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ORIGINAL PAPER

Bio-ecological control of chronic liver disease and encephalopathy

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Abstract Minimal encephalopathy was originally associated with chronic liver disease but is increasingly associated with most other chronic diseases and particularly with diabetes and also chronic disorders in other organs: kidneys, lungs, thyroid and with obesity. It is increasingly with dramatically increased and more or less permanent increase in systemic inflammation, most likely a result of Western lifestyle. Frequent physical exercise and intake of foods rich in vitamins, antioxidants, fibres, lactic acid bacteria etc in combination with reduction in intake of refined and processed foods is known to reduce systemic inflammation and prevent chronic diseases. Some lactic acid bacteria, especially *Lb paracasei*, *lb plantarum* and *pediococcus pentosaceus* have proven effective to reduce inflammation and eliminate encephalopathy. Significant reduction in blood ammonia levels and endotoxin levels were reported in parallel to improvement of liver disease. Subsequent studies with other lactic acid bacteria seem to demonstrate suppression of inflammation and in one study also evidence of clinical improvement.

Keywords Chronic liver disease · Liver cirrhosis · Encephalopathy · Inflammation · Life style · Lactic acid bacteria · Probiotics · Prebiotics

Minimizing hepatic injuries

Fifty years have passed since Rolf Olsson (24/3 1936–27/2 2008) (Fig. 1), later the first professor of hepatology in Sweden, and I started our research project aimed to

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Fig. 1 Professor Rolf Olsson

minimize and/or revert the extent of various types of injuries to the liver. We did during app one decade study various mainly acute but also chronic injuries: toxic (Bengmark and Olsson 1962a, b, 1963a, 1964b), liver resection (Bengmark and Olsson 1964a; Bengmark et al. 1964a, b, 1966a, b), biliary obstruction (Bengmark et al. 1966b) and in nutrition-induced liver cirrhosis (Bengmark et al. 1966c) mostly in rats, but also after liver resection in man (Almersjö et al. 1969). We knew little at that time about the innate immune system, inflammation, and the concept of apoptosis, but felt more or less instinctively that some substances might be favourable to protection against and healing of liver injuries. We observed early that female animals suffered greater toxic injuries than male, which stimulated us to try testosterone to minimize injury by supplementing testosterone both after toxic (Bengmark and Olsson 1962b, 1963c, 1964b), surgical injury (Bengmark and Olsson 1964a; Bengmark et al. 1966a) and in nutrition-induced cirrhosis (Bengmark et al. 1966c). The association between vitamin B12 and nucleic acid synthesis stimulated us also to try the effects of supplementation of this vitamin (Bengmark and Olsson 1962a, 1963a). We mainly looked at parameters such as wet and dry liver weight, transaminases in liver tissues, but also at influences on the changes in glycerides, cholesterol and phospholipids in the residual liver (Bengmark et al. 1964b) and the capacity to conjugate bile acids (Bengmark et al. 1964a). Positive effects of both treatments were reported, but it should last many years before these observed effects could be further explained.

Sustained exaggerated inflammation in focus

The progress in molecular biology and especially molecular genetics has provided new and important information about the innate immune system and the reactions to

both physical and mental stress—see further Bengmark (2001, 2004, 2006–2008). Increasing evidence suggest that inflammation precedes and paves the way for subsequent acute and chronic disease and complications to disease—"*the challenge in critical illness is less the infection than the exuberant inflammatory response*" (Taneja et al. 2004)—and the conditions are much the same also in most chronic illnesses. It has been observed in such chronic illnesses that signs of exaggerated systemic inflammation can be detected several years (example Alzheimer's disease) to a few weeks (example: mental depression) before clinical signs of disease are obvious. Numerous factors contribute to increased systemic inflammation, among these are, to mention only a few:

- *Low serum and tissue levels of vitamins and antioxidants*. It is well known that individuals living at high altitudes, North or South, suffer higher incidences of chronic diseases, which is strongly associated with low levels in serum of vitamins and antioxidants, due to lower consumption of fruits and vegetables but also to reduced exposure to sun. Vitamin D in serum for example is significantly lower at higher than lower altitudes and inversely associated to high incidence of coronary heart disease (Zittermann et al. 2005).
- *Lack of physical exercise*. Lack of exercise and restrictions in motility are known to be associated with increased vulnerability to oxidative and nitrosative stress and shown to be fundamental in the cascade of events resulting in neuronal degradation, especially in the hippocampi. Thus, physical exercise has been shown to reduce oxidative and nitrosative stress, reduce systemic inflammation and improve neuroendocrine autoregulation and counteract disease and age-related neuronal degeneration, brain ischemia and traumatic brain injury (Kiraly and Kiraly 2005).
- *Mental and physical stress*. Serum markers of inflammation increase significantly after both mental challenge and physical exercise and the levels of response are generally higher in patients suffering chronic diseases such as coronary heart disease (Kop et al. 2008). A strong association is found after mental challenge between markers of stress, increases in CRP and IL-6, and increased norepinephrine response.
- *Smoking and excessive use of alcohol*. Former smokers demonstrate compared to never smokers significantly higher levels of CRP and current smokers significantly elevated concentrations of most circulating inflammatory markers, supporting the association of smoking with a systemic inflammatory state (Levitzky et al. 2008). A significantly decreased HLA-DR expression, increased reactivity for CD123 and increased secretion of interleukin (IL) 1beta, IL6, IL12, and tumor necrosis factor-alpha (TNFalpha) by dendritic cells is observed in persons with chronic alcohol consumption, and so even if liver disease is absent (Laso et al. 2007).
- *High intake of proinflammatory foods*. High levels of glycated and lipoxidated proteins and peptides in the body are strongly associated with high level of systemic inflammation, chronic diseases and premature aging. Such molecules arrive in the body mainly through smoking, and to an even higher degree, through intake of food rich in such pro-inflammatory molecules. Heat-treatment,

irradiation and ionisation of foods are known contributors of dys-functioning and pro-inflammatory molecules, which are increasingly produced as the temperature of heated foods exceeds 80°C, see further Bengmark (2007) and Fig. 2. They are also formed when foods like powder milk, a common ingredient in many foods such as icecream, but also in clinical nutrition solutions and baby formulas, are stored for longer periods of time in room temperature (Baptista and Carvalho 2004). RAGE, a member of the immunoglobulin superfamily of cell surface molecules and receptor for advanced glycation end products, known since 1992, functions as a master switch, induces sustained activation of NF-κB, which in its turn activates more than 400 enzymes, suppresses a series of endogenous auto-regulatory functions and converts long-lasting pro-inflammatory signals into sustained cellular dysfunction and disease. This activation is associated with high levels of dys-functioning proteins in body fluids and tissues, and strongly associated with a series of diseases from allergy and Alzheimer to liver cirrhosis and Parkinson's disease. Other food-derived pro-inflammatory molecules are gluten in wheat, but also in rye and barley, and certain food-derived hormones like oestrogens, particularly 17-β oestradiol (Wolford and Argoudelis 1979; Malekinejad et al. 2006), and IGF-1 (Outwater et al. 1997; Holmes et al. 2002a, b) known for their pro-inflammatory and carcinogenic abilities. The main human source of these hormones is cow's milk. These hormones are increased about hundred times in pregnancy and modern commercial milk arrives to about 80% from pregnant cows. It is of considerable interest in this connection that most chronic diseases have increased in Japan during in recent years (1950–1998), for example prostatic cancer by 25 times, much in parallel to increase in intake of meat by 9 times and dairy products by 20 times (Ganmaa et al. 2002). High intake of dairy is also increasingly associated with neurodegenerative disease, especially with Parkinson's disease (Chen et al. 2007).

- *Low intake of anti-inflammatory foods*. Plants in general, and particularly vegetables, as well as some specific lactic acid bacteria (LAB) are increasingly recognized for their strong anti-inflammatory potentials—see further below.

HEATED DAIRY: powdered milk (ice cream, baby & clinical nutrition formulas) cheese, espec when heated: rich in pizza, tacos, nachos, salads, fast-food sandwiches and sauces & brown cheeses

HEATED GRAIN PRODUCTS: Bread esp. toasted bread, bread crusts & crisp breads

HEATED MEAT, POULTRY, FISH: especially cured meat (bacon, sausages). Content increases as one goes from boiling to oven frying: boiling (1000 kU/serving) < roasting (4300 kU)< broiling (5250 kU) < deep frying (6700 kU) < oven frying (9000 kU/serving). (Goldberg T et al. 2004)

OTHER FOODS: Egg yolk powder, lecithin powder, coffee, espec dark roasted, hard-cured teas, roasted and salted peanuts, dark and sugar-rich alcoholic beverages, broth, Chinese soy, Balsamic vinegar, Cola drinks etc

