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## Discussion

*Dr. Filler:* I'd like to cite a few differences between adult and pediatric cancer patients. First, chronic malnutrition in children is very unusual. When children are malnourished, it usually has been on a very acute basis. Second, these children do not have degenerative diseases. They are otherwise very healthy, and ordinarily by providing nutritional support for a short period of time, even as short as a month, as Dr. Rickard showed, one can get these patients back into what we would consider a perfectly good nutritional state. Tumors in children grow rather rapidly, and mothers and fathers quickly seek medical attention. By far the greatest problem in nutrition in the children with cancer occurs during therapy, as Dr. Donaldson said, and the therapy that's given for most childhood cancers involves surgery, radiation, and chemotherapy. The surgical procedures that we perform are major, but we rarely get involved with surgery of those areas which would inhibit nutritional intake following surgery. Children tolerate surgery very well, the wound infection rate is very much lower so that septic complications are fewer, and all of this tends to make a patient, from a nutritional standpoint, much less at risk. The malnutrition that we have seen in childhood cancer is documented in our own series. There were 68 patients in this study, and out of the 68, almost 50 of those patients required total parenteral nutrition for therapy-associated complications; when the therapy could not be given because of vomiting and diarrhea, total parenteral nutrition was started. In over two-thirds of those patients, the chemotherapy and radiation were continued despite the complications that had developed, and the chemotherapy and radiation were tolerated during that period of time. So while we might not be able to show a prophylactic effect in preventing the complications, it might very well be that we should look at it in a different way, that is, when the complications develop, how much good do we do by treating with nutritional means *versus* not treating with nutritional support. That might be a much better way to look at this problem.

*Dr. Jaffe:* I would like to complement some of the information that has been presented by Dr. Donaldson. As we've heard, both the tumor and therapy may be determinants of nutritional complications. The complications and the symptomatology may continue unabated with treatment despite apparent responses of the tumor, and I would like to present the results of an investigation which we conducted at the M. D. Anderson Hospital and Tumor Institute demonstrating that reduced dietary intake induced by chemotherapy was responsible for overt malnutrition. The effects appear to be more profound in preadolescent and early adolescent patients. These patients, although they received possibly more intensive treatment than the others, nonetheless did display more severe effects of the chemotherapy. In particular, these effects occurred despite apparent disappearance of disease and the beneficial responses to treatment. The patient population was as follows. All newly diagnosed patients referred to the M. D. Anderson Hospital and Tumor Institute from January 1979 to March 1980 were studied. In order to keep the study as clean as possible, eligibility required the absence of prior treatment with chemotherapy. Surgery and/or radiation prior to admission or during the first 3 months did not constitute a contraindication, provided that the radiation did not involve the gastrointestinal tract. In contrast, surgery, radiation, or a severe infection during the second 3 months after admission rendered the patient ineligible since these factors possibly cause malnutrition. A

