ABSTRACT

Because protein-calorie undernutrition is common in patients with neoplastic disease, nutritional support is often recommended. It is uncertain, however, that methods of supplemental alimentation successful in noncancerous subjects are suitable in cancer patients. We measured elemental balances, serum proteins, anthropometrics (triceps skinfold and mid-arm muscle area), and creatinine/height ratio in 15 undernourished patients with advanced cancer and in 10 noncancer undernourished controls during central venous or enteral hyperalimentation and found the following. (a) During central venous hyperalimentation, cancer patients showed significantly less improvement than the noncancerous controls in body weight (median increment, 5 kg in cancer patients and 8.5 kg in noncancerous), albumin (0.1 g/dl in cancer patients and 0.5 g/dl in noncancerous patients), creatinine/height ratio (4% of standard in cancer and 10% of standard in noncancer), and mid-arm muscle area (4% of standard in cancer and 11% of standard in noncancer). During enteral hyperalimentation, gains in body weight and albumin by cancer patients were significantly inferior to those in noncancerous subjects. Triceps skinfold increments, in contrast, were similar during both central venous and enteral hyperalimentation for cancer and noncancer patients, (b) While nitrogen retention was similar in cancer and noncancer patients, the cancer group retained significantly less magnesium and phosphorus (ΔMg in cancer patients, 3.2 mEq/day central, −2.7 mEq/day enteral; ΔMg in noncancer patients, 11.9 mEq/day central, 10.1 mEq/day enteral; ΔP in cancer patients, 0.13 g/day central, 0.07 g/day enteral; ΔP in noncancer patients, 0.27 g/day central, 0.33 g/day enteral). The poorer balances of cancer patients were caused by increased urinary, not fecal, loss.

These findings indicate a partial block in repletion of lean body mass or abnormal composition of newly deposited lean body mass when undernourished patients with advanced cancer receive hyperalimentation.

INTRODUCTION

In a recent report, we described progressive depletion of adipose tissue, skeletal muscle, and visceral protein in most advanced cancer patients in our hospital (48). Survival was decreased in patients with more severe undernutrition. Other factors associated with PCU include impaired cellular immunity, reduced tolerance to chemotherapy, and decreased function of major viscera (6, 50, 61). Since anorexia is a prominent component of this cancer cachexia syndrome (18), there has long been an interest in methods of bypassing the appetite and delivering adequate nutritional intake nonvollitionally. Most recently, the technique of CHA has been applied to patients with cancer (13, 20), and weight gain and positive nitrogen balance have been reported.

Enthusiasm for HA in cancer must be tempered, however, by animal studies which demonstrate that increasing the protein content of the diet stimulates tumor growth (3, 8, 9, 16, 58) and that most of the nitrogen retained in tumor-bearing animals is retained in malignant tissue rather than in the carcass (60). There have also been numerous reports of abnormalities of protein (10–12, 17, 25, 28–30, 36, 39–43, 46), carbohydrate (24, 32–34, 56, 63, 64), and lipid (4, 5, 15, 27, 37, 38, 44) metabolism in patients with cancer. Because of this diversion of nutrients to the tumor and these metabolic abnormalities in host tissue, it appeared premature to assume that the positive nitrogen balance and weight gain reported in cancer patients reflected restoration of normal lean body mass. We were therefore interested in evaluating the composition of the weight gained by these patients.

Metabolic balance studies provide an indirect noninvasive method for the evaluation of the composition of weight gain. We (54) and others (53) have demonstrated previously that, when lean body mass is restored, certain elements are retained by the organism in fairly fixed ratios, corresponding to the ratios in which they are found in normal protoplasm. If the nitrogen retention and weight gain reported in cancer patients reflects synthesis of normal lean body tissue, these patients should retain these elements in the same ratios. Significant deviation from normal patterns of element retention, however, would suggest that normal protoplasm was not being synthesized in response to HA. Previous balance studies in small numbers of patients with cancer treated with various nutritional regimens have demonstrated retention of some elements out of proportion to others, suggesting that indeed cancer patients may not synthesize normal lean body mass in response to HA (1, 22, 45, 61, 65, 66). We therefore performed elemental balance studies in 15 patients with advanced cancer receiving HA. These studies were also performed in 10 noncancerous patients with similar degrees of PCU receiving identical HA. It
was reasoned that these noncancerous patients would demonstrate patterns of element retention similar to those obtained in the past with other methods of nutritional support and would thus validate current measurements and techniques.

