994
7. Orenstein SR: Gastroesophageal reflux. Pediatr Rev 13:174–182, 1992
8. Morris CS, Lough LR, Weinberger E: Infant with lethargy, failure to thrive, and abnormal blood smear. Invest Radiol 25:1054–1057, 1990
9. Berkowitz CD: Cardiopulmonary problems and disorders of the head and neck. IN Failure to Thrive and Pediatric Undernutrition, A Transdisciplinary Approach. Kessler DB, Dawson P (eds). Brookes, Baltimore, MD, 1999, pp 227–238
10. Rudolph CD: Feeding disorders in infants and children. J Pediatr 125:S116–S124, 1994
11. Birch LL: Children's preferences for high-fat foods. Nutr Rev 50:249–255, 1992
12. Birch LL, Johnson SL: Appetite control in children. IN Appetite and Body Weight Regulation. Fernstrom JD, Miller GD (eds). CRC Press, Boca Raton, FL, 1994, pp 5–15
13. Black M, Hutcheson J, Dubowitz H, Berenson-Howard J, Starr RH: The roots of competence: Mother-infant interaction among low-income. African-American families. Appl Dev Psychol 17:367–391, 1996
14. Chatoor I: Feeding disorders of infants and toddlers. IN Handbook of Child and Adolescent Psychiatry: Volume I. Infants and Preschoolers: Development and Syndromes. Greenspan S, Wieder S, Osofsky J (eds). John Wiley & Sons, New York, 1997, pp 367–386
15. Rutter M: Psychosocial resilience and protective mechanisms. Am J Orthopsychiatry 57:316–331, 1987
16. Foy T, Czyzewski D, Phillips S, Ligon B, Baldwin J, Klish W: Treatment of severe feeding refusal in infants and toddlers. Infants Young Children 9(3):26–35, 1997
17. Krebs NF: Gastroiontestinal Problems and Disorders, IN Failure to Thrive and Undernutrition, A Transdisciplinary Approach. Kessler DB, Dawson P (eds). Brookes, Baltimore, MD, 1999, p 224
18. Foy T, Czyzewski D, Phillips S, Ligon B, Baldwin J, Klish W: Treatment of severe feeding refusal in infants and toddlers. Infants Young Children 9(3): 26–35, 1997
19. Moore MC, Greene HL: Tube feeding of infants and children. Pediatr Clin N Am 32:401–417, 1985
20. Luiselli JK, Luiselli TE: A behavioral analysis approach toward chronic food refusal in children with gastrostomy-tube dependency. Topics Early Childhood Special Ed 15(1):1–18, 1995
21. Cunningham KF, McLaughlin M: Nutrition. IN Failure to Thrive and Pediatric Undernutrition: A Transdisciplinary Approach. Kessler DB, Dawson P (eds). Paul H. Brookes Publishing Co, Baltimore, MD, 1998, pp 99–119
22. Satter E: How To Get Your Kid To Eat . . . But Not Too Much. Bull Publishing, Palo Alto, CA, 1987
23. Macht J: Poor Eaters: Helping Children Who Refuse To Eat. Plenum, New York, 1990
24. Toomey KA: [Caloric intake of toddlers fed structured meals and snacks vs. on demand]. Unpublished raw data, 1994
25. Frank D: Failure to thrive. IN Behavioral and Developmental Pediatrics: A Handbook for Primary Care. Parker S, Zuckerman, BS (eds). Mosby Year Book, St Louis, 1994, pp 134–140
26. Ashworth A, Millward DJ: Catch-up growth in children. Nutr Rev 44:157–163, 1986
27. Thomas K: Biorhythms in infants and role of the care environment. J Perinat Neonatal Nurs 9:61–75, 1995

28. Hellbrugge T, Lange JE, Rutenfranz J, Stehr K: Circadian periodicity of physiological functions in different stages of infancy and childhood. Ann NY Acad Sci 117:361–373, 1964
29. Birch LL, Fisher JA: Appetite and eating behavior in children. Pediatr Clin N Am 42:931–953, 1995
30. Cunningham KF, McLaughlin M: Nutrition. IN Failure to Thrive and Pediatric Undernutrition: A Transdisciplinary Approach. Kessler DB, Dawson P (eds). Paul H. Brookes Publishing Co, Baltimore, MD, 1998, pp 99–119
31. American Academy of Pediatrics. Committee on Nutrition: Commentary on breast feeding and infant formulas, including proposed standards for formulas. Pediatrics 58:276, 1976

DIABETES

Background

Most children with diabetes have type 1 diabetes mellitus, which involves an absolute lack of insulin secretion.[1] However, the incidence of type 2 diabetes mellitus in childhood appears to be increasing, particularly in the black and hispanic populations.[2] In this latter group of patients, the diabetes is usually related to obesity and is due to a relative lack of insulin secretion, along with insulin resistance.

