Module 12.1

Compromised Gut

Learning Objectives:

- To learn the anatomy of the gastro-intestinal tract;
- To learn the physiology of the gastro-intestinal tract especially with regard to nutrition;
- To learn the consequences of critical illness on the function of the gastro-intestinal tract;
- To learn the causes of disturbances in the balance between intestinal bacteria and their effects on the function of the bowel;
- To learn the consequences of anatomical pathology on the integrity and function of the intestinal tract;
- To appreciate the connections between intestinal inflammation and liver disease;
- To learn medical, surgical and nutritional interventions beneficial to the integrity and function of the gut;

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Key messages:

- Metabolic and digestive functions of the intestine reside predominantly in the proximal part of the small bowel (duodenum and jejunum). The distal part of the bowel have especially important functions in the resorption of bile acids and electrolytes. Apart from resorption of water and electrolytes the colon resorbs s short chain fatty acids derived from fermentation of soluble fiber;
• The degree of malfunction of the intestine in trauma and diseases depends on the severity of the disease and of the trauma. Several anatomical and functional abnormalities (stenoses, blind loops, pouches, constipation, severe disease, radiation) lead to inflammation and interfere with the adequate absorption of nutrients. Sometimes malabsorption occurs without inflammation or loss of intestinal length as in severe motility disorders such as pseudo-obstruction or scleroderma;
• Bacterial overgrowth is an important cause of malfunction of the intestine especially in chronic intestinal pseudo-obstruction;
• Compromised bowel (short bowel or/and bacterial overgrowth) may have deleterious effects on the liver. This happens in neonates and less often in adults;
• The composition of parenteral nutrition may induce of aggravate compromised bowel-associated hypertriglyceridemia, cholestasis and steatohepatitis;
• Correction of anatomical abnormalities (stenoses, defunctionalized small bowel segments, stagnant or dilated loops) and activation of the gut by (distal) enteral nutrition improves bowel function.

1. Physiology of the Gut

The appropriate intestinal structure and function is the result of the interaction between humoral, neural or local factors. Alternations of this complex relations may result in intestinal failure, which is the inadequate intestinal activity violating the ability to absorb nutrients effectively enough to maintain health.

The Knowledge of anatomical and physiological aspects of gastrointestinal tract is crucial for understanding of compromised gut.

1.1. Anatomy

The length of the GI-tract depends on the age, body size and the technique, which was used for measurement (i.e. in vivo or at autopsy, normal muscle tonus or relaxed). Consequently, during operation, only a rough estimate can be given for true length and size of gastrointestinal (GI) tract or its remnant. Taking above into consideration, it is assumed that individual parts of GI tract measure:
a/ the distance from oral orifice to the oesophagus is about 15 cm;
b/ oesophagus, which starts 15 cm from teeth and ends with in stomach inlet (cardia) – measures approximately 25-30 cm;
c/ an average estimate of the length of the stomach varies between 25 and 50 cm, but it must be remembered that its length depends on whether it is measured along the minor or greater curvature;
d/ duodenum, which derives its name from the fact that in medieval times it was considered to measure 12 fingers, which amounts to roughly 30 cm, and this is still regarded as the length of duodenum. It ends at the ligament of Treitz, where jejunum begins;
e/ small bowel, which can be divide into jejunum and ileum. The borderline between them is, however, not easy to mark, because instead of sharp transition there is just a gradual decrease in thickness of the intestine. The jejunum is at least twice as thick and more than twice as heavy per centimeter as the ileum, which is also reflected in its function. Total length of small intestine measured at surgery is close to 3-6 meters. Jejunum and ileum differs also in terms of motility: ileal transit is three-times slower than jejunal one.
f/ large bowel (colon), which starts at the the ileocecal valve Bauhin’s valve) and is approximately 100-120 cm long. The last part of large bowel, 15 cm long, is called rectum.
1.2 Digestion and absorption

The digestion commences in the oral cavity with the actions of amylase, which can be found in saliva. The esophagus does not contribute much to the process. Both oral cavity and the esophagus are resistant to hypertonic foods due to their multi-layered squamous epithelia.

