Invited Review

Nutrition in Clinical Practice
Volume 24 Number 4
August/September 2009 470-480

10.1177/0884533609339072
http://ncp.sagepub.com
hosted at
http://online.sagepub.com

# Intradialytic Parenteral Nutrition and Intraperitoneal Nutrition

M. Patricia Fuhrman, MS, RD, LD, FADA, CNSD

*Financial disclosure: Dr Fuhrman is employed by DCRX Infusion.*

Intradialytic parenteral nutrition and intraperitoneal nutrition are methods to provide supplemental nutrition support to patients with chronic kidney disease (also referred to as end-stage renal disease) while they are receiving dialytic therapy. There has been considerable controversy over indications and benefits of intradialytic parenteral nutrition and intraperitoneal nutrition. A major stumbling block had been problematic reimbursement for the therapy under Medicare. Medicare Part D has alleviated some of the reimbursement obstacles and has increased interest in reexamining the benefits and burdens of supplemental nutrition support therapies for patients receiving dialysis. (*Nutr Clin Pract.* 2009;24:470-480)

**Keywords:** parenteral nutrition; parenteral nutrition, total; kidney failure, chronic

In 2002, approximately 308,861 people in the United States and 1.2 million people worldwide were receiving dialysis.[1] Thus, based on the 2002 numbers and an average growth rate of 6% per year, about 438,125 people received dialysis in the United States in 2008. It is estimated that approximately 40%-50% of patients on dialysis are malnourished, and 10% of these patients are severely malnourished.[2,3] In the United States, this translates to about 43,812 severely malnourished patients on dialysis.

Intradialytic parenteral nutrition (IDPN) and intraperitoneal nutrition (IPN), as interventions for improving nutrition status, have a checkered history of acceptance and use. Initially, there was enthusiasm for both as adjunct nutrient sources for dialysis patients. As the nutrition scientific community focused on using the gastrointestinal (GI) tract as an avenue for providing nutrition, and as the difficulties of receiving reimbursement through Medicare for IDPN and IPN escalated, interest waned. Now that reimbursement issues are less problematic and clinicians continue to struggle with the challenges of convincing dialysis patients to consistently consume oral nutrition supplements, interest in IDPN and IPN has been renewed. This article discusses prevalence and incidence of malnutrition in the dialysis patient population, indications and contraindication for IDPN and IPN, and the current state of Medicare reimbursement for these therapies.

From DCRX Infusion, Sunrise, Florida.

Address correspondence to: M. Patricia Fuhrman, RD, LD, FADA, CNSD, DCRX Infusion, 1932 Prospector Ridge Drive, Ballwin, MO 63011; e-mail: nutrisha50@earthlink.net.

## Malnutrition in Chronic Kidney Disease

Malnutrition, similar to its effect in other medical conditions, contributes to an increased risk of mortality and morbidity in patients receiving hemodialysis and peritoneal dialysis.[4,5] To assess nutrition status, serum albumin levels are often monitored as a nutrition indicator in this patient population. The Centers for Medicare and Medicaid's End-Stage Renal Disease (ESRD) Program Interpretive Guidance provides the most recent guidance related to the Conditions for Coverage for ESRD Facilities.[6] The Measures Assessment Tool (MAT) recommends a goal for serum albumin levels of ≥4 g/dL. An outcome-oriented plan must be developed and implemented for all patients experiencing nutrition-related problems with progress toward goals documented. In the event that progress does not occur, all factors affecting the lack of progress must be identified and documented.

Although the role of serum albumin levels in determining nutrition status continues to be debated,[7-11] it is clear that hypoalbuminemia is a prognostic indicator for an increased risk of mortality and morbidity. Results of published trials show that implementation of nutrition interventions in chronic kidney disease (CKD) patients increased serum albumin levels an average of 0.2 g/dL (range, 0.1-0.3 g/dL).[12] The potential impact of changes in albumin levels on outcome risks and treatment costs in an existing patient database (n = 77,205) were analyzed by Lacson and colleagues.[12] A serum albumin level <3.5 g/dL was associated with a 2-fold increase in the risk of hospitalization and death compared with a serum albumin level of 4 g/dL ($P < .001$). It was also suggested that increasing the serum albumin concentration by ≥0.2 g/dL

**Table 1.** Factors That Contribute to Malnutrition in Patients With Chronic Kidney Disease[13-16]

| |
|---|
| Cultural factors |
| Depression |
| Gastrointestinal symptoms |
| Gastroparesis |
| Inadequate dialysis |
| Inadequate oral intake |
| Increased energy requirements |
| Increased nutrient losses |
| Inflammation |
| Lack of assistance with shopping and cooking |
| Malabsorption |
| Medications (interactions, side-effects, and pill burden) |
| Metabolic acidosis |
| Nutrient losses during dialysis |
| Poor understanding of the diet modifications |
| Restricted food and fluid intake |
| Sleep deprivation |
| Socioeconomic factors |
| Uremia |

reduced mortality rate, hospitalizations, and treatment costs. In economic terms, the potential benefit of increasing albumin levels in patients living in the United States receiving dialysis was hypothesized to save ~1400 lives, avoid ~6000 hospitalizations, and save ~$36 million for Medicare because of a decrease in ~20,000 hospital days.

A multitude of factors can affect the nutrition status of patients with CKD. Uremia contributes to decreased appetite and nausea.[13-15] Deranged metabolism attributable to kidney failure, chronic metabolic acidosis, and other comorbid diseases such as diabetes mellitus affects the assimilation and utilization of nutrients.[13,14] Socioeconomic and cultural factors can influence food procurement, preferences, and tolerance as well as result in disparities in healthcare access and linguistic challenges in communication that can hinder effective education.[14,16]

In addition to impaired intake and tolerance of foods, considerable nutrient losses from the dialysis process itself can occur. Patients undergoing hemodialysis can lose 10-12 g of protein per dialysis session as well as water-soluble vitamins and trace elements.[17-19] Likewise, peritoneal dialysis patients can lose 5-15 g of protein per day.[20] Because of the severe restrictions imposed by the renal diet, including fruits, vegetables, dairy, and fluids, patient compliance with the diet can also lead to challenges. When oral liquid supplements are used in an effort to increase oral nutrient intake, *taste fatigue* can develop, reducing patient acceptance and consumption. Oral supplements are frequently discontinued for economic reasons. Increased nutrient losses and decreased intake work in tandem to produce negative energy, protein, and micronutrient balances. Table 1 provides a list of factors that can contribute to malnutrition in patients with CKD.

