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ESPEN Guidelines on Enteral Nutrition: Gastroenterology ☆

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Summary Undernutrition as well as specific nutrient deficiencies have been described in patients with Crohn's disease (CD), ulcerative colitis (UC) and short bowel syndrome (SBS).

The present guideline gives evidence-based recommendations for the indication, application and type of formula of enteral nutrition (EN) (oral nutritional supplements (ONS) or tube feeding (TF)) in these patients. It was developed in an interdisciplinary consensus-based process in accordance with officially accepted standards and is based on all relevant publications since 1985.

ONS and/or TF in addition to normal food is indicated in undernourished patients with CD or CU to improve nutritional status. In active CD EN is the first line therapy in children and should be used as sole therapy in adults mainly when treatment with corticosteroids is not feasible. No significant differences have been shown in the effects of free amino acid, peptide-based and whole protein formulae for TF. In remission ONS is recommended only in steroid dependent patients in CD. In patients

Abbreviations: CD; Crohn's disease; UC; Ulcerative colitis; SBS; Short-bowel syndrome; TF; Tube feeding; ONS; Oral nutritional supplements; EN; Enteral nutrition. EN is used as a general term to include both ONS and tube feeding. When either of these modalities is being discussed separately this is specified in the text; PN; Parenteral nutrition; Normal food/normal nutrition; Normal diet as offered by the catering system of a hospital including special diets; Fortified and texture modified diets

☆For further information on methodology see Schütz et al.[147] For further information on definition of terms see Lochs et al.[148]

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with SBS TF should be introduced in the adaptation phase and should be changed with progressing adaptation to ONS in addition to normal food.

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Summary of statements: Crohn's disease

Subject	Recommendations	Grade[147]	Number
Indications	Indications for enteral nutrition are: prevention and treatment of undernutrition, improvement of growth and development in children and adolescents, improvements in quality of life, acute phase therapy, peri-operative nutrition, maintenance of remission in chronic active disease.		3
Active disease	In adults use enteral nutrition as sole therapy for the acute phase mainly when treatment with corticosteroids is not feasible.	A	3.4
	Use combined therapy (enteral nutrition and drugs) in undernourished patients as well as in patients with inflammatory stenosis of the intestine.	C	3.4
	In children with CD enteral nutrition is considered as the first line therapy.	C	3.6
Maintenance of remission	In case of persistent intestinal inflammation (e.g. steroid dependent patients) use oral nutritional supplements.	B	3.6
	In longstanding (>1 year) clinical remission and in the absence of nutritional deficits a benefit of enteral nutrition (oral nutritional supplements or tube feeding) or supplements (vitamins and trace elements) has not been demonstrated.	B	3.6
Peri-operative nutrition	Use peri-operative nutrition in CD patients with weight loss prior to surgery and low albumin.	C	3.5
Application	Use tube feeding and/or oral nutritional supplements in addition to normal food to improve nutritional status and to eliminate consequences of undernutrition such as growth retardation.	A	3.1/3.2
	Correct specific deficits (trace elements, vitamins) by supplementation.	C	3.1/3.2
	Use continuous tube feeding rather than bolus delivery because of the lower complication rate.	B	4.2
Route	Using oral nutritional supplements, a supplementary intake of up to 600 kcal/day can be achieved in addition to normal food.	A	4.1
	Use tube feeding if a higher intake is necessary.	C	4.1
	Tube feeding can be safely delivered by nasogastric tube or percutaneous endoscopic gastrostomy.	B	4.2

Type of formula			
Active disease	There are no significant differences in the effect of free amino acid, peptide-based and whole protein formulae for tube feeding.	A	4.4
	Free amino acid or peptide-based formulae are not generally recommended.		4.4
	Modified enteral formulae (fat modified, omega-3 fatty acids, glutamine, TGF-β-enriched) are not recommended because no clear benefits have been shown.	A	4.5
Undernutrition	Enteral nutrition may improve the quality of life in undernourished CD patients.	C	3.3

Grade: Grade of recommendation; Number: refers to statement number within the text.