The normal mechanisms that maintain euglycemia in the postabsorptive state and prevent hyperglycemia in the postprandial state are impaired, presumably because of excessive hepatic glucose release and impaired glucose uptake.[3]

Children who are stressed can have elevated blood glucose concentrations without a prior history of diabetes. In adults, severe stress is associated with elevations in the counterregulatory hormones (specifically, glucagon, epinephrine, cortisol, and growth hormone).[4,5] These hormones counteract the effects of insulin and lead to increased hepatic glucose release and decreased peripheral uptake of glucose. In pediatric patients with diabetes, stress can cause even greater derangement in glucose metabolism, because children are unable to produce additional insulin in response to the elevations in counterregulatory hormones.

Evidence

There are no prospective, randomized studies that define optimal glucose management in hospitalized children with diabetes. Most strategies are extrapolated from adult studies.

There is a growing body of evidence in adults that hyperglycemia increases the incidence of nosocomial infections in stressed, hospitalized patients.[6–10] The rate of central catheter infection was about five times higher in diabetic patients receiving PN compared with nondiabetic patients. In addition, elevated blood glucose concentrations have been reported to be the most common risk factor for candida infection. However, all of these reports have been in adults.

The explanation for these findings appears to be a direct effect of hyperglycemia on leukocyte function. In vitro studies have shown that high blood glucose concentrations are associated with abnormalities in granulocyte adhesion, chemotaxis, phagocytosis, and intracellular killing.[7,8] Respiratory burst function and superoxide anion production, as well as complement function, also seem to be adversely affected.[11]

Special Considerations

The etiology of diabetes in children is still uncertain. Recently, a close association between obesity and an increased incidence of non-insulin dependent diabetes mellitus has been found.[12,13] This finding strongly supports the control of childhood obesity to reverse this trend. The optimal glucose levels for hospitalized children with diabetes mellitus have not been established. However, it seems reasonable to maintain blood glucose concentrations between 100 and 200 mg/dL. These values avoid the extremes of hypo- and hyperglycemia. The former is particularly important, since identifying the neuroglyopenic and adrenergic symptoms of low blood glucose concentrations may be difficult in severely ill patients who are sedated and/or on mechanical ventilation.

The nutrition assessment, indications for nutrition support, and estimation of nutrition needs for critically ill diabetic patients are similar to those of the nondiabetic patient. Diabetic gastroparesis, which can be seen in adults with type 1 diabetes mellitus,[14] is rarely observed in children.

There are no established protocols existing for the optimal control of blood glucose concentrations in diabetic children. However, children with type 1 diabetes mellitus are particularly prone to develop ketoacidosis; therefore, prolonged elevation of plasma glucose concentrations should be avoided. Usually, if patients are receiving all of their feedings intravenously, a dose of 0.1 units of regular human insulin is added for each gram of dextrose in the infusate.[14] Such dosing is rarely associated with hypoglycemia; frequently, increased doses of regular insulin may be needed to keep blood glucose concentrations within the goal range. If enteral feedings are being given, short-acting insulin is usually given as intermittent boluses until it is clear the patient is tolerating feedings. Then, the patient can be switched to intermediate acting insulin. No data exist concerning the optimal formula to utilize in this situation.[14] Enteral formulas that are lower in carbohydrate and higher in fat have not been shown to lead to an attenuated glycemic response. Despite lack of controlled trials, the American Diabetes Association has established guidelines for pediatric and adolescent insulin dependent diabetes mellitus patients.[15] These include the provision of 50% to 65% of total calories as complex carbohydrates and with high fiber content. Protein should contribute 12% to 20% and fat less than 30% of caloric intake, with less than 10% saturated fat and less than 300 mg/d from cholesterol. Similarly, recommendations for the fiber content of the formula are the same as for the nondiabetic hospitalized child.