Inflammation is thought to play an integral role in the development of malnutrition in the dialysis patient. Inflammatory mediators contribute to the reprioritization of hepatic protein synthesis with increased cytokines and positive acute phase proteins, and decreased negative acute phase proteins.[7-11] The resting metabolic rate is also reportedly increased by 13% in dialysis patients with infections.[21] Protein catabolism, lipolysis, and anorexia are additional consequences related to inflammation. Obesity can contribute to the inflammatory state of the patient with CKD.[22] A C-reactive protein (CRP) level >3 mg/dL (<1 mg/dL = low risk; 1-3 mg/dL = average risk; and >3 mg/dL = high risk of cardiovascular disease [CVD]) was noted to be 2.5 times higher in patients on dialysis with a body mass index (BMI) ≥30 kg/m$^2$ compared with <25 kg/m$^2$.[22]

The cytokine interleukin-6 (IL-6) is a primary mediator of increased CRP, amyloid A, and fibrinogen levels that also decreases serum albumin levels.[23] Of note, elevated positive acute phase proteins and subclinical infections were observed in 25%-50% of patients with CKD.[21] Elevated CRP levels are also associated with an increased risk of CVD,[23,24] which is of concern given that approximately 50%-60% of patients with CKD die from CVD.[24] Qureshi and colleagues[24] reported that patients without inflammation, malnutrition, or CVD had a 0% mortality rate over a 36-month period; comparatively, patients exhibiting all 3 characteristics at baseline had a 75% mortality rate after 36 months. Honda et al[23] investigated whether biomarkers could be used to predict malnutrition, mortality, and CVD in patients on hemodialysis. The best predictors of malnutrition were IL-6 and CRP; the best predictor of CVD was IL-6; and albumin and IL-6 were noted to be the best predictors of mortality. The authors proposed that IL-6 may be the most reliable predictor of CVD and death in the dialysis population.[23]

The trilogy of malnutrition, inflammation, and CVD has been called malnutrition-inflammation atherosclerosis and malnutrition-inflammation complex syndrome.[25] Ikizler and associates[26] found that CRP, as the marker of inflammation, and bioelectrical impedance (BIA), as the marker of nutrition status, were independent predictors of incidence of hospitalization in patients with CKD. Together, the 2 markers produced an additive effect. However, the caveat to using BIA to assess body composition in CKD patients is the lack of specific equations in the BIA equipment for this patient population.

A malnutrition inflammation score (MIS) has been developed using subjective global assessment (SGA), BMI, serum albumin level, and total iron binding capacity (TIBC).[25,27] The MIS has 10 components that are scored based on 4 levels of severity from 0 (normal) to 3 (very severe).[25] A study that included 378 CKD patients (53%

male, 47% Hispanic, 55% diabetic) correlated MIS with CRP, IL-6, tumor necrosis factor, albumin, transthyretin, TIBC, creatinine, cholesterol, and normalized protein catabolic rate (nPCR).[25] MIS, CRP, and IL-6 correlated with the greatest relative risk of death and hospitalization. The authors suggested that MIS could be used to stratify a patient's risk of mortality and morbidity in place of the more expensive laboratory tests of CRP and IL-6. Ho and colleagues[27] investigated the cutoff points for probability of death based on MIS. They found that an MIS score of 3, 4, or 5 was associated with a 10%, 40%, or 80% probability of death within a year, respectively. The authors noted that an MIS >4 was associated with a significant risk of mortality. Afsar and colleagues[28] evaluated the use of MIS in 50 peritoneal dialysis patients; MIS was positively correlated with peritonitis, hospitalizations, erythropoietin requirements, and levels of CRP and ferritin. Negative correlations were observed with mid-arm muscle circumference and serum albumin, transthyretin, creatinine, hemoglobin, transferrin, and cholesterol levels.

It is clear that nutrition assessment involves evaluation of multiple subjective and objective data. The need to identify optimal parameters that accurately distinguish between malnutrition vs inflammation continues. This is of importance in order to select the nutrition intervention(s) that will effectively facilitate nutrition repletion.

## Intensive Nutrition Counseling and Diet Supplementation

Intensive nutrition counseling aimed at increasing the nutrient density of dietary intake is the first step when oral nutrient ingestion is insufficient. Studies have shown positive effects when patients consume oral nutrition supplements during dialysis or between dialysis sessions.[29-32] Consistent intake and an adequate nutrition intervention period are needed to achieve effective nutrition supplementation. In general, a minimum of 3-4 months may be required. The challenge lies in motivating the patient to continue ingestion of oral supplements (whether homemade or commercially prepared and purchased) given the limited time the registered dietitian has available for coaching the patient and family. Negative comments made by staff and other dialysis patients about recommended supplements can often be counterproductive. Additional barriers to intensive nutrition counseling for clinicians are time, staffing, and reimbursement issues. Barriers to success for patients are intolerance, lack of compliance, fluid restrictions, cost of the supplement, and lack of ongoing intensive counseling and encouragement.

Caglar and colleagues[29] examined the effects of oral nutrition supplement intervention in chronic dialysis patients (n = 85); patients served as their own controls. During a 3-month baseline period, the patients received intensive nutrition counseling. During the 6-month intervention period, the patients were given an oral supplement containing 475 kcal and 16.6 g of protein in 237 mL during each dialysis session. Nutrition intervention resulted in increases in serum albumin and transthyretin levels and SGA scores for patients consuming the supplement as directed. Twenty percent (n = 17) of the patients refused the oral supplement altogether; 11.7% (n = 10) of patients were considered noncompliant because of poor consumption (<75% of the supplement). The study was not randomized and not placebo-controlled.

In a metabolic study, Veeneman et al[30] investigated the impact of an oral supplement, containing yogurt, cream, and protein-enriched milk powder that provided 386 kcal/h, on protein metabolism in 12 patients undergoing dialysis. The supplement was given every 30 minutes over a 3-hour period. On the nondialysis day, the patients fasted in the morning and were given 6 small meals of the supplement in the afternoon. Patients were also studied during 2 dialysis sessions separated by 1 week—one of the sessions required the patients to fast and the other session required the patients to consume 6 small meals of the supplement. Whole-body protein metabolism was measured by constant infusion of L-[1-$^{13}$C] valine. Three patients agreed to consume the supplement on both the dialysis and nondialysis days. Nine of the 12 patients objected to fasting and would not participate in both protocols: 6 consumed the supplement only on a nondialysis day and 3 patients participated only during dialysis. The nondialysis day protocol results showed that the change from fasting to feeding resulted in a transition from a negative protein balance to a positive protein balance. Dialysis contributed to a worse negative protein balance during fasting than the fasted state on the nondialysis day. The oral supplement consumed during dialysis resulted in a positive whole-body protein balance comparable to the results of feeding during the nondialysis day.[30] Because of the extremely small number of patients participating in the full study, the benefits of consuming this type of oral supplement to improve protein metabolism is difficult to determine. In addition, because this study was a 1-day snapshot of supplementation, it did not address the compliance issue of consistent supplementation and the clinical effects of long-term oral supplementation.

In another study, various oral nutrition supplements (average 600 kcal and 30 g protein per day) were provided prospectively to 56 malnourished patients receiving dialysis over a 1-year period.[31] Subjects were to consume supplements daily. During each dialysis session, subjects were asked to quantify their supplement consumption. Compliant patients (54%; n = 30) improved serum albumin and transthyretin levels and dry body weight. Noncompliant patients (46%; n = 26), defined as those who consumed <50% of the prescribed nutrition supplement, did not demonstrate significant changes in measured parameters.