The next part of GI tract, which is stomach, continues digestive process thanks to its enzymes from chief cells. It is not, however, its only function – it creates hostile environment for bacteria because it secretes hydrochloric acid which protects protects other parts of GI tract from contamination and helps to digest meals. It also dilutes food components so they may become isotonic instead of hipertonic, releases predigested food gradually to duodenum protecting the intestine from large boluses that could result in dumping. The latter process is rapid for liquids, but slow and regulated by particles-size & nutrient type in case of solid food. Gastric emptying is also slowed down by the presence of intestinal content in the distal part of small intestine, it is, however, enhanced by small bowel resection. [1,2]

Dumping syndrome may occur in patients after gastrectomy. It may result in substantial loss of weight and fatigue, dizziness and even loss of consciousness, It is caused by the sudden and substantial release of hormones (mostly insulin) provoked by quick passage and large volume of predigested food into the jejunum.

The main part of secretion and absorption takes place in the small intestine, where intestinal enzymes together with pancreatic and bile secretion break down large food particles. The digestive process in occurring in the small intestine can be divided into three phases: intraluminal (mainly hydrolysis), brush border membrane phase (=muscosal phase – further degradation of polysaccharide and peptides + absorption) and the incorporation phase (transport to portal vein and lymphatic tract).

Detailed scheme of digestive process was presented in Fig 1.

![Figure 1: Location and absorption of macronutrients, bile acids, Ca, Fe, Folic acid, vit B12 in different parts of the intestine (Boron/Boulpaep, Medical Physiology, Saunders 2003)](image-url)
Proximal part of small bowel absorbs more vital nutrients that the distal part, except for bile salt and vitamin 12, which are absorbed in ileum. Jejunum is also the place of more intense metabolic processes of amino acids, carbohydrates and lipids. Particularly glutamine degradation and conversion to glutamate, alanine, citrulline and ammonia takes predominantly place in the jejunum.

The size of reabsorption may depend on the nature of the meal as well. [3] Low-osmotic meal, most of the fluid is absorbed in the jejunum, whereas high-osmolarity meal is mostly absorbed in ileum.

Water and electrolytes are in varying amounts released into the lumen and simultaneously absorbed again. Hypertonic solutions are diluted by water secretion, hypotonic solutions are made isotonic by secretion of cations (especially Na); both types of solutions are subsequently reabsorbed.

Because of mechanisms described above, a fluid flux across the GI tract occurs of approximately 8-10 liters. This flux leads in the healthy bowel to the net uptake of the quantity of fluid ingested orally and loss of negligible amounts of fluid in the stools. Absorption of water and electrolytes takes place in the all parts of small bowel and in the colon, which explains the fact that after resection of substantial parts of the small and large bowel water and electrolytes (Ca\(^{++}\), K\(^{+}\), Mg\(^{++}\), Cl\(^{-}\)) cannot be efficiently absorbed. (See also Chapter 12.2)

The impact of such a big fluid flux across the GI tract results in huge fluid intestinal retention in case of mechanical obstruction and causes potent water and electrolytes shift between extravascular and intravascular compartment as well as intra- and extracellular one. This fluid shift results in hypotension or even hypovolemic shock in emergency surgical patients. In is crucial that whenever possible, water and electrolytes abnormalities are corrected before surgery.

In addition to the absorption of water and electrolytes, the small bowel and particularly ileum plays also an important role in the re-absorption of bile acids. Loss of bile acids and subsequent shrinking of the bile acid pool, diminishes the emulsification of fat in the duodenum and jejunum leading to loss of fat in the stools and fat soluble vitamins and cations like Ca\(^{2+}\) and Mg\(^{++}\) bound to fatty acids.

Vitamins are absorbed mostly proximally, the only vitamin that is predominantly absorbed in the ileum is vitamin B12, hence the loss of this part of the intestine leads to anemia.

In the colon, the 1000-1500 ml of fluid bowel contents coming from the ileum is largely absorbed, producing a solid stool containing 100 – 300 ml of water. Large bowel is a potent part of GI tract as far as water absorption is concerned - colon’s efficiency in water absorption reaches 90%, thanks to tight intracellular junctions

Water is absorbed in 44% in jejunum and in 70% in ileum, while sodium in 13% and 72%, respectively [3]. Net absorption of water and electrolytes in the small and large bowel is largely driven by active ion-pumping of the Na\(^{+}\)-K\(^{+}\) pump, which induces transmembrane concentration differences and electro-chemical gradients which drive Na\(^{+}\) linked co-transport of important luminal components including amino acids, glucose, bile acids and others. This process is easily disturbed in infectious or inflammatory states where the electro-chemical gradient across the cell wall of the enterocyte cannot be maintained and where co-transporters and exchangers are internalized, leading to diarrhea [6].

