Evaluation of complications and prognostic factors associated with administration of total parenteral nutrition in cats: 75 cases (1994–2001)

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Objective—To determine frequency and types of complications, prognostic factors, and primary diseases affecting clinical outcome associated with administration of total parenteral nutrition (TPN) in cats.

Design—Retrospective study.

Animals—75 cats that received TPN for ≥ 12 hours.

Procedure—Medical records were reviewed, and information was obtained on signalment, history, problems at initial evaluation, physical examination findings, weight and changes in weight while receiving TPN, duration in the hospital before initiation of TPN, the type of TPN catheter used, duration of TPN administration, and final diagnosis. Laboratory results obtained immediately prior to TPN and at 24 and 96 hours following initiation of TPN administration were compared.

Results—Reports of weight loss at initial evaluation, hyperglycemia at 24 hours, or diagnosis of chronic renal failure were significantly associated with increased mortality rate. Greater serum albumin concentrations prior to and at 96 hours following TPN administration were significantly associated with decreased mortality rate. Mechanical and septic complications were infrequent and not associated with increased mortality rate. Most cats had multiple diseases. The overall mortality rate was 52%; among 75 cats, 36 recovered, 23 were euthanized, and 16 died as a result of their primary illness or complications associated with their illness.

Conclusions and Clinical Relevance—Results indicated high mortality rate in cats maintained on TPN that had multiple concurrent diseases associated with a poor prognosis. Indicators of poor prognosis included a history of weight loss, hyperglycemia at 24 hours following TPN administration, hypoalbuminemia, and chronic renal failure. (*J Am Vet med Assoc* 2004;225:242–250)

There is ample evidence of the deleterious consequences of malnutrition on cellular and humoral immune function in humans and rodent models.[1-3] Additional deleterious consequences of malnutrition include decreased tissue synthesis, delayed wound healing, and altered intermediary drug metabolism.[4,5] Nutritional support is an important component in the management of patients whose disease status limits their ability to acquire nutrients via ingestion in quantities sufficient to aid successful recovery. The goals of nutritional support include correction of any preexisting malnutrition, prevention of progressive protein-calorie malnutrition, optimization of a patient's metabolic state, minimization of the risks of illness and death, and shortening of recovery time.[6] The appropriateness of enteral versus parenteral nutrition in critically ill patients has been a controversial issue.[7-11] **Total parenteral nutrition (TPN)** avoids some of the disadvantages associated with enteral nutrition, such as diarrhea, nausea, vomiting, delayed gastric emptying, and bloating. However, compared with TPN, enteral nutrition is argued by many to be a more physiologically sound and less expensive process and is recommended when the patient has a functional gastrointestinal tract.[8] Heyland et al[9] conducted a meta-analysis of prospective randomized clinical trials that evaluated the outcomes of parenteral nutrition versus oral alimentation with IV administration of dextrose in humans that had undergone surgery or were critically ill and concluded that parenteral nutrition did not affect mortality rates. A recently published meta-analysis[10] in which data collected from 27 studies involving 1,828 patients were compared revealed that tube feeding and conventional oral feeding with IV administration of dextrose were associated with a lower rate of infection than that associated with parenteral nutrition in patients with compromised function of the gastrointestinal tract. However, in malnourished populations, mortality rate was higher and the rate of infection was greater with oral alimentation with IV administration of dextrose than the rates associated with parenteral nutrition.[10] These data clearly underscore the ongoing debate regarding the benefits and indications of parenteral versus enteral nutrition.

Compared with enteral nutrition, disadvantages of TPN ascertained from results of human and animal studies include intestinal atrophy; decreased mucosal resistance to bacteria; abnormal liver function; increased rate of administration line sepsis; and metabolic complications such as hyperglycemia, blood electrolyte abnormalities, and hyperlipidemia.[12,13] Because of these potential risks and the high cost associated with TPN, enteral nutrition has remained the preferred method of nutritional support for most veterinary patients.[14,15]

There have been numerous clinical studies to evaluate the use of TPN in humans, and guidelines for TPN administration in humans are well-estab-

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lished.[16-18] In contrast, to the authors' knowledge, only 3 retrospective studies[12,19,20] comprising a total of 18 cats that received TPN in a veterinary teaching hospital setting and 1 prospective study[21] that evaluated the use of TPN in 7 healthy cats have been published to date. The latter investigation revealed that all of the cats developed mild to moderate normocytic, normochromic, nonregenerative anemia and mild to severe thrombocytopenia after 14 days of TPN administration.[21] In addition, all cats that were administered a TPN formula, which had a caloric density in excess of their metabolic requirements, developed hyperglycemia, and all but 1 cat had high serum **alanine aminotransferase (ALT)** activity at some time during TPN administration.

The reports of the aforementioned retrospective studies[12,19-21] provide limited information pertaining to specific risk factors or variables that could be evaluated to better predict illness and death in cats receiving TPN. In addition, the development of hematologic abnormalities in the healthy cats receiving TPN warrants further evaluation, and additional information is needed to define the significance of these changes in clinically ill cats receiving TPN. The purpose of the study reported here was to determine the frequency and types of complications, prognostic factors, and primary diseases affecting clinical outcome associated with administration of TPN in cats.

Criteria for Selection of Cases

The medical records of all cats receiving TPN at the **Veterinary Medical Teaching Hospital (VMTH)** of the University of California, Davis, during September 1994 through May 2001 were reviewed by use of the VMTH computer access network database. Selection criteria for nutritional support included prolonged anorexia (> 5 days) with an expected delay (> 5 days) in regaining normal food intake as a result of treatment, primary disease, or poor nutritional status (ie, detection of 1 of the following: a body condition score ≤ 3/9; hypoalbuminemia; recent weight loss of > 10% body weight; and a diagnosis of hepatic lipidosis). These cats were selected for parenteral support rather than enteral nutritional support if ≥ 1 of the following criteria were present: intractable vomiting or diarrhea, short bowel syndrome, severe enteropathy with malassimilation of nutrients, severe pancreatitis, and altered state of consciousness. Cats were included in the study if they received TPN for at least 12 hours at the VMTH. Cats were excluded from this study if they received parenteral nutrition via a peripheral vein.

