Nutritional consequences in children undergoing chemotherapy for malignant disease

Inger Skolin
In memory of my father Josef Skolin
Contents

Abstract 3
Original papers 4
Abbreviations 5
Introduction 6
Paediatric cancer in Sweden 6
Food provision for the hospitalised child and the family 6
Factors affecting the eating pattern of healthy children 7
Factors affecting food intake during chemotherapy 8
Energy and protein requirements 9
Prevalence of malnutrition in paediatric cancer patients 11
Consequences of malnutrition 11
Mode of nutritional support in paediatric cancer patients 11
Aims 12
Methods 13
Participants 13
Data collection 14
- Dietary intake (I, II) 14
- Anthropometry (I, II, IV, V) 15
- Laboratory methods (II) 16
- Questionnaire (I, II, V) 16
- Taste acuity test (V) 16
- Interviews (III, V) 17
Statistical methods 17
Ethical considerations 18
Results 18
- Dietary intake (I, II) 18
- Anthropometry (I, II, IV, V) 20
- Laboratory methods (II) 21
- Questionnaire (I, II, V) 21
- Taste acuity test (V) 22
- Interviews (III, V) 22
- Clinical experience of enteral support via PEG 24
Discussion 25
Methodological considerations 32
- Dietary intake 32
- Anthropometry 33
- Taste acuity test 34
- Interviews 34
Summary 36
Conclusions and implications for nursing 37
Perspectives 38
Tables 1-6 39-44
Populärvetenskaplig sammanfattning 45
Acknowledgements 47
References 48
Appendix
Questionnaire (II)
Papers I-V
Abstract

**Background:** Chemotherapy has side effects that may interfere with food intake. Children suffering from a malignant disease are subjected to treatment with chemotherapy and may therefore become at risk of undernutrition during the period of treatment. This may increase the risk of infections and influence the outcome of treatment. Few studies have investigated how children undergoing chemotherapy for cancer perceive food and eating. Attempts to improve food intake and the nutritional status require an understanding of how eating patterns are altered during chemotherapy in children. **Study design:** Dietary information were collected after the initiation of chemotherapy in children admitted to the Paediatric Haematology and Oncology Unit at Umeå University Hospital. This initial study resulted in the establishment of new mealtime routines on the ward. A follow-up study was conducted with another group of children. Interviews were performed with a third group of children, their parents and attending nurses. Recognition thresholds for the basic tastes were determined with 10 of the oldest of these children and 10 healthy controls. **Results:** Before introduction of new mealtime routines, the average daily oral energy intake during hospitalisation was 58% of the Swedish Nutrition Recommendations, SNR. There was a significant weight loss up to three months after onset of chemotherapy. After the introduction of new mealtime routines, the average daily oral intake on hospital days was 61% of SNR and thus still lower than recommended despite efforts to serve palatable food on the ward. When enteral and parenteral nutrition was included, the energy intake came close to that recommended for healthy children, 91% of SNR. Both children and parents perceived that altered taste was an important cause of the children’s eating problems. The children also viewed food aversions, nausea and vomiting and pain as important causes, while the parents perceived nausea, food aversions and altered smell as significant factors. The nurses on the other hand, viewed nausea and the ward environment as important factors. The patients had significantly higher thresholds for bitter taste and made significantly more mistakes in taste recognition compared with controls. **Conclusion and clinical implication:** There seem to be changes both in the sense of taste as well as in the perception of food in children undergoing chemotherapy for malignant disease. Thus, single solutions such as providing a variety of “tasty food” in the hospital setting in order to improve food intake does not suffice for many paediatric cancer patients. The individual’s food preferences and aversions should be considered and combinations of oral, enteral and parenteral nutrition support should be provided.
Original papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals. Papers I-IV have been reprinted with the kind permission of the publishers.

I. Nutrient intake and weight development in children during chemotherapy for malignant disease.
Skolin I, Axelsson K, Ghannad P, Hernell O, Wahlin YB.

II. Energy and nutrient intake and nutritional status of children with malignant disease during chemotherapy after the introduction of new mealtime routines.
Skolin I, Hernell O, Wahlin YB.

III. Parents’ perception of their child’s food intake after the start of chemotherapy.
Skolin I, Koivisto Hursti U-K, Wahlin YB.

IV. Percutaneous endoscopic gastrostomy in children with malignant disease.
Skolin I, Hernell O, Vikström Larsson M, Wahlgren C, Wahlin YB.

V. Altered food intake and taste perception in children with cancer after start of chemotherapy: perspectives of children, parent and nurses.
**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASPEN</td>
<td>American Society for Parenteral and Enteral Nutrition</td>
</tr>
<tr>
<td>ALL</td>
<td>Acute lymphatic leukaemia</td>
</tr>
<tr>
<td>AML</td>
<td>Acute myelogenous leukaemia</td>
</tr>
<tr>
<td>BMR</td>
<td>Basal metabolic rate.</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CS</td>
<td>Conditioned stimulus</td>
</tr>
<tr>
<td>CTZ</td>
<td>Chemoreceptor trigger zone</td>
</tr>
<tr>
<td>DEXA</td>
<td>Dual-energy X-ray absorptiometry</td>
</tr>
<tr>
<td>DIT</td>
<td>Diet-induced thermogenesis</td>
</tr>
<tr>
<td>DLW</td>
<td>Doubly-labelled water</td>
</tr>
<tr>
<td>EE</td>
<td>Energy expenditure</td>
</tr>
<tr>
<td>EN</td>
<td>Enteral nutrition</td>
</tr>
<tr>
<td>5-HT</td>
<td>5-hydroxytryptamine</td>
</tr>
<tr>
<td>NCHS</td>
<td>National Centre for Health Statistics</td>
</tr>
<tr>
<td>NG tube</td>
<td>Naso-gastric tube</td>
</tr>
<tr>
<td>NNR</td>
<td>Nordic Nutrition Recommendations</td>
</tr>
<tr>
<td>NOPHO</td>
<td>Nordic Society of Paediatric Haematology and Oncology</td>
</tr>
<tr>
<td>PAL</td>
<td>Physical activity level</td>
</tr>
<tr>
<td>PEG</td>
<td>Percutaneous endoscopic gastrostomy</td>
</tr>
<tr>
<td>PN</td>
<td>Parenteral nutrition</td>
</tr>
<tr>
<td>PNET</td>
<td>Primitive neuroectodermal tumour</td>
</tr>
<tr>
<td>SD score</td>
<td>Standard deviation score</td>
</tr>
<tr>
<td>SNR</td>
<td>Swedish Nutrition Recommendations.</td>
</tr>
<tr>
<td>TEE</td>
<td>Total energy expenditure</td>
</tr>
<tr>
<td>US</td>
<td>Unconditioned stimulus</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual analogue scale</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
</tbody>
</table>
Introduction

Paediatric cancer in Sweden

Approximately 300 children are diagnosed with malignant disease each year in Sweden (1). Following a dramatic improvement in recent decades, the survival probability for childhood cancer now varies from 15% to 97% for different subgroups. Children with Hodgkin lymphoma, retinoblastoma, Wilms’ tumour and germ-cell tumours have survival probabilities exceeding 90%. Some rare cancer forms and subgroups of neuroblastoma have the poorest prognoses (2). Treatment includes chemotherapy, either alone or in combination with radiotherapy, surgery or bone marrow transplantation (2). The duration of chemotherapy usually varies from 3-4 months to 2.5 years (2). The chemotherapeutic drugs exert their cytotoxic effects by interfering with critical metabolic reactions in cancer cells. They also disrupt metabolic pathways in normal cells, which results in various side effects, some of which affect food intake. Consequently, the child may become at risk for malnutrition, which can affect tolerance to therapy, increase the risk for infections and influence overall survival (3). The questions constituting the starting point for this thesis, originated in my work as a nurse in paediatric oncology. It was my experience that adequate food intake was problematic due to the many factors that contribute to eating problems in these patients. Studies by others have confirmed the clinical impression that energy and nutrient intake are often decreased in this patient group (4, 5).

Food provision for the hospitalised child and the family

At the time when paper I was planned, the food service department (“Central Kitchen”) delivered two cooked meals daily and these were distributed by the nursing assistants on the paediatric oncology ward. Preprinted menus were handed out and patients were asked to make their selections one day in advance. Meals could also be prepared on an individual basis in the Central Kitchen, based on the child’s preferences, when requested one day ahead of time. Beside those meals, the ward provided breakfast and three snacks per day. The meals were free for the hospitalised child, while parents and siblings paid for their food. Parents had access to a kitchen close to the ward, where they could prepare food for themselves.
When meals from the Central Kitchen were served, many patients on the ward no longer felt like eating what they had ordered the previous day. For some children this food provision system was too rigid. The cancer therapy and its side effects resulted in unexpected changes in the food they wanted. Therefore, improved mealtime routines on the ward were instituted in 1994. We presumed that flexibility with regard to menus and the timing of meals as well as food enrichment, would give the children an opportunity to increase their energy and nutrient intake during the days they were hospitalised. Cooked meals continued to be provided by the Central Kitchen. The improved routines included assigning a nursing assistant to the ward kitchen during the daytime in order to prepare meals on short notice that the children would accept. The freezer was stocked with a variety of typical foods preferred by children and adolescents. Snacks were prepared that were particularly palatable and energy-dense. Enrichment of the hospital food and food prepared in the local kitchen was done using naturally energy-dense ingredients according to standard recipes. Beverages were enriched with tasteless and odourless glucose polymers and a variety of commercial liquid supplements were also provided. The nursing staff attended courses on paediatric clinical nutrition and a dietician associated with the unit was available for consultation.

**Factors affecting the eating pattern of healthy children**

Factors that stimulate children’s food intake are the taste of the food, the familiarity of the food served and the social context of the mealtime (6). The primary tastes include salty, sour, sweet, bitter and umami (7). The preference for the sweet taste, probably the preference for the salty tastes and the rejection of sour and bitter tastes are innate (8). Taste sensation involves stimulation of specific chemoreceptors in the taste buds, adequate saliva and intact neural pathways (9). Smell is associated with taste, and intact olfactory receptors in the nasal cavity are therefore important (9). Chemoreceptors provide the molecular specificity of the taste response. Nerve impulses are transmitted via taste pathways to the brainstem and then to the cerebral cortex. The salty and sour tastes are transduced mainly by ion channels and sweet, umami and bitter tastes by specific receptors (10). The threshold for stimulation of bitter is much lower than for sweet, salty and sour. Receptors for sweet and certain amino acids allow recognition of nutritionally rich food sources, while receptors for bitter elicit aversive responses to toxic stimuli (11). Being able to identify and reject bitter compounds might have had a certain evolutionary advantage (12).
Young children are unwilling to try novel or unfamiliar foods, i.e. foods never presented to them before. This food neophobia is manifested in the avoidance of new foods. From an evolutionary perspective the neophobic predisposition served a protective function (6). Neophobia can be reduced by repeated exposure (13). Role models, including parents, siblings and peers, can have powerful effects on the child’s food selection and can decrease this neophobia, especially when the model is regarded as particularly powerful, e.g. older peers (14). Children can learn to prefer foods eaten in a positive social context. On the other hand, coercing may decrease food intake and result in a dislike of the food items the child is coaxed to eat (15).

