Supportive Nutritional Intervention in Pediatric Cancer


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Abstract

Nutritional support of the child with cancer now is recognized as an important adjunct to cancer treatment. Protein-energy malnutrition frequently accompanies the diagnosis and treatment of children with neoplastic diseases. Common risk factors for the development of protein-energy malnutrition include advanced stages of disease, lack of tumor responses, intense treatment with curative intent (including chemotherapy cycles at ≤3-week intervals, abdominal operative procedures, or abdominal and pelvic irradiation), and the absence of a supportive health care team which implements effective nutritional support. The impact of malnutrition may be reflected in tolerance of treatment, tumor response, and survival as well as in the incidence of complications. The risks and benefits associated with enteral and parenteral nutritional support are reviewed. Preliminary data from our institution document the severity of alterations in nutritional status and the immunological competence associated with multimodal treatment of children with advanced cancer. The effectiveness of enteral and parenteral nutrition in supporting a satisfactory nutritional status and/or reversing protein-energy malnutrition was evaluated in 28 children, ages 1 to 19 years, with a variety of neoplasms (21 solid tumors, 7 leukemia-lymphoma). A comprehensive enteral nutrition program which included intense nutrition counseling and oral supplements was found to be ineffective in preventing nutritional depletion during initial intense treatment of most children. Sixteen of 21 patients who received a comprehensive enteral nutrition program had a decreased kilocalorie intake [48 ± 24% (S.D.) of the Recommended Dietary Allowance] and significant weight loss (16 ± 8%). On the other hand, total parenteral nutrition provided at a kilocalorie intake of 100% of the Recommended Dietary Allowance and 2.5 to 3 g amino acids per kg for 28 or more days effectively restored muscle and fat reserves, increased serum albumin and transferrin to normal concentrations, and, in most patients, reversed anergy to recall skin test antigens. A shorter period of total parenteral nutrition (9 to 14 days) did not restore appropriate weight for height, fat reserves, and albumin concentration, although transferrin concentration was normalized and quality of life was improved. Of the group of 28 patients, 9 children (ages 1 to 7 years) with Wilms' tumors had the most severe and predictable malnutrition. A dramatic loss of weight (22 ± 7% by 26 ± 17 days from the beginning of treatment) was associated with initial intense treatment in children who received enteral nutrition. Every patient who received parenteral nutrition gained weight despite continuing treatment. These data suggest that most children with advanced Wilms' tumors will benefit from early and continued provision of adequate nutrition, such as that provided by total parenteral nutrition. Once patients completed the initial phase of treatment, however, enteral nutrition was effective in restoring or maintaining muscle and fat reserves in patients who had no evidence of tumor. Further research is needed to determine the roles of enteral and parenteral nutritional support in children with specific tumor types, when and how to implement effective enteral nutrition programs, and the value of parenteral nutrition in the support of the nourished child.

Nutritional support of the patient with cancer is attracting considerable attention as an important adjunct to cancer treatment. Effective nutritional support has been one of the most important and potentially beneficial advancements in patient care in the last 10 years. This report identifies children at high risk for nutritional depletion, discusses the significance of nutritional support, reviews the risks and benefits of enteral and parenteral nutritional support, provides data regarding the effectiveness of these modes of nutritional support in selected populations of children with neoplasms, and summarizes conclusions regarding the use of enteral and parenteral nutrition in the clinical management of children with cancer.

Childhood Neoplasms with High Risk for PEM

PEM is frequently observed at the time of diagnosis and during treatment of childhood cancer (54, 59, 70). The incidence of PEM at diagnosis of childhood neoplasms varies from 6% to as high as 50% (Table 1), depending upon tumor type, stage of disease, and criteria for PEM. Although data regarding the incidence of malnutrition associated with specific tumor types of childhood neoplasms and their treatment are sparse, some generalizations can be made which are consistent with clinical observations previously noted at this institution. At initial diagnosis or at the time of relapse, children with advanced stages of solid tumors have a higher incidence of PEM than do children with localized disease or children with leukemias. Although PEM may not be present at diagnosis, it may occur frequently during treatment. A number of factors may significantly increase the risk of development of PEM in children with neoplasms (Table 2). The extent of disease at diagnosis or the intensity and mode of treatment designed to eradicate the neoplasm and tumor response are determinants for the development of PEM. In addition, the absence of a supportive health care team and lack of attention to enteral nutrition increase the

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1 Presented at the Pediatric Cancer and Nutrition Workshop, December 11 and 12, 1980, Bethesda, Md. Supported in part by Grants RO1 CA28005 and RO1 CA28531 from the National Cancer Institute, NIH, Bethesda, Md. 20205.

