Malnutrition in paediatric oncology patients

Malnutrition at the diagnosis of cancer is not an uncommon finding in childhood cancer in the developing world.

JUDITH SCHOEMAN, ***BDietetics, BCompt, MSc Dietetics***
Principal Dietitian: Oncology, Steve Biko Academic Hospital Oncology Complex, Pretoria
Judy Schoeman started her career in 1998 and since then has gained experience in various fields of dietetics. During 2001 she became involved in the nutritional management of paediatric oncology patients. Since then her work has become her passion – to work with paediatric cancer patients is a privilege!

ANDRE DANNHAUSER, ***BSc Dietetics, MSc Dietetics, PhD***
Professor and Head, Department of Nutrition & Dietetics, University of the Free State
Andre Dannhauser (née Brink) started her career in 1969 and since has gained experience in various fields of dietetics. Since 1972 she has become involved in tertiary education and nutrition research. Clinical nutrition is her passion, including nutrition management of cancer patients. She has published widely and has presented papers at various national and international conferences.

MARIANA KRUGER, ***MB ChB, MMed Paed, MPhil (Applied Ethics), PhD***
Professor and Executive Head, Department of Paediatrics and Child Health, Stellenbosch University and Tygerberg Hospital, W Cape
Mariana Kruger is a paediatric oncologist and currently executive head of the Department of Paediatrics and Child Health, Stellenbosch University and Tygerberg Hospital. She obtained her PhD from the Catholic University of Leuven, Belgium, with the title 'Granulocyte-macrophage colony stimulating factor – more than just a growth factor'. Her interests are paediatric oncology, research ethics and children's rights.

Correspondence to: judy.schoeman@gmail.com

Children more commonly present with protein energy malnutrition (PEM) at diagnosis of cancer in developing countries than in developed countries, depending on the type of cancer and extent of the disease.[1-3] PEM at cancer diagnosis is associated with delays in treatment, increased infections and a negative outcome.[2] There is still controversy regarding the ideal criteria to use to describe PEM, as there are many methods and cut-off points.

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Nutritional assessment and status at cancer diagnosis

Nutritional assessment is the evaluation of the nutritional status of an individual or groups of individuals (population). It involves anthropometry, biochemical indicators, clinical examination and nutritional history.

Criteria for assessment of PEM

Anthropometry is the measurement of body weight and height, body composition and the comparison with different standards for corresponding age and gender groups in order to determine the nutritional status of an individual or population.[4]

Height for age (H/A) of less than 95% of the median for age and gender indicates stunting (chronic malnutrition).[5] Weight for age (W/A) under 90% of median indicates underweight[5-7] and weight loss of more than 5% to pre-illness weight or in 1 month is regarded as serious.[2,6,7] The body weight of children with cancer can be influenced by tumours, oedema or amputation of limbs,[8] therefore weight alone is not sufficiently sensitive to identify malnutrition.[3,5,9] Body mass index (BMI) for age and weight for height (W/H) under the 10th percentile indicate wasting (acute malnutrition).[5,6]

Arm anthropometry involves measurements such as mid-upper arm circumference (MUAC) and triceps skinfold thickness (TSF) that are used to determine arm fat area (AFA) and arm muscle area (AMA), which indicate muscle and fat stores. TSF, AFA and AMA under the 5th percentile indicates depleted fat and muscle stores.[4,6]

A Z-score is a statistical measure of the difference between the value of the individual and the median of the reference value, expressed as a portion of the standard deviation (SD).[10] A Z-score of <-2SD below the reference median of above is an indicator of severe malnutrition.[6,7]

Biochemical assessment measures nutrients in blood, faeces or urine – e.g. serum albumin under 3.2 mg/dl[6,7] may be seen as an indicator of protein status.[4] Careful interpretation is needed, because other non-dietary factors are more often the reason for the decreased values.

