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Addressing Inflammatory Bowel Disease (IBD)

White Paper by
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Inflammatory bowel disease (IBD) refers to a group of chronic inflammatory disorders of unknown cause involving the gastrointestinal tract. Chronic IBD may be divided into two major groups:

- Chronic nonspecific ulcerative colitis, and
- Crohn's disease

The original description of the disease by Crohn, Ginzberg and Oppenheimer in 1932 localized the disease to segments of the ileum (the last part of the small intestine). However, the mucosa, esophagus, stomach and small bowel may also be involved. This is known as regional enteritis. In addition, a similar inflammatory site may occur in the colon, either alone or with accompanying small intestinal involvement.

Epidemiologic and Etiologic Considerations

The epidemiologic and etiologic considerations in ulcerative colitis and Crohn's disease share many features. These diseases are more common in Whites than in Blacks and Asians, with an increased incidence (3 to 6 fold) in Jews compared with non-Jews. Both sexes are equally affected. The incidence and prevalence of the two diseases differ slightly with most studies showing ulcerative colitis to be more common. A family incidence of IBD has been recorded with estimates that 2 to 5 percent of persons with Crohn's diseases or ulcerative colitis will have one or more relatives affected. An increased incidence of Crohn's disease in monozygotic twins provides strong evidence for a genetic component.

Symptoms

The major symptoms of ulcerative colitis are bloody diarrhea and abdominal pain, often with fever and weight loss in more severe cases. With mild disease, there may be one or two semi-formed stools containing a small amount of blood with no systemic manifestations. In contrast, the patient with severe disease may have frequent liquid stools containing blood and pus, complain of severe cramps, and demonstrate symptoms and signs of dehydration, anemia, fever and weight loss. With predominantly rectal involvement, constipation rather than diarrhea may be present. The major symptoms of Crohn's disease are fever, abdominal pain, and diarrhea often without blood, generalized fatigue and weight loss.

Systemic complications of inflammatory bowel disease include:

- Nutritional consequences such as weight loss, decreased muscle mass, growth retardation in children, and electrolyte deficiency (specifically potassium, magnesium and calcium)

- Hypoalbuminemia which is due to malnutrition and protein losing enteropathy
- Anemia
- Bile salt deficiency which occurs when the disease affects a part of the small intestine called the ileum
- Fat soluble vitamin deficiency
- Increased colonic oxalate absorption which may increase the risk for renal stones, and
- Increased lithogenicity of bile which may increase the risk for gallstones

Musculoskeletal consequences include:

- Peripheral arthralgia
- Arthritis
- Ankylosing spondylitis
- Sarcoidosis, and
- Granulomatous myositis (rare)

Liver and gallbladder consequences include:

- Fatty liver,
- Cholelithiasis,
- Pericholangitis,
- Biliary cirrhosis,
- Sclerosing cholangitis,
- Bile duct carcinoma,
- Chronic active hepatitis, and
- Cirrhosis.

Skin and mucous membrane consequences include:

- Erythema nodosum
- Pyoderma gangrenosum
- Aphthous stomatitis, and
- Crohn's disease of gingival and vagina

Consequences of the **eye** include:

- Iritis
- Uveitis, and
- Episcleritis

Regarding the **circulatory system** there is a risk for:

- Venous thrombosis, and
- Thromboembolism

The Nutritional Approach

Nutritional support can offer profound beneficial effects on inflammatory bowel diseases. The steps to addressing IBD include dietary modification, elimination of intestinal health antagonists, probiotic supplementation and targeted supplementation.

The Specific Carbohydrate Diet (SCD)

The principles of the specific carbohydrate diet began to take shape in 1951, after years of clinical research by Drs. Sidney and Merrill Haas. This research was continued by Elaine Gotshall, M.Sc, and published in 1985 in the journal *Acta Anatomica* (123:178). The basics of the diet are to avoid specific carbohydrates that may not be digested in individuals with inflammatory bowel diseases. The lack of digestion results in malabsorption of specific carbohydrates, fermentation, over growth of bacteria, and increased bacterial by-products and mucus production. These cause direct inflammation and damage to the intestinal lining.