Fig. 2 Examples of foods rich in pro-inflammatory molecules (glycated and lipoxidated products)

Gastrointestinal tract—the pacemaker of the innate immune system

The main concept was for long that the innate immune system has its main location in the bone marrow, spleen and lymph nodes. During the last 20 years, however, it has become increasingly evident that the gut is the main location of this important defense system. It is suggested that 70–80% of it is located in the gut (Brandtzaeg et al. 1989). The composition of the microbionta (microbial flora) and food that we eat has a profound effect on the function of the innate immune system, aging and development of disease. Crosstalk between microbionta and immune cells in the wall of the intestine is of immense importance for immune reactions. Under optimal circumstances is the gut expected to contain up to 2 kg of bacteria and about 2 million genes, to compare with the about 25,000 genes in the eukaryotic part of the body. However, some bacteria seem not to tolerate Western lifestyle, which is why the microbionta in modern man is considerably reduced in diversity and numbers of bacteria (Finegold et al. 1983; Ahrné et al. 1998). An increasingly reduced microbionto is also observed in elderly, and associated with deficient intestinal epithelial integrity and reduced production of intestinal barrier produced components such as sIgA, mucins, defensins and secretions such as gastric acid. CMV or other viral infections are common in these individuals and associated with further chronic impairment of immune functions and especially T-cell immunity expressed as low ratio of naive/memory T cells.

The deranged intestinal microbionta represents an important source of continuous antigenic stimulation and contribute to development of chronic diseases and to immunosenescence (van Tongeren et al. 2005; Pancer and Cooper 2006). The best strategy against such a development seems to be, in addition to a control of stress and proper nutrition

- continuous physical exercise (Kohut and Senchina 2004)
- reduction of the antigenic load from pathogens, such as influenza virus and cytomegalovirus (CMV) by vaccination (Candore et al. 2008). No such vaccine does yet exist.
- reduction of the antigenic load by dietary supplements containing prebiotics, probiotics, and a combination of these—synbiotics. Such treatments have shown capacity to down-regulate hypersensitivity reactions, such as food intolerance and atopic eczema, and to increase phagocytosis (Tlaskalová-Hogenová et al. 2004; Debarry et al. 2007; Woodmansey 2007).

Manifestations of chronic diseases

Several changes in the body are common in chronic endemic diseases, and most likely a result of Western lifestyle, permanent elevated systemic inflammation and intake of foods. Among these are paradontosis, osteoporosis and minimal encephalopathy, for long only identified mainly in connection with chronic liver disease, but increasingly identified in chronic kidney, chronic lung (COPD), chronic thyroid, diabetes, extreme obesity and other chronic conditions. All these manifestations are increasingly recognized as risk factors for coronary heart disease and diabetes, but also for other chronic diseases. It has long been puzzling why

osteoporosis is so frequent in Western Societies despite an intake of minerals which is many times higher than in some rural areas, where this condition is more or less non-existing. A recent American study recently reports significantly reduced bone density in older women consuming >3 Cola-drinks (rich in AGE and ALE) per week compared to matched controls consuming similar amounts of other carbonated soft drinks (Tucker et al. 2006). It has also been observed in COPD patients that those who consume cured meat (bacon, sausages, luncheon meats, and cured hams, all rich in AGE and ALE) more than 14 times a month demonstrate a significantly reduced ventilation capacity (FEV1) by 110 ml compared to those who eat such foods 3–4 times per month (−12 ml) (Jiang et al. 2008). This is especially interesting as it is reported that a rich intake of solid fruits and especially catechins (rich in tea and apple) is associated with an increase in FEV1 by no less than 130 ml and accompanied by significant reduction of the four main COPD symptoms: chronic cough, phlegm, breathlessness (Tabak et al. 2001). These observations might have implications also to other manifestations of chronic diseases, including various encephalopathies. As a matter of fact, a most recent study (Kuhad and Chopra 2007) reports a significant attenuation not only of oxidative stress, inflammation, cholinergic dysfunction but also cognitive deficit in diabetic rats supplemented 60 mg/kg bw of curcumin (ingredient of turmeric, known for its anti-inflammatory abilities—see Bengmark 2006, 2008).