Clinical assessment includes a medical history and physical examination. Clinical signs of PEM include loss of subcutaneous fat and muscle, recent weight changes (not related to fluid retention or loss), oedema at ankles or sacrum and hair changes. Symptoms suggestive of vitamin and/or mineral deficiencies and medication-nutrient interactions are looked for.[4] History of inability to chew and swallow, loss of appetite, vomiting, diarrhoea, constipation and gastrointestinal tract (GIT) dysfunction longer than 5 days are also signs of PEM.[6]

Dietary assessment includes surveys of the quantity of foods consumed during the past 24 hours or past week.[4] An intake of less than 70% of patient's requirements for 5 days or more is seen as inadequate.[6]

The prevalence of malnutrition in paediatric cancer patients depends on the criteria used to identify the malnutrition.

Nutritional status of paediatric cancer patients at diagnosis

The prevalence of malnutrition in paediatric cancer patients depends on the criteria used to identify the malnutrition, as shown by Sala *et al.*[5] PEM at diagnosis in children with cancer is estimated at 6 - 50%,[1,6,5,11] while a Pretoria study indicated 25% of patients had PEM.[10]

The authors compared different studies on children with cancer and found that there was no difference in W/H between children with cancer and the control group, but 23% of the patients had a TSF of ≤2SD and 20% of the patients had a MUAC under the 5th percentile.[5] MUAC and TSF are not influenced by the tumour weight, so they must be used as part of the assessment of nutritional status in children with cancer, since they are more sensitive than weight alone.[5,8] Furthermore,