### 1.3 Motility of gastrointestinal tract

Intestinal motility plays an important, yet belittled role in nutrients’ absorption. Animal studies demonstrated an adaptive response with slowed gastric emptying and slowed transit after proximal resection of small intestine [4] The prolongation of migrating motor complex (MMC), increase in MMC Phase II and reduction in MMC Phase I duration were observed. The intestinal remnant showed also post-prandial inhibition of MMC. Distal resection resulted only in minor changes. Moreover, studies in human showed that intestinal remnant was characterized by shorter duration of MMC-cycle after major resection (when only < 100 cm of intestine was left). All above confirmed the adaptive potential of intestine from motoric point of view.
2. Severe inflammatory illness

Severe inflammation or infection influences the whole organism regardless of the location of the primary site. Recent views are that inflammatory activity causes opening of tight junctions in the lung, kidney, liver, intestine and other organs which leads to passage of cells, proteins and fluid into the interstitium [7, 8]. In case of GI tract those processes impair digestive function and absorption not only of water, electrolytes, macro- and micronutrients, but also other substances such as bile acids. The degree of impairment depends on the severity of disease.

The disturbance of absorption is the result of impairment of ATP-driven ion-transport. Not only systemic changes may influence absorption; those processes may also occur because of local inflammatory sites in course of abdominal inflammatory processes such as appendicitis, exacerbated Crohn’s disease or diverticulitis. Even the intact intestine if walling off the infectious site can exhibit “collateral” inflammation, which harms active water and electrolyte transport. This mechanism explains the presence of intra-luminal fluid levels encountered around the inflammatory mass on plain abdominal X-rays and the presence of diarrhea in these patients.

Not only absorption is disturbed; also digestion and motility are compromised in either generalized inflammatory states or in local inflammatory processes in the abdomen. This is the result of cytokines’ release. Animal studies showed that endotoxin challenge interfered with normal progression of migrating motor complexes and peristalsis [9]. As a consequence of these disturbances patients with severe localized or generalized inflammatory illness can have diarrhea or obstruction.

Consequently, the feasibility of enteral nutrition varies depending on the severity of inflammatory illness. Enteral nutrition in patients with multiple organ failure (MOF) should be carefully initiated with small amounts of iso-osmolar nutrition, containing adequate amounts of sodium in patients with adequate GI passage.

Very often motility disorders are caused by generalized motility disorders in the whole gastro-intestinal tract, and are not limited only to stomach or large bowel. [10] Disturbances in passage can be restricted, however, to the proximal digestive tract in case of local impediments, such as necrotizing pancreatitis with a “locked-in” duodenum. Even in these situations enteral nutrition may be initiated by the use of thin feeding tube inserted into distal, intact part of intestine. Enteral diets should be administered continuously in the intestine, not in a bolus form, and should always be isotonic. Administration of water is not recommended as jejunum is less resistant to hypertonic or hypotonic feedings than the stomach. It is also important to use peptide enteral diet during jejunal feeding instead of whole protein formula to enable complete absorption.

In critical illness the blood perfusion of the bowel may be impaired and in those cases this state may be further aggravated by the infusion of enteral nutrition, leading even to intestinal necrosis [11, 12]. In such patients combinations of enteral and parenteral nutritional may be useful to cover protein-energy requirements.

The composition of the nutritional regimen is more critical in severe (infectious) illness than in metabolically stable patients. Metabolic instability includes insulin resistance and glucose intolerance as well as hypertriglyceridemia, therefore those patients require very careful monitoring (see Topic 18: Nutritional Support in ICU).

The goal of nutritional support in severely ill patients is to limit muscle breakdown on the one hand but more importantly to support host response. This includes the immune response (synthesis of acute phase proteins, complement factors, immune globulins, white cells, macrophages etc.) and wound repair. As long as inflammatory activity persists, net protein catabolism (more protein breakdown than synthesis) will persist, hence the nutritional support is necessary to survive in chronically ill patients. (see Topic 18: Nutritional Support in ICU).

