Learning Objectives

- To understand the epidemiological, environmental and genetic factors in the pathogenesis of inflammatory bowel diseases;
- To understand the role of the intestinal microflora and the gut associated lymphoid tissue in the pathogenesis of inflammatory bowel disease;
- To know the nutritional implications in inflammatory bowel disease patients;
- To understand the rationale for nutritional interventions;
- To perform evidence-based enteral and parenteral nutritional interventions.

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Key Messages

- The pathogenesis of inflammatory bowel disease (IBD) is not yet fully understood;
- Genetics, environment and intestinal flora play a role in the pathogenesis of IBD;
- The intestinal immune system plays a crucial role in the development of IBD;
- The diagnosis is established on the basis of the history of the patient, and on macroscopic, endoscopic, histological and laboratory findings;
The prevalence of nutritional deficiencies and undernutrition is higher in Crohn’s disease (CD) than in ulcerative colitis (UC);
Prednisone is more effective to induce clinical remission than enteral or parenteral nutrition in acute exacerbations of IBD;
Nutritional support with specific nutrients is more beneficial in CD than in UC than in ulcerative colitis;
Enteral nutrition is effective in children and adolescents with growth retardation;
Elemental diets are not superior compared with polymeric diets in Crohn’s disease;
The type of dietary fat in enteral diets influences the clinical course of CD;
Probiotics are beneficial in maintaining remission in ulcerative colitis and in preventing pouchitis;
Enteral nutrition is the preferred method for perioperative nutritional support. Parenteral supplementation can be necessary to achieve a positive energy and nitrogen balance and to allow secondary infectious complications to resolve.
1. Definition

Inflammatory bowel diseases (IBD) (Crohn's disease (CD) and ulcerative colitis (UC)) are inflammatory diseases of the gut with acute attacks followed by remission episodes. Crohn's disease is a relapsing transmural inflammatory disease of the gut that can involve the entire gastrointestinal tract from the mouth to the anus. The inflamed areas manifest themselves in a discontinuous fashion throughout the entire intestine and may lead to complications like strictures, abscesses or fistulas. The disease is located in the terminal ileum in 47%, in the colon in 28% and in the ileo-colon in 21%.

Ulcerative colitis is a relapsing inflammatory process, that is restricted to the mucosa of the colon. The inflammation can be restricted to the rectum (proctitis) but often the whole colon in affected (pancolitis) (1).

2. Epidemiology

In the past the prevalence of IBD was especially high in the Northern countries, the UK and USA. At present the prevalence in these areas increases only slightly whereas the rates in former low-incidence areas such as southern Europe, Asia and in most developing countries steadily increases. There are also large differences between different ethnic groups. The prevalence is higher in white than in black populations. In addition, the prevalence is higher in populations with higher socio-economic background. The diseases are more prevalent in urban that in rural areas (2).

3. Pathogenesis

The pathogenesis of IBD is not yet fully understood, but three factors are considered important:

- Environmental factors
- Genetic factors
- Intestinal microflora

3.1 Environmental factors

Epidemiological studies have revealed an increase in the number of IBD cases in urban compared to rural areas. The results suggested that industrialization, sanitation and hygiene play important roles. The incidence increases in immigrants moving from low incidence to a high incidence regions. A lower risk has been found in populations with no access to tap water or hot water, in large or/poor families and in populations consuming contaminated food (3).

Living in a area with high sanitation may prevent early exposure to environmental antigens and consequently may impair the maturation of the mucosal immune system. This can result in an inappropriate immune response to antigens in later life.

The role of nutrition in the development of IBD is still controversial. There are observations that breast feeding may be protective and that an excessive consumption of sugar or polyunsaturated fats have a promoting effect (4). Overall, at present the impact of nutritional factors in the pathogenesis of IBD can not be conclusively defined. Smoking was found to have a beneficial effect in ulcerative colitis with fewer relapses. On the other hand, in Crohn’s disease smoking aggravates the course of the disease, increases the rates of relapse and the dependence on corticosteroids (2). Data are controversial regarding the role of vaccines for measles, mumps and rubella, the use of contraceptives or non steroidal anti-inflammatory drugs.