Summary of statements: Ulcerative colitis

Subject	Recommendations	Grade[147]	Number
Indications			
Undernutrition	Initiate nutritional support in patients with undernutrition or inadequate nutritional intake.	C	9
Active disease	An influence of nutritional measures (nutritional counselling, oral nutritional supplements, tube feeding or parenteral nutrition) on the inflammatory activity in acute or in chronically active ulcerative colitis has not been demonstrated. Therefore, enteral nutrition is not recommended as treatment of active ulcerative colitis.	C	10
Maintenance of remission	Enteral nutrition is not recommended.	C	11
Application	Treat specific deficiencies with supplements.	C	9
Type of formula	The value of specific substrates (omega-3 fatty acids, glutamine, butyrate) on disease activity is controversial and not proven.		10

Grade: Grade of recommendation; Number: refers to statement number within the text.

Summary of statements: Short-bowel syndrome

Subject	Recommendations	Grade[147]	Number
Indication	Maintenance and/or improvement of nutritional status, improvement of residual bowel function (adaptation), reduction of diarrhoea, improvement in quality of life.		15
Route			
Postop. hyper-secretion phase	Parenteral nutrition is obligatory in order to guarantee adequate nutritional intake and fluid and electrolyte replacement.	C	17.1
Adaptation phase	Use continuous tube feeding-in limited amounts-depending on the enteral fluid loss to improve intestinal adaptation.	C	17.2

	With progressive adaptation provide enteral nutrition (even over night to increase time for absorption) as a supplement to normal food.	C	17.2
Maintenance/ stabilisation phase	Use oral nutritional supplements or tube feeding if normal nutritional status cannot be maintained by normal food alone.	C	17.3
Type of formula	No specific substrate composition is required per se. Depending on the extent of malabsorption a significant increase in energy and a modification of substrate intake may be necessary.	C	16
	A regime to accelerate intestinal adaptation with recombinant growth hormone, glutamine and special formula (low fat, high carbohydrates) is not generally recommended due to inconclusive results.	C	18

Grade: Grade of recommendation; Number: refers to statement number within the text.

Crohn's disease (CD)

1. What influence does CD exert on nutritional status and on energy and substrate metabolism?

1.1. Acute phase

Undernutrition with weight loss, protein deficiency and specific deficiencies in vitamins, minerals and trace elements are common in the acute phase of CD.

Anorexia, increased intestinal losses and systemic inflammation are the main causes of undernutrition.

In children and adolescents a decrease in growth velocity may occur, secondary to inadequate nutrition and steroid therapy. The relevance and extent of these deficiencies vary according to the site and extent of diseased intestine as well as disease activity.

Active CD causes the same non-specific alterations of substrate metabolism as are observed in starvation and/or inflammation. As these reflect inflammatory activity, they are therefore reversible by treatment.

Comments: Weight loss is observed in up to 75% of hospitalised adult patients with active CD.[1–8] A negative nitrogen balance caused by reduced intake, increased intestinal losses, and steroid-induced catabolism occurs in more than 50% of patients with active CD. Total body potassium may be decreased.[9]

Depending on the severity of diarrhoea, low serum concentrations of potassium,[10] magnesium,[11,12] calcium[13] and phosphate[14] have been described. A deficit in fat soluble vitamins correlates with the extent of steatorrhoea. Lower plasma concentrations of retinol, seen in active CD, usually remain subclinical and are normalised after drug treatment, without the need for supplementation. Low concentrations of 25(OH)-vitamin D are found in more than half the patients; however, only 45% of CD patients develop osteopenia or osteomalacia in the course of the disease.[15] Decreased levels of vitamin K are associated with reduced bone mineral density.[16]

Vitamin E levels correlate with both total blood cholesterol and total blood lipid concentration.

Regarding water-soluble vitamins, lower serum concentrations and deficits of vitamin B_{12} are well documented,[1,7,17,18] depending on the involvement or resection of the terminal ileum. Measurement of serum concentrations of ascorbic acid, nicotinic acid and biotin are not useful for estimating inadequate supply.

Resting energy expenditure may vary depending on inflammatory activity,[19] but total energy expenditure is similar to healthy subjects.[20] It is slightly increased only if calculated in relation to fat-free mass (FFM).[21] An intake of 25–30 kcal/kg BW/day is usually adequate to meet requirements.

Changes in substrate metabolism, with reduced oxidation of carbohydrates and increased oxidation of lipids,[9,22] are similar to the alterations in starvation and are not disease-specific. They are reversible when patients receive adequate nutritional support.

