Summary

This thesis deals with several aspects of the influences of intensive cancer chemotherapy on the nutritional status, the metabolism, and the gastrointestinal tract of the host and describes whether these results can be influenced by enteral hyperalimentation. We studied these aspects in patients with disseminated malignant melanoma.

Chapter 1 consists of a review of the literature regarding the effects of the localization of the tumor and the systemic effects of neoplastic diseases on nutritional status. Moreover, the nutritional consequences of cancer therapy, and the effects of nutritional support on the host, the tumor, the tolerance to treatment, and the response rates to therapy are considered. Finally, the aims of this study are discussed.

In chapter 2 and 3 the pretreatment taste sensitivity and the effect of combination chemotherapy (bleomycin, actinomycin D, vindesine, and DTIC) and of enteral hyperalimentation on taste sensation are reported. Five concentrations of sweet, salt, acid, and bitter were tested. The untreated cancer patients had both quantitative and qualitative disturbances in taste. They experienced the lowest concentrations of acid, sweet, and bitter significantly stronger than the normal controls. Furthermore, 37% of the patients could not recognize all taste qualities correctly.

Chemotherapy led to an increased sensitivity for the lowest taste concentrations and a loss in the ability to discriminate between different taste intensities. In the hyperalimentation group there was no evidence for an increase in the sensitivity for the lowest concentrations.

In chapter 4 and 5 the effect of enteral normoalimentation or hyperalimentation on various nutritional parameters during intensive chemotherapy was evaluated. The plasma vitamin C level was uniformly low before treatment, while other nutritional parameters were generally normal. During chemotherapy serum prealbumin was the first nutritional parameter to fall and seemed to be a very sensitive indicator of the occurrence of nutritional imbalance. Further negative changes developed in the anthropometric variables, the visceral proteins, and the vitamin levels. We concluded that during intensive chemotherapy nutritional imbalance arose quickly and during enteral alimentation with a quantity of calories equal to equilibrium could improved and during nutrition status of the patient though they were continuous drip in

Chapter 6 and 7 chloride, potassium patients, while after cytostatic therapy observed that in a fixed ratio of the normocaloric feed even demonstrated, even.

In the course of the study positive in the hyperalimentation the retention rate of nitrogen balance indicated and the patient to synthesis and after chemotherapy.

Chapter 8 demonstrated that spermidine in the course of intensive chemotherapy, with sophisticated chemotherapeutic agents. Baseline amount of tumor and found no relation increase in specific hematological toxicity.

In chapter 9 we related to the gas
of calories equal to the pretreatment intake of the patients. A metabolic equilibrium could not be obtained. Enteral hyperalimentation initially improved and during and after chemotherapy it conserved the nutritional status of the patient. All patients tolerated the tube feeding well even though they were nauseated by chemotherapy, provided an equal pace of continuous drip infusion was maintained.

Chapter 6 and 7 describe the results of balance studies of sodium, chloride, potassium, magnesium, calcium, phosphate, and nitrogen in the patients, while they received enteral alimentation before, during, and after cytostatic treatment. During synthesis of lean body mass it has been observed that in non-cancer patients N, P, K, Na, and Cl are retained in fixed ratios. We evaluated these ratios in the patients with a positive nitrogen balance. The ratios in the hyperalimentation group before chemotherapy were compatible with the previously described ratios. During normocaloric feeding synthesis of lean body mass could not be demonstrated, even if a positive nitrogen balance was present.

In the course of cytostatic treatment the nitrogen balance became progressively negative in the normoalimentation group, but remained positive in the hyperalimentation group. It is concluded on the basis of the retention ratios of N, P, K, Na, and Cl that hyperalimentation resulted not only in a positive N balance, but also enabled the cancer patient to synthesize lean body mass before and to some extent even during and after chemotherapy.

Chapter 8 deals with the changes in the serum level of the polyamine spermidine in the patients with disseminated malignant melanoma treated with intensive chemotherapy in order to find a more quantitative and sophisticated chemical parameter for the tumor response or the toxicity of chemotherapy. Basal blood spermidine levels did not seem to mirror the amount of tumor present nor were they predictive of response. We further found no relation between the occurrence of a tumor response and an increase in spermidine levels, nor between these levels and the hematological toxicity or the digestive tract toxicity.

In chapter 9 we evaluated a number of clinical and chemical parameters related to the gastrointestinal tract in patients treated with combination
chemotherapy to find quantitative indicators for gastrointestinal toxicity and to investigate the cause of the diarrhea after chemotherapy. The two clinical parameters - diarrhea according to the WHO criteria and daily fecal consistency - were closely correlated. The most important effects of the chemotherapy on the chemical parameters were an increased fecal fluid, potassium (K), and fat excretion. The fecal wet weight and K-excretion showed a high correlation with the two clinical parameters for toxicity. We presume that the mucosal injury resulting from chemotherapy leads to increased small intestinal fluid and electrolyte secretion and we conclude that fecal wet weight and K-excretion are probably the best quantitative indicators for gastrointestinal toxicity of cancer chemotherapy.

Chapter 10 describes the effect of combination chemotherapy on the human small intestinal morphology and disaccharidase activities and their relation with clinical and chemical parameters for gastrointestinal toxicity in patients receiving enteral normoalimentation. As clinical parameters we used the diarrhea grading system according to the WHO criteria and the daily fecal consistency. The chemical parameters were fecal wet weight and K-excretion. Furthermore the supposed protective effects of enteral hyperalimentation with an elemental diet on the aforementioned parameters of gastrointestinal toxicity were evaluated.

After CT a comparable decrease in villus height, total mucosal height, and mitotic index was found in both groups. In the normoalimentation group the crypt depth decreased in contrast to the hyperalimentation group. The disaccharidase activities in the hyperalimentation group deteriorated after chemotherapy to lower values than in the normoalimentation group. We found no correlations between the disaccharidase activities and the morphology, nor a correlation between these variables and the fecal parameters and clinical diarrhea. This suggested that the diarrhea occurring after chemotherapy was not due to the loss of mucosal tissue or to the decrease in the enzyme activities. Furthermore we conclude that there was no protective effect of hyperalimentation with an elemental diet on gastrointestinal toxicity.

In dit proefschrift werden onderzoek naar de voedingstoestand van kankerpatient behandeld. Deze onderzoekingen werden uitgevoerd bij patiënten met maligne melanoom.

In hoofdstuk 1 gevolgen, die de invloed van kanker hebben op de toelopende tumor, op de toleratie van chemotherapie beschreven. In deze studie ter illustratie werden de resultaten ter beschikking gesteld.

In hoofdstuk 2 werden de resultaten van de behandeling met polenterale hyperalimentatie van de smaak van de smaak van zout en bitter. Hierna werden de resultaten van deze studie ter beschikking gesteld.

Chemotherapie geeft geen schadelijke gevolgen aan de smaak van de smaak van zout en bitter. Hierna werden de resultaten van deze studie ter beschikking gesteld.

Geconcludeerd wordt als kwantitatieve veranderingen verst