3.2 Genetic factors

Familial occurrence of IBD is known for a long time. In Crohn’s disease and ulcerative colitis, the risk of developing IBD is increased in first degree relatives. Furthermore, the concordance for disease type, disease pattern, and the presence of extra-intestinal disease manifestation is high. The lifetime risk of developing Crohn’s disease in first degree relatives approximates 5% and of developing ulcerative colitis 1.6% (5).
The strongest evidence of genetic influences was found in twin studies. The concordance in monozygotic twins in Crohn’s disease is 38% and in ulcerative colitis 10%. The respective rates in dizygotic twins are 7% for Crohn’s disease and 3% for ulcerative colitis. These data suggest that a genetic background is more important in Crohn’s disease than in ulcerative colitis. IBD is a polygenic disease. Until now, susceptibility regions on 12 chromosomes were described. The best known chromosomal region is CARD15/NOD2 on chromosome 16. Mutations in this area are linked with ileal Crohn’s disease. Other important genes are located in chromosome 6 which encodes the major histocompatibility complex.

3.3 Intestinal microflora
The intestinal microflora, the epithelial barrier and the mucosal lymphoid tissue are closely connected. The intestine hosts approximately \(10^{12}-10^{13}\) mainly anaerobic bacteria. More than 500 species are known (6). Specific peptides as bacteriocins (produced by the commensal bacteria) and defensins (produced by the epithelial Paneth cells) are controlling the growth of the pathogen bacteria.

Several important mechanisms are involved to maintain tolerance to the different microbiota. The epithelial barrier with the mucus layer is the first line of defence. In addition, the activity of sIGA (secretory Immunoglobulin A) is an important defense mechanism.

The second line of defence is associated with the mucosal lymphoid tissue. A large amount of T-cells, B-cells, granulocytes, mast cells and killer cells are found here.

The immune cells and the intestinal microbiota are communicating with each other through specific cells (dendritic cells), the toll-like receptors (TLR) and the nucleotide binding oligomerization domain (NOD) receptors. It is important to distinguish between commensal and pathogen bacteria. Via these mechanisms, the T-cell response can be activated or suppressed (7).

3.4 Inflammatory response
At present, IBD is generally considered to result from an inappropriate response of a defective mucosal immune system triggered by the intestinal microflora. The presence of bacteria in the intestinal lumen is a prerequisite for the development of IBD. In animal models, mice incapable of expressing IL-2 or IL-10 invariably develop a colitis- or Crohn-like inflammation (8,9). No inflammation occurs if they grow up in a pathogen free environment or if they are fed with Lactobacillus species when exposed to environmental bacteria (10). Thus, the absence of luminal bacteria or bacteria with a different make-up prevent the development of inflammatory bowel disease in these models. Patients with IBD have been found to have decreased counts of Lactobacillus and/or Bifidobacteria spp. Furthermore, an increased number of pathogen bacteria adherent to the mucosa and within the epithelium have been demonstrated in quantitative studies (11). It appears that these bacteria trigger a strong mucosal immunological response, leading to inflammation and intestinal epithelial cell injury, mediated by activated T-cells, mononuclear cells and macrophages. If this response cannot be down-regulated by regulatory T-cells, numerous inflammatory cytokines are activated by stimulation of the intracellular transcription factor NF-κB (12). It has been shown that also bacterial lipopolysaccharides or peptidoglycans can activate NF-κB by binding to the specific receptors on the cell membrane (TLR) or intracellular NOD receptors.

It is still unknown why the pro-inflammatory response cannot be downregulated and why the inflammatory drive continues leading to mucosal damage resulting either in Crohn’s disease or ulcerative colitis (13).

4. Clinical appearance of IBD
The clinical symptoms in Crohn’s disease depend on the location of the disease and include diarrhoea, abdominal pain, fever, clinical signs of bowel obstruction, as well as admixture of blood and/or mucus with the stools.

The clinical symptoms in patients with ulcerative colitis are bloody diarrhoea, frequent defecation and abdominal cramps during bowel movements often invalidating patients. Usually in proctitis or
left-sided colitis the symptoms are less severe than in pancolitis but repeated urge leading to frequent bowel movements may be extremely cumbersome (1).

5. Diagnosis of IBD

There is no pathognomonic sign, allowing to differentiate between CD and UC. The diagnosis can be suspected on the basis of the patient’s history and the clinical findings.