**Table 2.** Examples of Intradialytic Parenteral Nutrition (IDPN) Formulations[35-38]

| | Amino Acids, Initial Concentration, % (Volume, mL) | Dextrose, Initial Concentration, % (Volume, mL) [Absolute Value, g] | Kcal/Protein, g | Volume, mL |
|---|---|---|---|---|
| Low protein/low dextrose | 10 (500) | 50 (150) [75] | 455/50 | 750 |
| Moderate protein/moderate dextrose | 15 (500) | 50 (250) [125] | 725/75 | 750 |
| High protein/high dextrose | 20 (500) | 70 (250) [175] | 995/100 | 750 |
| High protein/low dextrose | 20 (500) | 70 (100) [70] | 638/100 | 600 |
| High protein/very low dextrose | 20 (500) | 70 (65) [45] | 553/100 | 565 |

20% lipid emulsion can be added to any of the solutions to increase total kcal and final volume: 50 mL = 100 kcal (25 g of lipid); 75 mL = 150 kcal (37.5 g of lipid); 100 mL = 200 kcal (50 g of lipid), 150 mL = 300 kcal (75 g lipid).

If oral diet is not successful at increasing nutrient intake, the clinician may consider tube feeding. Nocturnal tube feeding enables the patient to eat during the day and continue normal activities while receiving nutrition supplementation at night. The amount to infuse every night can be based on oral intake during the day. However, tolerance of tube feeding is plagued by many of the same issues that impair oral intake: nausea, vomiting, gastroparesis, fluid restriction, and depression. Tube feeding is infrequently used in the dialysis population because of patient refusal and intolerance.

A meta-analysis and systematic review by Stratton and colleagues[32] looked at 18 studies in which CKD patients on dialysis received oral nutrition supplementation or tube feedings. Of the 541 patients, some were malnourished and others were well nourished; the patients were in various clinical settings. The review demonstrated that oral nutrition supplementation and tube feeding improved serum albumin levels by 0.23 g/dL, but there were insufficient data to demonstrate improved clinical outcomes. Variations in study design, intervention period, and outcome measurements make it difficult to determine benefits of enteral supplementation across studies. It appears that the greatest challenge is finding an oral diet regimen that meets the patients' needs and can be maintained over time.

## Intradialytic Parenteral Nutrition

Intradialytic parenteral nutrition (IDPN) should not be considered until after attempts at intensive nutrition counseling including oral or tube feeding supplementation have been unsuccessful.[33,34] IDPN alone is insufficient to meet the estimated energy, protein, and micronutrient requirements of the patient, but it does enable the clinician to provide a consistent amount of energy and protein with each dialysis session as a supplement to the patient's oral or tube feeding intake. IDPN can provide 500-1000 kcal and 50-100 g of protein in ≤1 L of volume per dialysis treatment.[35-38] However, approximately 10% of infused amino acids are lost in the dialysate.[39] The formula can be customized to meet the needs of each patient. Table 2 provides examples of IDPN formulas.

Clinical criteria used to select patients for IDPN include signs and symptoms of malnutrition. A combination of any 3 of the bullet points below in conjunction with a failed attempt to increase oral intake and/or an intolerance or nonacceptance of tube feeding suggests the need to consider IDPN.[33,36,40] The original SGA tool scored nutrition status as A (well-nourished), B (mild to moderately malnourished), or C (severely malnourished).[41] The tool has been expanded for patients with CKD to a 7-point scale: 6 or 7 (very mild nutrition risk to well nourished), 3, 4, or 5 (mild to moderately malnourished), and 1 or 2 (severely malnourished).[33]

- SGA indicating severe malnutrition, "C"[41] or "1 or 2"[33]
- Serum creatinine <8.0 mg/dL (3-month rolling average)
- Weight loss: 10% ideal body weight (IBW) or 20% usual body weight
- Weight <90% IBW
- Triceps skinfold values <6 mm (males) and <12 mm (females)
- Serum albumin ≤3.4 g/dL (3-month rolling average)
- Clinical examination consistent with moderate to severe malnutrition
- Protein catabolic rate <0.8 g/kg/d
- Diet history of protein <0.8 g/kg and <25 kcal/kg

According to the 2000 National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI), IDPN may be beneficial in patients who are malnourished or unable to consume adequate energy and protein to meet nutrient requirements, who are unable to tolerate oral feedings or tube feedings, and who are able to meet

their needs with the combination of oral diet or tube feeding plus IDPN.[33] If the combination of oral diet or tube feeding plus IDPN is insufficient to meet assessed nutrient needs, then parenteral nutrition (PN) should be considered to meet all or a portion of the nutrient requirements.[33] It is not known how many patients on dialysis are receiving IDPN, but at a minimum the estimated 10% of dialysis patients who are severely malnourished[2,3] meet the criteria for IDPN.

## Administration and Management of IDPN

IDPN is ordered and monitored by a nephrologist in collaboration with the dialysis unit's dietitian and nursing staff. Companies providing the IDPN product may also provide clinical expertise to assist the dialysis unit staff in selecting an IDPN formulation and troubleshooting administration challenges. Components of IDPN formulations generally include dextrose and amino acids with or without lipids. Vitamins and trace elements are not routinely added to IDPN because the additives can readily be lost in the dialysate. However, vitamins can be added during the last 30 minutes of the IDPN cycle for patients who do not tolerate oral multivitamin preparations.[37]

IDPN does not require additional intravenous access because the solution is infused through the venous drip chamber of the hemodialysis machine. Additional fluid provided in IDPN can be removed by ultrafiltration, thereby reducing the risk of volume overload. An additional benefit of using IDPN is that patient noncompliance with oral nutrition supplementation is bypassed as an obstacle to supplementing energy and protein nutriture.

## IDPN Formulations

### *Amino Acids*

As with all PN formulations given to patients with CKD, IDPN should provide an amino acid formulation that contains both essential and nonessential amino acids. The amount of amino acids that can be given will depend on the total volume to be infused. However, a 20% amino acid solution enables the clinician to provide 100 g of protein in 500 mL; the goal is generally to provide 1.2-1.4 g/kg of protein per dialysis session.[37]

### *Dextrose*

Glycemic control is a major concern with the use of IDPN. Serum glucose levels have been noted to increase by 20-100 mg/dL in patients without a diagnosis of diabetes an hour into the IDPN infusion.[42] Another study that did not include patients diagnosed with diabetes reported a maximum glucose level of 214 ± 38 mg/dL[43]; however, serum glucose levels 2 hours after dialysis were <120 mg/dL. The change in serum triglyceride levels was nonsignificant from predialysis to postdialysis measurements (89 ± 31 mg/dL and 108 ± 39 mg/dL, respectively). Patients with diabetes mellitus or insulin resistance may require insulin in the IDPN bag as well as subcutaneous insulin injections on a sliding scale. Peripheral glucose levels should be checked prior to starting IDPN and at least once during infusion with insulin given as needed. Because data concerning tight glycemic control for improved outcomes have come from studies of critically ill patients,[44] the ideal glucose level is unknown during an acute elevation of serum glucose levels, as occurs with IDPN infusion. The conventional guideline for adding insulin to PN for patients with diabetes is 0.1 unit of insulin per gram of dextrose.[34] However, because insulin action can be prolonged in the patient with renal failure, adding 5-8 units of insulin per liter of IDPN when serum glucose concentrations approach 300 mg/dL has been suggested.[36,38] If the patient receives insulin during IDPN, it is important to monitor the patient for potential hypoglycemia after IDPN is discontinued. If possible, provide a 15-g carbohydrate snack during the last half hour of IDPN.[37]

Another concern with dextrose amount infused with IDPN is the risk of refeeding syndrome. Patients who become severely malnourished are at greatest risk and should be monitored closely for a precipitous drop in serum potassium, phosphorus, and magnesium levels; an increase in serum glucose levels; and fluid retention.[45] The initial IDPN infusions should be tapered in rate based on the patient's metabolic response to the therapy. The current trend is to provide less than 100-g dextrose in an IDPN solution to reduce glucose fluctuations.