In children and adolescents with CD, growth retardation has been described in up to 40% and a

decrease in muscle mass and body fat in up to 60%.[23–25]

In nearly 90% of adolescent patients a decrease in height and/or growth velocity below the 3rd percentile is seen even before the diagnosis is made, and often prior to other symptoms of CD.[26,27]

Growth retardation persists in 20–40% of patients and final body height is below the 5th percentile in 7–30% of patients.[28–33] Nutritional treatment may restore growth velocity, after a period of retardation, but ultimate height still falls short of genetic potential.[32,33]

1.2. Remission

Most patients in remission have an apparently normal nutritional status. Undernutrition, if present, is mainly due to malabsorption resulting from previous surgery, with bile acid-induced diarrhoea, or even from the development of SBS, bacterial overgrowth, or drug treatment (vitamin B_{12} malabsorption after treatment with sulphasalazine). Specific deficits (calcium, vitamin D and vitamin B_{12} deficiencies) require special attention.

Comments: In remission, deficiencies of macronutrients are rare. A deficit of vitamins and trace elements is only observed in a few individual cases.[34]

There are conflicting results regarding nutritional status of patients in remission. For example, body mass index (BMI) varies from similar[35] to significantly decreased in CD-patients compared with healthy controls.[36,37] In CD patients, reduced body weight was found to be related to reduced body fat mass (FM), whereas FFM was maintained.[12,36] Alterations of substrate metabolism are still present in quiescent disease. As a result of a higher lipid oxidation rate, the non-protein respiratory quotient has been shown to be significantly lower compared with healthy controls.[38,39] The intake of energy and nutrients is sufficient[37] and comparable with that of a healthy population.[12]

In untreated patients, osteopenia caused by nutritional deficits (protein, vitamin D and calcium) and by inflammatory cytokines may develop as the disease progresses. In treated patients in remission, osteopenia is often an adverse effect of steroid medication.[38,40–44] An increased risk for fractures has been described in CD patients[45–48] and supplementation with calcium and vitamin D has been recommended in all patients on steroid treatment.[49] Standard dosing as recommended for osteoporosis with cholecalciferol 800–1000 IE/day and 1000 mg/day ionic calcium should be used. Although higher doses might be necessary due to malabsorption.

2. What influence does nutritional status exert on outcome?

Undernutrition has a negative impact on the clinical course, the rate of postoperative complications and mortality (III).

Comments: Mortality in CD is associated with volume deficits, protein-calorie undernutrition and derangements of water and electrolyte balance.[50] Preoperative undernutrition increases the likelihood of postoperative complications[51] and prolongs the length of hospital stay.[52]

3. What are the goals of enteral nutrition (EN) therapy?

As in other diseases, the primary goals are

- Prevention and treatment of undernutrition (3.1.).
- Improvement of growth and development in children and adolescents (3.2.).
- Improvements in quality of life (3.3.).

In addition there are specific indications for EN in CD

- Acute phase therapy (3.4.).
- Peri-operative nutrition (3.5.).
- Maintenance of remission (3.6.).

3.1. Treatment of undernutrition

3.2. Improvement of growth

Undernutrition as well as growth failure cannot be treated with nutritional counselling alone. TF and/or ONS, in addition to the normal food, improves nutritional status and eliminates the consequences of undernutrition such as growth retardation, and is therefore indicated (A). Specific deficits (trace elements, vitamins) can be corrected by supplementation (C).

Comments: Several studies have demonstrated that an improvement in nutritional status cannot be achieved by nutritional counselling alone[30,53] (Ib). In adults as well as in children, supplementary ONS or TF improves nutritional status[30,53,54] (Ib).

Patients with growth retardation defined as height/growth <3rd percentile or <4 cm/year for more than two or more years, as well as retarded bone age, 4–6 week periods of EN providing up to 1000 kcal/day and/or overnight TF, in addition to normal food, can stimulate growth[30] (Ib). Repeated treatments are useful. Intensified nutritional therapy has to be initiated before the epiphysial growth plate is completed if growth velocity is to be regained. Enterally fed patients show a significantly higher increase in growth and FFM compared with those receiving steroid therapy[55] (III). Without TF, 50% of growth retarded patients cannot regain their body weight with medical therapy alone: 28% of patients remain growth retarded after 40 months despite conventional drug treatment (5-ASA, steroids) and nutritional counselling[56] (III).

EN increases FFM and other body compartments (intra- and extracellular water) in children with CD.[55]

3.3. Improvement in quality of life

EN may improve the quality of life in undernourished patients with CD (C)

Comment: Improvement of nutritional status often leads to an improvement in general well-being. Whereas the negative effects of corticosteroids and the positive effects of immunosuppressants on the quality of life in CD patients have been well documented[76,77] (Ib), there are no systematic trials of EN in this context.