Procedures

In each cat, a triple-, double-, or single-lumen central-venous catheter was placed via aseptic technique in an external jugular vein.[a,b] One of the ports of a multilumen catheter was dedicated for TPN administration only, and fluids were administered IV through a separate port. Each cat's daily caloric requirements were calculated by use of standardized worksheets that utilized the following formula: **resting energy requirement (RER)** = (30 × weight [kg]) + 70.[22] The **illness energy requirement (IER)** was estimated as a multiple of RER (IER = 1.1 to 1.4 × RER).[22] The protein requirement for cats was estimated as 6 g/100 kcal/d.[22] Protein was provided as a crystalline amino acid solution that contained electrolytes,[c] and nonprotein calories were provided as a mixture of 50% dextrose solution[d] and 20% lipid emulsion.[e] Protein calories were not accounted for when considering total energy requirements. Each cat received 1 of 4 TPN formulas according to availability and the cat's underlying illness and electrolyte abnormalities (**Table 1**). Formula 1 was administered to all cats from the start of the study through July 1995, whereas formulas 2, 3, and 4 were available for administration from August 1995 through the end of the study period. Formula 2 was formulated for critically ill cats with normal renal and hepatic function. Formula 3 was formulated for critically ill hypokalemic or eukalemic cats with renal failure or a hepatopathy. Formula 4 was formulated for critically ill hyperkalemic cats with renal failure or a hepatopathy. The TPN solution was compounded aseptically as a total nutrient admixture under a horizontal laminar flow hood,[f] and potassium phosphate or potassium chloride was added to the solution. Fat and water-soluble vitamins were added immediately prior to administration of TPN to avoid degradation. The admixture was inspected closely for evidence of destabilization of the emulsion, which was characterized by a dark-yellow color in a line along the top portion of the nutrient admixture or by large yellow globules throughout the admixture. The total nutrient admixture was either administered immediately or stored in a refrigerator at 4°C for a maximum of 24 hours prior to administration. All prepared bags were replaced within 48 hours of nutrient admixture. In most instances, the nutrient admixture was administered at a rate to supply 50% of the cat's IER on the first day and was increased on the second day to supply 100% of the cat's IER. The daily volume of crystalloid solution administered IV was determined by subtracting the daily total volume of TPN formulation administered from the cat's calculated

Table 1—Formulations used to provide total parenteral nutrition (TPN) to 75 cats.

	Component							
Formula	50% Dextrose solution (mL)	20% Lipid solution (mL)	8.5% Amino acid solution* (mL)	Vitamin B complex (mL)	Potassium phosphate (mEq)	Potassium chloride (mEq)	Protein (g/100 kcal)	Caloric density (kcal/mL)
1	250	250	500	1	7.5	0	3.9	1.1
2	150	125	500	2	1	0	6.3	0.9
3	300	250	500	2	0	12	3.6	1.1
4	300	250	500	2	0	0	3.6	1.1

*The amino acid solution contained electrolytes.

daily fluid requirement. For each cat, TPN administration was discontinued when enteral intake was deemed adequate to support energy requirement or following resolution of the underlying disorder. Bacteriologic culture of the TPN solution or the catheter tip at catheter removal was not performed routinely.

Data collected from the medical records included signalment, history, reason for evaluation at the VMTH, clinical signs, physical examination findings, body condition score,[23] weight and weight changes during TPN administration, primary medical problems, reason for TPN selection, type of catheter used for TPN administration, duration of TPN administration, and final diagnosis. If data were available, results of a CBC, serum biochemical analyses, and blood gas analysis obtained immediately prior to (designated T0) and at 24 (T24) and 96 (T96) hours after initiation of TPN administration were compared. Platelet concentration was also assessed at 5 or more days after initiation of TPN administration (T ≥ 5 days). For those cats that received TPN for < 96 hours, the last recorded blood values during TPN administration were evaluated.

Complications associated with TPN administration were classified as mechanical, septic, or metabolic. Mechanical complications were characterized by occluded or leaky administration lines, problems associated with the jugular catheter, equipment failure, or technical problems interfering with the administration of TPN. Septic complications were characterized by infected catheter sites in febrile patients, bacterial growth obtained on culture of the TPN solution or catheter tip used in febrile patients, bacterial growth obtained on culture of blood, or an abnormally high neutrophil concentration during TPN administration that could not be attributed to other disease processes. Metabolic complications were defined by those laboratory variables that were determined to be within reference range prior to TPN administration but for which there was an abnormal increase or decrease during TPN administration. Hyperglycemia in cats was classified as a metabolic complication if serum glucose concentration was within the reference range prior to TPN administration but increased to > 134 mg/dL during TPN administration. An increase in serum glucose concentration of ≥ 100 mg/dL, compared with serum glucose concentrations obtained prior to TPN administration, was also deemed a metabolic complication. Cats with diabetes mellitus prior to TPN administration were excluded from this evaluation. Metabolic corrections were defined for those laboratory variables determined to be outside reference ranges prior to TPN administration but that returned to the normal reference range during TPN administration.