Practice Guidelines *Diabetes*

1. Children with diabetes mellitus are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)

2. Blood glucose should be maintained between 100 and 200 mg/dL in hospitalized children with diabetes. (B)
3. If PN is being given, intravenous insulin should administered starting with 0.1 units of regular human insulin for each gram of dextrose in the infusate. (B)
4. If EN is being given, subcutaneous insulin should be used to maintain the blood glucose level between 100 and 200 mg/dL. (C)

REFERENCES

1. Anonymous: Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 20:1183–1197, 1997
2. Dabelea D, Pettitt DJ, Jones KL, et al: Type 2 diabetes mellitus in minority children and adolescents: An emerging problem. Endocrinol Metab Clin N Am 28:709–729, 1999
3. Dinneen SF: The postprandial state: Mechanism of glucose intolerance. Diabetes Med 14(Suppl 3):S19–S24, 1997
4. Shamoon M, Hendler R, Sherwin R: Synergistic interactions among anti-insulin hormones in the pathogenesis of stress hyperglycemia in humans. J Clin Endocrinol Metab 52:1235–1241, 1981
5. Schade DS, Eaton RP: The temporal relationship between endogenously secreted stress hormones and metabolic decompensation in diabetic man. J Clin Endocrinol Metab 50:131–136, 1980
6. Hostetter M: Perspectives in diabetes: Handicaps to host defense: Effects of hyperglycemia on C3 and candida albicans. Diabetes 39:271–275, 1990
7. MacRury SM, Genmell CG, Paterson KR, et al: Changes in phagocytic function with glycemic control in diabetic patients. J Clin Pathol 42:1143–1147, 1989
8. McMahon M, Bistrain BR: Host defenses and susceptibility to infection in patients with diabetes mellitus. Infect Dis Clin N Am 1–9, 1995
9. Pomposelli JJ, Baxter JK, Babineau TJ, et al: Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. JPEN 22:77–81, 1998
10. Wallace LK, Starr NJ, Leventhal MJ, et al: Hyperglycemia on ICU admission after CABG is associated with increased risk of mediastinitis or wound infection. Anesthesiology 85:1286, 1996
11. Ortmeyer J, Mohsenin V: Inhibition of phospholipase D and superoxide generation by glucose in diabetic neutrophils. Life Sci 59:255–262, 1996
12. Pinhas-Hamiel O, Dolan LM, Daniels SR, et al: Increased incidence of non-insulin-dependent diabetes mellitus among adolescents [see comments]. J Pediatr 128:608, 1996
13. Scott CR, Smith JM, Cradock MM, et al: Characteristics of youth-onset noninsulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus at diagnosis. Pediatrics 100:84, 1997
14. McMahon M, Rizza RA: Nutitional support in hospitalized patients with diabetes mellitus. Mayo Clin Proc 71:587–594, 1996
15. Brink SJ: Pediatric, adolescent, and young-adult nutrition issues in IDDM. Diabetes Care 11:192, 1988

OBESITY

Background

Obesity may be the most refractory health problem facing health practitioners who care for children. In the United States, up to 1 in 4 children fit the criteria of being obese; even worse, the prevalence of this diagnosis appears to be increasing.[1] Newly released growth charts from the National Center for Health Statistics (NCHS) have chosen to use data from earlier National Health and Nutrition Examination Surveys (NHANESs) for older children because of the increase in the average weight of children in the United States.[2]

The etiology of childhood obesity appears to be multifactorial.[3–7] At least 20 genes, loci, or chromosomal regions have been identified that may be important in creating the human obesity phenotype. Recent data in children have demonstrated high serum leptin concentrations in obese children, similar to what has been reported in obese adults.

Many studies have suggested that obese and normal weight children have similar caloric intake, implicating differences in metabolic rate as being important in the etiology of this condition. However, no consistent differences in resting energy expenditure have been found between obese and normal weight children. Some data exist that overweight children may have a decreased food-induced thermogenesis. Previous theories blaming abnormalities in adipocyte number have not been substantiated. There are some recent studies suggesting that while obese children have similar caloric intake to normal weight children, the composition of their diets may be different, with obese children eating more fat and less fiber. There are also a number of studies showing an association between childhood obesity and decreased energy expenditure during exercise.

Evidence

One recent study shows long-term benefit from behavioral, family-based treatment of childhood obesity in children ages 6 to 12 years.[8,9] Up to a 10-kg improvement in weight was demonstrated 10 years later when compared with controls. No role for SNS in the treatment of childhood obesity uncomplicated by intercurrent illness has been established.

No prospective, randomized studies exist to help the practitioner decide the optimal support for hospitalized, obese children requiring SNS. Although maintenance energy and protein may be adequate in critically ill, obese adults to prevent fat storage and allow for preservation of lean body mass,[10] similar studies have not been carried out in children.