The carbohydrates to be avoided are usually disaccharides, which are two simple sugars bound together. Specific foods must be avoided to prevent the ingestion of these carbohydrates including all grain products, potatoes, yams, parsnips, chickpeas, soy, bean sprouts, all forms of sugar (except honey), and foods containing milk and lactose.

The SCD program should also focus on reducing omega 6 fats, increasing omega 3 fats and medium chain triglycerides, and eliminating foods and substances that may negatively challenge gastrointestinal health.

Intestinal Health Antagonists

Microparticles

In February 2001, a study in the *European Journal of Gastroenterology and Hepatology* presented ground breaking information – there are substances commonly found in our environment (such as in soil residue) that enter our food supply via processing, which could initiate an exacerbation of intestinal symptoms in patients with Crohn's disease. Thus, an avoidance of these substances could actually improve the intestinal health of patients with Crohn's. The study focused on what are called microparticles.

The most common microparticles are titanium dioxide, aluminosilicates, anatase, and naturally occurring calcium phosphate.

Items To Avoid That May Contain Microparticles:

- Ready made meals (frozen foods, TV dinners, complete microwave meals), processed meats/fish, and egg beaters
- Tea/coffee whiteners (such as non-dairy creamer)
- Flavored milk products
- Mozzarella, cottage and processed cheese
- Fibrous skins, skins from fruits and vegetables with soil residue, and dried/candied fruit
- Whole grain flour or bread, refined flour, breakfast cereals, instant noodles, and bakery products
- Icing, sugar, lemon curd, and confectionary products
- Processed sauces, sea salt, soft drinks, and spices with anti caking agents
- Soft drinks and instant hot drinks
- Calcium supplements containing calcium phosphate or calcium triphosphate
- Toothpastes containing titanium dioxide, or carrageenan (read the labels carefully)

Check labels on OTC pharmacy products, supplements, and mouthwash to make sure they do not contain titanium dioxide, aluminosilicates, or anatase.

Carrageenan

Carrageenan is classified as an algal polysaccharide produced from seaweed. Whether it was safe for human consumption was questioned in 1982 after scientists discovered that carrageenan could injure the intestines of laboratory rats. In animal studies, sulfated polysaccharides, such as carrageenan, increase hydrogen sulfide production that inhibits the metabolism of butyric acid and other short chain fatty acids, which in turn starve colonocytes, and induce lesions similar to ulcerative colitis.

Carrageenan is ubiquitous in our food supply, and can be found in all sorts of alternative milk products such as soy milk, rice milk, grain milks, rice cream, soy cream, and tofu products, veggie burgers, cereals, baked goods, tooth pastes, supplements, and soups. The worst offender is the herb Irish moss because it is pure carrageenan.

Other Antagonists

Dietary allergies must be identified and their sources eliminated from the diet. Also, avoiding sulfate consumption from preservatives such as sulfites and sulfur dioxide may be beneficial for IBD patients.

Lastly, Monosodium Glutamate has been shown to induce diarrhea, and exacerbate symptoms associated with irritable bowel syndrome, Crohn's disease and ulcerative colitis. Definite sources of MSG include hydrolyzed protein, sodium caseinate or calcium caseinate, autolyzed yeast or yeast extract.

Possible Pathogen Association to IBD Pathology

Pathogens (disease producing organisms) with potential association to ulcerative colitis and Crohn's disease include *Escherichia coli*, *Diplostreptococcus*, *Campylobacter*, *Clostridium difficile*, *Fusobacterium necrophorum*, *Shigella sp.*, *Salmonella*, *Helicobacter hepaticus*, RNA virus, *Bacteroides vulgatus*, *Mycobacterium avium* subspecies, Lymphogranuloma venereum (LGV), NON-LGV Chlamydia, Gonorrhea Tuberculosis, Measles virus, and *Yersinia sp.* Bowel lesions seem to occur more frequently in areas of the colon that have high bacteria concentration.