### *Lipids*

Hyperlipidemia and adverse reaction to lipids during IDPN infusion can be problematic in the hemodialysis patient. Serum triglyceride levels should be monitored prior to the first infusion and again 6-24 hours after the first infusion to determine adequacy of lipid clearance. A serum triglyceride level >250 mg/dL 6 hours after infusion or >400 mg/dL during infusion indicates poor lipid clearance.[34] Lipids should not be given to patients with egg or soy allergy. Lipids are also associated with thrombocytopenia and hepatic abnormalities, and should be used cautiously in the dialysis population.[38] The signs and symptoms associated with lipid intolerance include nausea, vomiting, headache, dizziness, fever, flushing, drowsiness, chest and back pain, pressure over an eye, and erythema at the infusion site.[36] It can be difficult to differentiate whether the symptoms are caused by the lipids, an underlying disease, or the dialysis process. Some clinicians will defer addition of lipids in IDPN for the first

week of therapy in order to determine overall tolerance to PN without the confounding factor of lipid intolerance. The lipid solutions available in the United States contain polyunsaturated fatty acids that are associated with the stimulation of inflammatory cytokines.[46] The specific effect of lipids on patients receiving IDPN is not well studied. Some clinicians prefer to forgo lipids altogether to reduce the risk of potential lipid-related complications.

## Therapeutic Effectiveness of IDPN

Short-term (2-3 dialysis sessions), small (6-8 subjects), cross-over studies with IDPN in well-nourished patients on dialysis have focused on amino acid uptake and protein homeostasis.[42,47-49] A finding from one of these studies was the positive impact of IDPN on the fractional synthetic rate of albumin.[47] In a series of studies, the authors found that IDPN plus exercise resulted in a 2-fold increase in amino acid uptake[48]; IDPN, exercise, and growth hormone reduced amino acid losses and produced an anabolic effect with a 22% increase in protein homeostasis over IDPN and exercise alone.[49] However, extrapolation of these outcomes to malnourished patients receiving chronic IDPN therapy is challenging. Although some dialysis units may offer opportunities to exercise during dialysis, the more debilitated, malnourished patient is less likely to have the strength and endurance to participate.

Studies have compared oral nutrition supplementation with IDPN and found similar outcomes regardless of the source of supplementation.[5,42,50] Pupim et al[42] performed metabolic studies before, during, and after hemodialysis in 8 patients with CKD under 3 separate conditions: (1) receiving IDPN, (2) receiving oral supplementation, and (3) receiving no nutrition intervention (control). The oral and IDPN supplementation resulted in a highly positive whole-body net protein balance. When patients received no intervention, they had a neutral balance. The anabolic effects of the oral supplementation persisted after intradialytic nutrition therapy whereas the anabolic effects of IDPN decreased to levels similar to the control condition. This study was performed in a research center and not continued over time to test compliance and tolerance of the oral supplement. Moreover, the oral nutrient supplement and IDPN were not identical in nutrient distribution.

Cano et al[50] conducted a prospective, randomized study with 186 patients, comparing an oral supplement alone to an oral supplement plus IDPN over 1 year. Outcomes were monitored for an additional year. Consumption of the oral nutrition supplement (500 kcal and 25 g of protein per day) was not restricted to dialysis sessions. IDPN was not standardized among the patients. Both groups had improved BMI, albumin, and transthyretin levels; reduced 2-year mortality; decreased number of hospitalizations; and improved well-being determined by Karnofsky score compared with baseline prior to the intervention. The authors did not find an additive benefit of giving IDPN with oral supplements. Compliance with oral supplements ranged from 61% to 75%. No data on total energy and protein intake were provided, so it is difficult to determine how IDPN and oral supplements affected overall nutrient intake. This study suggested that if patients consistently consume oral supplements, outcomes will improve, and IDPN should be reserved for patients who cannot tolerate or comply with the intake of oral supplements.

IDPN has been reported to improve weight, appetite, serum albumin levels, and survival in malnourished hemodialysis patients.[5,43,50-54] Many studies used serum albumin level as the primary outcome, thereby making it difficult to differentiate the role of nutrition vs inflammation.[43,51-53,55] However, as stated earlier, increasing the serum albumin level has been associated with improved prognosis for patients with CKD, and providing protein substrate in IDPN may be a facet of overall care to combat inflammation and its adverse effects on patient outcomes.[8]

A retrospective, intent-to-treat study examined the differences between patients who received IDPN and patients who did not receive IDPN over a 1-year period.[14] The patient selection criteria for IDPN and duration of IDPN were not available. The authors stated that most IDPN patients received 15 kcal/kg and 1.2 g/kg of protein at each dialysis session. The risk of death was decreased in patients with a serum albumin level <3.4 g/dL who received IDPN. The association was stronger as the serum creatinine concentration decreased. Serum levels of albumin ≤3 g/dL and creatinine ≤8 mg/dL resulted in an odds ratio (OR) of 0.63 in the group treated with IDPN ($P <$ .01). The study also found that providing IDPN to patients with normal serum albumin levels was associated with an increased risk of mortality (ie, IDPN group: albumin ≥4 g/dL and creatinine >8 mg/dL; OR 2.6, confidence interval (CI) 1.24 and 5.04, $P <$ .005; control group: CI 1.0). The survival disadvantage with IDPN in patients with a normal serum albumin level could be related to the risks outweighing the benefits when nutrition status is adequate or the differences could be related to selection bias.[14] Several potential explanations for the benefit of IDPN seen in patients with a serum albumin level <3.4 mg/dL were postulated by the authors: (1) IDPN provided the energy and protein to treat malnutrition; (2) a placebo-effect occurred (but why did it not have the same effect on the patients with high serum albumin levels?); and (3) the timing of IDPN coincided with recovery from an acute reversible clinical event (however, most of the patients had hypoalbuminemia >9 months prior to initiation of therapy).

In a nonrandomized, retrospective study, Capelli and colleagues[5] examined the effects of IDPN for an average

of 9 months (followed for 24 months) in 81 patients. Patients (n = 50) received IDPN if they had a serum albumin level <3.5 g/dL plus either <10% IBW or 10% weight loss for 2 consecutive months. Furthermore, nutrition counseling or oral supplements were not successful in improving nutrition status for the 2 months prior to the study. The control group (n = 31) had a serum albumin level <3.5 g/dL but did not meet the weight loss criteria. Forty-one percent (n = 33) of the patients were diabetic and 20 of these patients were in the IDPN group. The diabetic patients received approximately 670 kcal per dialysis treatment, and the patients who were not diabetic received an average of 725 kcal per dialysis treatment. Patients who received IDPN had a significantly improved survival rate (64%) over those who did not receive IDPN (52%; $P < .01$). There was no difference in survival rate between patients with and those without diabetes. However, IDPN patients without diabetes had the lowest mortality rate. Serum albumin levels increased in both groups. IDPN increased serum albumin levels by 12% in survivors. Body weight significantly increased by 5.5-11.8 kg in the IDPN group ($P < .01$), whereas the untreated group lost weight. Potential selection bias and intensive counseling of the control group could have affected the results. The authors noted that changes in serum albumin level and body weight required >4 months of IDPN. Another nonrandomized study in elderly patients (n = 28) also reported positive results that required 3 months for biochemical (albumin, transthyretin, total lymphocyte count, and amino acid concentrations) changes and 6 months for anthropometric (triceps skinfold thickness, mid-arm muscle circumference, dry weight, and body mass index) improvements.[43]