Statistical analyses—Cox proportional hazards regression models were fitted to evaluate the effect of any of the putative risk factors on the cohort of cats receiving TPN administration, with outcomes being either time to death after initiation of TPN or time to successful cessation of TPN. Models were adjusted for the category of primary underlying disease process according to the following disease processes: cats with pancreatitis; cats with nonneoplastic liver disease; cats with gastroenteritis; cats with pancreatitis and concurrent nonneoplastic liver disease, gastroenteritis, or diabetes mellitus; cats with chronic renal failure; cats with chronic renal failure and concurrent nonneoplastic liver disease or diabetes mellitus; and cats with neoplasia of the liver, pancreas, or gastrointestinal tract. **Hazard ratios (HRs)** and 95% **confidence intervals (CIs)** for changes in serum ALT, **alkaline phosphatase (ALP)**, and **aspartate aminotransferase (AST)** activities and serum glucose concentration were calculated on the basis of 100-unit increments; changes in serum total calcium and phosphorus concentrations, serum albumin concentration, serum BUN concentration, and serum ionized calcium concentration were calculated on the basis of 1-unit, 0.5-unit, 10-unit, and 0.25-unit increments, respectively. Proportionality was assessed by use of likelihood ratio tests, and linearity of variables was verified for each model with continuous variables. Logistic regression was also used to model the effect of putative risk factors on the probability of cats being successfully weaned off TPN. Results are presented as adjusted HRs or adjusted **odds ratios (ORs)**, with adjustment for the underlying disease process that determined the need for TPN. Values of $P < 0.05$ were considered significant.

Results

During the 81-month period, 75 cats were evaluated for TPN alimentation and accounted for 424.5 patient days on TPN. Domestic shorthair cats were the most common breed (n = 49), followed by domestic longhair (13), domestic medium hair (5), Persian (3), Siamese (2), Siamese mix (2), and Burmese (1). There were 46 male and 29 female cats included in the study; ages of the cats ranged from 8 months to 20.6 years (median age, 9.8 years). Body condition scores (0 to 9 scale) at initial evaluation ranged from 2 to 8 of 9 (median score, 5/9). Immediately prior to TPN administration (T0), weights of the cats ranged from 1.98 to 8.2 kg (4.36 to 18.04 lb; median weight, 4.8 kg [10.56 lb]). After 96 hours of TPN administration (designated T96), weights of cats (n = 25) ranged from 2.6 to 7.0 kg (5.72 to 15.40 lb; median weight, 5.2 kg [11.44 lb]). The change in weight from T0 to T96 in these 25 cats ranged from a loss of 0.5 kg (1.10 lb) to a gain of 0.99 kg (2.18 lb; median gain, 0.23 kg [0.51 lb]). Weight and body condition scores at initial evaluation and weight changes during TPN administration did not have a significant association with mortality rate.

The most common problems reported at initial evaluation included vomiting (n = 32), anorexia (24), lethargy (15), and weight loss (6). Although weight at initial evaluation and weight changes during the administration of TPN were not associated with mortality rate, cats that had a history of weight loss had a significantly ($P = 0.031$) increased mortality rate (adjusted HR, 2.44; 95% CI, 1.08 to 5.47) and were significantly ($P = 0.029$) less likely to be weaned off TPN (adjusted OR, 0.2; 95% CI, 0.049 to 0.85) than were other cats in the study. No other problems reported at initial evaluation had a significant association with mortality rate. Among the study cats, the most common clinical signs included anorexia (n = 38), vomit-

ing (38), dehydration (37), lethargy (29), and icterus (21). Eighteen cats had at least 1 of these clinical signs, 23 cats had 2 of these signs, 21 cats had 3 of these signs, 4 cats had 4 of these signs, and 5 cats had all 5 clinical signs. Those cats that were dehydrated at initial evaluation had a nonsignificant ($P = 0.18$) increase in mortality rate (adjusted HR, 1.71; 95% CI, 0.79 to 3.70) and were less likely to be weaned off TPN (adjusted OR, 0.44; 95% CI, 0.16 to 1.23; $P = 0.12$) than were cats that were not dehydrated. During the initial physical examination, 12 cats were hypothermic (rectal temperature, < 32.7°C [< 99.0°F]) and 12 cats were hyperthermic or febrile (rectal temperature, > 39.2°C [> 102.6°F]). Cats that were hypothermic or hyperthermic did not have a significant increased rate of mortality, compared with normothermic cats. Six of the 12 cats that were hypothermic at initial evaluation had acute or chronic renal failure. Most cats (n = 32) were quiet, yet alert and responsive, during physical examination. Of the remaining cats, 28 were obtunded; 12 were bright, alert, and responsive; 1 was comatose at initial evaluation. Two cats did not have their demeanors recorded in the medical records. Although the finding was not significant ($P = 0.099$), the 29 cats that were either obtunded or comatose at initial evaluation appeared to have an increased mortality rate (adjusted HR, 1.86; 95% CI, 0.90 to 3.91), compared with the 44 cats that were bright, alert, and responsive or quiet, alert, and responsive.

The duration of hospitalization before initiation of TPN ranged from 6 hours to 36.5 days (median duration, 1.5 days). For the cats that died, the median duration of hospitalization at the VMTH before initiation of TPN was 1.3 days (range, 0.25 to 36.5 days), whereas for the cats that survived, the median duration of hospitalization before initiation of TPN was 2.7 days (range, 0.5 to 32.5 days). There was no significant association between length of hospitalization before TPN administration and mortality rate. The overall duration of TPN administration ranged from 0.5 to 18.5 days (median duration, 4.75 days). For the cats that died, the duration of TPN administration ranged from 0.5 to 15 days (median duration, 2.9 days), whereas for the cats that survived, the duration of TPN administration ranged from 0.5 to 18.5 days (median duration, 6.0 days). There was a decrease in mortality rate (adjusted OR, 0.86; 95% CI, 0.75 to 0.89; $P = 0.036$) in cats with each additional day of TPN administration.