Prebiotics and Probiotics in IBD

Modification of the microflora by prebiotics, probiotics, and herbal compounds with antibiotic characteristics may be a rational approach for controlling intestinal inflammation.

Lactobacillus GG

One of the most studied probiotics is *Lactobacillus GG*. Children (median age, 14.5 years) with mildly to moderately active Crohn's disease despite therapy with prednisone and immunomodulatory drugs (such as 6-mercaptopurine, azathioprine, or methotrexate) were given *Lactobacillus GG* twice a day for six months.

The median pediatric Crohn's disease activity index score at four weeks was 73% lower (better) than at baseline, and three patients had a score of less than 10, indicating inactive disease. In some patients it was possible to taper the dose of prednisone by an average of 50% after 12 weeks of *Lactobacillus GG* treatment. Intestinal permeability, measured by a double sugar permeability test, improved in an almost parallel fashion. The researchers concluded that *Lactobacillus GG* may improve gut barrier function and clinical status in children with mildly to moderately active Crohn's disease.

A Probiotic/Prebiotic Combination

A study published in the February 2005 issue of the journal, *Gut*, found that administration of a probiotic and a prebiotic to patients with ulcerative colitis improved inflammatory symptoms and helped regenerate epithelial tissue. Researchers from Ninewells Hospital Medical School in Dundee, Scotland gave the freeze-dried probiotic *Bifidobacterium longum* combined with a prebiotic

consisting of a mixture of fructo-oligosaccharides and inulin to 8 patients with ulcerative colitis, while 8 patients with the disease received a placebo. Sigmoidoscopic examinations were conducted and rectal biopsies were obtained before and after the one-month treatment period. Participants were asked to keep records of their bowel habits so that any changes could be noted.

The examinations found that consuming the probiotic/prebiotic combination was associated with a reduction in mucosal inflammation, while the placebo group worsened. Inflammatory cytokines tumor necrosis factor alpha and interleukin-1 alpha were significantly reduced in the treatment group. The biopsies also revealed regeneration of epithelial tissue in those who received the probiotic.

E.coli and Mesalazine

E.coli (Nissle strain 1917) was as effective as mesalazine in preventing relapse of ulcerative colitis for 116 patients and again in 120 patients via two double-blind studies.

Germinated barley food-stuff (GBF)

Germinated barley food-stuff (GBF) is an insoluble mixture of glutamine-rich protein and hemicellulose-rich dietary fiber. GBF is utilized efficiently by *Bifidobacterium*, *Lactobacillus*, and *Eubacterium* and converted by them into lactate, acetate, and butyrate. In clinical studies GBF has attenuated intestinal inflammation in patients with ulcerative colitis and in experimental colitis models through prebiotic actions. The aim of one study was to compare the effect of GBF with that of probiotics and antibiotics in an experimental colitis model.

Colitis was induced by feeding male SD rats with a diet containing 3.0-3.5% dextran sodium sulfate (DSS). The therapeutic effect of oral administration of a prebiotic (GBF), probiotics (mixture of *Lactobacillus* and *Clostridium butyricum*), antibiotics (vancomycin, metronidazole), and the vehicle was determined by assessing clinical and pathological scores on day 6 after initiation of colitis. Butyrate concentrations in the cecal content were also determined.

GBF treatment significantly reduced colonic inflammation as assessed by clinical scores with an increase in cecal butyrate levels. Probiotic treatment with a mixture of *Lactobacillus* and *Clostridium butyricum* did not show such an effect. Both antibiotic treatments significantly attenuated clinical and pathological scores. However, in contrast to GBF, this treatment led to a significant decrease in cecal butyrate levels. These data suggest that modification of the intestinal microflora by prebiotics, including GBF, may serve as a useful adjunct in the treatment of ulcerative colitis as well as antibiotic treatment.

Venturir and colleagues reported that a 1 year, twice daily probiotic regimen containing *Bifidobacteria* and *Lactobacilli*, and *Streptococcus thermophilus* was

well tolerated and helped maintain remission in 15 to 20 patients with ulcerative colitis. Similar data was presented for maintenance of remission of chronic pouchitis.