2 The abbreviations used are: PEM, protein-energy malnutrition; TPN, total parenteral nutrition; RDA, recommended dietary allowance.
risk of PEM. The effects of therapy on nutritional status are discussed in detail elsewhere in this workshop (22).

Significance of Supportive Nutritional Intervention

The impact of malnutrition in children with cancer may be reflected in their tolerance of treatment (28, 71), response to chemotherapy (10, 43), and duration of survival (17). In a prospective study of more than 3000 adults with cancer, DeWys et al. (17) demonstrated a statistically significant effect of weight loss on median survival of patients with solid tumors when performance status and metastatic anatomic sites were categorized. The effect of weight loss on survival, however, was not significant in patients with acute nonlymphocytic leukemia, possibly because of their poor survival rate. Preliminary data from children with neuroblastoma at this institution support this observation (9). Nourished children with metastatic neuroblastoma at diagnosis appear to have a longer remission period and survive longer than do malnourished patients. Whether the malnutrition present at the beginning of treatment is simply a predictor rather than an influence on tumor response to treatment is yet to be determined. Suffice it to say, however, that nutritional support will not cure cancer; rather, it can function only as adjuvant supportive therapy which allows successful provision of oncological treatment.

Supportive nutritional intervention in children with cancer is based upon the idea that vital organ system function is better maintained when the nutritional status of the patient is preserved. The functions of the pulmonary, cardiac, gastrointestinal, hepatic, lymphoreticular, and hematopoietic organ systems have been studied in animals as well as in humans in various states of PEM. During PEM, alterations have been documented in each of these systems (Table 3). An adaptive phenomenon may preserve life of noncancer patients in states of mild and moderately severe malnutrition. However, patients with cancer may be stressed beyond adaptation because organ systems may be affected not only by malnutrition but also by the cancer therapy (5, 44). The ability of the liver to metabolize chemotherapeutic agents and of the gastrointestinal tract to absorb drugs and nutrients may be compromised in the malnourished state. In addition, malnourished children regularly have an impaired immunocompetence as evidenced by a frequent lack of response to skin test antigens (8, 25, 49). In the cancer patient, the immune status may be further compromised by chemotherapy (41) or by radiotherapy to large segments of the bone marrow resulting in granulocytopenia due to bone marrow suppression. Intercurrent infection and bleeding are frequent complications and common causes of death in these patients (38). The effects of PEM on organ function are further discussed elsewhere in this workshop (30).

Risks and Benefits of Enteral and Parenteral Nutrition

Successful nutritional support of the child with cancer is dependent ultimately upon the provision of adequate nutrients, regardless of the route of administration. Enteral nutrient requirements, however, may differ from parenteral nutrient requirements because of selective absorption of some nutrients by the gastrointestinal tract. Furthermore, nutrient requirements of cancer patients may differ from noncancer patients. Lawson (45) reported metabolic balance data which compared 9 patients hyperalimented centrally with 6 cancer patients hyperalimented enterally and with similarly treated malnourished controls. Cancer patients who received hyperalimenta-