To help confirm the conclusions of our balance studies with regard to changes in lean body mass, we also performed serial determinations of MMA (7) and creatinine/height ratio (7, 21). Visceral function was assessed by calculation of changes in serum albumin concentration in response to HA.

We hypothesized that if cancer patients demonstrated abnormal patterns of element retention they would also manifest less improvement in lean body mass as assessed by these parameters. Changes in the adipose organ were also monitored serially in the 2 groups by TSF measurements (7).

MATERIALS AND METHODS

Patients. Fifteen patients with moderate to severe PCU (defined as creatinine/height ratio and TSF below 80% of standard) were selected for study from the general medical oncology ward population of Emory University Hospital and transferred to the Clinical Research Facility. Clinical data of this patient population, including age, sex, diagnosis, location of metastases, and baseline nutrition indicators are shown in Table 1. Ten noncancerous patients with a comparable degree of PCU were studied in a similar fashion in the Clinical Research Facility. Clinical data of these patients are also given in Table 1.

No attempt was made to match patients for the mechanism(s) by which they became malnourished, i.e., anorexia, malabsorption, hypermetabolism, predominantly protein depletion, or combined protein-carbohydrate insufficiency.

Experimental Design. The study for cancer patients comprised 3 sequential periods (Table 2). Period 1 was the time from starting HA to the beginning of chemotherapy; it ranged from 10 to 14 days in duration. During Period 2, both HA and chemotherapy were given; this lasted 2 to 5 days. Period 3 was a postchemotherapy HA period, averaging 5 to 7 days. The total duration of HA was 17 to 26 days. Anthropometric measurements were performed every 3 to 7 days.

The noncancerous controls received similar HA for periods lasting 21 to 28 days, with nutritional evaluation every 3 to 7 days as above.

HA Techniques. Nine cancer patients received CHA and 6 received EHA. No patient selected for EHA had contraindications to the enteral route (intractable vomiting or diarrhea, intestinal obstruction, or upper gastrointestinal bleeding). Four of the 6 had undergone segmental bowel resection for removal of primary disease, but none had a colostomy. Five noncan-

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Table 1. Ten noncancerous patients with a comparable degree of PCU were studied in a similar fashion in the Clinical Research Facility. Clinical data of these patients are also given in Table 1.

No attempt was made to match patients for the mechanism(s) by which they became malnourished, i.e., anorexia, malabsorption, hypermetabolism, predominantly protein depletion, or combined protein-carbohydrate insufficiency.