Accumulation in the body of dys-functioning proteins

Increased levels in the body of various AGE /ALE-substances are reported in almost all chronic diseases from allergy and Alzheimer's disease to polycystic ovary syndrome and various urogenital diseases (Table 1). An association with dairy products is this far reported in conditions such as allergy, coronary heart disease, diabetes, Parkinson's disease, and in various cancers such as breast, prostatic, testicular, and ovarian malignancies (See further Bengmark 2007). Significantly increased AGE/ALE levels are also reported in diseases with hitherto obscure

Table 1 Diseases associated with with increased levels of AGEs and ALEs in the body

Diseases associated with elevated AGEs/ ALEs	
• Aging	• Cataract
• Allergy	• Glaucoma
• Autoimmune diseases	• Macula degeneration
• Alzheimer's disease	• Diabetes
• Parkinson's disease	• Hormone deficiencies
• Amyotrophic lateral sclerosis	• Polycystic ovary syndrome
• Huntington's disease	• **Liver cirrhosis**
• Stroke	• Chronic pulmonary disorders
• Familial amyloidotic polyneuropathy	• Rheumatoid diseases
• Creutsfeldt-Jakob disease	• Fibromyalogia
• Down's syndrome	• Ruptured Achilles tendon
• Atherosclerosis	• Osteoporosis
• Cardiovacular disease	• Nephropathies
	• Paradontosis

etiology such as rupture of the Achilles tendon (Reddy 2004) and fibromyalgia (Hein and Franke 2002). Of special interest in this connections are the observations of rich accumulation of AGE/ALE in chronic liver diseases such as NASH (Hyogo et al. 2007) and, even more in pronounced liver cirrhosis (Yagmur et al. 2006). The level of AGE/ALE in serum increases with Child stage of liver cirrhosis, similar to that of hyaluronan (Yagmur et al. 2006). Furthermore, The AGE/ALE levels are observed to be reduced but not normalized after liver transplantation (Sebeková et al. 2002), which could well explain the remaining higher risk of developing other chronic diseases even after liver transplantation.

It has been demonstrated that vegans much in contrast to meat-eaters and lacto vegetarians have significantly lower levels of AGEs/ALEs in the body (Sebeková et al. 2001). As a matter of fact it has been shown that lacto-vegetarians have slightly higher levels of AGEs/ALEs in the body than meat-eaters, which might be explained by a higher intake of dairy products, especially cheese, but might also be influenced by a higher intake of fructose. Significant health advantages are reported for vegans, when compared to lacto-vegetarian and omnivorous : statistically significantly lower levels of pro-inflammatory molecules such as cytokines and acute phase proteins, lower systolic and diastolic blood pressure, lower total cholesterol/s, lower LDL-cholesterol/s, lower fasting blood sugar and triglycerides and lower incidence of chronic diseases, especially diabetes and complications to diabetes.

Effects of pro- and synbiotics

Only a few probiotic strains have this far shown ability to eliminate or reduce unwanted pro-inflammatory molecures such as AGE, ALE, glutenoids and heterocyclic amines from foods. Furthermore, only a minority of several hundred tested probiotic strains have demonstrated ability to suppress inflammation in the body, when supplemented. Especially desirable strains are those that improve immune function by increasing the number of IgA-producing plasma cells, improve phagocytosis, and the proportion of Th1 cells and NK cells (Ouwehand et al. 2002). The genetic differences between different lactic acid bacteria are large, by some said to be larger than between fish and man. The choice of probiotics for clinical use is critical, especially as strains which carry the same name have often different and sometimes opposite effects. A recent study selected 46 strains of *Lactococcus lactis* from about 2,600 LAB and compared the ability to induce production of cytokines by strains was studied (Suzuki et al. 2008). Even if the different strains carried the same name did their ability to produce pro- and anti-inflammatory cytokines vary widely, which seems to underline the importance of a meticulous choice for clinical studies and use. Some strains, however, are more likely to have strong clinical effects, among them are strains like *lb paracasei* subsp *paracasei, lb plantarum,* and *pediococcus pentosaceus.* Especially *lb paracasei* has a solid record. It has been shown to induce cellular immunity and stimulate production of suppressive cytokines such as TGFβ and Il-10 and to suppress Th2 activity and CD4 T-cells (von der Weid et al. 2001; Ibnou-Zekri et al. 2003), suppress splenocyte proliferation (Nagler-Anderson 2000) and decrease antigen-specific IgE and IgG1 (Prioult et al. 2003). *Lb paracasei* was also shown to be the strongest inducer of Th1 and repressor