### Table 1

<table>
<thead>
<tr>
<th>Type of neoplasm</th>
<th>% of total childhood neoplasms (63)</th>
<th>Incidence of PEM at diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute leukemias</td>
<td>30.2</td>
<td>2/34; 6%(^a) (54)</td>
</tr>
<tr>
<td>Lymphocytic</td>
<td>25.7</td>
<td></td>
</tr>
<tr>
<td>Nonlymphocytic</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>Lymphomas</td>
<td>13.6</td>
<td></td>
</tr>
<tr>
<td>Hodgkin’s</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>NonHodgkin’s</td>
<td>9.3</td>
<td>10–15%(^b) (17)</td>
</tr>
<tr>
<td>Central nervous system tumors</td>
<td>16.6</td>
<td>?</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>7.7</td>
<td>9/10; 47%(^c)</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>2.6</td>
<td>?</td>
</tr>
<tr>
<td>Soft-tissue sarcoma</td>
<td>6.5</td>
<td>?</td>
</tr>
<tr>
<td>Wilms’ tumor</td>
<td>6.1</td>
<td>5/16; 31%(^d)</td>
</tr>
<tr>
<td>Bone sarcomas</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>2.3</td>
<td>1/8; 12.5%(^a) (70)</td>
</tr>
<tr>
<td>Ewing’s</td>
<td>2.3</td>
<td>4/6; 67%(^a) (70)</td>
</tr>
<tr>
<td>Liver tumor</td>
<td>1.2</td>
<td>?</td>
</tr>
<tr>
<td>All others</td>
<td>8.9</td>
<td>?</td>
</tr>
</tbody>
</table>

\(^a\) Based on weight:height ratio of 80% <50th percentile for age or serum albumin <3.0 g/dl.
\(^b\) Adults; based on >10% weight loss.
\(^c\) Children with metastatic neuroblastoma at diagnosis; based on weight-for-height <fifth percentile, >5% weight loss, or serum albumin <3.2 g/dl.
\(^d\) Based on weight-for-height <fifth percentile, >5% weight loss, or serum albumin <3.2 g/dl.

### Table 2

<table>
<thead>
<tr>
<th>Common risk factors for development of PEM in childhood neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced disease at diagnosis or during treatment</td>
</tr>
<tr>
<td>Lack of tumor response</td>
</tr>
<tr>
<td>Abdominal and pelvic irradiation</td>
</tr>
<tr>
<td>Intense frequent courses at ≤3-wk intervals of cytotoxic chemotherapy which cause nausea and vomiting, gastrointestinal toxicity, or hepatic toxicity in the absence of corticosteroids or appetite stimulants</td>
</tr>
<tr>
<td>Operative procedures of the abdomen or other abdominal complications such as adynamic ileus, etc.</td>
</tr>
<tr>
<td>Psychological depression, absence of supportive health care team, and lack of attention to enteral nutrition</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Organ system alterations associated with PEM in humans and animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
</tr>
<tr>
<td>Decreased cardiac output; atrophic heart muscle (42)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Morphological and cellular kinetic changes, resulting in short, flat villi with decreased absorptive area (61); decreased production of pancreatic enzymes, especially lactase (67); altered bile acid synthesis (62); decreased gastric motility and gastric emptying time (42); increased incidence of peptic ulcers (42)</td>
</tr>
<tr>
<td>Liver</td>
</tr>
<tr>
<td>Atrophy and fatty degeneration (42)</td>
</tr>
<tr>
<td>Spleen</td>
</tr>
<tr>
<td>Atrophy of lymphoid tissue and Malpighian bodies; reduction in splenic sinuses (42)</td>
</tr>
<tr>
<td>Renal</td>
</tr>
<tr>
<td>Relatively resistant (42)</td>
</tr>
<tr>
<td>Hematopoietic</td>
</tr>
<tr>
<td>Degeneration of fatty bone marrows; hyperplasia of red marrow (42); normocytic, normochromic anemia (42)</td>
</tr>
<tr>
<td>Lymphoreticular</td>
</tr>
<tr>
<td>Thymus, T-lymphocytes, and cell-mediated responses impaired (8, 27, 49); immunoglobulins usually normal or increased (8)</td>
</tr>
<tr>
<td>Neurological</td>
</tr>
<tr>
<td>Relatively resistant; peripheral neuropathies (7B vitamin deficiencies) (42)</td>
</tr>
<tr>
<td>Muscle</td>
</tr>
<tr>
<td>Atrophy</td>
</tr>
</tbody>
</table>

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tion centrally retained significantly less phosphorus and magnesium than did noncancer controls, and cancer patients who were given hyperalimentation enterally retained significantly less phosphorus, potassium, nitrogen, chloride, and magnesium than did controls. We are at the beginning of an era which hopefully will provide a better understanding of the nutrient requirements of children with cancer and increased effectiveness in nutritional intervention. Data regarding the roles of enteral and parenteral nutrition in support of children with specific tumor types, when and how to implement effective enteral nutrition support programs, and the value of parenteral nutrition in the support of the nourished child are sparse. Known risks and benefits of enteral and parenteral nutrition will be reviewed in the following sections.