Special Considerations

Because of concerns about energy restriction on growth and central nervous system development, SNS energy intake is not reduced in the obese hospitalized child requiring nutrition support.[11]

In patients with developmental delay, standard growth and energy requirements (eg, RDA) do not apply.[12] If EN is needed in such a patient, care must be taken to not overfeed the child (to avoid obesity). Typically, energy needs are two thirds of that of normally active children.

Practice Guidelines
Obesity

1. Obese children are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. Weight loss should not be a goal for the acutely ill, hospitalized obese child. (C)

3. SNS for the acutely ill, hospitalized child who is obese should be based on actual weight and not energy restricted. (C)

REFERENCES

1. Barlow SE, Dietz WH: Obesity evaluation and treatment: Expert committee recommendations. J Pediatr 102:e29, 1998
2. CDC Growth Charts: United States. Advance Data 314, 28 pp (PHS) 2000–1250
3. Klish WJ: Childhood obesity: Pathophysiology and treatment. Acta Paediatr Jpn 37:1–6, 1995
4. Bouchard C: Genetics of obesity: An update on molecular markers. Int J Obesity. 19:S310–S313, 1995
5. Hassink SG, Sheslow DV, de Lancey E, Opentanova I, Considine RV, Daro JG: Serum Leptin in children with obesity: Relationship to gender and development. Pediatrics 98:201–203, 1996
6. Gazzaniga JM, Burns TL: Relationship between diet composition and body fatness, with adjustment for resting energy expenditure and physical activity, in pre-adolescent children. Am J Clin Nutr 58:21–528, 1993
7. Kimm SYS: The role of dietary fiber in the development and treatment of childhood obesity. Pediatrics 96:1010–1014, 1995
8. Epstein LH, Valoski A, Eing RR, et al: Ten-year follow-up of behavioral, family-based treatment for obese children. JAMA 264:2519–2523, 1990
9. Epstein LH, Valoski A, McCurley J: Effect of weight loss by obese children on long-term growth. AJDC 147:1076–1080, 1993
10. Amato P, Keating KP, Quercia RA, et al: Formulaic methods of estimating caloric requirements in mechanically ventilated obese patients: a reappraisal. Nutr Clin Pract 10:229, 1995
11. Butte NF: Energy requirements. IN Nutritional Care During Infancy. Tsang RC, Lucas A, Uauy R, et al (eds). CV Mosby Co, St Louis, 1988, p 86
12. Spender QW, Crok CE, Charney EB, et al: Assessment of linear growth of children with cerebral palsy: Use of alternative measures to height or length. Dev Med Child Neurol. 31:2206–2214, 1989

HOME SPECIALIZED NUTRITION SUPPORT

Background

Indications for home SNS mirror those for hospitalized patients with the exception that the patient's clinical status has stabilized sufficiently to permit care in a the less acute home environment. With the transfer of technology into the home, patients are now being discharged who have more complex home care needs. Thus, before sending an infant, child or adolescent home, a critical evaluation of not only the nutritional requirements but of all the health care needs must be undertaken.

Often, nutrition needs must be integrated with other services to promote growth and development. Meeting all of the needs of children requiring high-tech support is often requires engagement of numerous health care services. Coordination of care requires innovative approaches to keep all health care workers informed of the child's status. A discharge plan should be initiated as soon as it is evident the child will recover and be sent home. Children discharged on home SNS must be physiologically stable, have caregivers who are willing and able to provide care, and have appropriate resources available including a safe home environment.

The establishment of interdisciplinary nutrition support teams has proven to be beneficial to hospitalized patients. Many home care organizations have extrapolated this concept into their practice.[1] Members of the home care team should include: parents or caregivers, pediatricians, case managers, nutrition case specialist, subspecialists, nurses, teachers, dietitians, pharmacists, and visiting nurses. Other individuals may include speech and occupational therapists and social workers. The team should develop a plan of care and disseminate it to all health care providers with updates as needed. Education of caregivers should begin in the hospital and carry over into the home. Written checklists ensure caregivers receive complete education. Repeat demonstrations of enteral and parenteral techniques help facilitate education and adaptation to care. Standards of care or guidelines have been established to reduce inappropriate variations in practice and to promote the delivery of high quality care.[2] The Joint Commission Accreditation of Healthcare Organizations (JCAHO) Standards for Home Care also assists home care organizations to develop high-quality care systems.[3]