For treatment of short-bowel syndrome (SBS), see the end of this chapter.

3.4. Primary therapy for active CD

EN (ONS and TF) is effective in the treatment of the acute phase of the disease. In adults, however, treatment with corticosteroids is more effective (Ia): therefore, in adults, EN as sole therapy for acute CD is indicated mainly when treatment with corticosteroids is not feasible, e.g. due to intolerance or refusal (A). Combined therapy (EN and drugs) is indicated in undernourished patients as well as in those with inflammatory stenosis of the intestine (C).

In children with CD, EN is considered the first-line therapy (C)

Comment: Several studies have shown the effectiveness of EN in the treatment of active phases of CD. Approximately 60% of all patients reach remission[57–67] (Ia). A recent Cochrane Review[60] (Ia) analysed four trials including 130 patients with active CD treated with EN and 123 with corticosteroids and confirmed the findings of earlier meta-analyses that corticoid therapy in adults is more effective than EN in inducing remission. Response rates to EN (intention to treat basis) vary between 53–80% after 3–6 weeks of therapy. The localisation of CD has no prognostic value for the response to EN. The supposedly impaired response in Crohn's colitis has not been confirmed.[58,65,66]

EN as primary treatment has a favourable impact on inflammatory processes, induces remission, treats undernutrition and its consequences, and avoids the side effects of conventional immune modulating and suppressing agents (5-ASA, steroids, azathioprine, 6-mercaptopurine).

The mechanisms of the above favourable effects of EN on inflammation in CD remain unclear: the hypotheses of bowel rest, improved nutrition or a reduced intestinal antigen load have not been proven. A reduction of intestinal permeability is assumed.

Total parenteral nutrition (PN) is no better than EN in the therapy of active CD and should therefore be restricted to patients with a contraindication to or intolerance of EN (Ib).[68–71]

Compliance of patients receiving ONS, especially with peptide-based formulae, is low.[65] More than 20% of randomized patients receiving ONS with peptide-based or whole protein formulae stop the treatment due to the unpalatability of the enteral formula or intolerance.[58] Withdrawal rate is significantly lower with nasogastric tubes (8%) than with oral intake (34%).[67]

With the tendency to high relapse rate in children, it is essential to optimise nutritional therapy to promote growth. The use of EN in children and adolescents with CD has the potential to reduce the need for corticosteroid treatment, and may have a prompt effect in reducing abdominal pain due to strictures.[59] EN, therefore, is commonly used as initial therapy in children with active CD.

3.5. Peri-operative nutrition

Postoperative complications are increased in CD patients with weight loss prior to surgery and low albumin (IIa). Peri-operative nutrition is therefore recommended in this patient group (C).

Comment: An increased frequency of postoperative complications has been shown in CD patients with severe nutritional risk,[51] being defined as weight loss >10% within the last 3–6 months, BMI <18.5 kg/m^2 and/or plasma albumin levels below 30 g/l. Although specific data concerning the effect of peri-operative nutrition in CD are lacking, there is a considerable body of evidence

about the effect of peri-operative nutrition in general gastrointestinal surgery and in critically ill patients. Patients with CD should therefore be treated accordingly. Recommendations concerning peri-operative nutrition are outlined in the chapter ''Surgery including Organ Transplantation'' (p. 224).

3.6. Maintenance of remission

The length of remission and subsequent relapse rate after remission induced by EN are comparable to that after treatment with corticosteroids in children and adults. (Ib). In the case of persistent intestinal inflammation (e.g. steroid dependent patients) ONS have been shown to be beneficial (B).

In longstanding (more than 1 year) clinical remission and in the absence of nutritional deficits, a benefit of EN (ONS or TF) or supplements (vitamins and trace elements) has not been demonstrated (B).

Comment: One-year relapse rates have been reported to be 25–42% after successful treatment of active CD by EN and 17–67% after steroid therapy (Ib).[29,64] One trial reported that the achievement of positive nitrogen balance during EN was followed by clinically sustained remission (III).[72]

If supplementary EN is continued after the active phase, it prolongs the relapse-free interval (IIa).[73–75] The localisation of CD has no impact on the chances of relapse.

In disease causing fistulae or strictures, relapse occurs early if long-term EN is discontinued. In children and adolescents, ONS can improve growth and prolong remission in some situations[74] (III), (Ib).[54] Remission may be prolonged in adults.