The most commonly administered TPN formula was formula 2 (36/75 [48.0%] cats), followed by formula 3 (32/75 [42.7%]), formula 1 (11/75 [14.7%]), and formula 4 (4/75 [5.3%]). Eight cats received ≥ 1 formula (ie, combinations of formulas 2, 3, and 4) during hospitalization. There was no significant association between the TPN formula administered and mortality rate. The most common replacement and colloid fluids administered concurrently with TPN were lactated Ringer's solution (n = 51), physiologic saline (0.9% NaCl) solution (24), dextran 70 (11), and an isotonic crystalloid replacement solution[g] (11). The most common fluid supplements administered IV were potassium chloride (n = 62) and potassium phosphate (8). The supplementation of fluids with potassium chloride was associated with a significantly ($P = 0.036$) decreased mortality rate (adjusted HR, 0.33; 95% CI, 0.12 to 0.83), and cats receiving potassium chloride were significantly ($P = 0.039$) more likely to be weaned off TPN (adjusted OR, 5.49; 95% CI, 1.09 to 27.47). Thirteen of the 75 cats did not receive supplemental potassium chloride for the following reasons: 7 cats were not administered fluids with their TPN, 5 cats were hyperkalemic (4 had renal failure and 1 had concurrent hepatic lipidosis, pancreatitis, and diabetes mellitus), and 1 cat received potassium phosphate. The most common blood products given to cats during the period of TPN administration were fresh whole blood (n = 13), stored whole blood (14), and fresh frozen plasma (12). Cats that received fresh whole blood appeared to be less likely to be weaned off TPN, although this finding was not significant (adjusted OR, 0.065; 95% CI, 0.008 to 0.56; $P = 0.065$). Cats that received fresh frozen plasma had a significant ($P < 0.001$) increase in mortality rate (adjusted HR, 6.25; 95% CI, 2.51 to 15.56), and none were successfully weaned off TPN (adjusted OR, < 0.001; no 95% CI or P value).

In 58 of 62 nondiabetic cats, serum glucose concentrations at T0 ranged from 45 to 312 mg/dL (median concentration, 154 mg/dL); overall, serum glucose concentrations at T0 were not significantly associated with mortality rate. In 47 of 62 nondiabetic cats, serum glucose concentrations at T24 ranged from 84 to 1,074 mg/dL (median concentration, 247 mg/dL). For each incremental increase in serum glucose concentration of 100 mg/dL from T0 to T24, cats had a significant ($P = 0.017$) increase in mortality rate (adjusted HR, 1.38; 95% CI, 1.06 to 1.80). In 38 of 62 nondiabetic cats, serum glucose concentrations at T96 ranged from 94 to 523 mg/dL (median concentration, 225 mg/dL); overall, serum glucose concentrations at T96 were not significantly associated with mortality rate. Insulin was administered to 21 cats that were transiently hyperglycemic. The duration of insulin administration ranged from 1 to 8 days (median duration, 4 days). Regular insulin was administered in 16 of the 21 cats, ultralente in 3 cats, NPH in 1 cat, and regular insulin with lente insulin in 1 cat. There was no significant association between insulin administration and mortality rate.

Serum ALP, ALT, and AST activities and BUN, creatinine, calcium, ionized calcium, phosphorus, glucose, and albumin concentrations at T0, T24, and T96 were assessed (**Table 2**). Blood gas concentrations (ie, total carbon dioxide and bicarbonate), partial pressure of carbon dioxide, and pH values were recorded at T0 in 41 cats, T24 in 36 cats, and T96 in 24 cats; there were no significant differences in these values among time points. Serum liver enzyme activities and glucose, total calcium, and ionized calcium concentrations were not significantly associated with mortality rate. At T0, cats with high serum BUN concentration had a significant ($P = 0.022$) increase in mortality rate for each incremental increase in BUN concentration of 10 mg/dL (adjusted HR, 2.03; 95% CI, 1.11 to 3.71). At T0, cats with chronic renal failure had an increased

Table 2—Results of serum biochemical analyses in 75 cats prior to (T0) and at 24 (T24) and 96 (T96) hours after administration of TPN.

Variable	Reference range	Median (range)
Alkaline phosphatase (U/L)	14–71	
T0 (n = 66)		46 (4–1,628)
T24 (27)		5 (79–1,670)
T96 (31)		86 (17–1,530)
Alanine aminotransferase (U/L)	26–106	
T0 (66)		94 (11–1,525)
T24 (27)		90 (3–2,090)
T96 (31)		92 (17–638)
Aspartate aminotransferase (U/L)	12–46	
T0 (64)		74 (3–2,100)
T24 (27)		55 (3–4,081)
T96 (31)		44 (0–954)
BUN (mg/dL)*	18–33	
T0 (68)		23 (5–267)
T24 (37)		18 (5–125)
T96 (33)		18 (3–54)
Creatinine (mg/dL)	1.1–2.2	
T0 (68)		1.4 (0.3–10.9)
T24 (37)		1.2 (0.3–5.2)
T96 (33)		1.2 (0.1–3.2)
Total calcium (mg/dL)	9.4–11.4	
T0 (68)		8.6 (5.5–11.7)
T96 (32)		8.7 (6.7– 0.6)
Ionized calcium (mg/dL)	0.7–1.27	
T0 (68)		1.00 (0.63–1.49)
T96 (32)		1.05 (0.86–1.96)
Phosphorus (mg/dL)†	3.2–6.3	
T0 (68)		4.1 (0.8–19.1)
T24 (37)		3.6 (1.1–13.0)
T96 (34)		4.5 (1.6–16.2)
Glucose (mg/dL)‡	73–134	
T0 (58)		154 (45–312)
T24 (47)		247 (84–1,074)
T96 (38)		225 (94–523)
Albumin (g/dL)§	1.9–3.9	
T0 (68)		2.2 (1.2–3.4)
T24 (35)		2.1 (1.1–3.0)
T96 (35)		2.1 (0.6–3.2)

Hazard ratios and 95% confidence intervals (CIs) for serum glucose, phosphorus, albumin, and ionized calcium concentrations were based on 100-unit, 1-unit, 0.5-unit, and 0.25-unit increments, respectively.