Joannidis et al[56] compared patients with malnutrition-inflammation complex syndrome (n = 6) receiving IDPN and well-nourished controls (n = 6) not receiving IDPN who were matched for age, gender, BMI, and comorbidities. IDPN significantly ($P = .03$) increased the dry weight of the intervention group (61.7 ± 7.7 to 63.9 ± 8.9 kg), whereas the weights of the control group did not change (66.3 ± 10.5 to 66.3 ± 10.6 kg, $P > .05$). Malnourished patients had higher serum levels of tumor necrosis factor throughout the study vs controls, although levels did not increase with IDPN. There was no difference between patient groups throughout the study with regard to serum levels of albumin, IL-6, CRP, soluble IL-2 receptor, and adipocytokines. Atherogenic factors (total cholesterol, low-density lipoproteins, and high-density lipoproteins) did not significantly differ between the control group and the IDPN group during the study period. Serum glucose levels were not reported. The authors concluded that 6 months of IDPN was effective at improving weight status without the risk of worsening the inflammatory process or contributing to the patient's risk of atherosclerosis; however, long-term studies are needed to identify the relationship of these laboratory changes to inflammation, CVD, and mortality.

Several studies have investigated the use of IDPN in children and adolescents, but the small numbers of subjects make it difficult to extrapolate or interpret the results.[54,57] Krause and colleagues[54] studied 4 patients ages 4-18 years over a 1-year period. IDPN was given during each dialysis session over 7-12 weeks and oral diet intake was monitored with a 3-day diet history. Oral intake and weight increased after the IDPN-treatment period. Another study looked at biochemical markers in 9 adolescent patients on dialysis receiving IDPN over 3-22 months.[57] An interesting finding of the study was that patients with a psychosocial etiology of malnutrition did not respond to IDPN therapy. It is doubtful that the adolescents with psychosocial issues consumed an adequate diet in conjunction with the IDPN to meet total nutrient needs. The authors also found nPCR to be a more reliable indicator of nutrition status than serum albumin level. Both studies reported minimal side effects of IDPN. A review of nutrition status in children requiring hemodialysis concluded that optimizing the outcomes of hemodialysis in children requires both adequate dialysis and nutrition.[58] Ideally, malnutrition should be prevented, but in the event that it does occur, it is imperative to identify and aggressively treat malnutrition with intensive nutrition counseling, oral nutrition supplements, and/or IDPN.

## Intraperitoneal Nutrition

Peritoneal dialysis removes waste products from the body with a hyperosmolar glucose-based dialysate using the peritoneal membrane as a filter. IPN replaces a portion of the glucose dialysate with amino acids for 1 or 2 exchanges per day. Each bag of IPN can provide 20-40 g of amino acids to counter the loss of 5-15 g of amino acids per day through the peritoneal membrane.[20,59-63] IPN can be accomplished by (1) providing a bag of amino acids without glucose in place of 1 or 2 standard dialysate bags; (2) removing some of the glucose from a standard dialysate bag and inserting the prescribed volume of amino acids into the bag; or (3) combining amino acids and glucose throughout all dialysis exchanges. Option 3 is used in Europe.[63]

The substitution of a solution containing amino acids for 1-2 standard glucose exchanges per day can reduce the absorption of excess energy from the glucose dialysate as well as decrease hypertriglyceridemia and hyperglycemia in patients with diabetes mellitus and insulin resistance. According to the KDOQI guidelines, IPN is indicated for patients who are malnourished and consume inadequate energy and protein intake, cannot tolerate adequate oral diet or tube feeding to meet estimated needs, can meet their needs with the combination of IPN

**Table 3.** Examples of Intraperitoneal Nutrition Formulations[64-67]

| Amino Acid, % | Protein, g | Fill Volume, L | mOsm, L | Equivalent Dialysate |
|---|---|---|---|---|
| 1 | 20 | 2 | 411-412 | 1.5% dextrose |
| 1 | 25 | 2.5 | 411-412 | 1.5% dextrose |
| 1 | 30 | 3 | 411-412 | 1.5% dextrose |
| 1.5 | 30 | 2 | 445 | 2.5% dextrose |
| 1.5 | 37.5 | 2.5 | 445 | 2.5% dextrose |
| 2 | 40 | 2 | 478 | 4.25% dextrose |

pH ranges from 5.2 to 5.25. Fill volume can vary according to the patient's intraperitoneal nutrition prescription. Reprinted with permission from DCRX Infusion, Sunrise, Florida.

plus oral diet or tube feeding, and have difficulty with glycemic and lipid control related to the carbohydrate content of the dialysate.[33]

## Formulas and Administration of IPN

Amino acid solutions of 1%-2% wt/vol have been used for IPN.[59-67] The amino acids provide supplemental protein and act as an osmotic gradient along with the glucose during peritoneal dialysis. Table 3 provides a list of IPN solutions and the equivalent peritoneal solution for different amounts of added amino acids.

IPN, performed by the patient or caregiver in the home, can be incorporated into manual and automated peritoneal dialysis modalities. It is important for the patient and caregiver to be trained in aseptic technique when handling all peritoneal solutions to reduce the risk of peritonitis. In the U.S., IPN generally is the last dwell of the cycle or day and is left in the abdominal cavity 4-6 hours. A longer dwell time could result in some of the infused amino acids crossing back into the peritoneal cavity and being lost when the waste product–containing dialysate is removed. The patient's peritoneal transport rate will also influence the absorption and retention of infused amino acids.[68]

## Effectiveness of IPN

Various short-term studies (<3 months) with small numbers of subjects (12-105) have shown improvement in nitrogen balance,[61,66] anthropometric measurements,[60,62,66] serum lipid levels,[66,67] serum albumin levels,[60,62,64] nPCR,[62] protein synthesis,[61,63,65] and anabolic response with IPN.[59-61] Taylor and colleagues[62] conducted a retrospective study of 22 IPN patients with an initial serum albumin concentration <3.5 g/dL. IPN was provided an average of 13.6 months (range, 6-26 months). Significant increases were seen in the serum albumin level from 2.25 ± 0.097g/dL (range, 1.4-3.3 g/dL) to 2.57± 0.12 g/dL (range, 1.6-3.5 g/dL) ($P$ = .0036) and nPCR from 0.898 ± 0.053 g/kg/d to 1.085 ± 0.056 g/kg/d ($P$ = .0057). Weight increases did not reach statistical significance. One episode of peritonitis occurred on average for every 23 treatment months. The low rate of peritonitis and absence of reported adverse effects led the authors to conclude that IPN was safe and effective during extended treatment. A reduction in serum phosphorus and potassium levels has also been reported with IPN.[60]

Although amino acids are lost via the peritoneal cavity, replacement of 1 glucose exchange with an amino acid solution has been shown to result in a net gain of amino acids (absorption greater than losses) over 24 hours.[59-63] However, substituting >1 amino acid-containing solution for peritoneal dialysis may increase the risk of metabolic acidosis, which could increase protein catabolism in patients with CKD.[60] As with IDPN, it may take several months of IPN to replete the nutrition state of a malnourished patient.