Enteral Nutrition. Provision of nutrition via the enteral route is the preferred method of feeding because it is more physiological, has a lower risk of infection and other catheter-related complications, is less expensive, and encourages more normal play activities and life style. Often the disease or its treatment interferes with eating, taste sensations, or function of the gastrointestinal tract (13–15, 18, 20, 21, 23, 51). Alterations in taste sensation noted in some adults are of particular interest. Changes in taste sensation have been correlated with symptoms of the patients, i.e., a general decrease in taste pleasurability with elevated sucrose thresholds (7, 73), meat aversion with low bitter thresholds (14), and preference for tart juices with increased sour acuity (73). In addition, elevated salt thresholds have been observed (7, 14, 73). Furthermore, taste abnormalities have been correlated with tumor extent (7, 14) and with reduced energy intake (7, 14, 32, 73). Conceivably, this information can be used to develop nutritional intervention strategies which enhance acceptance of food (7, 14, 15, 18, 73). For example, patients with an elevated sweet threshold may find that the addition of sugar enhances palatability, or patients who have an aversion to meat because of taste changes may enjoy alternate sources of protein such as eggs, peanut butter, and cheese.

A number of factors besides those directly due to the disease may contribute also to an inadequate food intake. For instance, misconceptions about food, fear of disease, unfamiliar foods, hospital routines which conflict with meals, lack of attention to the needs of a patient, learned food aversions (1–3, 65), trauma associated with medical procedures, and pain may interfere with eating. There are few data to evaluate the effectiveness of enteral nutrition when these factors are taken into consideration. An intense, individualized enteral feeding program that minimizes these obstacles still may provide an efficient method to support many children with cancer. Regardless of the effectiveness of parenteral support, the limitations of time and cost demand that enteral feeding be the primary mode for provision of nutrients during most of the treatment period.

Enteral nutritional supplementation (ad libitum) has been reported to provide some benefit in delayed hypersensitivity skin test responses (24) and in preventing PEM (26) in some selected types of adult cancers. A patient’s acceptance of enteral supplements may be influenced by taste alterations associated with cancer. Dewys and Herbst (18) reported significant differences in supplement preference scores between cancer patients and normal controls, and a correlation of bitter taste recognition threshold with overall preference scores. Unfortunately, the patients with a low bitter taste threshold were more likely to give negative preference scores than were those with a normal threshold. These findings are consistent with our observations that the children who have a reduced intake and a particular need for supplements may be the least likely to accept them. In our experience with children who have advanced cancer, supplements have provided some benefit in a small subgroup of older infants and toddlers, especially those who were being bottle fed. The role of supplements in the provision of enteral nutrition for children has not been extensively evaluated.

Donaldson et al. (23) suggested that the prophylactic use of a special diet may prevent acute and chronic radiation enteritis. This diet was devoid of gluten, cow’s milk protein, and lactose and was low in fat and residue. Several other investigators (4, 24) have reported the use of a defined formula for adult patients who were receiving abdominal or pelvic irradiation. Perhaps the most significant benefits observed in these patients were the preservation of cellular immunity (24) and the minimization of the decrease in total lymphocyte count following irradiation (4).

In children with neoplastic diseases, the currently available defined-formula diets with amino acids or hydrolysates substituted for intact proteins have been almost universally rejected by young children because of poor palatability, nonacceptance of a new and strange taste, or possibly aversive conditioning. Even more familiar foods may not be eaten during this time. Force feedings by nasogastric tube are not considered an acceptable option in very young children because of possible emesis with resulting aspiration, the potentiation of nausea during abdominal irradiation and chemotherapy, and the young patients’ resistance to insertion of a nasogastric tube. An older child may cooperate and can be taught to pass his own nasogastric tube. Continuous-drip enteral tube feedings during the night have been beneficial in a few patients with a functional gastrointestinal tract. Every effort has been made to make eating (and the hospitalization experience) a positive rather than an adverse experience. This is especially important because the duration of treatment may continue for several years and the child’s cooperation with regard to eating programs is essential over the long run. More acceptable options consist of either an enteral nutrition program which utilizes nutritious foods more familiar to children during treatment-free periods or parenteral nutrition programs.