*Hazard ratio for serum BUN concentration at T0 = 2.03 (95% CI, 1.11 to 3.71; $P = 0.022$). †Hazard ratio for serum phosphorus concentration in cats with chronic renal failure at T0 = 1.14 (95% CI, 1.04 to 1.24; $P = 0.013$). ‡Hazard ratio for serum glucose concentration at T24 = 1.38 (95% CI, 1.06 to 1.80; $P = 0.017$). §Hazard ratios for serum albumin concentration at T0 = 0.60 (95% CI, 0.39 to 0.93; $P = 0.022$) and at T96 = 0.14 (95% CI, 0.014 to 0.44; $P < 0.001$).

mortality rate for each incremental increase in serum phosphorus concentration of 1 mg/dL (adjusted HR, 1.12; 95% CI, 1.00 to 1.25; $P = 0.051$). In the 17 cats with chronic renal failure, the median serum BUN concentrations at T0, T24, and T96 were 63, 43, and 39 mg/dL, respectively. Cats had a decreased mortality rate for each incremental increase in serum albumin concentration of 0.5 g/dL at T0 (adjusted HR, 0.60; 95% CI, 0.39 to 0.93; $P = 0.022$) and T96 (adjusted HR, 0.14; 95% CI, 0.045 to 0.44; $P < 0.001$). In addition, cats were more likely to be weaned off TPN for each incremental increase in serum albumin concentration of 0.5 g/dL at T0 (adjusted OR, 1.87; 95% CI, 1.08 to 3.25; $P = 0.25$) and T96 (adjusted OR, 3.04; 95% CI, 1.15 to 8.05; $P = 0.025$), although this finding was only significant at T96.

The Hct and neutrophil concentration of all cats, with the exception of those that received fresh whole blood, stored whole blood, or packed RBCs during TPN administration, were evaluated (**Table 3**). At T0, T24, and T96, Hct values were below the lower reference limit in 21 of 42 cats, 14 of 19 cats, and 13 of 16 cats, respectively. In contrast, at T0, T24, and T96, Hct values were above the upper reference limit in 10 of 42 cats, 1 of 19 cats, and none of 17 cats, respectively. The change in Hct in 16 cats at T96 ranged from a decrease of 18.0% to an increase of 5.5% (median decrease, 6.7%). The Hct values at T24 and T96 were not significantly associated with mortality rate. At T0, T24, and T96, neutrophilia was reported for 49 of 71 (69%) cats, 21 of 30 (70%) cats, and 17 of 32 (53%) cats, respectively. Four cats with normal neutrophil concentration before initiation of TPN developed neutrophilia during TPN administration, and 2 additional cats became febrile without neutrophilia. In contrast, at T0, T24, and T96, 2 of 71 (2.3%) cats, 1 of 30 (3.3%) cats, and 2 of 32 (6.3%) cats were neutropenic, respectively. Neither neutrophil concentration nor the presence of toxic neutrophils was significantly associated with mortality rate. Assessment of platelet concentrations did not include data for cats that received fresh whole blood or stored whole blood during TPN administration. At T0, T24, T96, and T ≥ 5 days, 22 of 42 cats, 11 of 17 cats, 8 of 12 cats, and 8 of 13 cats were thrombocytopenic, respectively. The platelet concentration was not significantly associated with mortality.

Cats with pancreatitis (n = 35), hepatic lipidosis (25), chronic renal failure (17), and diabetes mellitus (13) constituted the largest proportion of patients receiving TPN administration. Compared with all other disease categories, cats with chronic renal failure (with or without concurrent nonneoplastic liver disease or diabetes mellitus) had a significantly ($P = 0.021$) increased rate of mortality (adjusted HR, 2.46; 95% CI, 1.29 to 4.60; **Table 4**). Thirty-six of the 75 cats were weaned off TPN because of apparent recovery, 23 cats were euthanatized, and 16 cats died as a result of their primary disease or complications associated with the disease. Six of the 36 cats weaned off TPN required enteral nutrition, whereas the other 30 resumed oral feeding. Euthanasia was elected for 18 of the 23 cats because of the severity of their primary disease and imminent death, whereas euthanasia was elected for the other 5 cats because of financial constraints. Of those 5 cats, 1 cat had gastroenteritis and hepatitis (euthanatized after 8 days of TPN), 2 cats had concurrent hepatic lipidosis and pancreatitis (euthanatized after 1 and 1.25 days of TPN, respectively), 1 cat had hepatic lipidosis (euthanatized after 8 days of TPN), and 1 cat had pancreatitis (euthanatized after 3.25 days of TPN). Of the 36 cats that recovered, 17 (47%) had more than 1 disease. The most common diseases among cats in this group included pancreatitis (n = 15), hepatic lipidosis (8), diabetes mellitus (7), chronic renal failure (4), and gastroenteritis (4). Nineteen of the 23 (82%) cats that were euthanatized had multiple disorders. The most common diseases among cats in this group included pancreatitis (n = 12), hepatic lipidosis (11), gastroenteritis (5), and chronic renal failure (5). Thirteen of the 16 cats that died as a result of illness had multiple disorders. The most common dis-

Table 3—Results of hematologic analyses in 75 cats prior to (T0) and at 24 (T24) and 96 (T96) hours and 5 or more days after administration of TPN.