“Good Yeast”

One of my favorite “good guys” of the gut is actually “good yeast”. *Saccharomyces boulardii* is good yeast that has been studied extensively for intestinal diseases and symptoms. It is wonderful for controlling diarrhea, especially if *Clostridium difficile* is the cause.

Thirty-two patients with Crohn's disease in clinical remission were randomly assigned to receive one of the following for 6 months:

- mesalamine (1 g 3 times per day), or
- mesalamine (1 g 2 times per day) plus *Saccharomyces boulardii* (1 g in the morning)

Clinical relapse, defined as a Crohn's disease activity index greater than 150 with an increase of 100 points over the baseline value for more than 2 weeks, occurred in 6 of 16 patients (37.5%) receiving mesalamine alone and in 1 of 16 patients (6.25%) receiving combination therapy ($p=0.04$).

Saccharomyces boulardii releases a protein that interferes with the binding of toxin A secreted by *C. difficile* to its receptor. In a randomized placebo-controlled trial, *Saccharomyces boulardii* in combination with vancomycin or metronidazole was well tolerated and reduced the relapse rate by 50%.

Antifungal Therapy

Many doctors have reported improvements in patient's IBD symptoms after initiating antifungal therapy, which may include antifungal herbs, probiotics and antifungal medication.

Looking Ahead

Fatty Acid: Short and Long Chain

Short chain fatty acids, such as butyric acid, propionic and acetic acids, are produced in the colon by fermentation of fiber. Butyric acid provides the primary fuel of colonocytes. Impaired metabolism of short chain fatty acids has been implicated as a possible factor for IBD. Larch arabinogalactan has been shown to increase butyrate formation and butyric acid enemas are often recommended to patients with IBD.

Fish oil may be a useful therapeutic agent in the management of IBD. Studies on the use of dietary supplements of fish-oil-derived long chain fatty acids have

indicated a beneficial effect on inflammatory bowel disease (Ross 1993; Steinhart 1997; Almallah et al. 1998).

Many published studies suggest that marine fish-oil supplements, which are rich in omega-3 fatty acids, may reduce the inflammation associated with ulcerative colitis and Crohn's. Fish oils may exert their anti-inflammatory effects by modulating tissue levels of certain immune factors that promote inflammation. In prospective, randomized, and controlled studies, omega-3 fatty acids have been shown to be therapeutically useful (Hillier et al. 1991; Aslan et al. 1992). Studies also show that fish oil reduces the doses needed of steroid drugs (Hawthorne et al. 1992; Grimminger et al. 1993; Williams 1993).

Oxidative Stress

Patients with ulcerative colitis and Crohn's disease show signs of increased oxidative stress in the intestinal mucosa, which may be secondary to inflammation. Mucosal biopsies have been shown to have increased reactive oxygen intermediates, DNA oxidation products (8-OhdG), and iron in the inflamed tissue.

In an interesting study, plasma antioxidant levels were measured in patients with ulcerative colitis and Crohn's disease. In both cases plasma levels of vitamins A and E and several carotenoids were very low compared to control groups.

There is a theory proposed by researchers that may explain the increased oxidative stress in patients with inflammatory bowel disease. Tumor necrosis factor alpha (TNF- α) production leads to the production of reactive oxygen species (ROS), which in turn activates Nuclear Factor-Kappa B (NF- κ B), which then enhances more TNF- α production, feeding the vicious cycle of ROS production.

Worm Therapy

Although not enticing, scientists say drinking a concoction containing thousands of pig whipworm eggs could protect people against bowel disease. Early trials of the drink called TSO, developed by German company BioCure, suggest it can dramatically reduce the abdominal pain, bleeding and diarrhea associated with inflammatory bowel disease (IBD).

BioCure hopes to have TSO approved by regulators and on the market in Europe by May 2005. Some scientists have long believed that the eradication of worms from human stomachs over the past 50 years may be behind the rise in IBD. Dr. Weinstock, a gastroenterologist at the University of Iowa, came up with the TSO idea after noticing that a rise in IBD cases coincided with a drop in infections caused by roundworms and human whipworms.