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Table 1. Clinical summaries of 15 cancer patients and 10 noncancerous patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Sites of metastases</th>
<th>Age</th>
<th>Sex</th>
<th>BW (% of ideal)</th>
<th>24-hr creatinine/height (% of standard)</th>
<th>MMA (% of standard)</th>
<th>TSF (% of standard)</th>
<th>Type of HA</th>
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<tr>
<td>Cancer patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>C1</td>
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<td>Liver</td>
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<td>59</td>
<td>M</td>
<td>70</td>
<td>54</td>
<td>64</td>
<td>32</td>
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</tr>
<tr>
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<td>Colon</td>
<td>Liver, lung, bone, nodes</td>
<td>51</td>
<td>M</td>
<td>89</td>
<td>66</td>
<td>85</td>
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<td>C4</td>
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<td>56</td>
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<td>78</td>
<td>75</td>
<td>65</td>
<td>25</td>
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<tr>
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<td>Head and neck</td>
<td>Liver</td>
<td>57</td>
<td>F</td>
<td>82</td>
<td>44</td>
<td>49</td>
<td>48</td>
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<td>Lung</td>
<td>67</td>
<td>M</td>
<td>61</td>
<td>43</td>
<td>66</td>
<td>24</td>
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<td>Liver, lung, bone, nodes</td>
<td>65</td>
<td>F</td>
<td>90</td>
<td>71</td>
<td>77</td>
<td>42</td>
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<td>68</td>
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<td>85</td>
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<td>54</td>
<td>M</td>
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<td></td>
<td></td>
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<td>35</td>
<td>M</td>
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<td>76</td>
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<td>41</td>
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<td>NC2</td>
<td>Regional ileitis (48)</td>
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<td>16</td>
<td>M</td>
<td>55</td>
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<td>65</td>
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<td>73</td>
<td>F</td>
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<td>70</td>
<td>76</td>
<td>38</td>
<td>CHA</td>
</tr>
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<td>M</td>
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<td>74</td>
<td>84</td>
<td>63</td>
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</tr>
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<td></td>
<td>53</td>
<td>M</td>
<td>72</td>
<td>72</td>
<td>80</td>
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<td>M</td>
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</tr>
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<td>F</td>
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<td>M</td>
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<td>30</td>
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<td>36</td>
<td>F</td>
<td>59</td>
<td>37</td>
<td>52</td>
<td>53</td>
<td>EHA</td>
</tr>
<tr>
<td>NC10</td>
<td>Malabsorption (36)</td>
<td></td>
<td>46</td>
<td>F</td>
<td>66</td>
<td>65</td>
<td>78</td>
<td>42</td>
<td>EHA</td>
</tr>
</tbody>
</table>

* Numbers in parentheses, duration of disease (months).
cereous patients received CHA and 5 EHA.

CHA was accomplished by the method of Dudrick (20). The composition of the solution (C1800) is given in Table 3. Delivery of this solution was increased during the initial 72 hr of HA to a rate providing 30 to 35 cal and 0.2 to 0.3 g nitrogen per kg BW per 24 hr.

Our nasogastric feeding techniques have been described elsewhere (31). Constant infusion of Isocal via a 16-gauge polyethylene catheter or pediatric feeding tube was performed to deliver 30 to 35 cal and 0.15 to 0.20 g nitrogen per kg BW per 24 hr (Table 3). The infusion was begun at 1000 ml/24 hr and increased 1000 ml/day to the desired level (approximately 3000 ml/24 hr). Full-strength diet was usually tolerated from the start, but occasionally half-strength diet was necessary initially with gradual increase to full strength. One patient received peripheral HA [P900, a 900-mosM/ml solution (Table 3; Ref. 35)] along with nasogastric feeding, a total of 30 to 35 cal and 0.15 to 0.20 g nitrogen per kg BW per 24 hr being administered.

**Clinical Methods.** The anthropometric techniques have been described previously (49). Chemotherapy of gastrointestinal cancers and adenocarcinoma of unknown primary site consisted of a 5-day constant infusion of 5-fluorouracil (20 mg/kg/day) along with methyl 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea p.o. (50 to 100 mg/sq m) once during the 5 days. Chemotherapy was repeated every 3 to 4 weeks. Patients with squamous cell carcinoma of the lung or head and neck received monthly high-dose methotrexate (300 to 500 mg/sq m) with leucovorin rescue. One patient with islet cell cancer of the pancreas was given streptozotocin (1 g/sq m/week). Attempts to measure changes in tumor growth rate in response to HA were unsuccessful.

**Metabolic Balance Study Methods.** Techniques of measuring daily balances of nitrogen, phosphorus, potassium, sodium, chloride, calcium, and magnesium are given in Ref. 53 and 54.

**Statistical Methods.** The balance studies were analyzed using the methods of Wilcoxon (47). The changes among the groups in BW, creatinine/height ratio, TSF, MMA, and albumin were analyzed nonparametrically (Wilcoxon independent-groups test) (BMIDPS2).

**RESULTS**

**HA of Noncancerous Patients**

Complications during HA. CHA and EHA in the noncancerous patients were tolerated well except for the following complications. Blood pressure rose into the hypertensive range after 2 weeks of CHA in one subject. This was corrected by reducing CHA content of NaCl and administering antihypertensive drugs. Pedal edema during CHA appeared in one subject but disappeared after NaCl intake was curtailed. During the first week of EHA, 2 subjects developed diarrhea as the rate of EHA infusion was increased towards the maintenance dose. The infusion rate was slowed, and the diarrhea was resolved in both cases. Maintenance was achieved by a more gradual increase of the EHA infusion rate.