Variable	Reference range	Median (range)
Platelets (platelets/μL)	200,000–600,000	
T0 (n = 42)		198,500 (43,000–875,000)
T24 (17)		180,000 (22,000–297,000)
T96 (12)		156,000 (73,000–944,000)
T ≥ 5 days (13)		191,000 (22,000–394,000)
Hematocrit (%)	29%–35%	
T0 (42)		29.5 (16.2–49.9)
T24 (19)		22.8 (14.8–38.2)
T96 (16)		22.7 (12.9–35.8)
Neutrophils (cells/μL)	2,500–11,300	
T0 (71)		14,184 (1,530–69,741)
T24 (30)		15,796 (759–59,490)
T96 (32)		14,630 (192–47,630)

Table 4—Most common diseases and associated percentage mortality in 75 cats receiving TPN.

Disease*	No. of cats	Percentage mortality	Median duration of TPN (days)
Pancreatitis	35	46	5.8
Hepatic lipidosis	25	52	5.3
Chronic renal failure	17	71	3.5
Diabetes mellitus	13	23	5.1
Gastroenteritis	13	62	4.0
Hepatitis or cholangiohepatitis	7	57	4.0

*Many cats had multiple diseases.

eases among the cats in this group included pancreatitis (n = 8), chronic renal failure (7), hepatic lipidosis (6), and gastroenteritis (4). The overall mortality rate was 52%; the mortality rate for the 14 cats administered TPN in the period from September 1994 through November 1996 was 64.3% (95% CI, 38.3% to 90.3%). For the 15 cats administered TPN in the period from December 1996 through February 1999, the mortality rate was 46.7% (95% CI, 20.6% to 72.8%). For the 46 cats administered TPN in the period from March 1999 through May 2001, the mortality rate was 50.0% (95% CI, 35.4% to 64.6%). There was no significant difference in mortality rates among these 3 study periods.

Complications—All complications were recorded and categorized as metabolic (n = 240), mechanical (19), and septic (6). The mechanical and septic complications represented all complications recorded during the entire duration of TPN administration, whereas the metabolic complications represented laboratory abnormalities recorded at T24 (n = 102) and T96 (138). Lipemia was detected at T0 in 18 of 75 (24%) cats, T24 in 13 of 67 (19%) cats, and T96 in 8 of 53 (15%) cats. The most common metabolic complications detected at T24 included hyperglycemia (diabetic cats excluded; 20/43 [47%] cats), hyponatremia (21/62 [34%]), hypokalemia (17/62 [27%]), hypocalcemia (6/44 [14%]), high total carbon dioxide concentration (5/37 [14%]), hypophosphatemia (4/32 [13%]), and hypoalbuminemia (4/33 [12%]). Both hyperglycemia at T24 (adjusted HR, 5.66; 95% CI, 1.71 to 18.79; $P = 0.005$) and an incremental decrease in serum albumin concentration at T24 (adjusted HR, 7.20; 95% CI, 0.89 to 58.38; $P = 0.04$) were significantly associated with an increased mortality rate. Cats that were hyperglycemic at T24 were less likely to be weaned off TPN (adjusted OR, 0.11; 95% CI, 0.021 to 0.54; $P = 0.007$), whereas none of the 4 hypoalbuminemic cats were successfully weaned off TPN (adjusted OR, < 0.001; no 95% CI or P value). Two of those 4 hypoalbuminemic cats were assessed as clinically dehydrated on physical examination at T24, whereas the other 2 cats had concurrent abdominal effusions (samples of which were classified as a mild purulent exudate on cytologic examination). The most common metabolic corrections during TPN administration at T24 included hypophosphatemia (5/16 cats), hyperkalemia (2/6), hyperphosphatemia (2/7), and hypochloremia (7/29 [24%]). The most common metabolic complications at T96 included hyperglycemia (diabetic cats excluded; 16/35 [46%] cats), hyponatremia (11/52 [21%]), hypochloremia (8/40 [20%]), high serum ALP activity (6/31 [19%]), hypophosphatemia (6/34 [18%]), hypokalemia (7/48 [15%]), and hyperchloremia (6/40 [15%]). Hypophosphatemia was associated with increased mortality rate at T96 (adjusted HR, 22.89; 95% CI, 2.13 to 245.9; $P = 0.01$). Of the 6 cats with hypophosphatemia, 4 had hepatic lipidosis among other diseases, 1 had hepatic lymphoma, and 1 had septic peritonitis secondary to dehiscence of jejunal anastomosis following resection of a jejunal adenocarcinoma. Three of the 6 hypophosphatemic cats were assessed as moderately to markedly underweight (body condition score, 1 to 3/9). The most common metabolic corrections during TPN administration at T96 included hypokalemia (16/32 [50%] cats), high serum AST activity (12/25 [48%] cats), low total carbon dioxide concentration (13/29 [45%] cats), and hypophosphatemia (5/11 cats).

Sixteen of the 75 (21%) cats had at least 1 mechanical complication. The most common mechanical complications included dislodgment of the jugular catheter (n = 6), kinking of the jugular catheter at the suture site (3), and occlusion of the administration line (2). The type of jugular catheter used for TPN administration was described in the medical records for 53 of 75 cats. Triple-lumen catheters were the most common catheter used (n = 41), followed by double-lumen catheters (11) and single-lumen catheters (1). The type of catheter used was not associated with mortality rate. Septic complications were not identified in this study population, although while receiving TPN, 4 cats developed neutrophilia and 2 additional cats became febrile. Three of the 4 cats that developed neutrophilia recovered and were weaned onto oral alimentation. The fourth cat that developed neutrophilia died as a result of bile duct carcinoma with concurrent pancreatitis and hepatic lipidosis. The 2 cats that became febrile during TPN administration had pancreatitis and hepatic lipidosis; both cats were euthanatized because of financial constraints. Bacteriologic cultures of the TPN catheters, TPN solutions, or blood samples were not performed for those 2 febrile cats; however, negative results were obtained via urinalysis in 1 of the cats. Results of bacteriologic culture were negative for samples obtained from the jugular catheter (n = 4), TPN solution (1), blood (3), pleural fluid (2), and burette chamber[h] attached to the infusion line (1). Bacteriologic culture yielded microbial growth for 3 of the 17 urine samples and 1 of the 3 peritoneal fluid

samples; positive culture results were not significantly associated with mortality rate.