3. Bacterial overgrowth

Bacterial overgrowth represents a threat to the whole organism due to risk of evoking mucosal inflammation, impairment of gut barrier, bacterial translocation and
bacteremia/sepsis. Symptoms include diarrhea, bloating, distension, abdominal pain, weight loss, fatigue and liver dysfunction.

There are two major components of bacterial overgrowth: increase in adherence and pathogenicity of bacterial strains forming the normal gut flora, particularly enterobacteriaceae (Klebsiella, E.Coli, Pseudomonas spp.) and the decrease in "protective" bacterial strains (Lactobacilli, Bifidobacteria spp) [13-16].

The overgrowth is enabled by the lower intestinal secretion of sIgA, which increase adherence and pathogenicity of bacteria strains as well as changes in phenotype of bacteria demonstrated by enhancement of virulence [17,18].

There are some conditions that predispose to bacteria overgrowth. They include:

a/ starvation or protein malnutrition
b/ stenosis of intestine
c/ dysmotility
d/ exclusion of bowel segment
e/ pouchitis

Starvation or protein malnutrition disrupts indigenous GI tract microflora by decreasing anaerobe and lactobacilli population, allowing overgrowth of aerobic bacteria. It impairs host defense. Fortunately, as shown by others, this condition does not lead to bacteria translocation.

There are several relatively rare conditions causing intestinal stenosis and dysmotility. An important cause is Crohn’s disease in which longstanding inflammation ultimately leads to fibrosis, scarring and contraction both in the transverse and in the longitudinal direction. The other reasons are post-surgical stenoses, stenoses due to radiation enteritis and stenoses due to malignancies. This last category is characterized by a subacute and progressive course, whereas the first category may develop over years and rarely leads to complete obstruction. Sometimes motility disorders are encountered in diabetes, some dysmotility syndromes, scleroderma but also in radiation enteritis. All these conditions lead to the situation, in which virulence factors of commensal bacteria will be stimulated, leading to bacterial overgrowth.

Exclusion enteritis is a clinical entity, detected at endoscopy in excluded colorectal segments. Excluded bowel segments show macroscopic and microscopic inflammatory signs. Not only do they show inflammatory activity in the excluded small bowel segment but evidence supporting the relevance of this inflammatory process is derived from the fact that these conditions respond favorably to treatment with antibiotics directed against potentially harmful strains[19]. The benefit is not only achieved in conditions where intestinal segments are surgically excluded, but also in pure starvation, e.g. during long term total parenteral nutrition[20, 21].

Pouchitis occurs in approximately 30% of patients with ileal pouches. Its symptoms include an increase in stool frequency, abdominal discomfort, pain and bleeding and sometimes steatorhea. Bacterial overgrowth, characterized by disturbances in the balance between Clostridia spp and Lactobacilli/Bifidobacteria and increased concentration of bile acids, plays an important role in the pathogenesis [22,23,24]. In most cases pouchitis generally responds favorably to antibiotics like Metronidazole or Ciproxin. Other causes of pouchitis include lack of nutrients like glutamine and butyrate and obstruction caused by pouch itself.[25]

4. Gut-Liver axis

4.1 Intestinal inflammation and liver disease

Whereas the data regarding the relevance of the specific influence of bacterial translocation on the occurrence of MOF are not very convincing, there is strong evidence that gut dysfunction is related to liver abnormalities [26,27,28]. The impairment of GI tract can be so advanced that surgeon use terms such as ‘abdominal catastrophe’ to emphasize the impact of such state on the whole organism.