**Table 4.** Parameters for Monitoring Outcomes of Intradialytic Parenteral Nutrition and Intraperitoneal Nutrition Interventions[16,35-37]

- Appetite changes
- Body mass index
- Diet history/food consumption
- Karnofsky score
- Laboratory values
  - Albumin
  - Blood urea nitrogen
  - C-reactive protein
  - Creatinine
  - Glucose
  - Interleukin-6
  - Triglycerides
- Malnutrition inflammation score
- Mid-arm muscle circumference
- Normalized protein catabolic rate
- Quality of life
- Subjective global assessment
- Triceps skinfold measurements
- Weight changes

## Monitoring Outcomes

As stated earlier, serum albumin level is a commonly used outcome monitor for the effectiveness of IDPN and IPN. Although this parameter is not nutrition-specific, it does have prognostic implications for mortality and morbidity.[8,12] The absence of a specific indicator of nutrition status makes it difficult to differentiate the changes in parameters attributable to nutrition intervention from changes induced by inflammation, disease processes, and overall health status. Table 4 provides a list of parameters that can be used

to monitor outcomes of IDPN and IPN therapy. Until a definitive nutrition measurement is identified, clinicians will have to rely on the combination of several laboratory and clinical parameters to determine the indications for and the effectiveness of nutrition interventions.

A lack of perceived improvement in the patient's nutrition status must be evaluated in terms of other factors that could affect the outcome parameters. Stopping IDPN or IPN in a patient with a nutrient intake deficit based on the patient's lack of improvement in serum albumin level can create a greater energy and protein deficit. Clinicians must consider the benefits of preventing nutritional and physical decline when weighing the benefits and burdens of nutrition therapy in a patient. The ultimate goal of therapy is to improve the well-being of the patient and enable the patient to eventually resume an adequate oral diet.

## Caveats of the Research

There is a need for more definitive research in this area of nutrition therapy. Many of the studies are small, short-term, uncontrolled, nonrandomized, retrospective, or observational. Study designs and patient populations are not uniform across studies for comparability.[14] Outcomes are measured in laboratory changes and weight changes, which can be affected by disease process, fluid status, and inflammatory mediators. Often, the total nutrient intake from oral diet and/or IDPN and IPN is not quantified. A major drawback to performing studies in this population is that it could take a year with >1300 patients per group to achieve a measurable treatment effect with a power of 80%.[50] Data are not available on the success of patients in maintaining nutrition status orally after discontinuation of IDPN and IPN. More research is needed to determine the effect of IDPN and IPN on not only mortality and morbidity but also quality of life.

## Reimbursement

Clinical criteria for starting IDPN and IPN should not be confused with reimbursement criteria. Historically, IDPN and IPN were evaluated under Medicare Part B, which requires documentation in the medical record of a permanent dysfunctional or nonfunctional gastrointestinal tract for financial coverage.[69,70] Patients had to demonstrate severe malabsorption that prevented "maintenance of weight and strength commensurate with the patient's overall health status."[71] This was almost impossible because the purpose of IDPN and IPN is to provide supplemental nutrient intake in addition to oral diet, thereby disqualifying the therapy. The frustrations over obtaining coverage under Medicare Part B made many clinicians wary of recommending IDPN and IPN for their patients who may have benefited from the therapies.

Medicare Part D has changed the criteria by which IDPN and IPN are covered under Medicare.[69,70] IDPN and IPN are on the formulary for coverage, although preauthorization is required. Medicare Part D will reimburse for IDPN and IPN if the patient has a serum albumin level of ≤3.4 g/dL (3-month average) *OR* has had a >5% weight loss over 3 months *AND* there has been an attempt to increase albumin or weight with an oral nutrition supplement and intensive nutrition counseling.

Despite coverage by Medicare Part D, there are still issues with reimbursement. Patients pay a premium that varies according to the plan selected, and each patient pays a deductible before benefits begin. In 2007, the deductible was limited to $265.[69] After the deductible is covered, the patient pays either a copayment (a set amount) or a co-insurance (a percentage of the cost). These amounts may be the same for all prescriptions or may be broken into tiers based on cost of generic vs brand name of the drug. The "doughnut hole" is a coverage gap. After the beneficiary reaches a preset amount ($2400 in 2007), the beneficiary pays 100% of drug costs until the gap is crossed ($3850 in 2007). Some Medicare Part D plans provide additional coverage to help beneficiaries cross the gap. A secondary insurance policy can also bridge the gap and assist with copayments. Copayments and the coverage gap can create financial challenges for patients. Grants from the National Kidney Foundation and assistance from IDPN and IPN providers are available. However, patients are often reluctant to complete financial disclosure forms to qualify for financial assistance.

## Conclusion

Malnutrition is common in patients receiving dialysis. The challenge is differentiating malnutrition from other factors that affect nutrition parameters. When malnutrition is identified, the first step in reversing the course is intensive nutrition counseling to increase total energy and nutrient intake. This can include oral nutrition supplements and tube feeding. IDPN and IPN should be considered when attempts to meet nutrient needs by oral diet or tube feeding have not been successful. IDPN and IPN are supplemental nutrition therapies that, when combined with oral diet and tube feeding, enable the patient to meet energy and nutrient needs and improve nutrition status. Medicare Part D has improved reimbursement for the therapies, but copayments and coverage gaps continue to challenge patients, clinicians, and providers.

Clinical guidelines are needed to assist healthcare practitioners with identifying candidates for IDPN and IPN as well as with effectively managing the therapy. Outcome research has been primarily limited to short-term parameters such as laboratory values and weight change. The long-term effects on mortality, hospitalizations, costs, and quality of life have yet to be adequately

addressed. More quantitative and qualitative research is needed to determine the optimal time to start IDPN and IPN as well as how to determine successful outcomes. Physicians, nurses, pharmacists, and dietitians must use their clinical judgment based on their patient population and the available scientific literature to determine whether and when to provide IDPN and IPN to their patients.