variety of established chemotherapeutic regimens were employed, and the side effects of these have already been described by Dr. Donaldson. A careful account of height, weight, hemogram, and renal and liver function studies including serum albumin and caloric intake was recorded. Patients also received dietary counseling on admission and frequently during therapy. Except for such counseling, nutritional support was not provided unless specifically indicated according to recognized criteria. A specific search was made for overt malnutrition which was defined as below 80% of the 50th percentile for weight for height. Our results were as follows. The number of new patients entered from January 1, 1979, to March 31, 1980, was 197. Twenty-two new patients previously treated with chemotherapy were excluded; 53 new patients with no malignant disease were also excluded. No data were subsequently available on 28 of the cancer patients after 6 months because they were referred elsewhere for treatment or lost to followup. This left a total of 94 patients, or 48% of the original admissions. Complete disappearance of tumor lasting a minimum of 6 months was achieved in 78 of these 94 patients (83%). The other 17% relapsed or did not achieve full remission. Marginal to overt malnutrition was diagnosed in 24% of these 78 patients. It was also of interest that overt malnutrition was diagnosed in 8% of new patients with cancer at first evaluation. Let us now outline the 24% who demonstrated overt malnutrition. The initial change in weight-height over the first 6 months demonstrated profound changes in patients with osteosarcoma, Ewing's sarcoma, and soft-tissue sarcoma. Patients with Hodgkin's disease, lymphoma, and leukemia did not demonstrate aberrations in nutrition, and it was determined that this was probably due to the corticosteroid administration which accompanied the chemotherapeutic regimen in these patients. Also, these patients seemed to have less nausea and vomiting accompanying the administration of chemotherapy. The average caloric intake (relative to recommended) of the initial 6 months was as follows: osteosarcomas, 75%; Ewing's sarcoma, 60%; neuroblastoma, close to 100%. Patients with soft-tissue sarcomas had close to 95% of the recommended caloric intake in contrast to those with osteosarcomas in whom profound nutritional disturbances were also detected. Now we had earlier brought up the question of the effects of different types of tumors, and I think that this is important. Possibly, some tumors do react differently than others; also the different chemotherapeutic agents may affect patients differently, and this may in fact be responsible for different nutritional aberrations observed in different groups. There was no difference in the albumin concentration in these patients despite the tremendous changes in weight that we observed and the caloric intake that the different patients experienced. We found that the average protein intake over the initial 6 months was quite satisfactory, and this was reflected in the serum albumin. The administration of aggressive chemotherapy during the first 6 months does not affect the serum albumin, and the protein intake is generally satisfactory. What was particularly interesting to me was the soft-tissue sarcoma patients. There was a tremendous weight-height loss, yet their intake was adequate. This contrasts with osteosarcoma patients for whom there was also a weight-height loss and there was a poor intake. I could account for that in the osteosarcoma group but not in the soft-tissue sarcoma patients.

*Dr. DeWys:* Your data suggest that patients with soft-tissue sarcomas were more likely to be hypermetabolic.

*Dr. Jaffe:* Right.

*Dr. DeWys:* Dr. Bernstein, does age have any impact on conditioned learning?

*Dr. Bernstein:* We have not seen that. We've looked for it in a population including children up to ages 16 and 18 and above, and we have not seen any age effect. It's easier to document diet aversions in children than in adults, and the reason for that is not clear. It seems to be that children have more aversions than adults, if we look at those aversions diffused in the diet.

*Dr. Morrison:* Something one must bear in mind is that food intake or metabolic costs are in effect differentials; that is, they are calories per day. But as a weight, body weight is an integral; it is something that is accumulated. It is not only technically much more difficult to get factual values in calories per day, whether as intake or as output, much more difficult than it is to measure body weight; it is also, as I said, differential and therefore very, very variable, very unstable when looked at as a numerical value. In addition to that, if you consider an average of a pound lost per week, which for pediatric patients is quite a substantial loss, the balance between intake and output in calories for that is barely within the limits of detectability with accuracy. So I think that these apparent discrepancies between body weight change and food intake and output have to be taken with several pinches of salt; that is, one cannot lay the same reliability on the intake/output data as

one can on the body weight data.

*Dr. Filler:* Can I ask Dr. Neumann, are we doing the right thing at puberty measuring height/weight ratios?

*Dr. Neumann:* No, the standards stop at puberty. Once you hit puberty, these weight-height measurements really don't hold, and it would be much more accurate to do grading of sexual maturation. As a proxy during that period, most people are just using weight for age and they resume weight for height after full development has occurred. They arrive at a relation; it's not valid really in that period of time to use weight for height.

*Dr. Holroyde:* Very briefly, chemotherapy itself can affect overall metabolism. We measured caloric expenditures serially in patients given chemotherapy for colorectal cancer and found that it had diminished. Different drugs can do different things. You don't make protein, a form of kinetic energy, and this is being shown clearly in the studies with Adriamycin. Further, if you give patients a given food load of protein and carbohydrate, some will burn more than others, and some will store more than others. We're measuring how much heat patients produce if given a standard protein load. It is quite different for cancer patients and normal patients. It is also different depending on the underlying status of nutrition, whether in the repairing phase, or whether catabolizing, and so on and so forth.