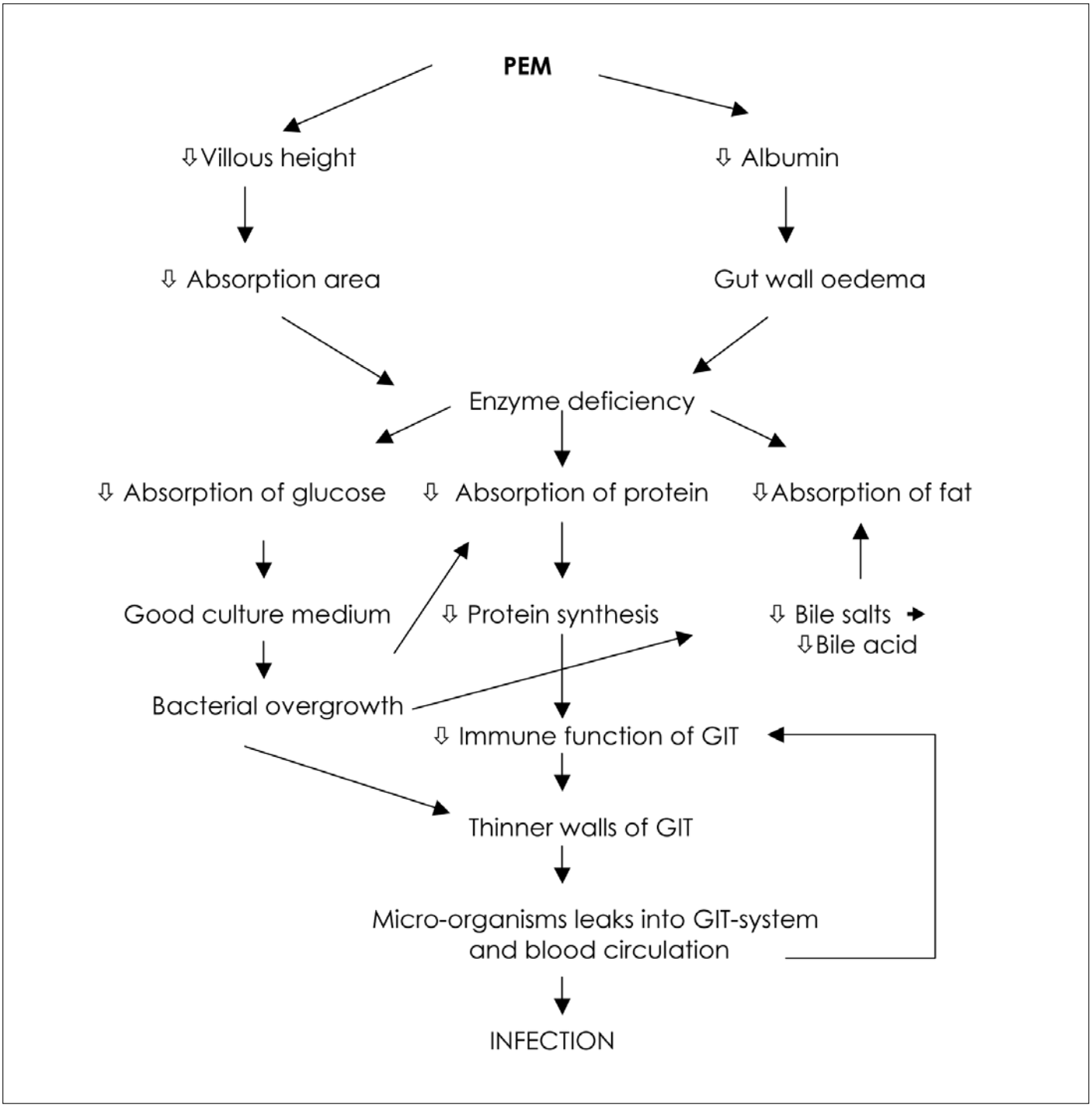

Fig.1. Effect of PEM on the gastrointestinal tract, compiled from literature.[1,2,3,5,9,12,13]

according to Garófolo *et al.*, malnutrition was observed in 40.2% of the patients with solid tumours in Brazil based on TSF, and 35.4% on MUAC, but only 18.9% based on W/H or BMI.[8] In the Pretoria study malnutrition was found in 41.8% of patients based on MUAC and 32.8% on TSF compared with only 25% on H/A and 24.3% on W/A.[10]

Effect of malnutrition on paediatric cancer patients

PEM in patients has a negative effect on the function of the GIT and immune system response to cancer treatment and on cancer outcome.

Effect of PEM on the gastrointestinal tract

The effect of PEM on the GIT is explained in Fig. 1. The villi of the GIT tend to flatten,[12] decreasing the absorption area,[13] leading to malabsorption or decreased absorption of nutrients.[12] Villi are covered with cuboidal cells and fatty acids, causing lack of enzymes for digestion of nutrients. Lactase is one of the enzymes that can become deficient, resulting in malabsorption of glucose and lactose.

PEM influences the normal function of the GIT, leading to decreased stomach acid, increased transit time and number of bacteria. The bacteria impair the formation of triglycerides (TG), phospholipids and micelles of bile salts that are needed for normal fat absorption, and these increase the risk for diarrhoea.[12]

Effect of PEM on the immune system

The immune system of children with PEM is compromised and they have a higher incidence of infection than well-nourished children,[7] as well as 20 times more complications.[8] The walls of the GIT are thinner and micro-organisms can leak into the GIT walls (Fig. 1), leading to bacterial overgrowth that impairs immune function

and leads to infections.[13] A higher incidence of neutropenia,[3] poor wound healing,[13] morbidity and mortality were also noted.[12,13]

Patients with leukaemia showed a significant association between poor nutritional status at diagnosis and rate of infection.[3]

Effect of PEM on response to cancer treatment

Malnourished patients respond poorly to medical interventions such as chemotherapy, radiotherapy and/or surgery,[2] with increased episodes of toxicity from chemotherapy[2,14] and reduced drug metabolism.[2]

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A decrease in tolerance to chemotherapy[1,3,5,7,9,14] leads to reduced doses in future cycles.[7] According to Sala *et al.*[5] malnourished patients only receive 50% of the doses of chemotherapy actually needed. This can lead to an impaired response to treatment[13] and increased risk for treatment toxicity.[1,11,14]

Drug metabolism may be altered in malnourished patients,[2,7] thiopurine methyltransferase activity may differ and fat stores may have an effect on pharmacokinetics.[3] Methotrexate, 5-fluorouracil, doxorubicin and penicillin have decreased clearance in under-nourished patients, suggesting decreased renal tubular secretions, an increased tumour response to chemotherapy and tubular damage.[1]

Effect of PEM on cancer outcome

The outcome in cancer can be seen as survival (disease free), relapse of disease or death.