**Metabolic Effects of HA.** During CHA, the average daily balances of the 7 elements were positive in all 5 individuals except for calcium in one patient. The average values (expressed per 70 kg BW) were: ΔN, 4.6 g; ΔP, 0.27 g; ΔK, 18.9 mEq; ΔNa, 23.4 mEq; ΔCl, 17.7 mEq; ΔCa, 0.06 g; ΔMg, 11.9 mEq (Table 4). BW, which initially averaged 74% of standard, showed a median increase of 8.5 kg. Creatinine/height, TSF, and MMA, which initially averaged 70, 44, and 77% of standard, showed median increases of 10, 8, and 11%, respectively. Albumin, initially depressed to an average of 3.1 g/dl, rose in all patients, the post-HA value averaging 3.6 g/dl.

During EHA in 5 noncancerous patients, generally similar changes occurred. No statistically significant differences were found between HA and CHA for any of the 7 elemental balances or for the HA-related improvements in BW, albumin, creatinine/height, TSF, or MMA (Table 4).

The ratios of retained nitrogen/phosphorus/potassium/sodium/chlorine/calcium/magnesium in these centrally hyper-
alimented noncancerous patients were 1/0.06/4.11/5.09/3.85/0.01/2.59. For the enterally hyperalimented noncancerous patients, these ratios were 1/0.06/2.87/3.79/2.49/0.03/1.91. There were no significant differences between the 2 routes of delivery, although some tendency toward increased sodium retention in CHA patients is noted.

Reifenstein et al. (53) noted that, because of the fixed ratios of nitrogen to phosphorus in protoplasm and of calcium to phosphorus in bone, it is possible to predict the balance of any one of these elements if the other 2 are known. Application of this formula to the centrally hyperalimented noncancer patients revealed that predicted phosphorus balance was +0.34 g; as shown in Table 4, the observed phosphorus balance was +0.27 g. The predicted phosphorus balance for the enterally hyperalimented noncancer patients was +0.44 g, which is in fairly close agreement with the observed balance of +0.33 g. Similarly, theoretical nitrogen balance can be calculated from potassium balance. For noncancerous patients receiving CHA, the theoretical nitrogen balance was +7 g, while actual nitrogen balance was 4.6 g. For enterally hyperalimented noncancerous patients, the theoretical nitrogen balance was +5.6 g; the observed value was +5.3 g. Thus, although the potassium balance of centrally hyperalimented patients was relatively higher than the nitrogen balance, these calculations generally support the contention that the nitrogen retained by these noncancerous patients was used for the synthesis of normal lean body mass (Table 6).

**HA of Cancer Patients**

**Complications during HA.** Both CHA and EHA in the 15 cancer patients were well tolerated. No patient aspirated while on nasogastric feeding. Septicemia, hemothorax, pneumothorax, clinically apparent pulmonary embolus, and significant electrolyte abnormalities did not occur during CHA. Three patients experienced hyperglycemia which required supplemental insulin, and one patient had congestive heart failure which responded to digitalis and diuretics. Two patients had local cellulitis around the central catheter. There was an increase in ascitic fluid or pleural effusion during HA in 2 patients, but a decrease in the sodium content of the HA fluid corrected this problem. Mild nasopharyngeal irritation from the enteral catheter occurred in 2 patients. Severe hepatic insufficiency and diarrhea did not occur during EHA.

**Metabolic Effects of HA.** During CHA, the 9 cancer patients showed positive average daily balances for all elements except for a slightly negative calcium balance. Among individuals, however, several instances of negative balances were seen. Calcium balance was negative in 3, and magnesium balance was negative in 3 of the 9 patients. Median gain in BW during the 3-week course of CHA was only 5 kg. Serum albumin level, which initially averaged 3.5 g/dl, rose an average of only 0.1 g/dl during the same period. It fell in 4 of 9 patients and was unchanged in one. Creatinine/height ratio and MMA showed median rises of only 4% of standard each, while TSF exhibited a median increase of 10% of standard (Table 4).