4. Practical implementation of EN

4.1. Which patients should receive ONS? When is TF indicated?

With ONS, a supplementary intake of up to 600 kcal/day can be achieved in addition to normal food (A).

If a higher intake is required, TF is necessary (C).

Comment: In a controlled cross-over study, an increase in the daily intake of 600 kcal has been achieved, using ONS, in patients with inactive CD (Ib).[54]

A higher intake is feasible for short periods in the treatment of active CD[65] (Ib); but it appears not to be tolerated over a long period. Most cases with growth retardation, therefore, require TF.

4.2. Are there special issues concerning the method of delivery or the formulae for EN in CD patients?

TF can be safely delivered by a nasogastric tube (NGT) or percutaneous endoscopic gastrostomy (PEG) (B).

Continuous administration of TF rather than bolus delivery is preferred because of the lower complication rate (B).

Comment: Continuous administration is associated with fewer complications than bolus delivery.[78] In children with growth retardation, overnight TF has been used successfully. Children learn quickly to pass feeding tubes every evening and are not inhibited in their daily life (Ib).[53,55]

If a NGT is not accepted or the duration of feeding required is anticipated to be more than 1 month, a PEG may be placed for long-term nutrition. This method is safe in CD, has no increased rate of complications, and does not result in persistent gastric or entercutaneous fistulae[79] (III), (IIa).[80] A starter regimen does not appear to be necessary, however, the risk of a refeeding syndrome has to be kept in mind in severely undernourished patients and simultaneous oral intake is possible (IIb).[81]

4.3. Are there contraindications to EN in CD?

There are no specific contraindications to EN in CD apart from those which apply generally.

Comment: EN in sub-ileus and high-grade stenosis does require special caution. A documented stenosis; however, is no contraindication to EN per se.[82]

4.4. Are free amino acid/peptide-based compared with whole protein formulae of benefit for TF in the treatment of active CD?

There are no significant differences in the effect of free amino acid, peptide-based and whole protein formulae for TF. Nutritional support with normal food is considered the treatment of choice. Free amino acid or peptide-based formulae are therefore not generally recommended (A).

Comment: In several randomised controlled studies the efficacy of free amino acid, peptide-based and whole protein formulae in active CD have been compared. No difference in response to the

different formulae was detected[58,60] (Ia) (Ib).[83–88] In some patients, who are intolerant to whole protein formulae AA or peptide-based formulae might however be tried.

4.5. Do specific enteral formulae offer any benefit in the treatment of active CD?

No clear benefit of using disease-specific formulae (fat modified, ω-3 fatty acids, glutamine, TGF-β-enrichment) has been shown (Ib). Therefore, these formulae are not recommended (A).

Comment: Modification of EN with a low content of long-chain triglycerides (LCT), or replacement of LCT with medium-chain triglycerides (MCT)[89,90] (Ib) is of no therapeutic benefit. The improvement in disease activity, increase in body weight, FFM and triceps skinfold is comparable between the different regimens (Ib).[90] However, the type of LCT might influence therapeutic outcome. Using standard formulae containing 35% energy from fat, a formula high in oleate worsened outcome significantly compared with an equal formula high in linoleate, with remission rates of 27% vs. 63%, respectively (Ib).[91] Glutamine-enriched whole protein formulae showed no advantage compared with standard formulae with regard to decrease in disease activity, or in terms of clinical and anthropometric parameters[92,93] (Ib). Delivery of EN enriched with transforming growth factor-β_2 (TGF-β_2) showed, in uncontrolled studies, reduced mucosal inflammation, a down-regulation of proinflammatory cytokines in the ileum and colon and an increase in TGF-β_2 m-RNA. A clinical advantage of modified over standard formulae, however, remains unproven in the absence of adequate clinical trials[94,95] (III).

Ulcerative colitis (UC)

5. What influence does UC have on nutritional status as well as on energy and substrate metabolism?

Global undernutrition, as well as specific deficiencies has been described in active UC. Specific deficits including anaemia due to iron and/or folate deficiency are described even in remission. Specific deficits may also be due to drug treatment (e.g. sulphasalazine).