Changed social circumstances, depression, loneliness and bereavement may have major impact on food intake (16). Food is also of social and cultural significance with respect to an individual’s identity (17). This is important in the hospital setting. Life in hospital causes patients to lose control and their autonomy becomes subordinated to hospital routines (18).

**Factors affecting the food intake during chemotherapy**

Chemotherapy-induced mucositis, which occurs in 52-80% of children with cancer (19, 20, 21), normally lasts for three weeks, beginning at three to four days and peaking at 7 to 14 days after start of chemotherapy (22). The ulcerative lesions are often very painful, requiring treatment with analgesics and nutritional support (23). Chemotherapy may also cause damage to the gastrointestinal tract mucosa, leading to abdominal pain, decreased absorption of nutrients and sometimes severe enterocolitis (24).

Chemotherapy-induced nausea and vomiting is common in cancer patients (25). Anticipatory nausea and vomiting can occur before acute chemotherapy symptoms would be expected to occur and is linked to visual, taste, smell and environmental factors associated with previously administered chemotherapy. Nausea and vomiting are generally considered to be part of the same process, with similar underlying mechanisms (26). Vomiting is mediated by the vomiting centre. This centre receives input from the chemoreceptor trigger zone, (CTZ), which is located in the vicinity of area postrema. Chemotherapeutic agents may induce vomiting either by stimulation of the vomiting centre itself or via direct or indirect stimulation of the CTZ. 5-hydroxytryptamine, (5-HT) and 5-HT\textsubscript{3} receptors play important roles in the mediation of chemotherapy-induced nausea and vomiting. Cells in the small intestines are
major producers of 5-HT. 5-HT₃ receptors are located throughout the human brain, including a high concentration in the area postrema (26). When chemotherapy is given, 5-HT is released from cells in the small intestine. 5-HT activates 5-HT₃ receptors, which act on abdominal vagal afferent nerves. These mediate the signal to the vomiting centre, which co-ordinates the autonomic and somatic reactions, leading to nausea and vomiting. This is a simplified model of a complicated system, parts of which are unknown. Selective antagonists of 5-HT₃ receptors are potent antiemetics (26).

Eating a food is usually followed by positive feelings of satiety. If, on the other hand, illness follows, aversion to the food is likely to develop. Food aversion learning is extremely robust and is suggested to be based on primitive associative mechanisms involving neural integration occurring in the brain stem (27). Nausea plays a unique role in this type of learning (28). The mechanism linking nausea and vomiting to food aversions is a form of classical conditioning by which an individual begins to avoid a food (conditioned stimulus, CS) that has previously been linked to illness (the unconditioned stimulus, US) (27). Strong aversions can be acquired after only one pairing of a CS and a US and can develop despite long delays between exposure to the food and the symptoms (29). Nausea-induced food aversion is frequently reported by adult (30, 31, 32) and paediatric cancer patients undergoing chemotherapy (33). Paediatric cancer patients may be especially sensitive to acquired food aversions, since food aversions develop more easily before the age of 20 (34).

The rapid turnover of taste cells (35) makes them sensitive to chemotherapy agents, which may result in taste changes (36). Post-chemotherapy taste changes in adult cancer patients include loss of taste, changes in bitter and sweet tastes, and distorted taste, i.e. rancid, bitter, metallic, or salty taste (37, 38). Alterations in taste acuity were found in adult cancer patients (39, 40) and paediatric cancer patients undergoing chemotherapy (41, 42). Some of the cytokines, secreted by macrophages and lymphocytes, are associated with loss of appetite and the multiple metabolic alterations seen in cancer patients (43).

**Energy and protein requirements**

Total energy expenditure (TEE) is the sum of several components of the energy equation (44). The largest part is the basal metabolic rate (BMR). The diet-induced thermogenesis (DIT) corresponds to the increase in energy metabolism above basal due to digestion of food and
metabolism of nutrients. The physical activity level (PAL) integrates the energy expended on all types of activities over a period of 24 hours. PAL is defined as TEE divided by BMR. An individual’s BMR may be estimated from weight, height, age and sex (45). PAL values have been estimated for different lifestyles and activity levels in adults (46) and for low, moderate and vigorous habitual levels of physical activity in children and adolescents (47). Generally, PAL values vary between 1.2 and 2.5 (46). A PAL value of 1.2 corresponds to the lowest possible physical activity of a free-living individual (46), although lower values for PAL have been reported in wheelchair-dependent children (48). The energy cost for growth in children can be divided into two components: the energy deposited in new tissue and the energy costs of synthesis of new tissue (49). Dietary protein has two roles in nutrition, a specific role as a source of nitrogen and amino acids and a non-specific role as an energy source. For optimal dietary protein utilisation, the energy requirements of an individual need to be met. The recommended protein intake of healthy children aged two to 17 years is 0.9 g per kg body weight per day according to Nordic Nutrition Recommendations, NNR (50).

Children with cancer have nutrient requirements for growth that must be met also during extended periods of treatment. In order to prevent or reverse the effects of malnutrition and to increase the well-being of the child, nutritional support is an important part of the therapy (51). However, the true energy requirements for a given paediatric cancer patient are difficult to estimate. On the one hand, PAL is generally decreased during illness. On the other disease processes may result in elevated energy requirements secondary to inflammatory processes, wound healing and elevated body temperature (52). Energy needs in infants and children should be estimated using standard formulas or nomograms and then adjusted according to the clinical course of the child (53). Studies on energy requirements in paediatric cancer patients have reported increased (54, 55) or normal energy requirements depending on the phase in the treatment protocol (56). Diagnoses particularly associated with malnutrition are Ewing’s sarcoma, Wilms’ tumour, head and neck tumours, advanced lymphoma and neuroblastoma (57, 58, 3). The age of the child also presents a risk factor. Children younger than 3 years and teenagers have problems in satisfying their energy demands because of the higher growth rate during these ages (57).
Prevalence of malnutrition in paediatric cancer patients

It has been estimated that between eight to 32% of paediatric cancer patients present with evidence of malnutrition (59). Some investigators have found that malnutrition is relatively common as early as at the time of diagnosis in children with leukaemia (60, 61), in children with brain tumours (62) and in children with a variety of paediatric malignancies (63). Other investigators have found that malnutrition is uncommon at diagnosis (64, 65, 66, 67), but that treatment intensity is likely to result in malnutrition (4, 68, 65, 69). This lack of congruency is probably a consequence of heterogeneity with respect to diagnoses, sample sizes and differences in nutritional assessment methods.

Consequences of malnutrition

Malnutrition may result in altered pharmacokinetics, impaired drug metabolism, increased drug toxicity and altered response to treatment (70). Studies have shown that children with cancer and malnutrition have more infections, reduced remission rates and increased death rates compared with non-malnourished patients (71). They have a higher risk of early relapse and tolerate chemotherapy poorly as compared with children with normal nutritional status (72, 73).

Mode of nutritional support in paediatric patients

Children should be considered in need of nutritional support if they have an acute weight loss, a weight for height less than 90%, inadequate weight gain or a significant decrease in the usual growth percentile, increased metabolic requirements, impaired ability to ingest or tolerate oral feedings and documented inadequate provision or tolerance of nutrients (74). Oral diet counselling is considered the simplest and preferred method of dietary intervention in children at low nutritional risk. Enrichment of foods can be achieved by adding energy-dense natural ingredients. Other alternatives are glucose polymers in liquid or powder form that can be added to food items. In addition, commercial liquid supplements can be provided. Attempts to increase oral food intake may fail or be insufficient in children undergoing intensive chemotherapy (62, 57). Enteral nutrition (EN), i.e. nutritional support via nasogastric (NG) tube, may improve nutritional status (75), was found to be safe and cost-effective (76) and was associated with fewer fever episodes and fewer positive blood cultures than standard dietetic counselling alone (77). However, the NG tube may be traumatic to the fragile mucosa. Psychological distress, difficulty maintaining tube placement and cosmetic
disadvantages make NG tubes difficult to accept for many children. EN via percutaneous endoscopic gastrostomy (PEG) presents an alternative to the NG tube feeding for individuals with frequent vomiting and vulnerable oral mucosa, and for individuals with eating problems that persist for an extended period of time (78). The tube is placed in the stomach directly through the abdominal wall, either surgically or endoscopically. PEG resulted in significant weight gain in paediatric oncology patients (62) and is considered safe and cost effective (79, 62, 80, 81). Parenteral nutrition is considered for patients in whom the gastrointestinal tract is not functioning or enteral support is inadequate. It is associated with increased risk for infections and requires regular blood sampling to monitor nutritional status and possible side effects (82, 77, 83).

**General aims**

Few studies have investigated how children undergoing chemotherapy for cancer perceive food and eating. The main hypothesis underlying the present study was that food intake is altered after the initiation of chemotherapy. Parents are admitted to the paediatric ward together with their child and they play a crucial role in the care. Improved knowledge about the children’s actual food intake, their perceptions of food and eating, and the parents’ and nurses’ attitudes regarding the children’s food intake after initiation of chemotherapy. Such information could help to individualize the nutritional care and well-being of this patient group in the future.

**Specific aims**

- To assess whether the average daily oral intake of energy and macronutrients met the Swedish Nutrition Recommendations, SNR (84), in children after onset of chemotherapy (I)
- To assess whether the average daily oral intake of energy and macronutrients met SNR after the establishment of new mealtime routines (paper II)
- To assess the children’s own (V) perception of food and eating during days of hospital stay after onset of chemotherapy, and the parents’ (III, V) and nurses’ (V) attitudes regarding the incidence and the nature of possible eating problems, food preferences and avoidances (V).
• To assess possible taste alterations by a taste acuity test (V).
• To communicate our clinical experience of nutritional support via gastrostomy (paper IV).