Relapse of disease

In developed countries undernutrition is resolved quickly and therefore not associated with relapse,[3] but, untreated, can lead to cancer death.[13]

Malnourished children on maintenance therapy receive half the dose of oral chemotherapy, causing relapse of disease.[8] In patients with solid tumours, malnourished patients were more likely to relapse, especially those with neuroblastoma.[6]

Death

PEM is a negative prognostic factor in patients and children with cancer,[1,2,7,9] leading to as many as 20 - 25% of cancer deaths.[13]

Among 102 malnourished acute lymphoblastic leukaemia patients, 9.8% relapsed, 45% died and 46% were still alive compared with the well-nourished group, where only 19% died and 59% were still alive.[15] A W/H of less than 80% of the expected median in 455 children with cancer had a significant negative effect on their survival.[6] A study of paediatric oncology patients in Kalafong Hospital (Pretoria) indicated that children with depleted MUAC and AMA on admission had an increased risk of death.[11]

It is clear that PEM has a significant effect on treatment, and studies have shown an association between PEM at diagnosis and poor outcome in children with cancer.[6,8,10,14]

Nutritional status and intervention during cancer treatment

The medical treatment of cancer has side-effects that can lead to PEM, and nutritional support is important to prevent this becoming severe.

Side-effects of treatment

The medical treatment for cancer can cause taste alterations, anorexia, mucositis, dysphagia, reflux, early satiety, vomiting, diarrhoea, constipation or malabsorption. All these side-effects are worsened if there is lack of support by family and friends, and can lead to decreased oral intake, weight loss and eventually PEM.[5]

Development of PEM during treatment

Children have decreased energy reserves compared with adults, and treatment can lead to deterioration of the nutritional status of the patient if nutritional intervention does not take place.[1,9] PEM is caused by the increased energy expenditure due to tumour growth that uses the child's body stores for fuel. GIT discomfort can occur because of enlarged organs pressing on the stomach. GIT toxicity and neutropenia can develop and cause bacterial sepsis, fever, neutropenic enterocolitis and pain. This decreases the ability of the body to absorb nutrients efficiently and leads to further nutritional depletion.[11]

Sala *et al.*[5] described Mexican children who were evaluated after 1 month's chemotherapy and found that more than 10% of the patients with high-risk disease had decreased muscle stores, compared with patients with low-risk disease. The Pretoria study indicated a worsening of patients' degree of stunting, underweight and wasting but an improvement in TSF and MUAC after 3 months.[10]

Nutritional intervention

The nutritional goals in a child with cancer are to maintain nutritional status,[7] prevent PEM and poor growth and improve the quality of life. The best time to start nutritional intervention is at the time of diagnosis.[13] It is important to remember that every child is unique and will tolerate cancer treatment differently.

There are different types of nutritional intervention.

Oral intake

A high-energy high-protein diet can provide patients with sufficient energy to meet their nutritional needs and increase their physical performance and may also be used to try to increase their treatment tolerance and decrease therapy-related side-effects.

Appropriate diets given to patients between chemotherapy cycles and before radiotherapy is started, increase their tolerance to treatment and improve their outcome.[14]

Nutritional supplements

Nutritional supplements are nutrient-dense beverages available in different flavours and packaging.

Sala *et al.*[5] found that supplements alone were not effective in preventing malnutrition when given during treatment. The Pretoria study indicated an improvement in BMI, TSF, AMA and AFA after 3 months of supplementation.[10]

It is important to remember that patients with cachexia will not respond to nutritional supplementation alone[13] and nutritional repletion cannot be achieved in a short period of time.