Parenteral Nutrition. Parenteral nutrition bypasses the limitations of reduced caloric intake from nausea and vomiting as well as from anorexia (15, 34, 47, 66) associated with tumor burden, cancer treatment, and/or PEM. Cost of parenteral nutrition is substantial, and a high quality of care is essential. Known risks or complications (e.g., infection, liver dysfunction, hepatomegaly, thrombus formation, and a multiplicity of metabolic complications) may be associated with TPN. Risks can be minimized or safely controlled with careful patient management and strict adherence to a parenteral nutrition protocol. In a multiinstitutional study of complications observed in adult patients randomized to either TPN (125 patients) or control, non-TPN (126 patients) groups, Mullen (48) reported that the administration of TPN adds little serious morbidity and mortality. An increased incidence of fever (p < 0.003), anemia (p < 0.09), and pulmonary dysfunction (p < 0.13) was observed in
the TPN group; however, the frequencies of the latter 2 complications were not significantly different from those of the control group. Although incidence of fever was higher in the TPN group, both groups had a similar incidence (25%) of documented infections at distant sites. In the TPN group, 6% had catheter tip infections and 4% had infections at the catheter exit site. Thus, 30% in the TPN group and 11% in the non-TPN group had fevers of unexplained etiology. Van Eys et al. (28) reported a 3% incidence of catheter-related infections and a 10% incidence of sepsis unrelated to the catheters in a series of 25 children who received TPN. Of interest was the fact that the infection rate was higher in malnourished children. Filler et al. (28) reported a sepsis rate of 8% associated with TPN administered to a series of 65 children with cancer. The possibility that TPN stimulates tumor growth in excess of host repletion needs to be considered, although clinically this has not been observed when aggressive treatment is given simultaneously. In fact, it is conceivable that TPN may beneficially stimulate cell replication and increase effectiveness of cell cycle-specific drugs, although this has not been apparent in several recent prospective controlled studies of adults with specific types of tumors (50, 53).

The expense and risks associated with parenteral nutrition need to be carefully considered in relation to potential benefits. Several controlled prospective studies of parenteral nutrition given by central vein to selected populations of malnourished children with neoplastic disease have demonstrated the following benefits: effective reversal of PEM (59, 71); restoration of immunocompetence in some patients (57, 59); and fewer dose adjustments of chemotherapy (71). The benefits of parenteral nutrition for nourished children with cancer and for malnourished children with specific tumor types remain to be established.

**Effectiveness of Enteral and Parenteral Nutrition: The Riley Hospital Experience**

**Patients and Methods.** In the absence of sufficient data in the literature relating to the nutritional management of children, the effectiveness of enteral and parenteral nutrition regimens was evaluated in children with advanced cancer (59) (Table 4). These children had the most aggressive treatment and, therefore, were expected to have the most significant nutritional problems. Similar treatment protocols were used for each tumor type. Children with Stage III and IV solid tumors and second-relapse leukemia-lymphomas were assigned to 2 groups at diagnosis according to nutritional status (nourished, depleted).

Children received a comprehensive enteral nutrition program if they were considered nourished at diagnosis. This consisted of intense nutritional counseling and p.o. supplements. A concerted effort was made to encourage adequate p.o. intake through age-appropriate individual counseling, provision of pediatric menus, readily available snacks, an atmosphere conducive to eating in age-related-play dining rooms, child-oriented nutritional education experiences (19, 58), play activities, and parent care facilities. Continuity of nutritional care was provided by the same pediatric dietitian. Neither vitamin nor iron supplementation was used.