Methods

Participants

Diagnoses and clinical characteristics of the participating children are presented in Table 1. An overview of participants and assessments used in papers I-V is presented in Table 2. The data collection for the studies took place at the Paediatric Haematology and Oncology Ward at Umeå University hospital, one of six centres in Sweden, where treatment for malignant disease is initiated in children younger than 18 years. Consecutively admitted children aged two years and older whose chemotherapy for cancer was being initiated were eligible for inclusion in papers I, II and V.

Since 1994 percutaneous endoscopic gastrostomy (PEG) has been used on the ward for children with cancer who are at increased risk for malnutrition. Ten percent of the 200 children initiating treatment from November 1994 to April 2000 received a PEG for nutritional support. The criteria for inclusion in paper IV were an age below 18 years, a diagnosis of malignant disease, and receiving a PEG for nutritional support. Nineteen children fulfilled these criteria. One child had to be excluded because of incomplete medical record.

Medical treatment and nutrition support

Side effects regarding food intake (85, 86, 23) of the chemotherapeutic agents most frequently administered to the children are presented in Table 3. Radiotherapy, which may have a negative impact on food intake (26) and height development (87), was given to 12 children before the last anthropometric data were collected and before the interviews were performed with the parents in paper III and the children and parent/s in paper V: two in paper I, three in paper II and three in paper V, and four in paper V. None of the children participating in the taste acuity test received radiotherapy before the test. Most children, especially those with acute lymphatic leukaemia, received corticosteroids in doses that may affect appetite (88). Antiemetic drugs, primarily 5-HT3-receptor antagonists were given in scheduled doses at the time of chemotherapy. Intravenous glucose was administered according to current treatment
protocols during the dietary recording and some children also received parenteral nutrition in addition (papers I, II). Enteral nutrition via NG tube was given to one child in paper I for a limited number of days, and via PEG to one child in paper II, two children in paper V and 18 children in paper IV.

Parents of the children participating in papers II and V were eligible for inclusion in papers III and V. In most cases both the mother and father stayed with the child during hospitalisation. The intention of paper III was to interview one parent of each child in paper II. The intention of paper V was to interview both parents, which was done for eight children.

Out of 23 attending nurses, 17 were interviewed (74%). Twelve were registered nurses and five were nursing assistants. The median (range) number of years since graduation was 11 years (<1-44) and the median (range) of years of paediatric oncology experience was 7 years (<1-33). Registered nurses and nursing assistants will collectively be referred to as nurses in the text.

**Data collection**

Nutritional status was assessed by dietary intake estimates, anthropometric and laboratory measurements.

**Dietary intake (papers I, II)**

Dietary intake is assessed either by prospective or retrospective methods. Prospective methods record dietary intake at the eating occasion, or shortly thereafter. In estimated food record (food diary), all foods, snacks and beverages consumed for a specific time period are recorded (89). For composite dishes, the amount of each ingredient used in the recipe and the amount consumed are recorded. The standardised 7-day recording instrument for dietary intake, the National Food Administration’s food diary (90), was used in papers I and II. It contained illustrations of food items and meals, which helped the parent estimate the intake of foods in household measures. The standardised 7-day recording instrument has been judged as adequate for assessing energy and macronutrient intake, and provides a reasonable compromise between optimal precision, investigator workload and subject compliance (91).

The recording period comprised three consecutive weeks starting the day before (paper I) and the first day (paper II), respectively, of chemotherapy initiation. The parents were responsible
for the recording. They recorded whether each food item was consumed on days at home or in the hospital, and whether it consisted of regular hospital food or was bought and prepared by the parents. Days with dietary information could thereby be divided into three groups. One group consisted of days when all meals were eaten in the hospital (“hospital days”). The meals comprised either regular hospital food or food purveyed by the parents. A second group comprised days when the child was at home and had all meals at home (“home days”). The third group comprised days when the patient had eaten food in the hospital and at home on the same day (“mixed days”).

The estimated volumes of the consumed food items were converted into grams and analysed using the computerised food data bank of the National Food Administration. The software program (92) related the intakes of energy, protein, fat and carbohydrate to the recommended daily intake according to the 1989 Swedish Nutrition Recommendations, SNR (84), in relation to age, and also to sex for children older than 10 years. The daily intake of sucrose was expressed as percentage of the daily total energy intake. Based on the parents’ recording of type and volume of food and beverages consumed by the child, it was possible to calculate the contribution of the food enrichment to the total food intake (paper II).

**Anthropometry (paper I, II, IV, V)**

Weight for age and height for age are related to the mean of a sex- and age-specific reference population and expressed as a standard deviation score (SD score). Any child whose weight or height is more than 2 standard deviations greater than or less than the appropriate mean is considered at risk of having significant growth deviations (89). During periods of nutritional deprivation in children, a weight deficit is the first abnormality to be noted, followed by a height deficit (89). In contrast to weight for age, weight for height differentiates between nutritional stunting, when weight may be appropriate for height, and wasting, when weight is low for height as a result of deficits in tissue and fat mass. Weight for age, height for age, weight for height and BMI (weight in kg/height in m\(^2\)) are commonly used in the assessment of nutritional status in paediatric cancer patients (62, 4, 60, 69).

The patients’ body weight and height were measured according to the routines on the ward. The weight data were collected on admission and weekly up to six weeks after initiation of chemotherapy, and at three months (papers I, V), six months (paper II) and 12 months (paper IV) after treatment start. Height data were collected on admission and at three months (paper
V), six months (paper II) and 12 months (paper IV) after start of treatment. The data in papers I, II, IV were related to the National Centre for Health Statistics, NCHS (93) growth curves and expressed as SD scores. The data in paper V were related to the updated Swedish growth charts (94).

**Laboratory methods (paper II)**
The human body does not store protein as a dispensable source of energy. Decreased levels of serum albumin and prealbumin reflect a reduced supply of amino acid precursors (89). Levels of albumin and prealbumin are therefore reported as useful in detecting malnutrition in paediatric cancer patients (68, 67). Blood samples for analysis of serum albumin and plasma prealbumin were collected on admission and up to six months after initiation of chemotherapy. They were analysed immediately according to the routines at the Department of Clinical Chemistry, Umeå University Hospital.

**Questionnaire (papers I, II, V)**
During the dietary recording period in paper I and II the parents were also responsible for completing a questionnaire developed for the purpose of the study. The questions concerned the child’s experiences regarding food aversion, altered sense of taste or smell, loss of appetite, nausea and vomiting. In paper I, all questions were constructed to be answered with “yes” or “no”. Vomiting was graded according to frequency of vomiting during the day. In paper II, the items in the questionnaire concerning appetite and nausea were revised and pain was added. These questions were evaluated on a visual analogue scale, VAS (95). In paper V, the questionnaire was intended only for the children who participated in the taste acuity test. The questions concerned experience over time of alteration in appetite, taste and smell and possible avoidance of certain foods. The questions were constructed to be answered with “yes” or “no”. The patient was also asked to write a description in his or her own words.

**Taste acuity test (paper V)**
Alterations in taste sensation may be assessed by a taste acuity test in which the basic tastes are presented to the test person. The detection threshold is determined as the lowest concentration at which a taste can be distinguished from the medium (water). The recognition threshold is the lowest concentration at which a taste can be correctly identified (9). Ten of the children aged 11 to 17 years, in paper V performed the taste acuity test, as did 10 age- and sex-matched, non-nicotine taking healthy children. They were children of the staff at the
Department of Odontology, Umeå University. The procedure was performed between two chemotherapy cycles and was carried out in the child’s ward. Taste thresholds were determined for four basic tastes according to Nilsson & Holm (96). The concentrations increased in 9 steps and were presented in random order and in increasing concentrations.

Interviews with children (paper V), parents (papers III, V) and nurses (paper V)
The interviews were intended to capture information about experience over time. Thus, it was desirable that the children were in different phases of treatment. The interviews, which lasted from 15 to 90 minutes, were semistructured and were transcribed verbatim. In paper III, the parent was alone with the interviewer. In paper V, the child and the parent/s were interviewed separately, except in the case of children younger than six years. Paper III concerned the parents’ perceptions of their child’s eating pattern after onset of chemotherapy and the strategies they used to cope when eating problems arose. Paper V concerned the children’s perceptions, and parents’ and nurses’ interpretation of and attitudes toward the children’s food intake after onset of chemotherapy.

Content analysis (97) was used to analyse the interview data. This method is used to draw valid conclusions about manifest messages in a communication by objective and systematic identification of specified communication characteristics. Answers to open-ended questions are suitable for this technique. Words and sentences in the interviews are classified into mutually exclusive categories, which reflect central messages in the interviews. The categories are then grouped into main categories and subcategories depending on the level of abstraction. With access to the recording units, central characteristics and boundaries of the categories, an additional assessor independently assigned all identified recording units to the categories and subcategories. The boundaries and central characteristics of each category were discussed by the authors until consensus was reached.

Statistical methods

In paper I, paired Student’s t-test were used for compare energy and nutrient intake during days with all meals consumed at the hospital ("hospital days") versus days with all meals eaten at home ("home days"). In paper II, the Mann-Whitney U test was used for comparisons of dietary intake between groups, e.g. means of energy and nutrient intakes during "hospital days" and "home days", respectively, and for comparisons of energy from carbohydrate, fat
and sucrose, respectively, from regular hospital food and food purveyed by the parents, and for comparisons between subgroups of children with respect to changes in weight and height (paper IV). The Wilcoxon signed rank test was used for paired data, such as changes in weight and height (papers I, II, IV, V) and serum albumin and plasma prealbumin in the same individual (paper II). For the taste acuity test in paper V, a power analysis showed that a sample size of 10 test persons and 10 controls would be sufficient to detect a difference of 10% between the groups at a $\alpha$ level of 0.05 with 80% power. The Mann-Whitney U test was used for comparison of ordinal data, e.g. taste thresholds in the cancer patient group and the control group. For comparison of nominal data, for example the frequency of taste recognition errors in the two groups, the Chi-square test was used. P values <0.05 were considered statistically significant.

**Ethical considerations**

Papers II, III, V were reviewed and approved by the Regional Ethics Committee at the Medical-Odontology Faculty of Umeå University. The diet recording (paper I) and the medical records review (paper IV) were considered to be quality evaluations of already existing care routines. For ethical reasons it was not possible to evaluate the effect of PEG on anthropometric development, since such a study design would have required a control group of children with equivalent conditions who were not provided with a PEG.

**Results**

**Dietary intake**

Before introduction of new mealtime routines, baseline study (paper I). The total number of recorded days for each child varied between 7 and 21 (median 19 days). The median oral intake of energy and protein expressed as a percentage of the recommended daily intake, calculated on all 240 recorded days, was 64% and 69% respectively, of the 1989 SNR shown in Table 2 in paper I. The average daily oral intake during “hospital days”, “home days” and “mixed days” is presented in Table 4 in paper I.