Common laboratory findings are elevated, including CRP levels and leucocytes. Low haemoglobin levels and iron deficiency are more often found in ulcerative colitis and micronutrient and vitamin deficiency are more often encountered in Crohn’s disease. During exacerbations low albumin levels are common in both diseases.

A final diagnosis is made on the basis of the clinical findings and behaviour of the disease. In IBD of longer duration the transmural character of CD (inflammatory masses, strictures, obstruction, abscess formation, fistulae) and the mucosal colonic localization of UC (frequent and debilitating bowel movements of loose bloody stools), the proximal spread of CD are hallmarks of the diagnosis. Confirmation can be obtained by endoscopic, macroscopic (at operation and pathology) and histological features (1).

6. Treatment of IBD

The first step is to treat the active disease and to achieve remission.

In mild to moderate Crohn’s disease, sulfasalazine, mesalazine or topical corticosteroids are used most often. In patients who do not respond to this treatment or if they have more severe activity, corticosteroids are the treatment of choice. In severe disease or corticosteroid dependency anti-TNFα treatment is indicated.

For maintenance of remission azathioprine, mercaptopurine, methotrexate or continuing TNFα-blockers are effective. Surgery is indicated to treat fibrotic strictures, abscesses generally present in the presence of fibrotic strictures, and intestinal fistulas resulting from transmural perforating disease activity and from residual tracts after abscess drainage (1). In the presence of long standing strictures, abscesses and fistulae, corticosteroid treatment is of little benefit and may even be contraindicated. Instead, a surgical approach should be considered.

For ulcerative colitis, 5-aminosalicylic acids are the drugs of choice for mild to moderate disease. If there is an inadequate response, oral or i.v. corticosteroids are the next step.

For maintaining remissions 5-aminosalicylic acids are continued. Patients with relapses or steroid dependency are treated with azathioprine or mercaptopurine. In very severe cases anti-TNFα-treatment has been shown to induce remission in slightly less than half of the patients treated. Emergency surgery is indicated in patients with life-threatening complications not responding to medical treatment.

Elective surgery is indicated in patients with severe dysplasia, cancer or refractory to medical treatment as demonstrated by a severely compromised quality of life(1).

7. Nutritional aspects in IBD

7.1 Effect of inflammation on the nutritional status and metabolism

The inflammation of the GI-tract with the associated symptoms of pain, nausea, and diarrhea lead to reduced food intake and uptake leading to malnutrition. The prevalence of nutritional deficiencies and malnutrition is higher in patients with Crohn’s disease than in patients with ulcerative colitis. Unfortunately, this subject is not well studied in ulcerative colitis. Weight loss in Crohn’s disease is observed in up to 75% of adult hospitalized patients. A negative nitrogen balance is found in more than 50% of the patients during active disease (14). Patients with ulcerative colitis have often a relatively good nutritional status, but during acute attacks, a negative nutrient balance and inflammation may rapidly lead to a state of malnutrition (14).
The aetiology of malnutrition and the deficiencies of various vitamins, minerals and trace elements is multifactorial. Cytokine induced catabolism of fat free mass and anorexia are the main causes of IBD-associated malnutrition and growth failure in children. In addition, extensive inflammation or resection of the gut itself limits absorption of nutrients. Medication, increased exsudative losses of protein or small bowel bacterial overgrowth are additional causes of malabsorption (15). When patients with IBD are in complete remission, energy and substrate metabolism is normal. During the acute phase of Crohn’s disease, an increase in energy expenditure with a relative increase in fat oxidation and a decrease in carbohydrate oxidation can be found (16,17).

Suboptimal levels of micronutrients and vitamins are often found in children and adults with Crohn’s disease, but symptoms of these deficits are seldom evident (except for iron, vitamin B12, folic acid and zinc). Anaemia and iron deficiencies are more prevalent in patients with ulcerative colitis. In patients with severe diarrhoea, low levels of potassium, magnesium, calcium and phosphate can be encountered. The levels of fat soluble vitamins correlate with the severity of steatorrhea. Low vitamin D levels have been associated with bone disease independent of glucocorticoid treatment in patients with Crohn’s disease. Glucocorticoid treatment itself is associated with osteoporosis. In children glucocorticoid treatment leads to growth failure. The main nutritional deficiencies in Crohn’s disease and ulcerative colitis are summarized in Table 1.