Discussion

To the authors' knowledge, the study reported here is the first comprehensive evaluation of TPN administration in a large cohort of cats. The lack of improved survival rate through the 7 years of the study (despite improved nursing care and enhanced selection of parenteral formulations) is most likely a reflection of the increasing complexity and severity of the cases with advanced disease that were presented to the VMTH during those years. The high mortality rate of the cats (52%) in the study of this report reflected the critically ill status of these patients; furthermore, most (82%) of these cats had multiple concurrent diseases, including chronic renal failure, pancreatitis, liver disease, and diabetes mellitus.

There were few variables at initial evaluation that served as indicators of prognosis. Cats that were obtunded or comatose at initial evaluation had a nonsignificant increase in mortality rate, compared with cats that were bright, alert, and responsive or quiet, alert, and responsive. In addition, cats with a history of weight loss had a significant increase in mortality rate. The weight loss in those cats may have been a result of prolonged periods of inappetence or anorexia associated with chronic diseases, such as renal failure and pancreatitis. Malnourished humans with a history of weight loss who are hospitalized have also been shown to have increased illness and death.[24,25]

The most common metabolic complication during TPN administration was hyperglycemia. Thirty-four of 58 (59%) cats had blood glucose concentrations above the upper limit of the reference range prior to initiation of TPN, reflecting the high incidence of stress hyperglycemia in cats.[26] This finding was similar to that of a retrospective study[20] evaluating TPN administration in 12 cats in which 4 of 9 cats with glucose intolerance had hyperglycemia before TPN administration. The stress response associated with hospitalization or blood collection in cats has been associated with hyperglycemia secondary to increased serum lactate concentration and norepinephrine release.[26,27] In a large retrospective study[13] of dogs receiving TPN, hyperglycemia was also found to be the most common metabolic complication. Hyperglycemia commonly occurred during the first 24 hours of TPN administration in that study but returned to within reference range after 48 hours, which is consistent with findings of studies[28,29] of humans receiving TPN. In contrast, hyperglycemia persisted for > 96 hours in most cats in the study of this report, reflecting the unique challenge of successful regulation of blood glucose concentrations in cats.

Severe illness is known to affect blood glucose concentrations. In critically ill humans undergoing surgery, the severity of illness rather than the TPN itself was the dominant factor associated with glucose intolerance in the perioperative period.[30] In addition, the cats in the study of this report were mostly middle-aged and old cats; in humans, increasing age has been associated with alterations in glucose homeostasis, including hyperglycemia, glucose intolerance, and insulin resistance.[31] In humans, the higher incidence of hyperglycemia was attributed to decreased insulin secretion and increased renal threshold for glucose[32]; however, to the authors knowledge, this has not been determined in cats to date.

Hyperglycemia was also the most commonly reported metabolic complication in 3 previous retrospective studies[12,19,20] evaluating cats receiving TPN. In 1 prospective study[21] in which healthy cats were evaluated, hyperglycemia was only detected in those cats for which the caloric content of the TPN administered exceeded their metabolic requirements. In the study of this report, a significant association was identified between hyperglycemia and increased mortality rate at 24 hours, but not at 96 hours, after initiation of TPN. Treatment with insulin may be indicated to maintain more precise glycemic control during TPN administration, similar to recommendations made in human medicine. Effective control of glycemia in critically ill human patients has been associated with a marked reduction in the incidence of bloodstream infections, reduction in the incidence of acute renal failure requiring dialysis or hemofiltration, reduction in the number of blood transfusions required, and reduction in the incidence of critical illness-associated polyneuropathies, compared with those required for patients with poor glycemic control.[33,34] Intensive insulin treatment in critically ill human patients partially prevents the anticipated postoperative decrease in neutrophil phagocytic function, ameliorates the depression in oxidative function of the alveolar macrophages, and reverses the decreased intracellular bactericidal activity in leukocytes.[33,34]

Evaluation of Hct values and platelet concentrations were of particular interest in the study of this report because of findings of a previous investigation[21] of anemia and thrombocytopenia associated with TPN administration in 7 healthy cats. The underlying causes of anemia and thrombocytopenia in that study were not elucidated, and RBC and platelet concentrations were not discussed in the previous retrospective studies[12,19,20] involving cats receiving TPN. Poor lipid clearance is associated with anemia and thrombocytopenia in humans receiving TPN.[35,36] One evaluation of children receiving long-term cyclic TPN identified a temporal link of intermittent thrombocytopenia with IV administration of a lipid emulsion.[37,e] The authors of that study attributed the decreased platelet life span and increased platelet destruction to reticuloendothelial system hyperactivation. However, the actual occurrence of this complication remains unclear because other studies[38,39] evaluating IV fat infusions have not detected similar changes in platelet concentration. Although the mean platelet concentration of cats in the study of this report was below the lower reference limit at 24 hours after initiation of TPN administration, platelet concentrations before TPN administration, at 24 and 96 hours, and after 5 days of TPN administration were not significantly different. Although the Hct values of the study cats were below the lower reference limit at 24 and 96 hours, the Hct values were not significantly different from the mean Hct value obtained prior to TPN administration. The decrease in the Hct

may be partially explained by the concurrent administration of parenteral fluids and the hemodilution effects of TPN. In addition, many cats in the study of this report were thrombocytopenic and anemic prior to TPN administration, making interpretation of the alterations in these variables more challenging.