“Hospital days”

During the 159 “hospital days” the median oral energy intake was only 58% of that recommended. The intake of protein was only 61% of the recommended intake. Three of the 14 children, diagnosed with sarcoma, Wilms’ tumour and CNS tumour, respectively, were
unable to take anything by mouth for a total of seven days. They received intravenous glucose, providing an additional 22% of the energy recommended intake. One of these children received NG tube feedings for one day and thereby received 59% of the recommended energy intake. During the following two days the patient received parenteral nutrition, which provided 49% and 29%, respectively, of the recommended daily intake.

“Home days”
During a total of 56 of the recorded days all meals were eaten at home. The median energy and macronutrient intake on “home days” was significantly higher compared with that of “hospital days” (p<0.05, Student’s t-test).

Intake of sucrose
In regular hospital food, the median energy from sucrose was 12% of the total daily energy intake, which is almost in accordance with the recommended 10%. In food purveyed by the parents during ”hospital days”, the energy from sucrose was particularly high, comprising 22% of the total daily energy intake, (Table 6 in paper I).

Follow-up study (paper II)
After the establishment of improved mealtime routines on the ward, data were collected with the aim of studying whether the daily energy and macronutrient intake were in accord with the recommended intake. The total number of recorded days for each child varied between five and 21 (median 20). The average daily oral intakes of the 11 children during “hospital days”, “home days” and “mixed days” are presented in Table 3 in paper I.

“Hospital days”
Ten of the 11 children had days with all their meals in the hospital. The mean daily oral energy intake of these 10 children was 61% of that recommended intake, and was still lower than recommended in spite of efforts to prepare palatable food on the ward. Energy intake from regular hospital food comprised 49% of the total intake. The energy from food purveyed by the parents was 11% which was as large as before the institution of new mealtime routines. Enrichment of the hospital food provided only 3% of the recommended daily intake. Two children received parenteral nutrition for a limited number of days, and one child received enteral nutrition via PEG for the entire dietary recording period. The total energy intake for the whole study group, including oral intake, enteral and parenteral nutrition as well as
intravenous glucose on treatment days, came close to that recommended for healthy children, median 91% of the recommended intake.

In healthy children older than three years, protein should ideally provide 10 to 15% of the total daily energy intake, fat should provide 30%, and carbohydrate 55 to 60% (84). In regular hospital food, protein comprised 15% and fat 34% of the oral intake, which is almost in accordance with the recommendations. In food purveyed by the parents on the other hand, 9% of the energy intake came from protein and 42% from fat. The difference in energy intake from protein in hospital food and food purveyed by the parents was statistically significant (p<0.05). Sucrose in food purveyed by the parents on “hospital days” continued to be higher than that recommended and comprised 19% of the average oral daily energy intake.

For the purpose of this thesis, the daily oral energy intake for each child in papers I and II was recalculated using the adjusted energy reference values of the Nordic Nutrition Recommendations, NNR (50). The children’s average daily energy intake and their estimated energy requirements according to NNR 2004 are presented in Table 4. The recalculation showed that out of the 25 children who participated in papers I and II, 14 (56%) had an average energy intake lower than 75% of these reference values for healthy children.

**Anthropometry (papers I, II, IV, V)**

The newly diagnosed children in paper I were born during the period 1976-1987, those in paper II were born during the period 1980-1993 and those in paper V during the period 1986-2000. For the purpose of this thesis and for uniformity, weight and height data from papers I, II and V were recalculated and related to the same standard, the 1976 Swedish growth curves (98). Weight and height data on admission and at different time points after onset of chemotherapy for the children in papers I, II and V are presented in Table 5.

On admission the median SD score for weight for age was below (paper I) and above (papers II and V), respectively, the standard reference value (98). After the initiation of chemotherapy, there was a reduction in weight for age that was statistically significant (p<0.05, Wilcoxon paired data) at one week (papers I, II and V) and that persisted up to three months after the initiation of chemotherapy (paper I). There was no statistically significant difference in median weight for age on admission between paper I and papers II and V.
On admission, the median SD score for height for age was below the reference values (98) in paper I and slightly above those values in papers II and V. After the initiation of chemotherapy, height development was significantly decreased at three months (paper II, V) and at six months (paper II) compared with admission height (p<0.05, Wilcoxon paired data).

Children provided with a PEG for nutritional support (paper IV).
Eighteen children were provided with a PEG for nutritional support (paper IV). Ten of these children received their PEG at treatment start, since they had been identified at diagnosis as being at risk for malnutrition as defined by the locally formulated nutrition support program (99). Eight children were considered at diagnosis as being at average risk for malnutrition. They received their PEG at a median time of 3.4 months after treatment start. The SD scores for weight for age at two, three, sex and 12 months after the PEG placement were compared with the SD score at PEG placement (93). The comparison between the two groups, in which the children still had the PEG in use, showed a significant difference in body weight at three months (p<0.05 Mann-Whitney) after PEG placement, indicating more favourable weight development in the group of children who were at average risk for malnutrition at the time of diagnosis.

On admission, the median height for age was +0.03 SD for the whole group of 18 children. The median height at one year after PEG placement was -0.31 SD, indicating that the linear growth for the whole study group was retarded at one year after PEG placement. There was no statistically significant difference in height development between the group of 10 children, who were identified at diagnosis as being at high risk for malnutrition and the group of eight children, identified as being at average risk for malnutrition.

**Laboratory methods (paper II)**
On admission, the serum albumin levels were within the reference values for age and sex, except in one child. A small but statistically significant decrease was seen six weeks after initiation of chemotherapy. The prealbumin levels showed minor variations over time. There was no consistent deviation from the reference range.

**Questionnaire (papers I, II, V)**
In paper I, the children experienced loss of appetite on 50%, nausea on 36%, vomiting on 12% and food aversion on 37% of the recorded days. Food was considered to have an
unpleasant taste on 34% and a different smell on 19% of the recorded days. In paper II, eight of the 11 children (73%) experienced nausea and five (45%) vomiting as well. Seven (66%) suffered from lack of appetite and six (55%) from pain in the mouth, throat or abdomen. Four children (36%) experienced food aversion and three (27%) altered taste. Six children experienced more than two of these problems. In paper V, 10 children participating in the taste acuity test filled in the questionnaire. Seventy percent of them reported alterations in taste since the start of chemotherapy.

**Taste acuity test (paper V)**

There was a significant difference in recognition thresholds for bitter taste between the groups, where the patients were less sensitive compared to controls, median (range): 0.015 mmol/L (0.002-0.006) and 0.004 mmol/L (0.002-0.06) respectively (Mann-Whitney U test, p<0.05). There were no significant differences in recognition thresholds for sweet, salty and sour. The taste acuity test also showed that significantly more patients made taste recognition errors compared to the controls (Chi-square, p<0.05). Further analysis, comparing the type of error for type of stimulus between the groups, revealed that the patients incorrectly reported bitter taste at a higher rate compared with the controls (Mann-Whitney U test, p<0.05).

**Interviews (paper III, V)**

Table 2 in paper V shows the cause and frequency of eating problems among the 21 children participating in paper V. Selected subcategories (in italics) are briefly presented below. The view of both children and parents was that altered taste was the predominant cause of the children’s eating problems. This means that according to the children, 43% of them had experienced altered taste and according to the parents, 76% of the children had experienced altered taste. The children also viewed learned food aversions, nausea and vomiting and pain in the mouth, abdomen and extremities as important causes, while the parents perceived nausea, pain, learned food aversions and altered smell as significant factors. The nurses, on the other hand, viewed nausea, feeling ill, the ward environment, and food refusal as a way of gaining some influence over the situation and as a protest against the situation as important factors. The older children seemed to be more affected by altered taste, learned food aversions, and nausea as compared to the younger children. The parents of the youngest children believed pain to be very important with respect to eating problems.
Initially, the children seemed to be satisfied with the regular hospital food and dishes composed upon request by the Central Kitchen. This indicates that they did not have any prejudice against hospital food. However, after initiation of chemotherapy, food choices changed in some way for all of the children. *Preferred foods* during periods of poor appetite were mainly well-known foods and dishes the children had liked previously. These were often purveyed by the parents. *Avoided foods* were mainly protein-rich foods such as red meat, chicken, hot dogs and fish. They were said to have a strange taste. Chocolate and ice cream were avoided because they were associated with nausea that had been experienced close in time to chemotherapy administration.

The older children were generally more negative towards regular hospital food than the younger children. The children, and also many parents, criticized its taste, preparation and lack of variation. Eighty-five percent of the parents said that they purveyed food for their child. Some of these parents stated that they paid no attention to whether the food they purveyed was nutritious. Being flexible and providing food they thought the child would accept was of greater importance. The statements made by the nurses indicated that the regular hospital food was generally rejected, especially by the older children, in favour of foods purveyed by the parents. It was the nurses’ perception that by rejecting the hospital food, the children may have been trying to manifest their autonomy. Providing food was perceived by the nurses as a crucial parental task and an important part of their coping strategy. It relieved anxiety and was also a way for the family to maintain some autonomy on the ward.

Four children, aged 8-17 years, said that they avoided all kinds of food, including food purveyed by the parents and meals and snacks prepared by the nurses on the ward, because food was perceived as “disgusting”. One parent’s opinion was that the child rejected a previously accepted, well-known, brand-name soft drink when it was served on the ward because then the product was perceived as “contaminated” even though it was in its original container. The same product, when consumed outside the hospital, was accepted by the child. After initiation of chemotherapy, there seemed to be changes in how the study children perceived food.

During periods of poor appetite, the children were offered commercial liquid supplements, which were available in a variety of flavours. These were not popular among the children and
were perceived to have a strange taste. The nurses on the other hand, offered these liquids as the first choice for nutritional support. The nurses emphasised the importance of how the drink was presented to the child. Acceptance was perceived to be better if the drink was served in an attractive way, thereby avoiding the association with “medicine”.

Interviews with parents (paper III) showed that *emotional support and practical help*, i.e. encouragement, help with cooking, ordering alternatives or serving alternative meals from supplies in the local kitchen when the child rejected the regular hospital food were appreciated. This may indicate that for some parents the feeling of being responsible for the daily provision of food was distressing. Parents described their feelings when the staff considered *intervention through enteral nutrition* via an NG tube or PEG when their child’s eating problems resulted in weight loss. Although the parents understood that the nutritional support was needed, the NG tube was perceived as a threat to the child’s self-esteem. None of the children actually got an NG tube, but one child received nutritional support via PEG. The PEG was perceived by the parents as positive in the long-term perspective. It made the previously distressing mealtime situations more positive.