IBD is rare in developing countries where parasitic infections are more common. When TSO was tested twice a month on 100 IBD patients, symptoms such as abdominal pain, bleeding and diarrhea, disappeared. Fifty percent of patients with ulcerative colitis and 70 percent of Crohn's sufferers went into remission.

Digestive disease specialists at the University of Iowa are now organizing additional clinical trials to gather more data and knowledge about this potential treatment of inflammatory bowel disease. Worm therapy is not being used as a routine clinical treatment for patients with inflammatory bowel disease. The encouraging results of the initial research must be tested and substantiated by further research. Researchers are only using this agent under a strictly controlled research protocols. Bottom line: it is not ready for prime time.

The Vitamin D Connection

The standard treatment for inflammatory bowel diseases such as Crohn's and ulcerative colitis is through steroids, which help reduce the inflammation. However, they can cause bleeding, and bone loss, which can lead to osteoporosis later in life.

Vitamin D deficiency may be more common in people who have inflammatory bowel disease. Vitamin D deficiency may worsen the symptoms of Crohn's disease, but it is still unclear whether lack of the vitamin could be a cause, or simply an effect of the disease.

In a study, genetically engineered mice set to develop Crohn's disease and ulcerative colitis, were divided into two groups. Half were starved of vitamin D in their diet, while the other half was given a supplement. The treated mice not only had less bowel inflammation, but also survived when the untreated mice started dying after only a few weeks.

The research team pointed out other factors, which might suggest a link between IBD, and vitamin D. Rates of IBD are higher in North America and Northern Europe, which receive less sunlight. However, a UK expert questioned whether vitamin D was the principal factor behind the high rates of Crohn's disease. Dr. Nick Thompson, a consultant gastroenterologist, carried out a study of 250 Crohn's patients and found only three who could be classed as vitamin D deficient. He also pointed out that rickets has virtually disappeared in recent years, while Crohn's has soared.

It is interesting to note that patients with Crohn's disease may actually have high levels of vitamin D in their blood, indicating risk for toxicity if they took additional vitamin D. It may not be the best idea to start prescribing vitamin D for patients without testing 25 hydroxyvitamin D levels. As Abreu's team explains in the medical journal, *Gut*, under certain circumstances too much active vitamin D can actually contribute to the breakdown of bone, leading to osteoporosis. In that

same journal, researchers found "inappropriately high" blood levels of the active form of vitamin D in 42 percent of the 138 people they studied with Crohn's disease. This was true of only 7 percent of 29 patients with ulcerative colitis. In addition, the higher the blood levels of active vitamin D in Crohn's patients, the lower their bone density -- regardless of whether they were treated with steroids. The researchers believe that high vitamin D levels are most likely a manifestation of the underlying gut inflammation. Immune system cells produce vitamin D as part of the immune response (vitamin D is required for cell differentiation).

A high vitamin D level is an additional risk factor predisposing some Crohn's disease patients to development of osteoporosis. Treatment of the underlying inflammation, may improve metabolic bone disease. Bottom line: get a 25 hydroxyvitamin D blood test for patients with Crohn's or colitis. It seems that colitis patients are better candidates for medically supervised vitamin D therapy.

Say No to NSAIDS

It is already known that people with IBD should avoid ibuprofen (like Motrin, Advil, and Nuprin). Now researchers think other anti-inflammatory drugs like Ecotrin, and anything containing aspirin should be avoided as well.

A study published in the August edition of *The American Journal of Gastroenterology* takes the position that people with IBD should not take nonsteroidal anti-inflammatory drugs. Taking an NSAID may exacerbate existing disease or even cause the onset of IBD in persons who are predisposed.

Sixty patients that were hospitalized for serious flare-ups of IBD were queried about their NSAID use. In one-third of the patients, researchers found a relationship between the use of NSAIDs and flare-ups.

What About Erythema Nodosum?