Children received TPN if they were considered nutritionally depleted. Children were considered nutritionally depleted if they had a recent weight loss greater than 5%; were below the fifth percentile on weight-for-height grids, or had a serum albumin concentration of less than 3.2 g/dl. Parenteral nutrition provided a synthetic nutrient mixture of amino acids (2.55 g amino acids per dl); Free Amino II; McGaw Laboratories, Milwadgeville, Ga.), glucose, minerals, and vitamins (1 ml Multivitamin Infusion; USV Pharmaceutical Corporation, Tuckahoe, N. Y.). Nutrients were administered through a central hyperalimentation catheter placed into the superior vena cava under sterile conditions. The catheter was attached to on-line micropore filters and pumps; catheter care techniques were described previously (59). Additionally, several nutrients were given weekly by i.m. injection including: 1 mg folate acid; 100 mg hydroxycobalamine; and 1 mg vitamin K. Also, a fat emulsion was administered (2 g fat per kg per day) via peripheral veins 3 times per week. Concentrations of glucose (15 to 25 g/dl) and rate of administration were increased over a 5- to 7-day period to provide an arbitrarily set goal of 100% of the RDA for kilocalories, since parenteral nutrient intake standards for children with cancer do not exist.

**Children with Advanced Disease.** At the beginning of therapy, 21 patients received an enteral nutrition program while 7 received TPN. Sixteen of the 21 children who were considered nourished and received enteral nutrition at the beginning of cancer treatment had a decreased nutrient intake [48 ± 24% (S.D.) RDA] and significant weight loss (16 ± 12%). Although enteral nutrition was generally ineffective, TPN provided for 28 or more days was quite effective. A total of 18 children received TPN for an average of 24 days; kcal averaged 90 ± 26% RDA during weight gain. TPN effectively restored muscle and fat reserves, increased serum albumin from 3.06 ± 0.38 to 3.48 ± 0.53 g/dl; increased serum transferrin from 175 ± 62 to 236 ± 40 mg/dl, and, in most patients, restored recall skin test reactivity to several antigens. At the beginning of TPN, only 1 of 18 patients was reactive to recall skin test antigens, whereas 7 of 11 children retested at the end of TPN were reactive. The total lymphocyte count, however, decreased from 1102 ± 966 to 737 ± 677 despite nutritional repletion with TPN.

Since duration of TPN from the beginning to the end varied from 7 to 60 days, biochemical and anthropometric measurements were further evaluated at short intervals (9 to 14 days) or long intervals (28 days) of TPN. TPN for 28 days significantly improved weight gain, subcapular skinfold measurements, serum albumin, and transferrin (Table 5). In contrast, TPN for

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**Table 4**

<table>
<thead>
<tr>
<th>Type of Neoplasm</th>
<th>No. of Affected Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilms' tumor</td>
<td>9</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>5</td>
</tr>
<tr>
<td>Ewing's sarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>3</td>
</tr>
<tr>
<td>Non-Hodgkin's lymphoma</td>
<td>3</td>
</tr>
<tr>
<td>Second relapse leukemia-lymphoma</td>
<td>3</td>
</tr>
<tr>
<td>Hodgkin's lymphoma</td>
<td>1</td>
</tr>
<tr>
<td>Embryonal cell carcinoma</td>
<td>1</td>
</tr>
</tbody>
</table>

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9 to 14 days restored neither serum albumin concentrations, nor skinfold reserves, nor appropriate weight for heights (although weight increases were significant). These data documented nutritional and immunological benefits of a 28-day course of TPN for malnourished children who were receiving intense treatment for advanced cancer. In addition, TPN allowed patients to continue vigorous treatment protocols which otherwise may have been jeopardized or impossible due to lack of tolerance. The small and heterogeneous group of patients from this early study did not allow conclusions regarding the relationship of a satisfactory nutritional status throughout treatment to tumor response or to length of survival.

Children with Wilms' Tumors. Of the group of 28 patients initially studied, 9 children (ages 1 to 7 years, 8 female) with Wilms' tumors had the most severe and predictable malnutrition (60). These children received treatment outlined in the National Wilms' Tumor Study II Protocol. Initial, intense treatment consisted of operative removal of primary tumor, 5 days of actinomycin D, weekly vincristine, and abdominal irradiation to the tumor bed. Maintenance chemotherapy treatment included 5-day courses of actinomycin D and vincristine at 3, 6, 9, 12, and 15 months from diagnosis. In addition, 4 patients received Adriamycin between the 3-month cycles. At diagnosis, 8 children received a comprehensive enteral nutrition program while one received TPN. Four of those who initially received enteral nutrition subsequently received TPN.