**Clinical experience of enteral support via PEG (paper IV)**

The medical records review showed that the median (range) time for PEG use for the whole group of 18 children was 12.3 months (1.2 – 24.0). Ten of these children were identified at diagnosis as being at considerable risk for malnutrition. They received their PEG at treatment start and had it in use for a median time of 13.4 months. Eight children were considered at diagnosis to be at average risk for malnutrition. They received their PEG at a median of 3.4 months after treatment start and had it in use for a median time of 7.7 months. The majority of complications were local or systemic infections, leakage of gastric juice, and feeding intolerance. The most serious PEG-related complications were documented in two children receiving palliative treatment. There was no significant difference in the rate of complications between the 10 children identified at diagnosis as being at increased risk for malnutrition and the eight children at average risk for malnutrition. Taking into consideration the medical condition of the children in the study group and the length of time with the PEG in place, nutrition via PEG was rarely associated with other than minor complications.
Discussion

In general, the impact of cancer on nutritional status in children is likely to be minimal at the time of diagnosis. Many of the side effects of chemotherapy interfere with food intake and cause the patient to be at risk for malnutrition. Malnutrition contributes to increased susceptibility to infections, decreased tolerance to therapy and poorer treatment outcomes (3).

Studies of children under treatment for cancer show oral energy intakes that are considerable lower than age-based nutrition recommendations (4, 5). Our data before the institution of new mealtime routines are in agreement with an average daily oral energy intake during “hospital days” of only 58% of that recommended. Regular hospital food constituted 50% and the difference comprised food purveyed by the parents, indicating their efforts to improve the intake. The average daily oral protein intake was 61% of the recommended intake. We assumed that improvements in the mealtime routines on the ward would give the patients an opportunity to increase their food intake and to choose food with an adequate composition of nutrients, thereby improving nutritional status. However, the follow-up showed that the average daily oral intake of energy and protein on “hospital days” was still below that recommended for healthy children, 61% and 64%, respectively, despite the efforts to provide palatable food on the ward that the children would accept. The contribution of energy from purveyed food was as high as before the institution of new mealtime routines. The energy from enrichment of the hospital food provided only a small proportion of the average energy intake. However, the total energy intake for the whole study group, including oral intake, enteral and parenteral nutrition as well as glucose on treatment days, was 91%, i.e. close to that recommended.

The energy intake from sucrose in food purveyed by the parents during “hospital days” was particularly high, comprising 19% of the total daily energy intake. It is recommended that the energy intake from sucrose should ideally not exceed 10% of the daily energy intake. Some of the interviewed children and parents in paper V related that taste alterations made the child avoid sweet foods. The dietary recordings in paper I and II on the other hand, showed that the average energy intakes from sucrose were considerably higher than that recommended. This incongruence might be explained by the fact that the children may have decreased their usual
consumption of sweets or that the contribution of sucrose in sweetened beverages consumed may have been underestimated by the children and the parents. It may also be due to the timing of the interviews and the dietary recordings in relation to the development of taste alterations as well as heterogeneity with respect to diagnoses and treatment protocols. If mostly nutritious foods are consumed, empty calories from sugar may be an acceptable addition to the diet in healthy, physically active individuals, while a child who is ill and has a low food intake is in need of nutrient-dense foods, allowing less empty calories.

The SNR are levels of intake of essential nutrients judged as adequate for meeting the needs of practically all healthy individuals and are not intended to be used on an individual level, particularly not if the individual has special requirements, such as is the case for children with chronic diseases. In contrast to the recommendations for nutrients, the value set for energy is not generous. It is set at the mean of the population’s estimated requirements, representing the average needs of a group of individuals and not to meet the exact need for all individuals. Growing children and adolescents with chronic diseases, may have increased requirements, although the extent to which they are increased is not known. The application of the doubly labelled water (DLW) technique has revealed that previous estimates of energy expenditure in healthy infants (100), children and adolescents (47) have been overestimated. The estimated energy reference values have been reduced for children aged 2 to 9 years and adjusted with regard to different levels of physical activity in children aged 10 to 17 years (50). Thus, the recommended energy intake according to the 1989 SNR (84), to which the energy intakes of the children studied in paper I and II were related, might have been too high. Recalculation of the energy intakes of the children in papers I and II showed that 56% had an average energy intake lower than 75% of these new reference values for healthy children (50).

This study tries to identify some of the problems regarding food intake in children with cancer after the initiation of chemotherapy. In addition to physiological factors such as altered taste sensation, nausea and pain, psychological aspects such as learned food aversions, a negative attitude towards hospital food, a negative impact of the hospital environment, and food refusal judged as a means of gaining some control over the situation were mentioned as important causes. The younger children seemed to be more affected by pain and altered taste, as judged by their parents. Older children were able to describe their symptoms over time and emphasised altered taste, learned food aversions and nausea. The nurses perceived that nausea
was the most important cause. This may indicate that the nurses focused on more easily managed complaints and underestimated the impact of alterations in taste.

The taste acuity test showed that the patients had a significantly higher recognition threshold for bitter as compared with controls. Previous studies in paediatric cancer patients showed significantly higher recognition thresholds for salty taste (41) and for all four tastes (42) after start of chemotherapy compared with admission values. The results are not quite consistent with ours, which is probably a consequence of heterogeneity with respect to diagnoses and the time point of the taste acuity test in relation to initiation of chemotherapy. The patients also made mistakes and were more frequently uncertain about the right taste category as compared with the controls. None of the patients actually complained of any bitter background taste, although five of them answered “bitter” when they were presented with very low concentrations of salty and sour solutions as well as with water, which served as a blank. These findings probably do not account for all the abnormal food taste changes reported by the children, but may indicate a phantom taste of bitter, meaning a distortion of taste where there is no stimulation (11), and/or some other taste dysfunction related to bitterness. It is possible that the existence of such dysfunction may act as a masking stimulus and elevate the bitter threshold, since the individual has to detect increments over the background taste. Theoretically, a possible phantom taste of bitter may make these children avoid certain foods and prefer spicy and strong tastes. However, it can be concluded that providing a variety of “tasty” food in the hospital setting did not suffice for many of the children.

Pain caused by mucositis was perceived by some of the children and the parents as the most important causes of eating problems. Some children who were treated with corticosteroids had good appetite and were hungry, but oral mucositis made eating impossible. Children with mucositis received treatment with saline mouthwash, topical analgesics and opioids were sometimes used for pain control. To date there is no optimal treatment and there is controversy regarding different treatment approaches (101).

Fallon and co-workers (102) developed a taxonomy for rejection of foods. They described four basic types of reasons, which are not totally mutually exclusive. Three of these, i.e. distaste, danger and disgust, may be applicable to our findings. Distaste means that the food is rejected because of the taste, smell and or texture. Danger is rejection based on anticipated harmful consequences of ingestion such as nausea. Disgust is based on ideational grounds and
has a strong affective component. Disgusting foods are disliked because of the idea of what they are, their nature or their origin and there are also strong objections to their taste, smell, texture or appearance. Batsell and Brown (103) found support for “traditional” as well as “cognitive” food aversions. In the traditional aversion, it is typical for the flavour of the food to be associated with an episode of nausea, whereas in the cognitive aversion, mental images are associated with the food. Learned food aversions were commonly reported in the interviews and aversive food items included for example red meat, ice cream and chocolate. This finding is in accordance with previous research (42). Protein-rich food and food with a strong flavour, such as chocolate, easily become targets for food aversions (27). One explanation is that gastric emptying generally is slower for protein than for carbohydrate and digestion is also slower than for carbohydrate (27). Theoretically, proteins are associated with more severe symptoms when nausea occurs. This is unfortunate because red meat is energy dense food and is also nutritionally significant in terms of protein and iron intake. In the present study, children, parents and nurses reported that nausea strongly contributed to the eating problems. The prevention of nausea is important, because it plays a unique and potent role in the development of learned food aversions (28). In accord with the routines on the ward, antiemetic drugs were given as prophylaxis before nausea develops and at intervals thereafter. Although 5-HT\textsubscript{3} antagonists were given in association with chemotherapy administration, complete control of nausea was obviously not attained for all patients. The efficacy of antiemetics is influenced by patient characteristics such as sex, age, prior history of motion sickness, high anxiety levels and poorly controlled nausea in previous chemotherapy cycles (25). This may explain why paediatric cancer patients continue to suffer from chemotherapy-induced nausea in spite of powerful antiemetics (104). Hopefully, more effective and individually tailored medical treatment for managing nausea and vomiting will reduce these problems in the future.

The older children were generally more negative than the younger children towards the regular hospital food. The children criticised its taste, preparation and lack of variation. It was rejected in favour of foods purveyed by the parents. Some of the older children refused to eat anything while they were admitted to the ward, since they found all foods served on the ward “disgusting”. Furthermore, well-known brand-name products were sometimes rejected when served on the ward, even though still in the original packaging. The parent believed the products to be perceived as “contaminated” by the child. These reactions may indicate the cognitive type of food aversion (103, 102). Food aversions are more likely to be directed
towards unfamiliar foods (34). Although the hospital menu provided well-known dishes, food neophobia may play an important role regarding the children’s rejection of the hospital food. Unfamiliar foods do not have to be totally new products, but may be a new brand of previously well known foods (105). Changes in the child’s taste perception, may make hospital food seem unfamiliar and therefore aversive because of food neophobia. Rejection of the commercial liquid supplements may be explained by the fact that the children perceived them as medicine rather than food, or as food representing the hospital or simply as unfamiliar food. It can be concluded that nausea and taste alterations contributed to learned food aversions, and that disgust and neophobia negatively affected the appetite, leading to food rejection in our patients. Energy enrichment by means of hospital food is not likely to make significant nutritional contribution to the child receiving chemotherapy who has eating problems.

It has been shown that cooperation between staff and parents in preparing of food on the ward can result in increased food intake in paediatric cancer patients (5). Involving the parents in cooking was not the intention of the improved mealtime routines on our ward. One can speculate as to whether active involvement on the part of the parents would have resulted in less rejection and better acceptance of the hospital food. None of the parents asked for such involvement. On the contrary, they stated that they appreciated the nursing assistants’ practical help in preparing the food.