During EHA in 6 cancer patients, average balances were significantly lower ($p < 0.05$) for phosphorus, potassium, sodium, chlorine, and magnesium compared to CHA (Table 4). Negative balances for phosphorus (3 of 6), potassium (5 of 6), chlorine (6 of 6) and magnesium (4 of 6) occurred fairly often.
in these subjects. The median increase in BW during the month of EHA was only 3.5 kg. Serum albumin concentration fell in 2 of 6 and was unchanged in a third. Median improvements of 8, 3, and 14.5% of standard occurred in creatinine/height, MMA, and TSF, respectively.

Fecal contents of all 7 elements on the average remained within normal ranges for the CHA patients. These ranges, expressed per day, were: nitrogen, <1.5 g; phosphorus, <0.5 g; potassium, <20 mEq; sodium and chloride, <15 mEq; magnesium, <15 mEq; calcium, <600 mg. The negative balances of phosphorus, potassium, chlorine, calcium, and magnesium observed in these patients resulted entirely from abnormally large urinary excretion. The EHA patients had greater fecal loss than the CHA patients, but the negative balances were the result of abnormal urinary excretion in these patients as well.

Average balances in the cancer groups did not differ significantly between Periods 1 and 2 or between Periods 2 and 3 (Table 5). During chemotherapy (Period 2), however, fecal excretion of nitrogen, phosphorus, potassium, sodium, and chlorine did increase significantly in 4 cancer patients.

While cancer patients retained the same amount of nitrogen as noncancer subjects, they retained some minerals to a lesser extent. Thus, the elemental balances deviated from the profile seen in normal lean body mass. In cancer patients receiving CHA, the ratios of retained nitrogen/phosphorus/potassium/sodium/chlorine/calcium/magnesium averaged 1/0.03/3.67/3.82/2.47/−0.01/0.63; in cancer patients receiving EHA, these ratios were 1/0.01/−0.65/−0.71/−1.15/0.02/−0.56. The predicted phosphorus balance (53) for centrally hyperalimented cancer patients was +0.34 g; however, the observed phosphorus balance was only +0.13 g. For the enterally hyperalimented cancer patients, these values were: predicted, +0.37 g; observed, +0.07 g. The predicted nitrogen balance based on potassium balance for centrally hyperalimented patients was 6.9 g, with an observed value of 5.1 g. This discrepancy is similar to the one observed in noncancerous patients and may reflect an effect of this route of delivery. However, for enterally hyperalimented cancer patients, the theoretical nitrogen balance was −1.1 g, compared to an observed nitrogen balance of +4.8 g. Since observed balances differ from predicted in these cancer patients, the equations developed by Reifenstein et al. (53) cannot be used to analyze the composition of the weight gain. Specifically, these data do not support the contention that the retained nitrogen was utilized for the synthesis of normal lean body mass (Table 6).

**HA in Cancer versus Noncancerous Patients**

With CHA, the following significant (p < 0.05) differences were found. Magnesium balance was less positive in cancer subjects and was negative in some. Improvements in BW, albumin, creatinine/height ratio, and MMA were also significantly less. With EHA, the balances for sodium, chlorine, potassium, and magnesium were significantly less positive in the cancer group, as was the HA-related improvement in BW (Table 4). Improvement in adipose mass as judged by TSF was similar in the cancer and noncancerous patients.

In noncancerous patients, the 2 routes of HA gave similar results in both balances and nutritional indicators. In cancer subjects, however, use of the enteral route resulted in less retention of sodium, chlorine, phosphorus, potassium, and magnesium. Despite this, improvements in BW, albumin, creatinine/height, TSF, and MMA were similar between the 2 groups (Table 4). Given the small number of patients observed, it is possible that to some extent these variations reflect patient selection rather than true differences in the manner in which cancer patients respond to HA by these 2 routes.

Comparison of all hyperalimented cancer patients with all noncancerous patients revealed significantly lower phosphorus, sodium, chlorine, and magnesium balances in the cancer patients, with no significant differences among nitrogen, potassium, and calcium balances. Cancer patients also showed less improvement in BW, MMA, and serum albumin than controls with nonmalignant diseases (Table 4).