## References


1. Global dialysis: dialysis standards and statistics. http://globaldialysis.com/stats.asp. Updated March 1, 2007. Accessed September 28, 2008.
2. Mehrotra R, Kopple J. Nutritional management of maintenance dialysis patients: why aren't we doing better? *Annu Rev Nutr*. 2001;21:343-380.
3. Wang AY, Sanderson J, Sea MM, et al. Important factors other than dialysis adequacy associated with inadequate dietary protein and energy intakes in patients receiving maintenance peritoneal dialysis. *Am J Clin Nutr*. 2003;77:834-841.
4. Davies SJ, Russell L, Bryan J, Phillips L, Russell GI. Comorbidity, urea kinetics, and appetite in continuous ambulatory peritoneal dialysis: their interrelationship and prediction of survival. *Am J Kidney Dis*. 1995;26:353-361.
5. Capelli JP, Kushner H, Camiscioli TC, Chen S, Torres MA. Effect of intradialytic parenteral nutrition on mortality rates in end-stage renal disease care. *Am J Kidney Dis*. 1994;23:808-816.
6. Centers for Medicare and Medicaid, Department of Health and Human Services. Conditions for Coverage for ESRD Facilities, 42 CFR Part 494. Fed Regist. April 15, 2008. Effective October 14, 2008.
7. Fuhrman MP, Charney P, Mueller C. Hepatic proteins and nutrition assessment. *J Am Diet Assoc*. 2004;104:1258-1264.
8. Kaysen A, Levin NW. Why measure serum albumin levels? *J Ren Nutr*. 2002;12:148-150.
9. Kaysen GA, Dubin JA, Muller HG, Rosales L, Levin NW, Mitch WE. HEMO Study Group. Inflammation and reduced albumin synthesis associated with stable decline in serum albumin in hemodialysis patients. *Kidney Int*. 2004;65:1408-1415.
10. Fein PA, Mittman N, Gadh R, et al. Malnutrition and inflammation in peritoneal dialysis patients. *Kidney Int*. 2003;64(suppl 87):S87-S91.
11. Gabay C, Kushner I. Acute phase proteins and other systemic responses to inflammation. *N Engl J Med*. 1999;340:448-454.
12. Lacson E, Ikizler A, Lazarus M, Teng M, Hakim RM. Potential impact of nutritional intervention on end-stage renal disease hospitalization, death, and treatment costs. *J Ren Nutr*. 2007;17:363-371.
13. Riella MC. Malnutrition in dialysis: malnourishment or uremic inflammatory response? *Kidney Int*. 2000;57:1211-1232.
14. Chertow GM, Ling J, Lew NL, Lazarus JM, Lowrie EG. The association of intradialytic parenteral nutrition administration with survival in hemodialysis patients. *Am J Kidney Dis*. 1994;24:912-920.
15. Moore E, Celano J. Challenges of providing nutrition support in the outpatient dialysis setting. *Nutr Clin Pract*. 2005;20:202-212.
16. How PP, Lau AH. Malnutrition in patients undergoing hemodialysis: is intradialytic parenteral nutrition the answer? *Pharmacotherapy*. 2004;24:1748-1758.
17. Gil H, Yang J, Lee E, Lee E, Choi JS, Hong S. The effect of dialysis membrane flux on amino acid loss in hemodialysis patients. *J Korean Med Sci*. 2007;22:598-603.
18. Malgorzewicz S, Debska-Slizien A, Rutkowski B, Lysiak-Szydlowska W. Serum concentration of amino acids versus nutritional status in hemodialysis patients. *J Ren Nutr*. 2008;18:239-247.
19. Bossola M, Muscaritoli M, Tazza L, et al. Malnutrition in hemodialysis patients: what therapy? *Am J Kid Dis*. 2005;46:371-386.
20. Jones MR, Gehr TW, Burkart JM, et al. Replacement of amino acid and protein losses with 1.1% amino acid peritoneal dialysis solution. *Perit Dial Int*. 1998;18:210-216.
21. Utaka S, Avesani CM, Draibe SA, Kamimura MA, Andreoni S, Cuppari L. Inflammation is associated with increased energy expenditure in patients with chronic kidney disease. *Am J Clin Nutr*. 2005;82:801-805.
22. Ramkumar N, Cheung AK, Pappas LM, Roberts WL, Beddhu S. Association of obesity with inflammation in chronic kidney disease: a cross-sectional study. *J Ren Nutr*. 2004;14:201-207.
23. Honda H, Qureshi AR, Heimburger O, et al. Serum albumin, C-reactive protein, interleukin 6, and fetuin A as predictors of malnutrition, cardiovascular disease, and mortality in patients with ESRD. *Am J Kidney Dis*. 2006;47:139-148.
24. Qureshi AR, Alvestrand A, Divino-Filho JC, et al. Inflammation, malnutrition, and cardiac disease as predictors of mortality in hemodialysis patients. *J Am Soc Nephrol*. 2002;13(suppl 1):S28-S36.
25. Kalantar-Zadeh K, Kopple JD, Humphreys MH, Block G. Comparing outcome predictability of markers of malnutrition-inflammation complex syndrome in hemodialysis patients. *Nephrol Dial Transplant*. 2004;19:1507-1519.
26. Ikizler TA, Wingard RL, Harvell J, Shyr Y, Hakim RM. Association of morbidity with markers of nutrition and inflammation in chronic hemodialysis patients: a prospective study. *Kidney Int*. 1999;55:1945-1951.
27. Ho LC, Wang HH, Peng YS, et al. Clinical utility of malnutrition-inflammation score in maintenance hemodialysis patients: focus on indentifying the best cut-off point. *Am J Nephrol*. 2008;28:840-846.
28. Afsar B, Sezer S, Ozdemir FN, Celik H, Elsurer, Haberal, M. Malnutrition-inflammation score is a useful tool in peritoneal dialysis patients. *Perit Dial Int*. 2006;26:705-711.
29. Caglar K, Fedje L, Dimmitt R, Hakim RM, Shyr Y, Ikizler A. Therapeutic effects of oral nutritional supplementation during hemodialysis. *Kidney Int*. 2002;62:1054-1059.
30. Veeneman JM, Kingma HA, Boer TS, et al. Protein intake during hemodialysis maintains a positive whole body protein balance in chronic hemodialysis patients. *Am J Physiol Endocrinol Metab*. 2003;284:E954-E965.
31. Azar R, Smessaert C, Clicteur K, et al. Effects of oral nutritional supplementation on nutritional status in malnourished chronic hemodialysis patients [abstract]. *J Ren Nutr*. 2008;18:S33.
32. Stratton R, Bircher G, Fouque D, et al. Multinutrient oral supplements and tube feeding in maintenance dialysis: a systematic review and meta-analysis. *Am J Kidney Dis*. 2005;46:387-405.
33. National Kidney Foundation. K/DOQI clinical practice guidelines for nutrition in chronic renal failure. *Am J Kidney Dis*. 2000;35(suppl):S1-S104.
34. A.S.P.E.N. Board of Directors and The Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients [published correction in *JPEN* 2002; 26:144]. *JPEN J Parenter Enteral Nutr*. 2002;26(suppl):1SA-138SA.
35. McCann L, ed. *Pocket Guide to Nutrition Assessment of the Patient with Chronic Kidney Disease*. 4th ed. New York, NY: National Kidney Foundation, 2009.
36. Fuhrman MP. Parenteral nutrition in kidney disease. In: Byham-Gray L, Wiesen K, eds. *A Clinical Guide to Nutrition Care in Kidney Disease*. Chicago, IL: American Dietetic Association; 2004:159-174.
37. Moore E, Lindenfield SM. Intradialytic parenteral nutrition: a nutrition support intervention for high-risk malnutrition in chronic kidney disease. *Support Line*. 2007;29:6-13,16.
38. Serna-Thome MG, Padilla-Rosciano AE, Suchi-Bernal L. Practical aspects of intradialytic nutritional support. *Curr Opin Clin Nutr Metab Care*. 2002;5:293-296.