PEM is caused by the increased energy expenditure due to tumour growth that uses the child's body stores for fuel.

Nasogastric enteral feeds (NG)

NG feeds should be considered in paediatric cancer patients with PEM. It is also indicated in patients with 5% weight loss since the time of admission,[9] a decrease in MUAC of 10%,[4] severe oral mucositis[9] and when their oral intake is less than 60 - 80% of their nutritional requirements.[1]

Enteral feeds are effective as the primary source of nutrients for children with

cancer.[1] No complications were observed in neutropenic patients or patients with a low platelet count. The majority of children tolerated the tube feeds without complications[1] such as epistaxis, sinusitis, tube-related infections[11] and vomiting or diarrhoea, even while receiving chemotherapy.[1,9]

Nutritional intervention is a valid and inexpensive method to improve the outcome in cancer patients.

Continuous, constant infusion of NG feeds with a feeding pump is better tolerated than bolus feeds, and fewer complications occur. Nocturnal feeds are the best for children, because they can then lead a normal life and are not pressurised to eat adequately.[9]

Total parenteral nutrition (TPN)

TPN consists of the intravenous (IV) administration of nutrients to meet patients' nutritional needs. Indications are typhlitis, continuous vomiting, inability to access the GIT and diarrhoea. Supplementary TPN is given where oral intake is inadequate or requirements cannot be met by oral diet or enteral nutrition.[1]

Patients with relapse of leukaemia/lymphoma received 90% of their RDA through TPN and have shown a decrease in malnutrition. W/H, TSF, albumin and transferrin concentrations normalised after 28 days.[6]

Conclusion

All patients with cancer are at risk of malnutrition and deterioration in their nutritional status due to the effect of the chemotherapy and/or radiotherapy and this can increase the risk for a negative outcome. It is recommended that they undergo nutritional assessment on a regular basis and receive early and ongoing nutritional intervention to maintain their nutritional status.

Different types of nutritional intervention can be used in the form of oral supplements, NG feeds and TPN that can maintain and improve a patient's nutritional status. Nutritional intervention is a valid and inexpensive method to improve the outcome in cancer patients.

References available at www.cmej.org.za

In a nutshell

- Nutritional assessment is the evaluation of the nutritional status of an individual or groups of individuals (population).
- Protein energy malnutrition at cancer diagnosis is common in developing countries.
- Malnutrition in patients has a negative effect on the function of the GIT.
- Malnourished patients respond poorly to medical interventions.
- Nutritional goals for paediatric oncology patients are to prevent deterioration of the nutritional status and poor growth, and improve their quality of life.

Single Suture

Gene switch the key to youthful brain

A genetic switch linked to memory impairment in elderly mice has been flipped back on, restoring their failing brains to a more youthful state. If a similar switch exists in people it may provide a way to keep human brains young.

To find out more about what underlies the cognitive decline that occurs with age, André Fischer of the European Neuroscience Institute in Göttingen, Germany, and colleagues analysed DNA from the brains of both young and old mice that had been set tasks involving learning and memory.

They found that when young mice are learning, a molecular fragment – an acetyl group – caps a particular site on the histone protein that DNA wraps itself around. The cap ends up close to a cluster of genes on the surrounding DNA that are involved in learning and which became more active during learning tasks.

By contrast, in older mice set the same tasks, the acetyl cap was missing and no boost in gene activity occurred during learning.

The team concludes that the acetyl cap acts as an on switch for the crucial genes. By injecting older mice with an enzyme that encourages the binding of acetyl groups, Fischer's team were able to flip the switch on, which improved the mice's learning and memory performance.

Unpublished post-mortem studies have linked acetyl caps to brain decline in humans. It's not clear if flipping them would similarly improve brain function or how many switches control brain decline in humans.

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