Comment: The information regarding undernutrition in UC derives mainly from case reports. There are no epidemiological studies that would allow estimation of the prevalence of underweight and weight loss, although weight loss is commonly observed in acute exacerbations of the disease. Specific information on alterations of body composition in UC, ie relative changes in lean and fat mass, are not available.[13,36,96]

Anaemia, defined as haemoglobin under 10 g/100 ml, was found in 37% of a defined group of patients,[97,98] iron deficiency in 55% and zinc deficiency in 10%.[99] Epidemiological studies on the general prevalence of these deficiencies in UC are not available. Folic acid deficit has been reported frequently with sulphasalazine therapy.[100,101] Reduced bone mineral density (BMD), selenium deficiency or general antioxidant deficiency have not been described in UC.[102,103]

The activity of UC does not influence the development of specific vitamin and trace element deficiencies. As pointed out before, measurement of plasma concentrations does not help in the diagnosis of deficiencies of most micronutrients. In order to assess folate status, for example, its erythrocyte content has to be determined, since normal plasma concentrations do not rule out a deficiency.

6. Does disease activity influence oral nutritional intake?

Inadequate intake of protein or energy has been reported in acute UC. Nutritional intake is not compromised in remission.

Comment: There are no epidemiological studies addressing this issue. However, it has been shown in one study that patients with UC in remission have a normal intake.[104] Studies of nutritional intake during acute UC are only available for limited patient groups.[96,105]

7. What influence does drug treatment have on nutritional status?

There are no studies investigating the effect of drug treatment on nutritional status in UC.

Comment: In CD steroid therapy increases nutritional intake (protein as well as energy); however, it does not lead to positive nitrogen balance.[106] It can be assumed that effects of steroids on eating habits/patterns and metabolism are similar in UC.

8. What influence does nutritional status exert on outcome?

Whereas information on the association between undernutrition and increased risk for postopera-

tive complications is available for CD, there are no such data available for UC. A similar relationship may reasonably be assumed in UC.

9. Is EN indicated in order to treat undernutrition in UC?

If undernutrition or inadequate nutritional intake are present, nutritional support should be initiated (C). Specific deficiencies must be treated with supplements (e.g. iron deficiency) (C).

Comment: Specific dietary regimens are not generally required in order to maintain or improve nutritional status in UC. There are no data on supplementation with ONS in UC. By analogy with CD, supplementation with 500–600 kcal ONS/day can be considered of value in patients with reduced oral intake. TF should only be administered in exceptional cases. There are currently no indications that free amino acid, peptide-based or other special formulae yield superior results over whole protein standard formula. PN should only be considered in severe acute UC, when adequate oral intake is not possible, or in pre- and postoperative situations.

In patients with UC or CD suffering from iron deficiency, oral or i.v. supplementation of iron was successful in improving anaemia as well as quality of life in 80%.[107]

10. Is EN indicated in the therapy of active UC?

An influence of nutritional measures (nutritional counselling, ONS, TF or PN) on the inflammatory activity in acute or in chronically active UC has not been demonstrated. The value of specific substrates (ω-3 fatty acids, glutamine or butyrate) on disease activity of UC is controversial and not proven. EN is therefore not recommended as treatment of active UC (C).

Comment: Two retrospective studies with small sample sizes have investigated the role of EN: remission rates of approximately 33% are reported with the use of peptide-based TF, corresponding to the rate of spontaneous remission (III).[108,109]

Another study assessed the value of bowel rest in combination with steroid therapy in acute UC (parenteral vs. oral nutrition), but found no advantage (Ib).[110]

A further study compared PN with EN in acute UC and found similar effects on nutritional status and disease activity, as well as similar complication rates (Ib).[111] Neither PN nor EN exert favourable effects on inflammation in UC.

Data regarding specific substrates are controversial. It has been shown that ω-3 fatty acids improve the histological index as well as the leukotriene B4/leukotriene B5 ratio (IIb).[112] A clinical effect however has not been proven (Ib).[113] There is a lack of data on glutamine administration and on the effect of complex carbohydrates, which are metabolised to short-chain fatty acids in the colon. The data on the effect of topically administered short chain fatty acids are controversial (Ib).[114,115] A general recommendation cannot, therefore, be given. Combined therapies (steroids/whole protein/peptide-based TF formulae) have not yet been evaluated in clinical studies.

11. What value does EN have in the maintenance of remission?

There are no clear data on the effect of disease-specific formulae or nutritional therapy on maintenance of remission. EN is therefore not recommended for this purpose (C).

Comment: There have been no specific studies on the role of diet in the maintenance of remission in UC. Trials assessing the effect of ω-3 fatty acids have found no clinically relevant advantage (Ib).[116]

12. Contraindications and complications

Contraindications and complications do not differ from other patient groups.