It was the perception of some of the nurses that the child wanted to manifest his/her autonomy by rejecting the hospital food. Being hospitalised causes patients to lose control and their autonomy becomes subordinated to hospital routines (18). When loss of control occurs, the children may strive to maintain control. Rejecting hospital food may serve as a target of such control. There are social aspects of food that are related to an individual’s identity (17), which is important in the hospital setting. Food purveyed by the parents may represent the identity of the child, the family and life outside the hospital, and may therefore be better accepted. Hospital food may also represent an area in which both the parents and the child feel free to criticise hospital services (106).

Many parents related that they purveyed food for themselves instead of paying for the hospital meals. This may have implications for the patient’s choice of food. Eating is a social event, and models, e.g. persons important to the patient may have a powerful influence on food
selection (15). Hence, parents and siblings are likely to influence a child’s food preferences. When the hospitalised child sees parents and siblings consume purveyed foods, he or she is likely to prefer purveyed food and reject hospital food.

Coaxing and stressful mealtime situations were described by some of the parents. Parents of paediatric cancer patients experience high levels of psychological distress (107). Altered eating pattern by the child with cancer is of considerable symbolic value to parents and when eating patterns change, parents are reported to feel helpless and to become preoccupied with their child’s eating (5, 108, 109). When the child eats well, parents take this as a sign that the child wants to fight the disease, while loss of appetite or weight loss may be perceived as a sign of defeat (106). Anticipatory nausea and food aversions were seen more frequently in paediatric cancer patients whose parents relied more on coaxing when managing their children in fearful situations (110). Paediatric cancer patients were reported to be coaxed more by their parents during mealtimes as compared with healthy children (42). It is most probable that parents who are anxious to increase the child’s food intake, unintentionally exacerbate the eating problems. These findings highlight the need to recognise the parents’ feelings of distress and the need for continuous support from health care professionals.

Flexible mealtime routines are important, since they show the child and the family that they are important and that food preferences and aversions are taken into consideration. However, efforts to encourage food intake are sometimes insufficient. Intervention by means of an NG tube or a PEG was discussed with the parents. Previous studies have shown that children with cancer who receive a PEG either gain or maintain their weight, or at least returned to a desired weight (79, 62, 111, 80, 81). The weight development of children who were at average risk of malnutrition was more favourable as compared with the weight development of children considered to be at increased risk of malnutrition. Less favourable weight development may reflect a catabolic condition that is not easy overcome even with intensive nutritional support. However, a PEG may presumably make it easier for parents to administer sufficient nutrition and necessary enteral medication, and thereby relieve some of their distress and allow them to improve the quality of life of the child and the family. These psychological aspects are difficult to quantify.

The present study support previous research showing that newly diagnosed children with cancer are generally not underweight on admission (66, 67), but that treatment results in
weight loss for most of the children. High doses of corticosteroids may increase the appetite and prevent weight loss in children with leukaemia (88, 42). Interviews with children and parents showed that periods of increased appetite were perceived to be related to corticosteroid treatment. However, we could not confirm an effect of corticosteroid dosage on energy intake or weight development. This may be explained by sample size and heterogeneity with respect to diagnoses and treatment protocols.

It has been reported that Swedish children have become taller and heavier in recent decades (94). The newly diagnosed children were born in 1976-1987 in paper I, in 1980-1993 in paper II, and in 1986-2000 in paper V. Although the median weight on admission was -0.34 SD for the children in paper I, +0.39 SD for the children in paper II and +0.42 SD for the children in paper V, there were no statistically significant differences in median weight on admission between the children in paper I and those in papers II and V. The secular trend of increased body weight could not be confirmed in the present study.

The genetically predetermined linear growth potential may be comprised by variations in nutrient intake (89). Retarded longitudinal growth was seen at three months and at six months. Twelve of our patients received radiotherapy before recording of height was completed. Administration of radiotherapy to paediatric cancer patients may reduce their final height (87). Thus, linear growth may be compromised by factors other than malnutrition in children with cancer. Although inconclusive, our results suggest that the reduced growth rate may be explained partly by altered nutritional intake and partly by the illness and treatment itself. To what extent hospitalization itself affect growth is not possible to conclude in absence of a control group.

Serum albumin and prealbumin have been reported to be useful in detecting malnutrition in children with malignancies (68, 67). However, these indices did not prove to be useful indicators of protein deficiency in the present study. This may be explained by the fact that both albumin and prealbumin are influenced by causes other than malnutrition, e.g. decreased synthesis, increased losses and fluid overload (112) or that few study children, if any, suffered from severe malnutrition.

A relevant question concerns what methods are best for detecting an increased risk of malnutrition in paediatric cancer patients. Anthropometric and laboratory methods, e.g. serum
albumin and prealbumin, reflect past rather than current nutritional status. Based on clinical symptoms that alter food intake, a scoring system was designed to assess nutritional status on a day-to-day basis (113). The symptom scores were significantly related to fever and a fall in neutrophil count, but there was no correlation with anthropometric indices. These results suggest that the nutritional status of children undergoing chemotherapy can be sufficiently assessed by a few clinical parameters and an open dialogue with the parents about altered food intake. To assess the quality of growth in cancer patients’ body composition analysis, e.g. dual-energy X-ray absorptiometry, DEXA scan (114), should give valuable information.

**Methodological considerations**

Paediatric cancer is rare and there are methodological problems such as small and heterogeneous patient groups with respect to ages and diagnoses (115). This may have consequences regarding the generalisability of the findings. Out of the 20 consecutive children who met the criteria for inclusion in paper I, the parents of 14 agreed to let their child participate (70%). In papers II and V, 79% of the eligible children participated. The children, who declined participation, represented various age groups and diagnoses, so that systematic biases are unlikely. The Umeå University Hospital catchment area covers approximately 50% of the area of the country and 10% of the Swedish population. We believe that the participants are representative for paediatric oncology patients at large.

**Dietary intake**

The total number of observation days for the 14 children in paper I was 294. For 54 of these, (18%) no dietary recording was done. The corresponding figures for the 11 participating children in paper II were 231 and 32 (14%), respectively. This may reflect the psychological burden on the parents. The children were newly diagnosed and the families were under considerable strain. The researchers’ follow-up visits were conducted in a supportive way so as not to add to the parents’ psychological distress.

The major sources of error that affect validity in dietary recording are the difficulties the test person has in accurately estimating the kinds and amounts of food consumed and the tendency to over- as well as underreport food intakes (116, 117). In a Swedish study, adolescents tended to underestimate their intakes (118). Generally, young children tend to overestimate and older children tend to underestimate their food intake (119). However, when the dietary
recording was carried out by the parents and the children had no unsupervised access to supplementary sources of food and snacks, the energy intake and energy expenditure were reported to be very close to one another (120). The parents in papers I and II were motivated to participate in our study, which is why a high degree of compliance might be expected. The children had practically no unsupervised access to supplementary sources of food during days of hospitalisation. One way of validating dietary intake data is to calculate the quotient between reported energy intake and estimated BMR (121). Ratios below 1.0 would indicate that the food intake may have been under-estimated. Recalculation of the dietary recording in papers I and II showed that many of the children studied in papers I and II had a median oral energy intake below their estimated BMR (45). Energy intake equal to BMR is not sufficient to maintain body weight. Almost all the children in our study groups lost weight during their dietary recording period. Taking into consideration the reported eating problems, the recorded low food intake of many of the children is likely to have been reasonably accurate, particularly when related to the new requirements based on the DLW method (50).

There are certain differences between the two computerised data bank versions used in these studies, one of which is of importance for papers I and II. In Dietist DOS version 5.2 (92), which was used in paper I, dietary fibre was added to the carbohydrates and was thus counted as an energy provider. In the updated version of Dietist Windows 95.2 version 1.0, used in paper II, it was not. The fact that fibre contributed to the energy in paper I while it did not do so in paper II would have had consequences regarding interpretation if the results of these studies had been compared. The aim of paper II was to see whether the energy intake met the recommended daily intake according to the 1989 SNR (84) after the new mealtime routines were initiated, and not to compare the intakes in papers I and II.

Anthropometry
The weight and height data were obtained according to the routines of the hospital ward and were extracted from the medical records. This might have affected the precision of the measurements, but systematic bias is unlikely. The NCHS growth curves provide international reference values for children from birth to 18 years and consist of measurements of 200 children in each age group, born between 1963 and 1974, and are mainly cross-sectional (89). The Swedish growth curves of Karlberg et al. (98) and Albertsson Wikland et al. (94) are longitudinal and consist of measurements of 212 children born between 1955 and 1958 and measurements of 3650 children born between 1973 and 1975, respectively.
The NCHS (93) growth curves were used in papers I and II. Recalculation of weight and height data using the curves of Karlberg et al. (98) showed the same results regarding statistically significant differences in the studies. The correlation coefficients varied between 0.98 and 0.99 when the weight and height data of the boys and girls were computed in both standards. This shows a good agreement between the two standards.

However, weight alone is not reliable for assessing nutritional status in paediatric cancer patients. Some children may have tumour masses large enough to add to their body weight at diagnosis, and loss of tumour mass due to treatment may contribute to weight loss after chemotherapy (57). The administration of fluids and diarrhoea and vomiting reduce the reliability of weight-related indices in assessing nutritional status. High doses of corticosteroids may alter the muscle mass and cause retention of salt and fluid and reduce linear growth (57).

**Taste acuity test**
When taste thresholds are measured, the test person may detect nontaste sensations and confuse them with taste. For example, sodium chloride, citric acid and quinine may produce stinging sensations in some people. Thus, even if the test person has no taste function at all, he or she may be able to correctly detect that these taste solutions differ from water (122). It would have been desirable to include umami in the taste acuity test. Unfortunately, this was not possible. The control group comprised healthy children to the staff at the Department of Odontology, who volunteered for the test. Hence, they may not necessarily be representative for the population at large. All the patients were receiving combination chemotherapy. Direct information about the effect of particular medications or length of time of the medication was not investigated.

**Interviews**
Although all the children were on active treatment, 45% (paper III) and 35% (paper V) of the children and their parents were interviewed more than six months after initiation of chemotherapy. This time period may have resulted in recall bias regarding the most intensive treatment phase. On the other hand, the interviews took place after the children were no longer hospitalised for an extended period of time. Thus, they were less dependent on the
hospital, which probably allowed them to express their criticism of hospital routines more freely.

In paper V, registered nurses and nursing assistants are collectively referred to as “nurses” and it was not our aim to analyse differences between these groups. To a great extent, they take active part in communication about food and eating with the patients, their parents and the attending paediatric oncologists. Therefore, it is reasonable to believe that registered nurses and nursing assistants would agree on many aspects. Nevertheless, there might be different perceptions due to differences in their educational background. Gender perspectives with respect to patients and nurses could not be investigated, since boys comprised the majority of patients and women the majority of nurses.