Bacteria and bile acids can play a prominent role in the genesis of intrahepatic cholestasis, because bacterial hydroxylation of primary bile acids yields secondary bile
acids, some of which are cholestatic [29, 30]. Bile acid metabolism is changed in short bowel syndrome and patients with bile acid malabsorption are more prone to develop diarrhea and cholestasis. The exact mechanism is not fully elucidated but secondary bile acids are cytotoxic both for the biliary tree and for the colon. Mechanisms that prevent from hepatotoxicity include intricate mechanisms, such as balanced bile acid composition, effective secretory pathways depending on hepatocyte nuclear receptors, cytokines, ileal peptides and adequate phospholipid secretion [31, 32]. Several reports demonstrated also beneficial effects of ursodeoxycholic acid on cholestasis due to it normalize bile acids pool [31, 32, 34]. Secretory IgA (sIgA) also is of utmost importance in the mechanism of liver failure due to gut-liver axis, because it constitutes a major defense mechanism against bacterial invasion of the gut mucosa. The decrease of its concentration increases bacterial mucosal adherence, the proliferation of enterobacte thus impairs mucosal defense, as precisely showed in studies in rats [28] Starvation of the gut always results in the decrease of sIgA in bile, even if the organism is fed parenterally. [27] The clinical case of patient, presented in Fig 2, proves that gut impairment can lead to liver dysfunction and treatment of this condition may help to recover. This patient suffered from a bowel wall disruption and a jejunal fistula opening into the wound as a double barrel stoma. In this patient the proximal output of the fistula was collected and re-infused into the distal part of the small bowel. He required total parenteral nutrition and developed cholestasis (increased Alkaline Phosphatase, gamma-GT and bilirubin) accompanied by hypertriglyceridemia and fatty liver. However, after re-infusion of gut secretion into the distal defunctionalized part of the small bowel these values normalize [26]. Refunctionalisation of the gut relieved the liver abnormalities.

![Image](image-url)

**Figure 2**: Proximal jejunal fistula in the midline of the abdomen. Suction drain brown yellow. Infusion drain white.

### 4.2. Pathological states and the Gut-Liver axis

#### 4.2.1. Short Bowel Syndrome (SBS)

After a major ileal resection, there is interruption of the enterohepatic cycle of bile salts. This disturbance of gut-liver axis may result in severe liver steatosis and cholestasis, progressing to fibrosis, cirrhosis and liver insufficiency. The clear demonstration of such situation are premature birth infants with necrosing enterocolitis (NEC) which led to major resection and SBS requiring total parenteral nutrition (TPN). Those patients develop liver failure quickly, which proves the existence of the importance of gut-liver axis [33, 35, 36]. Their liver condition may be also worsened by depletion of body mass, lack of glutamine and bacterial overgrowth as well as the parenteral feeding regimen itself [37].
4.2.2. Bypass operations for morbid obesity and blind loops

The existence of an active Gut-Liver axis is also supported by the severe liver insufficiency that may arise in patients undergoing bypass surgery for morbid obesity. In the last decade a number of reports in the literature mentions liver transplantations performed for this condition [38, 39]. This pathological state proves that in the iatrogenic “short bowel” situation parenteral nutrition is not required to develop liver disturbances. The functional short bowel situation itself that is created and the presence of a blind loop are important causative factors for liver disease. Evidence supporting the last contention comes from the observation that treatment with Metronidazole relieves part of the fatty liver component of the disease in patients [19]. Similarly removal of the blind loop in dogs has been shown to be beneficial [40].

4.2.3. Kwashiorkor

Kwashiorkor represents one of three types of malnutrition (the other are marasmus and mixed type), but in contrary to other two, in this type inflammatory processes are superimposed. [36]. Some of kwashiorkor patients develop liver steatosis due to ongoing inflammation, while the others demonstrate hepatomegaly and cholestasis [41,42,43].

4.2.4. Cholestasis and Primary Sclerosing Cholangitis

The presence of a normal bile acid pool and normal composition of bile acids and content of sIgA is important for the resistance of the gut and the liver against bacterial actions. The absence of normal bile and sIgA during extrahepatic cholestasis may therefore lead to a vicious circle and aggravate the situation by adding an intrahepatic component to the extrahepatic component. In clinical practice it may be advisable to administer bile enterally when bile can be drained in case of extrahepatic biliary obstruction.

Primary Sclerosing Cholangitis (PSC) is an enigmatic disease usually accompanying Inflammatory Bowel Disease. Recently circumstantial (epidemiological) evidence has been presented that patients with primary biliary cirrhosis have leakier guts than control patients. It is debatable whether the hepatic inflammatory process is the result or the cause of the diminished mucosal barrier function. Stronger support can be derived from the observation that patients with celiac disease have an increased risk to develop liver cirrhosis. The inflammatory signs in the liver are alleviated by strict adherence to a gluten-free diet and improvement of gut morphology and function. An important question is why in IBD specifically the bile ducts are affected whereas this is not the case in celiac disease. Several potential explanations can be offered. New epidemiological data suggest that IBD may also coincide with primary biliary cirrhosis (PBC), implying that IBD is not specifically or exclusively related to PSC [44]. Secondly the severity of the inflammatory process in the gut may be a determinant of the inflammatory process in the liver. Furthermore there may be a genetic heterogeneity in the pro-inflammatory and anti-inflammatory effects of the cytokine cascade.