A dramatic loss of weight (22 ± 7% by 26 ± 17 days from the beginning of treatment) was associated with initial, intense treatment in the children who received enteral nutrition. On the other hand, every patient gained when receiving parenteral nutrition. During the period of intense treatment and weight loss, intake of kilocalories averaged 64% RDA whereas TPN provided 105 ± 9% RDA during weight gain. At the lowest weight (during enteral nutrition), 7 of the 8 patients were below the fifth percentile on weight-for-height grids (35) and below the tenth percentile on skinfold grids (40). Initial data indicated that 10 days of TPN was not sufficient for restoring an appropriate weight for height and, furthermore, that TPN was needed until the end of the intense treatment period (abdominal irradiation). Longer intervals (28 or more days of TPN) restored an appropriate weight for height, significantly increased serum transferrin and albumin concentrations, and reversed anergy (11). Longer intervals (28 or more days of TPN) restored an appropriate weight, fat reserves, and serum albumin.

Conclusions and Implications for Clinical Management

A comprehensive enteral nutrition program was not effective in preventing severe nutritional depletion during the initial and intense phases of cancer treatment for most of the children with advanced disease, although some benefits from this program were observed. Emotional support and understanding were provided for the child and his family during the treatment of a disease which may otherwise engender an overpowering sense of helplessness. A continuing relationship and sound nutrition philosophy were developed which facilitated the later success of an enteral nutrition program, once the child was past the most intense phase of his treatment. Nutritional depletion of children with Wilms' tumors was the most dramatic and predictable. Once a patient became malnourished, anorexia and other complications associated with PEM (6, 61, 62, 67) were compounded by the side effects and complications of almost continuous cancer treatment for 40 to 60 days (operative resection at diagnosis, chemotherapy, and abdominal irradiation of 1800 to 4000 rads). Preliminary data from these patients suggest that most children with advanced Wilms' tumors will benefit from early and continued provision of adequate nutrition, such as that provided by TPN, throughout the initial and intense treatment periods. Adjunctive TPN (or other effective nutritional support) seems imperative for patients with Stage IV disease, patients with unfavorable histology who receive the most rigorous treatment, and those severely malnourished at the onset. In these patients, nutrient intake is unlikely to be adequate for maintenance of a satisfactory nutritional state or for repletion during the first 40 to 60 days of treatment.

Based upon previous data, however, some nourished and marginally nourished children can be adequately supported with enteral nutrition. Usually, these are older children who are in maintenance phases of treatment, who respond to treatment, or who have less advanced disease. While it is possible to maintain nutrition enterally in some nourished children, it is very difficult if not impossible to replenish patients enterally. Parenteral nutrition is delayed often in hopes that the malnourished child will start eating. It is our experience that the child who is malnourished at diagnosis will remain so throughout intense treatment with curative intent. Furthermore, the child often becomes more severely malnourished and suffers numerous complications if not given adequate nutritional support.

TPN given for 28 or more days (at 90 to 100% RDA for kilocalories) was effective in nutritionally repelling patients. Administration of TPN for 9 to 14 days was not sufficient to restore an appropriate weight, fat reserves, and serum albumin.
concentrations, although serum transferrin concentration was normalized and quality of life was improved. These observations suggest that a 10-day interval of TPN provided at 100% RDA for kilocalories (in the absence of parenteral nutrient standards for children with cancer) and 2.5 to 3 g amino acids per kg is the minimum duration of treatment which provides benefit for the malnourished child. Usually, 21 or more days of TPN are necessary for restoration of an appropriate weight for height and for normalization of serum proteins in the severely malnourished child. Weight, skinfold measurements, and serum proteins provide only a gross estimate of renourishment. The repletion of the cancer patient may not be such a simple process since body weight may increase with an unchanged cell mass and other minerals may remain depleted (45). Inadequate repletion noted in several recent TPN studies (50, 64) with adults who have cancer may be related to altered host metabolism (29, 36, 47, 72), to the composition of the nutrient mixture, to a nonoptimal route and schedule of delivery, and to insufficient duration of therapy (16). The timing of parenteral nutritional support in relation to chemotherapy may be also critical in determining the myelotoxicity and cell cycle-specific drug effectiveness (56). These are significant areas of concern which need further research.