Young children can recall and describe experiences related to earlier adverse events, such as illness and hospitalisation (123). This enables researchers to select appropriate interviewing strategies in order to describe children’s experiences. The young children told about their perception of food, but were not able to describe their perceptions over time. However, we regard their verbal contribution as valuable. Verbal reports have their weaknesses. It may be questioned whether respondents really feel the way they say they do, particularly if their responses could potentially require them to admit to socially unacceptable behaviour (124). There were discrepancies between the views of the children, the parents and the nurses concerning the causes of the children’s eating problems. This may indicate the proxy problem, i.e. whose assessment should be regarded as most “true”. Parsons and co-workers (125) have argued for the need to reframe the question about proxy reporting from “who is right?” to “what does each informant contribute to our understanding?” We believe that the results are valuable in identifying patterns of experiences.

Two types of reliability are pertinent to content analysis: stability and reproducibility (97). Stability refers to the extent to which the results of content classification are invariant over time and can be determined when the same content is coded more than once by the same coder. Reproducibility, sometimes called intercoder reliability, refers to the extent to which content classification produces the same results when the same text is coded by more than one coder. Whether two persons find the same pattern in the data in an inductive study is debatable. According to Patton (126), it is helpful to have more than one person code the data, and the results should then be compared and discussed. In order to ensure the reliability of the
analysis in papers III and V, co-assessment of the transcribed interviews was therefore performed.

Summary

- The average oral energy and protein intake during hospital stay were only 58% and 61%, respectively, of recommended intakes for healthy children according to the 1989 SNR (84). Therefore, improved mealtime routines were instituted for the purpose of increasing energy and nutrient intake during in-hospital days.

- The follow-up study (paper II) showed that the average daily energy intake during in-hospital days was still lower than recommended, despite efforts to increase the oral intake. The average oral energy intake comprised 61% of the SNR. Food purveyed by the parents comprised 11% of this intake. The energy intake from enrichment of hospital food provided only a small proportion, 3% of SNR. Oral intake and additional enteral and parenteral nutrition came close to the recommended intake, 91% of SNR. A more effective protocolised nutrition journal is obviously needed during the intensive phase of treatment.

- Altered taste was by both children and parents the most frequently mentioned cause for the children’s eating problems. The children also viewed learned food aversions, nausea and vomiting and pain in the mouth and abdomen as important causes, while the parents perceived nausea, pain, food aversions and altered smell as significant factors. The nurses on the other hand, viewed nausea, feeling ill, the ward environment, and food refusal as a way of gaining some influence over the situation and as a protest against the situation as important factors.

- The taste acuity test showed that the cancer patients had a higher threshold for bitter taste and made more taste recognition errors compared with controls. The patients incorrectly reported bitter taste at a higher rate compared with the controls. Thus, changes seemed to exist in the sense of taste as well as in perception of food in these patients. It can be concluded that serving “tasty” food to children undergoing chemotherapy is not always successful.
• The coping strategy of most parents was to provide food for their child. They seemed satisfied if the child ate at all, even if the child’s food selection was very limited. Emotional support and practical help in preparing food from the nursing staff were appreciated. The study indicates that parents need continuous support in order to play an optimal role in the nutritional care of their child.

• Our clinical experience with 18 children, who were provided with a PEG for nutritional support for a median duration of more than 12 months indicated that PEG has several advantages and is rarely associated with other than minor complications.

• The median weight for age at admission was below (paper I) and slightly above (paper II, V) the reference value. Compared with the admission weight, there was an average weight reduction that was statistically significant at one week (papers I, II, V) and at three months (paper I). Linear growth was significantly retarded at three (paper II, V) and six months (paper II).

Conclusions and implications for nursing

The present study shows that the requirements for energy and macronutrients are difficult to meet by food intake for many children undergoing chemotherapy for malignant disease. At least part of the explanation is that there are changes in the sense of taste and the perception of food as well as in eating behaviour in these children. The nurse plays a vital role in the daily assessment of the child’s nutritional status and can, in close collaboration with the parents, identify factors that interfere with the child’s food intake. The parents should be informed early in the treatment about common problems that interfere with food intake, e.g. alterations in taste and smell, nausea, and development of food aversions. This will help to minimise their burden. Nutritional intervention should be timely and anticipate nutritional needs. Early intervention is important. Screening for risk of nutritional problems should be done at diagnosis and continue throughout treatment. A nutrition record should be kept and nutritional screening should include a history of decreased or unusual food intake, an estimation of energy intake in relation to calculated needs and expected weight and height development. The individual child’s food preferences should be considered. Spicy food should be on the
menu and served when appropriate, because spices may mask a possible phantom taste of bitter. Elimination of odours that adversely affect appetite in smell-sensitive patients should be included in food preparation and presentation. Nausea plays a potent role in learned food aversions. Without effective prophylaxis, nausea and vomiting and consequently learned food aversions become debilitating and impaire the patient’s quality of life. It is also important to individualise combinations of oral, enteral and parenteral support. Optimal nutrition promotes a better outcome for cancer patients. The overall goals of nutritional care are to prevent and correct nutritional deficiencies and to minimise weight loss.

**Perspectives**

The role of certain nutrients that seem to have pharmacologic effects on gut function and on inflammatory and immune responses has been studied over the last two decades. Substances such as glutamine, omega-3 fatty acids, arginine, and nucleotides have been added to standard nutritional support solutions and the use of these solutions is known as immunonutrition (127). The significant nutritional and metabolic ramifications of cancer and its therapy deserve consideration. There might be a need for disease-specific nutritional support for the cancer patient. Further studies are required to evaluate the putative beneficial effects of immunonutrients in cancer therapy.
Table 1. Characteristics of the participating patients in papers I-II, IV-V.

<table>
<thead>
<tr>
<th></th>
<th>Paper I</th>
<th>Paper II</th>
<th>Paper IV</th>
<th>Paper V</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>Sex, boys/girls</td>
<td>7/7</td>
<td>4/7</td>
<td>10/8</td>
<td>16/6</td>
</tr>
<tr>
<td>Age, years, median (range) at diagnosis</td>
<td>10 (5-16)</td>
<td>7 (2-15)</td>
<td>2.5 (0.5-14)</td>
<td>9 (2-17)</td>
</tr>
<tr>
<td>Diagnostic groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukaemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- acute lymphoblastic leukaemia, ALL</td>
<td>4</td>
<td>4</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>- acute myelogenous leukaemia, AML</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Lymphoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hodgkin lymphoma</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>- non- Hodgkin lymphoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- histiocytosis</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central nervous system, CNS tumours</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ependymoma</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- astrocytoma</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>- medulloblastoma/PNET</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Solid tumours</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Wilms’ tumour</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>- hepatoblastoma</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- osteosarcoma</td>
<td>1</td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>- Ewings’s sarcoma</td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>- rhabdomyosarcoma</td>
<td>3</td>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Therapy status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- on chemotherapy</td>
<td>14</td>
<td>11</td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>- off chemotherapy</td>
<td></td>
<td></td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>Nutritional support</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- NG/PEG</td>
<td>1/0</td>
<td>0/1 a)</td>
<td>0/18 a)</td>
<td>0/2</td>
</tr>
<tr>
<td>- parenteral</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>9</td>
</tr>
</tbody>
</table>

* a) One child participated both in paper II and paper V
Table 2. Participants, study design, measurements and assessments used in papers I-V.

<table>
<thead>
<tr>
<th>Paper</th>
<th>Participants</th>
<th>n</th>
<th>M/F</th>
<th>Age, yrs (median, range)</th>
<th>Assessments</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Children newly diagnosed with cancer during an 11-month period from 1992 to 1994</td>
<td>14</td>
<td>7/7</td>
<td>10 (5-16)</td>
<td>Baseline. Prospective dietary recording and questionnaire-based assessment of eating problems during 3 consecutive weeks after initiation of chemotherapy. Weight up to 3 months after onset of chemotherapy.</td>
</tr>
<tr>
<td>III</td>
<td>One parent of each child in study II</td>
<td>11</td>
<td>1/10</td>
<td></td>
<td>Retrospective. Interviews with focus on the child’s eating pattern after initiation of chemotherapy.</td>
</tr>
<tr>
<td>IV</td>
<td>Children with cancer, provided with a PEG during the period 1994-2000</td>
<td>18</td>
<td>10/8</td>
<td>2 (0.5-14)</td>
<td>Retrospective. Medical records review regarding PEG-related complications. Weight, height up to 12 months after PEG placement.</td>
</tr>
<tr>
<td>V</td>
<td>Children newly diagnosed with cancer during a 21-months period from 2002 to 2004</td>
<td>22b)</td>
<td>16/6</td>
<td>9 (2-17)</td>
<td>Retrospective. Interviews with focus on the child’s eating pattern after initiation of chemotherapy. Weight, height up to 3 months after onset of chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Parent/s of 21 children</td>
<td>29</td>
<td>12/17c)</td>
<td></td>
<td>Taste acuity test and a questionnaire-based assessment of eating problems</td>
</tr>
<tr>
<td></td>
<td>Nurses</td>
<td>17</td>
<td>2/15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

b) One boy participated only in the taste acuity test; c) for 8 children both the mother and the father were interviewed.
Table 3. Side effects with impact on food intake caused by chemotherapy agents most frequently received by the participants in papers I, II, V. Most children were receiving combinations of the chemotherapeutic drugs.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Side effect with impact on food intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asparaginase</td>
<td>Nausea (^{d})</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Nausea (^{d}), taste changes (^{f})</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Nausea (^{d}), taste changes (^{f})</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>Nausea (^{d}), mucositis (^{e})</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Nausea (^{d}), mucositis (^{e}), taste changes (^{f})</td>
</tr>
<tr>
<td>Dactinomycin</td>
<td>Nausea (^{d}), mucositis (^{e}), taste changes (^{f})</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Nausea (^{d}), mucositis (^{e}), taste changes (^{f})</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Nausea (^{d}), mucositis (^{e})</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>Nausea (^{d}), mucositis (^{e})</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Nausea (^{d}), mucositis (^{e}), taste changes (^{f})</td>
</tr>
<tr>
<td>Thioguanide</td>
<td>Nausea (^{d}), mucositis (^{e})</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>Nausea (^{d}), mucositis (^{e})</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>Nausea (^{d})</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Nausea (^{d}), taste changes (^{f})</td>
</tr>
</tbody>
</table>

\(^{d}\) Modified from Hesketh et al. (86), \(^{e}\) modified from Wohlschlaeger (23), \(^{f}\) modified from Bender (85).
Table 4. Average daily oral energy intake according to diet recordings of the girls and boys participating in papers I - II and their estimated energy requirements according to NNR (50). PAL values used for girls and boys aged 10-17 years were 1.50 and 1.55, respectively.