### Table 1 Nutritional deficiencies in IBD (adapted from (15))

<table>
<thead>
<tr>
<th>Nutritional deficiencies</th>
<th>Crohn’s disease frequency (%)</th>
<th>Ulcerative colitis frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>65-75</td>
<td>18-62</td>
</tr>
<tr>
<td>Hypoalbuminaemia</td>
<td>25-80</td>
<td>25-50</td>
</tr>
<tr>
<td>Intestinal protein loss</td>
<td>75</td>
<td>seldom</td>
</tr>
<tr>
<td>Negative nitrogen balance</td>
<td>70</td>
<td>seldom</td>
</tr>
<tr>
<td>Anaemia</td>
<td>60-80</td>
<td>66</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>39</td>
<td>81</td>
</tr>
<tr>
<td>Vitamin B12 deficiency</td>
<td>48</td>
<td>5</td>
</tr>
<tr>
<td>Folic acid deficiency</td>
<td>54</td>
<td>36</td>
</tr>
<tr>
<td>Calcium deficiency</td>
<td>13</td>
<td>possible</td>
</tr>
<tr>
<td>Magnesium deficiency</td>
<td>14-33</td>
<td>possible</td>
</tr>
<tr>
<td>Potassium deficiency</td>
<td>6-20</td>
<td>possible</td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>11</td>
<td>no data</td>
</tr>
<tr>
<td>Vitamin B1 deficiency</td>
<td>possible</td>
<td>no data</td>
</tr>
<tr>
<td>Vitamin C deficiency</td>
<td>possible</td>
<td>no data</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td>75</td>
<td>possible</td>
</tr>
<tr>
<td>Vitamin K deficiency</td>
<td>possible</td>
<td>no data</td>
</tr>
<tr>
<td>Zinc deficiency</td>
<td>40</td>
<td>possible</td>
</tr>
<tr>
<td>Cu deficiency</td>
<td>possible</td>
<td>possible</td>
</tr>
</tbody>
</table>

Overall, the presence of malnutrition is linked to adverse outcome. Defects in cellular and humeral immunity have been reported. Malnutrition increases the risk of postoperative complications.

### 7.2 Nutritional assessment

The diagnosis of malnutrition depends on the patient’s history, physiological examination, and selective laboratory tests. Several anthropometric and biochemical parameters (weight, height, skinfold thickness, body composition analysis, serum albumin) are routinely used. It is also important to record the food intake in the last one or two weeks. IBD patients often consume an unbalanced diet which may lead to nutritional deficiencies (18). For screening purposes, the NRS-2002 may be recommended (see Module 3.1).

### 7.3 Energy and protein requirements
Resting energy expenditure varies depending on inflammatory activity. Energy requirements have been calculated with the Harris-Benedict equation using an adjustment factor of x1.75 for net catabolic state (15). This adjustment overestimates actual energy expenditure significantly (approximately 45 Cal/kg/24h). Energy requirements are often not greater than the predicted requirement if patients are not very lean with low fat mass (19). However, physical activity, inflammatory activity and malabsorption should be taken into account when calculating actual nutrient requirements. Also the degree of obesity should be taken into account. The more obese the less energy/kg is required and vice versa, the leaner a patient the higher energy requirement per kg BW. Consequently requirements may be calculated on the basis of ideal BW (or adjusted BW) and may amount to 25-30 Cal/kg ideal BW/24h (14).

Protein requirements in patients with IBD are generally increased in the presence of inflammatory activity. Inflammation induces a catabolic response with endogenous proteolysis and ensuing negative nitrogen balance. To limit nitrogen losses in patients with active IBD, 1.5 g/kg BW protein per day should be provided. Although solid data are lacking it has been recommended to increase protein intake to 2g protein/kg BW/24 h in infectious or severely malnourished patients (15).

In remission, IBD patients often have a normal nutritional status. Patients with Crohn’s disease with short bowel syndrome or with longstanding strictures may have very low body weights with low fat free mass and low fat mass.

8. Nutritional support in IBD

The aims of nutritional support in IBD are to treat or to prevent nutritional deficits, to reduce disease activity, to improve growth and development in children and adolescents, to reduce the need for surgery or aggressive medical treatment, and to maintain remission.