4.3. Parenteral Nutrition and Liver disease

Parenteral nutrition itself may be the reason of liver insufficiency. The disease is called parenteral nutrition associated related liver disease (PNALD), with the end-stage of liver cirrhosis of fibrosis. Severe form of PNALD, called severe liver disease (SLD) is characterized by encephaloapathy, ascites, portal hypertension, GI bleeding and coagulopathy.

Causes of PNALD can be divide into:

a/ patient-related: presence of SBS without ileum or SBS < 150 cm with ileum, colonic exclusion, sepsis, bacterial translocation
b/ nutrition-related: energy overfeeding (> 40 kcal/kg/day), excess of glucose administration (> 7 g/kg/d), lack of essential fatty acids and choline, continuous regime of PN, multi-bottle system (instead of all-in-one admixtures), LCT lipid emulsions. Treatment must be usually multimodal and include change of PN regime (isocaloric feeding, MCT/LCT or omega-3-FA or olive oil based emulsions), reconstruction of GI tract, antibiotics, bowel SCFAs flushes, taurine administration, cyclic feeding and the use of ursodeoxyxolic acid.

5. Therapeutic measures to improve gut integrity

Many studies confirmed increased intestinal uptake of nutrients and fluids after even extensive resections due to increased mucosal surface area. The adaptive response of enterocytes starts within hours after resection, as in case of Na+/glucose transporter or the activity of digestive enzymes. In most cases those positive mechanisms are not sufficient enough to assure proper absorption and some therapeutic measures can be helpful.

5.1. Restoration of GI tract continuity and supportive treatment

The restoration of the normal passage of food and enterohepatic cycle of bile acids should be one of main goals of treatment, as mentioned in 4.1. The other include refunctionalisation of blind loops or widening of stenotic segments, which may help to liquidate obstruction, bowel distention and bacterial overgrowth. Antibiotics are often necessary to delete potentially pathogenic flora. Supplementation with bile acids (ursodeoxyxolic acid) helps to normalize the size and composition of the bile acid pool [34]. Strategy for maximizing intestinal adaptation should focus on: restoration of continuity, provision of optimal dietary constituents, augmentation of growth factors and at the same time suppression of inhibitory factors.

5.2. Specific enteral and parenteral formulas

Enteral nutrition regimen may have beneficial effects on the gut flora and consequently on intestinal inflammation. These adaptations especially regard adaptations of the amino acid composition, the fat content, and the pre- and probiotic composition of the enteral nutrition.

5.2.1. Amino acid and fatty acids composition

Formulas containing arginine, omega-3 fatty acids and RNA have shown favorable effect on intestinal function, especially in elective surgery patients [46]. The multimodality character of the adapted formula has precluded identification of the specific component in the intervention responsible for the benefit, nor it was possible to identify the mechanism underlying the benefit, however it possible that omega-3 fatty acids change the composition of pro- and anti-inflammatory mediators. As proven by metaanalyses, the addition of glutamine to the parenteral feeding regimen (approximately 20 g in adults/day) has beneficial effects in some studies in surgical patients and in other patients not receiving enteral nutrition, improving mucosal barrier function and in critically ill patients for less well explored reasons [47, 48, 49, 56]. The non-critically ill patient population with compromised bowel is not specifically studied for obvious ethical reasons. Enteral glutamine showed also beneficial effect in trauma and burned patients [42].

5.2.2. Pre- and probiotics

The use of pre- and probiotics seemed to be helpful in in chronic IBS and constipation patients. Although a beneficial trend can be identified, the multitude of different pre- and
probiotic-mixtures precludes specification of a particular pre- and probiotic mixture achieving the highest benefit. Especially Oligofructoses and Inulin have been shown to have specific effects in IBS (in combination with probiotics) [50] and pouchitis [51, 52, 53] respectively. These soluble fibers are normal food constituents and non-toxic, and therefore prescription of moderate amounts may also be considered when bacterial overgrowth is diagnosed.