**DISCUSSION**

Despite considerable experience with HA in the cachexia of cancer, the question of whether the tumor poses obstacles to the restoration of lean body mass not found in other wasting diseases remains controversial. In this study, we used anthropometric measurements, the elemental balance technique, and serial measurements of serum albumin to assess the composition of the weight gain in patients with and without cancer receiving CHA and EHA.

Calculation of changes in body composition from elemental balance studies is based on the observation that normal lean body mass contains certain elements in relatively fixed proportions (53, 54). Retention of these elements in these ratios

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**Table 5**

Comparison of Period 1 with Period 2 and Period 2 with Period 3 for elemental balances in cancer patients

<table>
<thead>
<tr>
<th>Type of HA</th>
<th>Period</th>
<th>ΔN (g)</th>
<th>ΔP (g)</th>
<th>ΔK (mEq)</th>
<th>ΔNa (mEq)</th>
<th>ΔCl (mEq)</th>
<th>ΔCa (mEq)</th>
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<td>23.0</td>
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<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>2 vs. 3</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Table 6**

Correlation between observed and predicted nitrogen and phosphorus balances based on the equation of Reifenstein et al. (53)

<table>
<thead>
<tr>
<th>Phosphorus balance based on nitrogen and calcium balance (g)</th>
<th>Nitrogen balance predicted from potassium balance (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted</td>
<td>Observed</td>
</tr>
<tr>
<td>CHA, noncancerous</td>
<td>0.34</td>
</tr>
<tr>
<td>CHA, cancer</td>
<td>0.34</td>
</tr>
<tr>
<td>EHA, noncancerous</td>
<td>0.44</td>
</tr>
<tr>
<td>EHA, cancer</td>
<td>0.37</td>
</tr>
</tbody>
</table>

*NS, not statistically significant (p > 0.05).*
suggests that normal lean body mass is being synthesized. If
an organism retains these elements, especially nitrogen, phos-
phorus, and calcium, in abnormal ratios, the conclusion that
normal lean body mass is being restored is unwarranted. The
noncancerous subjects in this study confirmed previous obser-
vations (53, 54) by demonstrating retention of these elements
in proportions similar to lean body mass. Predicted and ob-
served phosphorus balances were in close agreement. Anthro-
pometric measurements indicated that muscle mass had in fact
increased, and increases in serum albumin suggested improve-
ment in visceral protein status; both these indicators tend to
support the contention that normal lean body mass was being
restored in these patients.

In the cancer patients, however, the elements examined were
retained in abnormal ratios, although nitrogen retention was
similar in the 2 groups. Observed phosphorus balance was far
less than that predicted by the nitrogen and calcium balances.
Thus, the composition of the weight gain cannot be calculated.
Specifically, there is no basis for the conclusion that normal
lean body tissue was being synthesized. Anthropometric meas-
urements indicated that, although some increase in muscle
mass did occur, this improvement was less than that noted in
similarly malnourished noncancerous patients receiving similar
nutritional support. Serum albumin concentration also showed
less improvement in the cancer patients than in their counter-
parts without cancer, confirming previous studies (26, 51, 52).
Adipose tissue, however, was equally responsive to HA in both
groups. Thus, the results of our study support the conclusions
that the cachexia associated with cancer results not from
anorexia alone but also from metabolic aberrations peculiar to
patients with cancer and that attempts to overcome loss of lean
body mass in cancer patients by nonvolitional means will be
less successful than in subjects without cancers.