of Th2 cytokines when more than one hundred strains were compared (Fujiwara et al. 2004). A recent study compared in rats compared the ability of four different strains: *Lactobacillus paracasei*, *Lactobacillus johnsonii*, *Bifidobacterium longum*, or *Bifidobacterium lactis* to control *Trichinella spiralis*—induced infection, only *lb paracasei* but not the other LAB were able to reduce the infection-associated Th2 response, muscle levels of TGF-β, COX-2 and PGE2—attenuate infection-induce muscle hypercontractility (Verdú et al. 2004). An even more recent study compared three probiotic strains: *Bifidobacterium lactis* NCC362, *Lactobacillus johnsonii* NCC533, and *Lactobacillus paracasei* NCC2461 and their effects on stress-induced changes in gut permeability & on sensitivity to colorectal distension. Again only *Lb paracasei* but not the other LAB did significantly prevent visceral hyperalgesia, reduce visceral pain and restore normal gut permeability (Eutamene et al. 2007). But also Lb plantarum has an excellent record. When the ability of fifty different LAB to control 23 different *Clostridium difficile* (C diff) strains were studied, only *Lb paracasei* and *Lb plantarum* were effective to eliminate all C diff strains—more than half of the tried LAB strains were totally ineffective, and some only against a few (Naaber et al. 2004). Some LAB can be potentiated by simultaneous supply of prebiotic fibres (probiotics + prebiotics => synbiotics) but there are great differences in their ability to utilize, especially semi-fermentable fibres such as oligofructans. When 712 different LAB strains were tested did only a handful demonstrate ability to ferment inulin and phlein, namely : *Lactobacillus plantarum* (several), *Lactobacillus paracasei* subsp. p*aracasei, Lactobacillus brevis* & *Pediococcus pentosaceus* (Müller and Lier 1994).

After analysis of the anti-inflammatory effects of more than 550 different lactic acid bacteria strains was a new synbiotic composition constructed, consisting in *Lactobacillus plantarum*, *Lactobacillus paracasei* subsp. p*aracasei, Lactococcus raffinolactis* and *Pediococcus pentosaceus.* To the composition was added four different fibres known for their strong bioactivity: betaglucan, inulin, pectin and resistant starch and the composition given the name of Synbiotic 2000, a composition, which successfully has been tried in a series of especially acute disorders.

Pro- and synbiotic effects on liver and brain functions

Increasing evidence suggest that probiotics, alone and/or in combination with plant antioxidants and fibres, possess strong neuro-endocrine modulatory effects and alleviates effects of physical and mental stressors both early (Gareau et al. 2007) as well as later in life (Eutamene and Bueno 2007). We have undertaken two studies with the above-mentioned synbiotic in patients with liver cirrhosis and minimal encephalopathy (MHE), the first in a mainland China population (Liu et al. 2004) and the second in an Australian population (Riordan et al. 2007).

In the first study 55 patients with MHE were randomized to receive for 30 days Synbiotic 2000 (n=20), the fibres in the compostion alone (n=20), or placebo (n=15). Cirrhotic patients with MHE were found to have substantial derangements in the gut micro-ecology, with significant fecal overgrowth of potentially pathogenic *Escherichia coli* and *Staphylococcal* species. Synbiotic treatment significantly

increased the fecal content of non-urease-producing *Lactobacillus* species at the expense of these other bacterial species. This modulation of the gut flora was associated with a significant reduction in blood ammonia levels and reversal of MHE in 50% of patients. Synbiotic treatment was also associated with a significant reduction in endotoxemia. The Child-Turcotte-Pugh functional class improved in nearly 50% of cases (Liu et al. 2004). Treatment with fermentable fibres alone was also of benefit in a substantial proportion of patients. This study was received with some enthusiasm by hepatologists world-wide and leading hepatologists (Solga and Diehl 2004) commented: "The study by Liu et al. merits attention as a big step forward in the translation of such research to humans. Their finding that gut therapy improved hepatic inflammation, and overall liver function in cirrhotic patients (mostly with viral hepatitis) has implications for the pathogenesis of liver disease, as well as its clinical management." "Liu et al. have made a major contribution to the application to gut flora therapy to humans with liver disease. We expect this research will stimulate further interest in the study of gut flora therapy and the "gut-liver" axis, because the liver does, indeed, care about the gut."