In humans maintained on TPN, hypophosphatemia has been identified in association with the refeeding syndrome,[40] although this finding has been poorly documented in the veterinary medical literature. In contrast to the findings of Lippert et al,[20] cats with hypophosphatemia in our study had an increased mortality rate at 96 hours after initiation of TPN administration. Also, hyperphosphatemia was associated with an increased mortality rate at T0 in cats with chronic renal failure. Six of the 10 hyperphosphatemic cats in the study of this report had hyperphosphatemia secondary to chronic renal failure prior to TPN administration. In the other 4 cats, the development of hyperphosphatemia was most likely associated with excessive potassium phosphate supplementation in fluids given IV prior to TPN administration. Prior to TPN administration, the mean serum phosphorus concentration for these cats was 8.2 mg/dL, compared with a value of 4.1 mg/dL for the remainder of the study population. Cats with chronic renal failure and cats with high serum BUN concentration at T0 also had a significantly increased rate of mortality, which probably explains the associated increased mortality rate in those cats that were hyperphosphatemic.

The findings of the study of this report support those of previous studies[41,42] in humans that indicated a correlation between decreasing serum albumin concentration and increased mortality rate. In our study, cats with high serum albumin concentration before TPN administration and at 96 hours after TPN administration had a significantly decreased mortality rate. Although serum albumin concentration appeared to be a good prognostic indicator in the study of this report, the administration of TPN did not affect mean albumin concentrations. The short duration of TPN administration in the study cats (median, 4.6 days) is a likely reason for this finding. In addition, results of studies[43-45] in humans have indicated a strong correlation between a patient's underlying disease status and serum albumin concentration. Total parenteral nutrition was associated with an increase in serum albumin concentration after resolution of the underlying inflammatory processes in humans undergoing surgery that had a variety of diseases.[44] Furthermore, studies[45,46] in humans undergoing dialysis and patients with end-stage kidney disease have revealed a correlation between the concentration of acute phase proteins and fractional catabolic rate of albumin and rate of albumin synthesis.

Mechanical complications occurred infrequently in the study of this report and were not associated with increased mortality rate. The most common complications involved the dislodgment or kinking of the jugular catheter. Sixteen of 75 (21%) cats had at least 1 mechanical complication, which is less than that reported in a large study[13] of 209 dogs receiving TPN (in which 37% of the dogs experienced at least 1 mechanical complication). In that study, dogs were more likely to have complications associated with leaking or chewed administration lines, which reflects their behavioral characteristics. The lower incidence of mechanical problems in our study may also reflect the improved personnel skill and training in recent years.

It is difficult to comment on the lack of septic complications in the cats of the study of this report because only samples from 4 jugular catheters and 3 blood samples were submitted for bacteriologic culture. However, the low number of samples submitted also reflects the lack of clinical suspicion of sepsis in these patients. Four of the 75 (5.3%) cats in the study of this report developed neutrophilia, whereas 2 (2.7%) became febrile after the initiation of TPN. These findings are similar to those in dogs and humans maintained on TPN in which 4.4% to 21% of patients developed a septic complication.[13,25,47] One of the 7 healthy cats in the investigation by Lippert et al[21] developed mild neutrophilia with a left shift on the last day of TPN administration, and WBC variables were not evaluated in the previous retrospective studies.[12,19,20] The lack of septic complications in the study of this report may reflect the increased utilization of TPN in recent years and improved aseptic technique.

With the increased availability and familiarity of TPN in veterinary medicine, proper identification of suitable recipients and utilization of TPN are of utmost importance. It seems intuitive that for each additional day that cats received TPN, there was a decreased rate of mortality, but this factor is important to consider during patient selection. In humans, TPN is not thought to be beneficial unless it is administered for at least 2 weeks.[17] The mean duration of TPN administration in the study of this report was 5.7 days, which is similar to the duration reported in a study[13] of the use of TPN in dogs (4.4 days) and similar to another previous report[15] in the veterinary literature. This duration is substantially shorter than that reported in the human medical literature (10 to 26 days)[17,48] and is far shorter than the current recommendations for treatment of humans.[17] The reasons for the shorter duration of TPN administration in veterinary patients may be related to financial constraints of many pet owners and our limited ability to assess the nutritional status of those patients that would allow for early identification of TPN candidates.[13]

Overall, the study of this report revealed a high mortality rate in cats maintained on TPN (52%) and underscored the critically ill nature of cats with multiple concurrent diseases that afforded the animals a poor to grave prognosis independent of TPN intervention. Poor prognostic indicators (based on selection criteria for TPN at T0) included diagnosis of chronic renal failure, history of weight loss, and hypoalbuminemia. The presence of hyperglycemia at T24 during TPN administration was also associated with a poor outcome. In contrast, increased duration of TPN administration and the supplementation of IV fluids with potassium chloride during TPN administration were associated with decreased mortality rate. The lack of early intervention with TPN in many cats following hospitalization cannot account for the poor outcome because there was no significant association between length of hospitalization before TPN administration and mortality rate. Additional prospective

studies are warranted to compare TPN versus enteral alimentation in critically ill cats.

[a]L-CATH intravenous catheter placement unit, Luther Medical Products Inc, Tustin, Calif.
[b]Double-lumen and triple-lumen central venous catheterization sets, Arrow International Inc, Reading, Pa.
[c]Travasol 8.5% with electrolytes, Baxter Healthcare Corp, Deerfield, Ill.
[d]Dextrose solution, VEDCO Inc, St Joseph, Mo.
[e]Intralipid, Pharmacia Inc, Clayton, NC.
[f]NUAIRE Bioloical Safety Cabinet, NUAIRE Inc, Plymouth, Minn.
[g]Plasma-Lyte 148, Baxter Healthcare Corp, Deerfield, Ill.
[h]Buretrol Solution Set, Baxter Healthcare Corp, Deerfield, Ill.

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