Abnormal electrolyte and mineral retention in cancer has
also been noted in other studies. In 1898, Milroy and Malcolm
(45) noted that a patient with chronic leukemia excreted far
less urinary phosphorus as an absolute amount and relative to
nitrogen than a normal control. White and Hopkins (66) re-
ported similar findings in another patient with chronic leukemia
the following year. Adams et al. (1) noted marked phosphorus
retention during baseline balance studies of a patient with
acute leukemia, with negative nitrogen, phosphorus, and po-
tassium balances during successful treatment with cortisone or
adrenocorticotropic hormone. Fenninger et al. (22) found that
phosphorus balances were relatively more positive than nitro-
gen balances during periods of growth of leukemia and lym-
phoma tissue and were relatively more negative during periods of
successful treatment. Watkin (65) reported that patients with
various cancers had periods of inactive disease when nitrogen,
phosphorus, and potassium were retained in ratios that sug-
gested restoration of normal lean tissues but that these same
patients tended to show abnormal elemental balances during
periods of active disease. Elemental balances were also poorly
correlated with weight gain in these cancer patients. Terepka
and Waterhouse (61) performed 9 balance studies in 8 patients
with advanced cancer both prior to and during forced feedings
by nasogastric tube. These authors also noted that phosphorus
retention exceeded that predicted by nitrogen and calcium
balances and that all weight gain in their patients was ac-
counted for by intracellular fluid and fat, as determined by
indirect measurements.

The phosphorus retention in our cancer patients was not
significantly lower than control (p < 0.01). This is in contrast
to the reports noted above, in which phosphorus retention was
observed to be greater than expected. Our patients and those
of Watkin (65) and Terepka and Waterhouse (61) demonstrated
a wide range of phosphorus balances relative to nitrogen
balance. Thus, phosphorus retention appears to be increased
in some cancer patients and decreased in others and appears
to have lost its relationship to nitrogen balance.

The present study extends previous observations to CHA.
Although this technique does cause nitrogen retention and
weight gain as reported previously (20), more complete ele-
mental balance studies do not permit the conclusion that nor-
mal lean body mass is being restored; anthropometric meas-
urements confirm that similarly malnourished noncancerous pa-
tients demonstrate more increase in lean tissue for the same
amount of HA than cancer patients. We have demonstrated
previously that withholding nitrogen, phosphorus, potassium,
sodium, or chloride from patients receiving nutritional support
effectively blocks restoration of lean body mass even if the
other elements are provided (54). Patients who are in negative
balance for any of these elements in effect make them una-
available for tissue synthesis; thus, absence of improvement, or
minimal improvement, in anthropometrics is not surprising in
such subjects. In contrast, the provision of glucose calories
alone is sufficient to permit fat synthesis (54); cancer patients
showed improvement in TSF equal to that of controls despite
abnormal elemental balances.

The decreased magnesium retention in cancer patients, with
actual negative balance in many, has not been described
previously, although Frazier et al. (23) noted that patients with
cancer were much more likely to become hypomagnesemic
during HA than noncancerous patients. Decreased intracellu-
lar magnesium concentrations compared to normal liver have
been found in the noninvolved hepatic tissue of tumor-bearing
animals (57). Given the importance of magnesium in oxidative
phosphorylation, maintenance of mitochondrial integrity, and
DNA and RNA metabolism and given the efficiency of the
normal kidney in conserving magnesium (2), it appears that
these abnormalities of magnesium metabolism may be of im-
portance in understanding the basic processes of the effects of
cancer on the host.

It appears unlikely that abnormal uptake of these elements
by the tumor tissue itself accounts for the changes in element
retention observed in this study; it seems more plausible that
these differences reflect anomalies in host tissue induced by
the tumor (14, 61). In recent years, abundant evidence has
accumulated to suggest that host tissues not directly involved
with tumor show aberrations that appear to be due to the
cancer. Plasma amino acid levels in subjects with cancer are
different from those in normals or in malnourished controls (12,
39). Incorporation of leucine into hepatic proteins is increased
in cancer patients (41); this is not due to alterations in the
precursor pool (42). Lysosomal enzyme activities are also
increased in the livers of tumor-bearing mice and humans (41);
for cathepsin D, at least, the alteration in enzyme activity does
not appear to be due to nutritional deprivation alone (43). Other
alterations in hepatic enzyme activity under the influence of a
tumor have been noted (17, 28–30, 36, 46).

Skeletal muscle metabolism is also affected by the presence
of a growing neoplasm. Increased lysosomal enzyme activity

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REFERENCES

Hyperalimentation of the Cancer Patient with Protein-Calorie Undernutrition


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