Short-bowel syndrome (SBS)

SBS is a complex condition resulting from either loss of intestine and/or an impairment of absorptive capacity of the remaining small bowel. SBS is not defined by a certain length of the remaining bowel but rather by the loss of absorptive function. The main causes of SBS are resections after mesenteric infarctions, extensive resections in CD, trauma, and bowel damage from radiotherapy.

13. What influence does the disease exert on nutritional status as well as on energy and substrate metabolism?

Malabsorption is an integral part of the definition of SBS. The extent and the type of undernutrition depend on the extent and site of resection as well as on the integrity and adaptation of the remaining bowel. Alterations

in energy and substrate metabolism have not yet been demonstrated.

Comment: Pathophysiological consequences depend on the extent and site of bowel resection.

Resection of the jejunum is better tolerated if the remaining/residual bowel is intact.[117,118] Loss of the ileum has more consequences with regard to nutrition and metabolism, since areas for the absorption of specific substances are lost (bile salts, fat and vitamin B_{12}).[119] Chologenic diarrhoea occurs if more than 1 m of ileum is resected. Unabsorbed bile salts, which reach the colon, induce a high net secretion of water with loss of relevant ions. If more than 1 m is resected, the loss of bile salts exceeds the functional capacity of de novo synthesis.

The resection of large parts of the colon or the whole colon and parts of the small intestine can result in loss of sodium, potassium, and water as well as in accelerated intestinal transit, due not only to the loss of absorptive surface but also to altered gastric emptying. Gastric emptying time is shortened due to loss of the ileal brake[120] and gastric secretion (H_2, volume) is increased. If the ileocaecal valve is missing, the contact time between food and the mucosa is significantly reduced. Furthermore, bacterial colonisation of the small bowel occurs.

14. What influence does nutritional status exert on outcome?

The prognosis of SBS patients depends on the degree of malabsorption, and the magnitude of oral intake. In addition, the range of complications associated with life-sustaining nutritional support usually determines the morbidity and mortality of patients.

Comment: Since malabsorption is an integral part of the diagnosis, nutritional support is mandatory depending on the extent of malabsorption. The type and extent of nutritional therapy also depend on the functional capacity and the adaptation of the residual small intestine.

15. What are the goals of nutritional therapy?

The goals are maintenance and/or improvement of nutritional status, improvement of residual bowel function (adaptation), reduction of diarrhoea and improvement in quality of life.

Comment: The goal of nutritional therapy in SBS is to meet nutritional requirements and to maintain the balance of electrolytes, trace elements and vitamins, without increasing stool frequency and volume.

16. Does SBS require specific substrate composition?

No specific substrate composition is required per se. Depending on the extent of malabsorption a significant increase in energy and a modification of substrate intake may be necessary.

Comment: Woolf et al. measured, in eight SBS patients, an absorption of 62% of delivered energy; the absorption of fat, carbohydrates and of proteins was 54%, 61% and 81%, respectively.[121] In order to keep energy balance and body weight constant, energy intakes of up to 60 kcal/kg BW/day orally or via a TF may therefore be necessary.[122] Increasing oral energy intake up to 200–419% of the basal metabolic rate can avoid the need for PN in more than half of all patients with SBS.[123] Protein requirements from normal food and/or EN are frequently 1.5–2 g/kg BW/day. If the colon is intact, the delivery of large amounts of carbohydrate can improve energy absorption due to the synthesis of short-chain fatty acids.[124] Patients with malabsorption are often able to compensate for the absorption deficit through increasing food and carbohydrate intake (compensatory hyperalimentation/hyperphagia).[125]

Recommendations concerning the quantity and type of fat are controversial. Fat tolerance has to be evaluated individually.[126] After resection of more than 1 m of the ileum but with an intact jejunum and colon, restriction of fat can reduce fatty acid-induced diarrhoea.

Patients with an intact jejunum benefit from a modified fat regimen, replacing some long-chain triglycerides with 20–60 g medium chain triglycerides per day. With a high fat intake, a loss of divalent ions occurs, which need to be substituted.[121,126] In patients with a jejunostomy, the relative proportions of carbohydrate and fat are without significance.

17. What role does EN have in the various phases of SBS?

The route of delivery (ONS or TF) and length of nutritional therapy depend on the disease activity and residual intestinal function.