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Girls, n</th>
<th>Median (range) oral energy intake, kcal/d according to dietary recording</th>
<th>Estimated energy requirements, kcal/d for girls</th>
<th>%</th>
<th>Boys, n</th>
<th>Median (range) oral energy intake, kcal/d according to dietary recording</th>
<th>Estimated energy requirements, kcal/d for boys</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1</td>
<td>1010 (1010)</td>
<td>1065</td>
<td>95</td>
<td>1</td>
<td>662 (662)</td>
<td>1133</td>
<td>58</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1310 (1310)</td>
<td>1426</td>
<td>92</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>813 (813)</td>
<td>1958</td>
<td>42</td>
<td>1</td>
<td>333 (333)</td>
<td>1386</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>1615 (1615)</td>
<td>1229</td>
<td>131</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td></td>
<td>1</td>
<td>578</td>
<td>1</td>
<td>1638 (1638)</td>
<td></td>
<td>35</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>702 (702)</td>
<td>1611</td>
<td>44</td>
<td>1</td>
<td>663 (663)</td>
<td>1833</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1931 (1931)</td>
<td>1625</td>
<td>119</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2117 (2117)</td>
<td>1654</td>
<td>128</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td></td>
<td>1</td>
<td>1112</td>
<td>1</td>
<td>2031 (2031)</td>
<td></td>
<td>55</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td></td>
<td>1</td>
<td>839</td>
<td>1</td>
<td>2011 (2011)</td>
<td></td>
<td>42</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>2504 (2504)</td>
<td>2006</td>
<td>125</td>
<td>1</td>
<td>1889 (1889)</td>
<td>2640</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1436 (1436)</td>
<td>1695</td>
<td>85</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>1</td>
<td>1280 (1280)</td>
<td>1464</td>
<td>87</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>780 (780)</td>
<td>2713</td>
<td>29</td>
<td>1</td>
<td>2171 (2171)</td>
<td>2350</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2480 (2480)</td>
<td>1961</td>
<td>126</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1580 (1580)</td>
<td>2143</td>
<td>74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td></td>
<td>1</td>
<td>2001</td>
<td>1</td>
<td>3346 (3346)</td>
<td></td>
<td>60</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td></td>
<td>2</td>
<td>1458</td>
<td>2</td>
<td>2401 (2401)</td>
<td>644</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>3711 (3711)</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>16</td>
<td>1</td>
<td>1699 (1699)</td>
<td>1990</td>
<td>85</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td></td>
<td>Total 14</td>
<td></td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 5. Weight and height data for the children in papers I, II and V on admission and of different time points after onset of chemotherapy. Data related to Karlberg et al. (98).

<table>
<thead>
<tr>
<th>Study no./time point in relation to start of treatment</th>
<th>n</th>
<th>Weight for age Median (range) SD score</th>
<th>Height for age Median (range) SD score</th>
<th>BMI Median (range) SD score</th>
<th>Weight for height, % Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study I, n=14</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On admission</td>
<td>14</td>
<td>-0.340 (-1.33-2.33)</td>
<td>-0.330 (-0.86-2.24)</td>
<td>-0.415 (-1.32-1.49)</td>
<td>97.5 (78-128)</td>
</tr>
<tr>
<td>One week after</td>
<td>12</td>
<td>-0.605 (-1.10-1.91)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Six weeks after</td>
<td>10</td>
<td>-0.160 (-0.85-2.94)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three months after</td>
<td>13</td>
<td>-0.380 (-1.10-1.72)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Study II, n=11</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On admission</td>
<td>11</td>
<td>+0.390 (-0.83-2.80)</td>
<td>+0.130 (-0.97-1.79)</td>
<td>+0.450 (-2.24-2.27)</td>
<td>106.0 (87-148)</td>
</tr>
<tr>
<td>One week after</td>
<td>7</td>
<td>+0.370 (-1.08-2.65)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Six weeks after</td>
<td>9</td>
<td>+0.580 (-1.40-2.09)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three months after</td>
<td>9</td>
<td>+0.490 (+0.08-1.95)</td>
<td>-0.160 (-1.18-1.63)</td>
<td>+0.900 (-1.80-2.54)</td>
<td>113.5 (89-127)</td>
</tr>
<tr>
<td>Six months after</td>
<td>11</td>
<td>+0.270 (-0.81-2.87)</td>
<td>-0.200 (-1.32-1.84)</td>
<td>+0.590 (-0.93-3.17)</td>
<td>112.0 (90-132)</td>
</tr>
<tr>
<td><strong>Study V, n=22</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On admission</td>
<td>20</td>
<td>+0.415 (-1.98-1.78)</td>
<td>+0.120 (-1.32-1.29)</td>
<td>+0.280 (-1.46-1.97)</td>
<td>103.0 (88-135)</td>
</tr>
<tr>
<td>One week after</td>
<td>15</td>
<td>-0.050 (-2.55-1.64)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Six weeks after</td>
<td>19</td>
<td>+0.3100 (1.56-2.34)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three months after</td>
<td>17</td>
<td>+0.240 (-1.30-1.95)</td>
<td>-0.070 (-1.62-1.42)</td>
<td>-0.050 (-2.08-2.47)</td>
<td>102.0 (84-124)</td>
</tr>
</tbody>
</table>

\(^{a)}\) Weight compared with weight on admission (p<0.05 Wilcoxon, paired data).

\(^{b)}\) Height compared with height at admission (p<0.05 Wilcoxon, paired data).

<table>
<thead>
<tr>
<th>Cause of eating problems</th>
<th>Age interval, years</th>
<th>Children</th>
<th>Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered taste</td>
<td>&lt; 4 y&lt;sup&gt;)&lt;/sup&gt;</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>4-7</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Learned food aversions</td>
<td>&lt; 4 years</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>4-7</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>&lt; 4 years</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>4-7</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Pain</td>
<td>&lt; 4 years</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>4-7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>&lt; 4 years</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>4-7</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Feeling ill</td>
<td>&lt; 4 years</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4-7</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Altered smell</td>
<td>&lt; 4 years</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4-7</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Ward environment</td>
<td>&lt; 4 years</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4-7</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gaining some influence</td>
<td>&lt; 4 years</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>over the situation</td>
<td>4-7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Protest against the</td>
<td>&lt; 4 years</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>situation</td>
<td>4-7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8-12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>13-17</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>)</sup> Number of children in each age interval: <4 years, n=5; 4-7 years, n=5; 8-12 years, n=4 and 13-17 years, n=7.
Populärvetenskaplig sammanfattning


Den initiala datainsamlingen visade att det genomsnittliga dagliga födointaget under sjukhusdagar endast gav 58% av rekommenderat energiintag enligt Svenska Näringsrekommendationer, SNR. Viktutvecklingen var negativ upp till tre månader efter behandlingsstart. Efter införandet av de nya, mer flexibla måltidsrutinerna var det genomsnittliga energiintaget genom mat och dryck fortfarande lågt, 61% av SNR. Med ordinerat näringsstöd uppnåddes dock 91% av SNR. Intervjuerna med barn och föräldrar visade att smakförändringar var den oftast nämnda orsaken till ätproblem. Barnen nämnde också mataversioner, illamående och smärta som viktiga orsaker, medan föräldrarna nämnde illamående, smärta, mataversioner och luktförändringar. Barn- och sjuksköterskorna å sin sida, ansåg att illamående, allmän sjukdomskänsla och vårdmiljön var de vanligaste orsakerna samt att avvisande av mat kunde vara ett sätt för barnet att söka påverka sin situation.
Smaktestet visade att patienterna jämfört med de friska kontrollerna oftare placerade smak i fel smakkategori och hade högre smakröskel för besk smak.

Acknowledgements

I wish to express my sincere gratitude to:

**Olle Hernell**, Head of Paediatrics, Department of Clinical Science, Umeå University, my advisor, for excellent scientific guidance and mentorship, continuous encouragement and support.

**Ylva Britt Wahlin**, Associate Professor of Paedodontics, Department of Odontology, Umeå University, my co-advisor, for introducing me to this project and for your encouragement, generous support and friendship during all these years and for cheering me up when I best needed it.

**Ulla-Kaisa Koiviso Hursti** at the Department of Public Health and Caring Sciences, Uppsala University and **Daniel Broman** at the Department of Psychology, Umeå University, my co-authors for stimulating collaboration.

**Fredrik Serenius**, Head of the neonatology ward, Umeå University Hospital, for introducing me to scientific work in general and computer programs and statistics in particular.

**Tor Lindberg**, Professor Emeritus of Paediatrics, for introducing me to paediatric research.

**Erik Forestier**, **Per Erik Sandström**, **Kjell Johansson**, paediatric oncologists at the Paediatric Haematology and Oncology Ward, Umeå University Hospital, for your constructive comments.

**Marita Vikström Larsson**, RN and co-author, **Gerd Israelsson**, **Siv Inger Eliasson** and my former work mates at the Paediatric Haematology and Oncology Ward, Umeå University Hospital. **Margareta Holmgren**, Department of Odontology for carrying out the taste acuity tests. **Claes Wallentinsson**, Kost och näringsdata and **Lena Carling**, Pfizer for computer support. **Hans Stenlund**, Department of Epidemiology, Umeå University, for statistical support. **Jane Wigertz** for language revision. **Karin Vigren**, university secretary, Paediatrics, Department of Clinical Science, Umeå University, for your valuable assistance.

All participants; children, parents, health care personnel who so generously have given me their time and their thoughts.

My supervisors and colleagues at the Division of Clinical Physiology, Department of Laboratory Medicine, Karolinska Institutet, Huddinge. Special thanks to **Eva Jansson**, professor, **Staffan Ljungfeldt** and **Ulla Olivemark**, lecturers, for your helpful and understanding attitude.

My friends and relatives. Special thanks to: **Hans Skolin**, **Ruben Skolin**, **Maud Ederin**, and **Alexander Edgren**, for your great support and patience, and **Bo Schenkman**, for your scientific criticism. This work was supported by grants from the Children’s Cancer Foundation in Sweden, the Center for Health Care Sciences at Karolinska Institutet, the Mary Béve Foundation for Paediatric Cancer Research, the Foundation for Scientific Research in Memory of Sigurd and Elsa Golje and Gunnar Nilsson’s foundation for Cancer Research.
References