Malnutrition in Crohn’s disease is associated with a negative clinical outcome and increased postoperative complications. Patients with ulcerative colitis in general have less malabsorption and consequently may sustain better nutrient equilibrium. When inflammatory activity is high this will lead, despite nutrient equilibrium, to loss of fat free mass. Patients with severe diarrhea and frequent bowel movements often eat less to diminish stool frequency. Malnourished patients with high disease activity need adequate nutritional support. Unfortunately, nutritional counselling alone does not suffice to improve nutritional status (20). The nutritional support required during an acute exacerbation differs from the nutritional regimen during remission. Oral, enteral and parenteral nutritional support have especially been studied during exacerbations.

8.1 Oral supplements

Overall, the compliance of oral nutritional supplements is low. More than 20% of the patients discontinue using supplements due to unpalatability or intolerance of these feeds. In Crohn’s disease patients with malnutrition or with growth retardation daily ingestion of 500 kcal of a polymeric oral supplement can be beneficial to improve nutritional state if compliance is maintained (21).

There are no specific data available for ulcerative colitis to improve or to maintain nutritional status with oral supplements. In analogy with Crohn’s patients, supplementation with 500 calories can be considered in patients with a reduced oral intake (14).

8.2 Enteral versus parenteral nutritional support

Specific nutritional support is more beneficial in Crohn’s disease than in ulcerative colitis. Enteral nutrition is the preferred route for nutritional repletion because of the potential trophic effects on the intestinal mucosa, the preservation of gastrointestinal function, and the beneficial effects on the intestinal flora and mucosal barrier integrity. In addition, complication rates and costs have been reported to be lower than with parenteral nutrition. For a long time, it was suggested that bowel rest with total parenteral nutrition may reduce intestinal inflammation and decrease disease activity in patients with IBD.

The concept of bowel rest has been abandoned because no effect on outcome could be demonstrated. Total parenteral nutrition (TPN) as primary treatment was studied in 8 trials in
Crohn’s disease and 4 trials in ulcerative colitis. The total number of patients studied amounted to 117 in Crohn’s disease and 60 with ulcerative colitis. TPN was more effective in Crohn’s disease than in ulcerative colitis. In Crohn’s disease an initial remission was achieved in 81% and in ulcerative colitis in 37% (14). Crohn’s disease patients that came in remission with TPN developed in a high proportion of cases early recurrences. Consequently TPN was abandoned for patients with primary uncomplicated exacerbations of their disease. Crohn’s disease patients with secondary infectious complications (abscess, stricture, fistulae, inflammatory masses) often do not tolerate enteral nutrition well and may benefit from parenteral nutrition. In this situation in most cases an operation is necessary which can be postponed to allow the infectious process to become quiescent and nutritional state to improve. Parenteral nutrition is of limited benefit in ulcerative colitis. Sometimes parenteral nutrition is instituted to decrease a debilitating defecation frequency, when patients are hospitalized with acute toxic colitis.

With enteral nutrition (EN) around 60% of Crohn’s patients with primary exacerbations reached remission, but the time to induce remission is rather long (22). A meta-analysis and a Cochrane Review demonstrated that the response with corticosteroids is higher and faster than with EN (23,24). Unfortunately, a combination of EN and corticosteroids has not been studied.

Enteral nutritional support is indicated in Crohn’s disease patients with an acute exacerbation and with malnutrition and in children and adolescents with growth retardation. In addition, corticosteroids can be reduced in children when they are fed enterally. Adult patients with acute disease should receive 25-35 kcal/kg ideal BW/d by a continuous infusion via a naso-gastric tube. Enteral tube feeding has shown to be ineffective in patients with active ulcerative colitis. The remission rates are not higher than the rate of spontaneous remission when patients consume normal food. A comparison of TPN with EN in acute ulcerative colitis showed similar effects on nutritional status, disease activity and complications, but neither TPN nor EN had a positive effect on inflammatory activity (25).

### 8.3 Specific diets

#### 8.3.1 Elemental versus polymeric diets

Several randomized controlled trials with formulations containing free amino acids, peptides or whole protein did not show a clear difference in disease activity in active Crohn’s disease (22-24). Enteral oligomeric diets have a slightly higher osmolarity and are not recommended for primary use. In patients intolerant to polymeric diets, an elemental or peptide-based diet can be tried.