Monitoring of growth, biochemical parameters, energy intake, macronutrients and micronutrient status, and gastrointestinal function should be undertaken to prevent complications. Complications can be categorized into four groups: mechanical, infectious, nutritional, and metabolic. Monitoring of SNS patients at home varies from program to program; there are no established national standards or evidence-based recommendations. Caregivers should monitor weight, fluid status, intake, and output on a daily basis, with temperature and urine glucose readings daily to weekly. Physical exam, weight, height, and head circumferences (if the child is less than 1 year of age) should be performed on a routine basis and plotted on growth curves. Published schedules of biochemical monitoring recommend electrolytes, BUN/creatinine, calcium, phosphorus, magnesium, acid–base status, visceral proteins, liver function tests, glucose, triglycerides and complete blood counts initially weekly to monthly with the frequency decreasing over time.[4,5] Iron studies, platelet, folate/vitamin B-12, and carnitine levels should be obtained as indicated. Trace element studies every 2 to 6 months and fat-soluble vitamin assessment every 6 to 12 months are appropriate.

Evidence

Providing SNS in the home has been demonstrated to be cost-effective. Additionally, children can gain weight and stature with both PN and EN.[6–11] In children receiving PN long term, improvements have been seen in neurologic and intellectual development 6 months after hospital discharge.[9] For children who require frequent rehospitalization, delays are seen in nonverbal performance, attention, and perceptual-motor abilities. These rehospitalizations may occur because of need for surgery because of the child's primary medical problem or catheter placement, cholestatic jaundice, catheter sepsis, and other significant infections.[10] Children who receive home EN and their caregivers have reported difficulties with sleep disturbances, mostly due to nocturia, vomiting and infusion pump monitoring and malfunction.[11] Although data are limited, numerous studies confirm that favorable outcomes may be achieved with long-term home PN

as measured by maintenance of growth and weight gain.[12]

Practice Guidelines
Home Specialized Nutrition Support

1. Children receiving home SNS are at nutrition risk and should undergo nutrition screening to identify those who require formal nutrition assessment with development of a nutrition care plan. (B)
2. SNS should be initiated for the indications appropriate to the underlying disease. (C)
3. Discharge planning and follow-up care for home SNS patients should be interdisciplinary. (C)
4. Education of caregivers for home SNS patients should begin before discharge and continue in the home care setting. (C)
5. SNS, in a home environment, should only be given if patients have caregivers who are willing and able to provide care, and have appropriate community resources to assure a safe environment. (B)
6. Routine monitoring of home SNS should be performed to prevent complications. (C)

REFERENCES

1. Nehme A: Nutritional support of the hospitalized patient. JAMA 243:1906–1908, 1980
2. A.S.P.E.N Board of Directors: Standards for home nutrition support. Nutr Clin Pract 14:151–162, 1999
3. Joint Commission on Accreditation for Healthcare Organization Board of Directors: 2000 Comprehensive Manual for Home Care. Oakbrook, IL, 1998, 1999
4. Davis AM. Pediatrics: IN Contemporary nutrition support practice: A clinical guide. Matarese LE, Gottschlich MM (eds): WB Saunders Company, Philadelphia, PA, 1998, pp 347–364
5. Ireton-Jones C, Orr M, Hennessy K: Clinical pathways in home nutrition support. J Am Diet Assoc 97:1003–1007, 1997
6. Greene HL, Helinek GL, Folk CC, et al: Nasogastric tube feeding at home: A method for adjunctive nutritional support of malnourished patients. Am J Clin Nutr 34:1131–1138, 1981
7. Bisset WM, Stapleford P, Long S, et al: Home parenteral nutrition in chronic intestinal failure. Arch Dis Child 67:109–114, 1992
8. Dahlstrom KA, Strandvik B, Kopple J, et al: Nutritional status in children receiving home parenteral nutrition. J Pediatr 107: 219–224, 1985
9. Ralston CW, O'Connor MJ, Ament M, et al: Somatic growth and developmental functioning in children receiving prolonged home total parenteral nutrition. J Pediatr 105:842–846, 1984
10. O'Connor MJ, Ralston CW, Ament ME: Intellectual and perceptual-motor performance of children receiving prolonged home total parenteral nutrition. Pediatrics 81:231–236, 1988
11. Holden CE, Puntis JWL, Charlton CPL, et al: Nasogastric feeding at home: Acceptability and safety. Arch Dis Child 66:148–151, 1991
12. Leonberg BL, Chuang E, Eicher P, et al: Long term growth and development in children after home parental nutrition. J Pediatr 132:461, 1998