In the second study thirty cirrhotic patients were randomized to receive Synbiotic 2000 or placebo preparations for only 7 days. Viable faecal counts of Lactobacillus species, Child-Pugh class, plasma retention rate of indocyanine green (ICGR15), whole blood tumour necrosis factor alpha (TNF-a) mRNA and interleukin-6(IL-6) mRNA, serum TNF-a, soluble TNF receptor (sTNFR)I, sTNFRII and IL-6 and plasma endotoxin levels were measured pre- and post-treatment (Riordan et al. 2007). The treatment with Synbiotic 2000 was associated with significantly increased faecal lactobacilli counts and significant improvements in ICGR15 and Child-Pugh class. Significant increases in whole blood TNF-a mRNAand IL-6 mRNA, along with serum levels of sTNFRI and sTNFRII, were also observed and TNF-a and IL-6 levels correlated significantly, both at baseline and post-synbiotic treatment. Synbiotic-related improvement in ICGR15 was significantly associated with changes in IL-6, both at mRNA and protein levels, but was unrelated to plasma endotoxin values. No significant changes in any study parameter followed placebo treatment. It was concluded that even short-term synbiotic treatment modulates significantly gut flora and improves liver function in patients with cirrhosis (Riordan et al. 2007).

Four other studies have subsequently been done. Twenty-two non-alcoholic fatty liver disease (NAFLD), 20 alcoholic liver cirrhosis (AC) and 36 HCV-positive patients were treated with 450 billion of VSL#3 for 3 months (Loguercio et al. 2005). Improvements were observed in plasma markers of lipid peroxidation in both NAFLD and AC, but not in HCV-positive patients, in malondialdehyde (MDA) & 4-hydroxynonenal (4-HNE) and only in AC patients in cytokines (TNF-a, IL-6, and IL-10). It was also reported that "routine liver damage tests" were improved at the end of treatment in all groups. No information was provided on effects on encephalopathy or infections. Significant improvement of the intestinal colonization ($P<0.001$) and trends to lowered endotoxemia ($P=0.07$) and improvement in Child-Pugh score ($P=0.06$) was reported from a study in 39 patients with liver cirrhosis receiving either *E. coli Nissle* or placebo for 42 days (Lata et al. 2007). However, no information was given to effects on encephalopathy. A composition consisting in *Bifidobacterium longum +2.5 g* fructoligosaccharides or placebo was supplemented

for 90 days to 60 cirrhotic patients (Malaguarnera et al. 2007). Significant reductions in fasting ammonia (P=0.003) and improvements in various neuropsychiatric tests (Trail Making Test-A & B, symbol digit modalities, test block design p=.000) and in Mini Mental State Examination (MMSE) were reported. A small study in 12 patients with alcoholic cirrhosis, who during 4 weeks were supplemented three times daily with 65 ml of a probiotic drink containing *Lb casei* Shirota was recently reported. Baseline neutrophil phagocytic capacity was significantly lower compared to healthy controls (73% versus 98%, $p<0.05$), but normalised by the end of the study. TLR2, 4 and 9 were over-expressed in the patients and TLR4 expression normalized by the end of the study. Soluble TNF-receptor (sTNFR)-1 and-2 and interleukin (IL)10 were significantly elevated in patients' plasma, but was not altered by the treatment. However, no "improvement was seen in disease control" (Stadlbauer et al. 2007).

Final words

Aging and various chronic diseases are all associated with an increasingly deranged function of the neuro-endocrine axis resulting in an increased status of inflammation (Bengmark 2001, 2004, 2008; Vasto et al. 2006). This affects the intestinal microbionta, which becomes reduced both in diversity and numbers. Minimal encephalopathy is increasingly recognized as an ingredient in most chronic diseases and strongly associated with a discrete but sustained level of increased systemic inflammation. Continuous supplementation of pro- and synbiotics, but also plant fibres and antioxidants, provides a promising alternative in order to suppress inflammation, reduce the risk of developing other chronic diseases or complications to disease and to considerably improve quality of life for these patients. It is of the greatest interest that suppression of inflammation by treatment with Synbiotic 2000 will in surgical operations such as liver transplantation reduce, not to say, eliminate the problem of postoperative infections (Rayes et al. 2005). Synbiotic treatment has also in animal models shown a unique ability to suppress inflammation: neutrophil accumulation in tissues, release of markers of inflammation: myeloperoxidase, malondialdehyde, nitric oxide and to prevent destruction of tissues (Tok et al. 2007). This offers great hope for the future.

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