References


Discussion

Dr. Morrison: I’m confused. Are you equating what you call “comprehensive enteral nutrition program” with encouraged voluntary food intake? I just feel that’s a little misleading and not what I expect from enteral nutrition, which I think of as being tube feeding.

Dr. Jaffe: I think it would be important to indicate the extent of the radiation treatment received by these patients with Wilms’ tumor, whether they received total abdominal irradiation or hemiabdominal irradiation. There are a number of patients with Wilms’ tumor here, and 9 patients receiving abdominal irradiation. I would like to know exactly the extent of the radiation they received.

Dr. Rickard: The radiation was 1800 to 4000 rads. Dr. Jaffe: And how many received hemiabdominal and how many received total abdominal irradiation?

Dr. Rickard: There were 4 that received total and the rest hemiabdominal, and the radiation was 1800 to 4000 rads, age-adjusted to the maximum ability to receive radiation.

Dr. Jaffe: Was there any difference between the total abdominal group versus the hemiabdominal group?

Dr. Rickard: All of the 8 children who had Wilms’ tumors lost weight. I do not go further in noting the percentage of weight loss, because we interrupted that weight loss with TPN. Usually, the ones who received the full abdominal irradiation received TPN in order to continue their radiation.

Dr. Jaffe: Let me emphasize that that question was asked because I think a lot of patients can get away with normal radiation without TPN, and it would be something of a disservice to the individual to indicate that all patients receiving abdominal irradiation require TPN. I think the information regarding the extent of weight loss should be provided, whether it was hemiabdominal or total abdominal irradiation, and the like.

Dr. Nixon: Both our results and your study showed that hyperalimentation puts fat on the cancer patient. The question is, is that a good thing to do? Does fat weight help the cancer patient?

Dr. Rickard: Let me clarify. First of all, when we followed the children, we found that they actually improved their weight:height ratios first and then subsequently we began to see improvements in skinfolds, especially the subscapular skinfold. We didn’t necessarily see the increase in fat at the onset. I’m saying that I’m not sure we necessarily saw repletion of fat with short intervals of treatment.

Dr. Nixon: Does your data indicate that the weight-for-height increase was something other than fat?

Dr. Rickard: That’s a sticky question. The one thing I can say is that we did notice that, with 28 days of TPN, visceral proteins increased to normal concentrations.

Dr. Nixon: The most important point of the data I presented was that the balance studies indicated that we were not repleting the lean body mass with hyperalimentation. The argument has been presented, not here but elsewhere, that we weren’t hyperalimenting long enough, and I fail to understand why 6 months, for example, of hyperalimentation would make any difference when 1 month didn’t replete lean body mass. In a second group of patients with advanced colon cancer that was hyperalimented, their profiles of mood states increased; they told us that they felt better, but their performance status in most cases actually decreased. We should be careful about interpreting the subjective good that hyperalimentation does.

Dr. Rickard: I appreciate that and I think that’s a very difficult aspect to measure. Let me say, though, that it might depend on the way you manage the TPN patient, in terms of what sort of a flexibility they have relative to normal activity. Certainly with children, we saw a dramatic improvement in play activity.

Dr. van Eys: Dr. Rickard made an apology for what she said was a very trite statement, but I think it is not repeated often enough in these discussions, namely, that children are different, and what they do with calories is very different from what adults do with calories. If you have a 3-year-old given inadequate calories, the child will not grow. If you give the calories, growth rather than storage is the rule. So we have to be very careful that we do not jump too quickly from a 60-year-old colon carcinoma patient to a 3-year-old child that has been deprived of growing by inadequate calories. You will see differences.

Dr. DeWys: I want to comment about the rate of weight loss in the Wilms’ patients. Because it was so rapid, one has to consider that much of it is probably drawn from body muscle, with its high water content. You can lose weight more rapidly from muscle than you can from fat.
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Cancer Res 1982;42:766s-772s.

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