#### 8.3.2 Diets with different fat components

Lipids in diets have been extensively studied in relation to the inflammatory response. Dietary lipids induces changes in the cell membrane phospholipids which, in response to an inflammatory trigger, synthesize eicosanoids with different degrees of pro- or anti-inflammatory activities through an up- or downregulation of the expression of pro- or anti-inflammatory cytokines and adhesion molecules (26). Several lipid compositions in enteral diets were studied in Crohn’s disease, but the results are still controversial.

Enteral diets with a low content of long-chain triglycerides (LCT), or with replacement of part of the LCT with median-chain triglycerides did not achieve clear beneficial effects (27,28). In a Cochrane analysis in 2001, no clear benefit could be demonstrated for a low-fat diet compared to a high fat diet (24). Different types of LCT were compared, one high in oleate and the other high in linoleate in patients with active Crohn’s disease. The remission rates with linoleate were significantly higher than with oleate (63% vs. 27%) (29).

The effect of n-3 fatty acids on the inflammatory response was studied in Crohn’s disease and ulcerative colitis. The reported effects showed mixed results. In a systematic review, 13 controlled trials were analyzed. Fewer than 6 were identified that assessed the effects of n-3 fatty acids on a single outcome parameter. In 3 studies, a reduction of corticosteroid requirements were found, although statistical significance was shown in only one of these studies. At present, it is not possible to draw a clear conclusion regarding the effects of n-3 fatty acids on clinical, endoscopic or histological scores and on remission or relapse rates (30). The effects of different types of lipids on inflammatory activity deserve further study.
8.3.3 Diets containing transforming growth factor-β
Transforming growth factor-β (TGF-β) enriched formulas are commercially available. TGF-β is an anti-inflammatory cytokine acting as a downregulator of the inflammatory response in patients with IBD. Enteral diets enriched with TGF-β were mainly used in uncontrolled studies in children or adolescents with Crohn’s disease. Mucosal inflammation could be reduced, a downregulation of proinflammatory cytokines and a upregulation of TGF-β mRNA was found, and disease activity decreased (31, 32). A recently published randomized open-label study used a TGF-β enriched polymeric diet alone in comparison with corticosteroids in the treatment of active pediatric Crohn’s disease. This study showed that a short course of this diet was more effective than corticosteroids in inducing healing of gut inflammatory lesions whereas similar clinical remission rates were achieved (33).

8.3.4 Diets containing glutamine
In one randomized study no evidence was found that a glutamine enriched polymeric diet has a more beneficial effect than a standard diet in active Crohn’s disease (34).

9. Alternative nutritional treatment components
Pre- and probiotics have been shown to be beneficial in gastrointestinal diseases.

Prebiotics are soluble poli- or oligo-saccharides (inulin, pectin, fructo- and galacto-oligosaccharides) and serve in the intestine as substrates for fermentation (36, 37).

Probiotics are non-pathogenic bacteria which are able to exert positive health benefits in the gastrointestinal tract. They are able to adhere to the intestinal mucosa and can stimulate the secretion of sIgA and mucus production. They may reduce the levels of pro-inflammatory cytokines (TNF-α, IL-1, IL-6) and increase levels of anti-inflammatory cytokines (IL-10, TGF-β). Furthermore, they can produce defensins and heat shock proteins (37-40).

Pre- and probiotics can interact with the commensal intestinal bacteria and may therefore influence the intestinal ecosystem. This effect is eminent in the colon, where anaerobic bacteria can ferment non-absorbable dietary carbohydrates. Through fermentation, the intestinal pH decreases, which stimulates the growth of non-pathogenic bacteria (prebiotic effect) and liberate short chain fatty acids (butyrate, acetate, and propionate). Butyrate is the main energy source for the colonic epithelial cells and inhibits the activation of NF-κB. This prevents the expression of specific genes encoding cytokines intensifying the inflammatory response (41, 42). In addition, butyrate increases apoptosis of inflammatory cells (43, 44).

So far, the use of pre-and probiotics was found to be more beneficial in ulcerative colitis than in Crohn’s disease. The use of a fermentable Plantago ovate (dietary fibre) supplementation achieved similar relapse rates in ulcerative colitis as Mesalazine (45).