17.1. Postoperative hypersecretion phase

In the hypersecretory phase PN is obligatory in order to guarantee adequate nutritional intake and fluid and electrolyte replacement (C).

Comment: After extensive resection of the small intestine, increased secretion of gastric acid and a subsequent derangement of the intestinal pH milieu occur at least temporarily. Medical treatment includes H2 receptor blockers or proton pump inhibitors.

In cases with extensive fluid loss through high-output jejunostomy, glucose-electrolyte solutions (oral rehydration) given orally or via TF can reduce jejunal mineral and water loss. In some cases, it is possible to begin oral intake early using small amounts of free amino acid or peptide-based ONS or TF formulae, as this helps to accelerate the adaptation process.

17.2. Adaptation phase

Continuous TF-in limited amounts-depending on the enteral fluid loss is recommended in patients with SBS to improve intestinal adaptation (C).

With progressive adaptation, EN (even overnight to increase time for absorption) can be provided as a supplement to normal oral intake (C).

Comment: Adaptation after bowel resection is characterised by cellular hyperplasia, villous hypertrophy and alteration of motility. The duration of adaptation is controversial. Even after 1 year, function can still improve (IV).[127–129] In the phase of adaptation EN should be initiated early, even in parallel with PN. It is disadvantageous to discontinue PN prematurely (IV).[130]

When enteral fluid loss is below 2.5 l per day minimal EN is initiated (i.e. 250 ml/day). Continuous rather than bolus delivery is tolerated best (IV).[131]

The feed rate is increased depending on tolerance. To utilise the sodium/glucose cotransport (peptides, glucose, amino acids), it is recommended to increase the sodium concentration of the ONS or TF formulae in situations with high sodium loss (e.g. in patients with jejunostomy) to 80–100 meq/l. The addition of sodium chloride (e.g. 3 g/l enteral formula) adjusts the concentration appropriately.

There is no agreement about whether free amino acid, peptide-based or whole protein ONS or TF formulae should be used during adaptation. Patients with accelerated transit and apparent (distinctive) malabsorption may benefit from a free amino acid or peptide-based formula (IV).[132–134] This has gained acceptance in practice although patients with a high jejunostomy do not need a special formula (III).[135] Four comparative studies that included critically ill patients, liver transplant and major upper gastrointestinal surgical patients have shown no disadvantage of EN compared with PN in terms of intestinal absorption and/or permeability.[136–139]

17.3. Maintenance/stabilisation phase

ONS or TF are indicated, if normal nutritional status cannot be maintained by normal nutrition alone (C).

Comment: In the maintenance phase, energy expenditure does not differ from that in healthy subjects. Resting energy expenditure is about 24 kcal/kg BW/day. Nonetheless, energy and substrate intake have to be adapted to absorption capacity (see above). Electrolyte and fluid balance vary, but are balanced in most patients.

EN is not generally superior to normal food in maintaining the nutritional status of these patients.

If an adequate oral intake is not possible, supplementary continuous overnight TF is recommended. This has a positive impact on absorption, nutritional status and gastrointestinal symptoms. However, it has to be considered that distal tube placement reduces the available absorptive area. Using ONS can avoid infusion therapy in some cases. This can be achieved despite the fact that ON or TF are not necessarily better absorbed than normal food. In short term experiments, the use of free amino acid formula led to reduced jejunal villous height (III),[140] (IV).[141]

Avoidance of PN and restriction to EN as the only nutritional therapy is contraindicated if the absorptive capacity of the bowel is so low that maintenance of normal body weight without PN cannot be achieved. If the stool volume is around 3 kg/day with an energy supply of more than 2000–2500 kcal/day, PN cannot be avoided (III).[142] PN can supplement EN.

18. What role does pharmaconutrition have as adjuvant therapy in SBS?

A regimen to accelerate intestinal adaptation with recombinant growth hormone, glutamine and special formula (low fat, high carbohydrates) is not generally recommended due to inconclusive results (C).

Comment: Glutamine exerts a trophic effect on the small intestine and can induce augmentation of

absorption. Improvement in bowel function has been reported when a high-carbohydrate, low-fat normal intake was enriched with 30 g glutamine and growth hormone was delivered subcutaneously. The results were better in cases with more residual bowel.[143,144] However, in a randomised controlled double-blind cross-over trial in eight patients, no significant effect of 0.45 g glutamine/kg BW/day could be observed[145] (IIa),[146] (IV).

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