In pouchitis inulin decreased the concentration of secondary bile acids and improved the balance between potentially pathogenic enterobacteriaceae, and beneficial bifidobacteria and lactobacilli species [54]. Similar recommendations can be given regarding probiotics. There is a multitude of potentially beneficial strains (for example Lactobacillus spuriun, Lactobacillus acidophilus, Lactobacillus plantarum 299V, Lactobacillus GG, Bifidobacterium lactis, Lactobacillus lactis, Streptococcus thermophiles), which makes definitive conclusions impossible at this stage.

Promising results are available with a probiotic mixture (8 different strains) for prevention and treatment of refractory pouchitis [55]. A word of caution should be expressed regarding the use of probiotics in critically ill patients. Recently probiotics given twice daily (10^10 bacteria total/day) to patients with severe pancreatitis receiving a fiber containing enteral formula proved to cause non occlusive small bowel necrosis in a high proportion of cases [56]. At present is therefore not advisable to use probiotics in critically ill patients.

A very interesting development consists of the genetic modifications of Lactobacillus lactis strains with human genes producing IL 10 [57, 58]. At present the focus of this research is Crohn’s disease, in which a continuing disbalance between pro-inflammatory cytokines (TNF-alpha, IL 1) and anti-inflammatory cytokines (IL 10) is considered to be the cause of ongoing inflammation. Other applications in some of the disease states, described in this module may also be considered.

5.3 Factors promoting intestinal adaptation

Generally, factors promoting intestinal adaptation may be divided into:

a/ Luminal contents
   - luminal nutrients
   - luminal secretions
b/ gastrointestinal regulatory peptides

   - growth factors
   - hormones
   - cytokines
d/ neural influences
e/ changes in blood flow
f/ mesenchymal factors

The role of those nutrients is particularly true after proximal resection, and intestine response in blunted if nutrients are administered intravenously, and not orally. The stimulation depend on the type of nutrient: glucose acts on proximal intestine, whereas fat on mid-part. LCTs stimulates adaptation to greater extent than MCTs, disaccharides are more effective than monosaccharaides. It is also important to avoid deficiencies, such as of zinc or vitamin A – those states impair adaptation. Some gastrointestinal regulatory peptides, such as calcitonin gene-related peptide (CGRP), cholecystokinine (CCK), glucagon-like peptide-2 (GLP-2), gastrin, gastric inhibitory polypeptide (GIP)peptide YY, neurotensin or neuropeptive Y may influence adsorption and stimulate adaptation. Of those, GLP-2 express the greatest potential and gives hope for development of new methods of treatment for SBS patients. [57] On the other hand, hormones such as somatostatin or vasoactive intestinal polypeptide (VIP) counteract the adaptation. [4]
6. Summary

Most of the digestion and absorption of macronutrients occurs in the proximal part of the intestine (oral cavity to jejunum) whereas electrolytes and fluid are absorbed in the whole gut. The distal ileum absorbs bile acids and vitamin B₁₂. In the colon soluble fiber is fermented and short-chain fatty acids produced and absorbed. Many surgical or disease related anatomical abnormalities (stenoses, blind loops, bypasses, motility disorders, pouches) lead to bacterial overgrowth, inflammation of the gut wall and malabsorption of nutrients. All aspects of gut function (motility, digestion, absorption) are disturbed in critical illness due to inflammatory activity, induced in the gut (as well as in all other tissues/organs in the body). The role of increased permeability as a sign of intestinal inflammation, in translocation of bacteria and in the genesis of multiple organ dysfunction syndrome is uncertain, but there is a clear pathogenetic connection between inflammatory activity in the intestine and cholestasis, steatosis and possibly steatohepatitis. Fat in parenteral nutrition may aggravate these abnormalities and a combination of nutritional and intestinal factors may ultimately lead to liver insufficiency especially in neonates.

Treatment of the compromised gut consists of surgical or/and medical restoration of normal bowel passage and function as well as of treatment of primary infection/inflammation. Adaptation of the nutritional regimen (immuno-nutrition) may play an adjunctive beneficial role.

7. References