39. Hakim RM. Proposed clinical trials in the evaluation of intradialytic parenteral nutrition. *Am J Kidney Dis*. 1999;33:217-220.
40. Lazarus MJ. Recommended criteria for initiation and discontinuing intradialytic parenteral nutrition therapy. *Am J Kidney Dis*. 1999;33:211-216.
41. Detsky A, McLaughlin J, Baker J. What is subjective global assessment of nutritional status? *JPEN J Parenter Enteral Nutr*. 1987;11:8-13.
42. Pupim LB, Majchrzak KM, Flakoll PJ, Ikizler TA. Intradialytic oral nutrition improves protein homeostasis in chronic hemodialysis patients with deranged nutritional status. *J Am Soc Nephrol*. 2006;17:3149-3157.
43. Hiroshige K, Iwamoto M, Kabashima N, Mutoh Y, Yuu K, Ohtani A. Prolonged use of intradialysis parenteral nutrition in elderly malnourished chronic hemodialysis patients. *Nephrol Dial Transplant*. 1998;13:2081-2087.
44. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. *N Engl J Med*. 2001;345: 1359-1367.
45. Fuhrman MP. Complication management in parenteral nutrition. In: Matarese LE, Gottschlich MM, eds. *Contemporary Nutrition Support Practice: A Clinical Guide*, 2nd ed. Philadelphia, PA: Saunders, 2003:242-262.
46. Hise ME, Brown JC. Lipids. In: Gottschlich MM, ed. *The A.S.P.E.N. Nutrition Support Core Curriculum: A Case-Based Approach—The Adult Patient*. Silver Spring, MD: The American Society for Parenteral and Enteral Nutrition. 2007:48-70.
47. Pupim LB, Flakoll PJ, Ikizler TA. Nutritional supplementation acutely increases albumin fractional synthetic rate in chronic hemodialysis patients. *J Am Soc Nephrol*. 2004;15:1920-1926.
48. Pupim LB, Flakoll PJ, Levenhagen DK, Ikizler TA. Exercise augments the acute anabolic effects of intradialytic parenteral nutrition in chronic hemodialysis patients. *Am J Physiol Endocrinol Metab*. 2004;286:E589-E597.
49. Pupim LB, Flakoll PJ, Yu C, Ikizler TA. Recombinant human growth hormone improves muscle amino acid uptake and whole-body protein metabolism in chronic hemodialysis patients. *Am J Clin Nutr*. 2005;82:1235-1243.
50. Cano NJM, Fouque D, Roth H, et al. Intradialytic parenteral nutrition does not improve survival in malnourished hemodialysis patients: a 2-year multicenter, prospective, randomized study. *J Am Soc Nephrol*. 2007;18:2583-2591.
51. Dezfuli A, Ricker M, Scholl D, Lindenfeld SM, Kalantar-Zadeh. Severity of hypoalbuminemia is related to the effectiveness of intradialytic parenteral nutrition (IDPN) in hemodialysis patients [abstract]. *J Ren Nutr*. 2008;18:S33.
52. Scholl D, Dowling R, Ricker M, Lindenfeld S. Intradialytic parenteral nutrition (IDPN): changes in albumin, total protein, dry weight, BUN, and creatinine after 3 to 12 months of therapy [abstract]. *J Ren Nutr*. 2007;17:162.
53. Smolle KH, Kaufmann P, Holzer H, Druml W. Intradialytic parenteral nutrition in malnourished patients on chronic haemodialysis therapy. *Nephrol Dial Transplant*. 1995;10:1411-1416.
54. Krause I, Shamir R, Davidovits M, et al. Intradialytic parenteral nutrition in malnourished children treated with hemodialysis. *J Ren Nutr*. 2002;12:55-59.
55. Madigan KM, Olshan A, Yingling DJ. Effectiveness of intradialytic parenteral nutrition in diabetic patients with end-stage renal disease. *J Am Diet Assoc*. 1990;90:861-863.
56. Joannidis M, Rauchenzauner M, Leiner B, et al. Effect of intradialytic parenteral nutrition in patients with malnutrition-inflammation complex syndrome on body weight, inflammation, serum lipids and adipocytokines: results from a pilot study. *Eur J Clin Nutr*. 2008;62:789-795.
57. Orrellana P, Juarez-Congelosi M, Goldstein SL. Intradialytic parenteral nutrition treatment and biochemical marker assessment for malnutrition in adolescent maintenance hemodialysis patients. *J Ren Nutr*. 2005;15:312-317.
58. Srivaths PR, Wong C, Goldstein SL. Nutrition aspects in children receiving maintenance hemodialysis: impact on outcome. *Pediatr Nephrol*. 2009;24:951-957.
59. Garibotto G, Sofia A, Canepa A, et al. Acute effects of peritoneal dialysis with dialysates containing dextrose or dextrose and amino acids on muscle protein turnover in patients with chronic renal failure. *J Am Soc Nephrol*. 2001;12:557-567.
60. Jones M, Hagen T, Boyle CA, et al. Treatment of malnutrition with 1.1% amino acid peritoneal dialysis solution: results of a multicenter outpatient study. *Am J Kidney Dis*. 1998;32:761-769.
61. Kopple JD, Bernard D, Messana J, et al. Treatment of malnourished CAPD patients with an amino acid based dialysate. *Kidney Int*. 1995;47:1148-1157.
62. Taylor GS, Patel V, Spencer S, Fluck RJ, McIntyre CW. Long-term use of 1.1% amino acid dialysis solution in hypoalbuminemic continuous ambulatory peritoneal dialysis patients. *Clin Nephrol*. 2002;58:445-450.
63. Tjiong HL, Rietveld T, Wattimena JL, et al. Peritoneal dialysis with solutions containing amino acids plus glucose promotes protein synthesis during oral feeding. *Clin J Am Soc Nephrol*. 2007;2: 74-80.
64. Faller B, Aparicio M, Faict D, et al. Clinical evaluation of an optimized 1.1% amino-acid solution for peritoneal dialysis. *Nephrol Dial Transplant*. 1995;10:1432-1437.
65. Afreen S, Goodship THJ, Kirkwood A, Ward MK. The nutritional/metabolic and hormonal effects of 8 weeks of continuous ambulatory peritoneal dialysis with a 1% amino acid solution. *Clin Nephrol*. 1990;33:192-199.
66. Bruno M, Bagnis C, Marangella M, Rovera L, Cantaluppi A, Linari F. CAPD with an amino acid dialysis solution: a long-term crossover study. *Kidney Int*. 1989;35:1189-1194.
67. Young GA, Dibble JB, Hobson SM, Tompkins L, Gibson J, Turney JH. The use of an amino-acid-based CAPD fluid over 12 weeks. *Nephrol Dial Transplant*. 1989;4:285-292.
68. McCann L. Nutrition management of the adult peritoneal dialysis patient. In: Byham-Gray L, Wiesen K, eds. *A Clinical Guide to Nutrition Care in Kidney Disease*. Chicago, IL: American Dietetic Association; 2004:57-69.
69. Centers for Medicare and Medicaid. Medicare Parts B/D Coverage Issues. http://www.cms.hhs.gov/pharmacy/downloads/partsbdcoverageissues.pdf. Updated November 27, 2007. Accessed October 1, 2008.
70. Medicare: The official U.S. government site for people with Medicare. http://www.medicare.gov. Updated March 28, 2008. Accessed September 28, 2008.
71. Department of Health and Human Services. Centers for Medicare and Medicaid Services. DME Information Form. http://www.cms.hhs.gov/cmsforms/downloads/cms10126.pdf. Updated October 26, 2007. Accessed October 1, 2008.