In two studies administration of E. coli Nissle 1917 (46, 47) and in one study administration of Lactobacillus GG (48) was compared with Mesalazine. In all three studies probiotics maintained remission at similar rates as Mesalazine.

Good clinical results were also published using probiotics in patients with pouchitis. In chronic relapsing pouchitis a significant reduction in the relapse rates was found with a combination of eight different bacteria (VSL#3) compared to placebo (49). In addition, treatment with VSL#3 reduced the pouchitis rate when given after surgery compared to placebo (50).

10. Nutritional support in the remission phase
Most patients with IBD in remission have a normal nutritional status. There are no specific diets recommended if the patients are in remission and can eat normally. A normal “healthy” diet rich in fruits, vegetables and fish can be recommended. In patients with ileum resection or sulfasalazine
treatment, vitamin B12 levels have to be monitored. Calcium and vitamin D status should be carefully controlled and especially in patients treated with corticosteroids.

After an initial study, showing great benefit of supplementation of the diet with n-3 fatty acids containing enteric coated capsules in Crohn’s disease, there was a great hope to reduce relapses (51). These beneficial effects could not be reproduced in two large, recently published studies (52).

11. Perioperative nutritional support

Patients with weight loss and low albumin concentration have an increased postoperative complication rate (14). Preoperative nutrition is therefore recommended in these patients if the operation can be postponed safely. If possible the operation should be delayed until the albumin levels are over 30 g/l. Enteral nutrition is preferable but parenteral nutritional supplementation can be necessary if requirements cannot be met by enteral route alone. Several meta-analyses in patients undergoing abdominal surgery for different diseases have demonstrated that parenteral nutrition is especially beneficial in patients that are malnourished and do not tolerate enteral nutrition. A parenteral nutrition course of 7 days before operation appears sufficient to achieve benefit, despite body weights not having normalized (53). Longer courses of parenteral nutrition are beneficial, when inflammatory/infectious activity can be effectively treated. This is especially the case in Crohn’s disease patients with stricturing, penetrating lesions that have led to secondary infectious complications. Crohn’s disease is a transmural inflammatory disease which can lead to slow perforation, abscess formation, rupture of the abscess to skin scars or to adjacent bowel or bladder, or surgical drainage of the abscess. When abscesses have perforated or are drained in most instances fistulae remain which may close spontaneously in patients receiving parenteral nutrition. They will recur however if normal oral food is re instituted. In almost all these patients the bowel has strictured due to longstanding inflammation and fibrous scar formation. In view of the fibrous stricture these patients cannot truly achieve remission by medical means and ultimately require operation. If parenteral nutrition can be diligently administered without causing catheter sepsis and without hyperalimenting patients, this decreases the risk of postoperative infectious complications (54). An additional benefit of this approach is that the inflammatory masses with which patients present initially, will be largely resolved and can be dissected more easily without causing undue harm to healthy intestine surrounding the original abscess and the (closed) fistula. When such patients are operated in the acute stage more (healthy) bowel is often resected and complications are more frequent. In patients with short bowel syndrome parenteral nutrition may be indicated (see Module 12.2 and Topic 19).

Postoperative nutritional support is not different from other surgical patients.

12. Summary

The pathogenesis of IBD is still not fully understood, but genes, environment and gut flora are involved. Crohn’s disease and ulcerative colitis show different clinical patterns, although the underlying pathophysiology may share common features.

Nutritional deficiencies and malnutrition are more often seen in Crohn’s disease than in ulcerative colitis. Nutritional deficiencies need to be treated like in any other disease, in view of their negative effect on outcome.

There is evidence that specific nutritional regimens can influence the immune response, by treating malnutrition but in addition, by influencing specific inflammatory pathways in the intestine. Enteral nutrition is the preferred mode of nutritional support in IBD patients. Parenteral nutrition may be indicated in very severe cases of Crohn’s disease, with secondary infectious complications, in most instances as a preparation for operation. The supplementation of specific nutrients or changing the lipid composition is of interest, but further studies are still required to establish their value in the future. In addition, the potential of pre- and probiotics to modify the course of IBD appears to be promising. Good results were shown in maintaining remission in ulcerative colitis and in preventing pouchitis.

References