Skin disorders are a common extra intestinal symptom of IBD, occurring in up to 25% of people with ulcerative colitis and Crohn's disease. Some of these skin conditions are pyoderma gangrenosum, aphthous ulcers, and erythema nodosum. Erythema nodosum is a skin condition that most often affects people with Crohn's disease, but can also develop in those who have ulcerative colitis. Corrections of deficiencies, olive leaf extract, fish oil, and probiotics have helped patients reduce the incidence of skin disorders during IBD therapy.

Kidney Stones and IBD

Many patients with IBD are also hyperoxaluric, suggesting that excess oxalate may be a complicating factor in the disease, or may lead to increased risk of kidney stones.

At the institute of Urology in Milano, Italy, researchers analyzed the frequency of renal stones in patients with chronic inflammatory bowel disease and their urinary patterns. During a 20-year period, 1,941 consecutive patients with renal stone disease underwent routine laboratory procedures including a fasting blood sample for chemistry profile and a 24-hour urine collection for analyses of electrolytes. Thorough histories including the presence of chronic inflammatory disease or ileal resection were obtained.

Urinary oxalate excretion was significantly higher and urinary citrate lower in stone patients with ileal disease than in idiopathic stone formers and stone patients with ulcerative colitis. Urinary volume was significantly lower in patients with ulcerative colitis. The researchers concluded that malabsorption associated with ileal disease causes increased oxalate absorption by increasing oxalate solubility in the intestinal lumen and permeability of the colonic mucosa. A reduced citrate excretion is associated with mild acidosis due to the loss of bicarbonate in the liquid stool. In ulcerative colitis, especially if an ileostomy is present, urine is scanty and concentrated, and urine pH falls, leading to uric acid or mixed stones. Diet strategies may include a low oxalate diet; the Specific Carbohydrate Diet can be adjusted to reduce total oxalate.

Nutrient Deficiencies

Vitamin K deficiency and low plasma vitamin E is common in patients with IBD. In an Australian study, biopsies of colon tissue revealed low levels of reduced ascorbic acid. Calcium, magnesium, iron, carotenoids, biotin, B1, B2, B3, B12, folic acid, and selenium are also common deficiencies for the IBD patient.

Zinc and copper balance is usually disrupted in IBD. Zinc status is important in maintaining enzyme function of metallothionein, and ROS reduction. Copper levels may actually increase, thus increasing ROS activity.

Be very careful when you replete iron. Remember that ROS production is a major player in the etiology of IBD, and iron is a pro-oxidant. An attempt to avoid iron supplements should be made unless they are an absolute necessity.

Supplementation

EGCG, an extract of green tea may help reduce inflammation associated with Crohn's disease and ulcerative colitis. In addition, green tea appears to be helpful for preventing colon cancer; this would be an added benefit for those with IBD because they are at a higher risk for that disease. In a recent study, scientists may have uncovered one of the mechanisms behind this effect. It was determined that EGCG can inhibit interleukin 8, a pro-inflammatory cytokine.

L-glutamine, an amino acid that is the main source of energy for the mucosal cells that line the intestines, and helps them heal. Dosage is adjusted for each patient. The common dose range is 6 to 25 grams divided into 3 doses per day, 30 minutes before meals. Dr. Alan Gaby reported in the *Townsend Letters for Doctors and Patients* (October 2001, p 19, based on *J Parenter Enteral Nutr* 2000; 24:196.) that glutamine might increase T-cell attack in Crohn's disease. In the Crohn's patient glutamine may also be metabolized into citrulline, which is converted to arginine, a substrate for nitric oxide synthesis. Excessive nitric oxide has been shown to contribute to tissue injury and inflammation in Crohn's disease. L-glutamine seems to be effective in ulcerative colitis.

Lactobacillus GG is a strain of beneficial flora that is extensively researched in gastrointestinal health, discovered by Drs. Gorbach and Goldin of Tufts University. Dosage: 1 capsule (10 billion cells), twice per day, away from food.

Essential formulas probiotic supplement contains 12 strains of live lactic acid bacteria in a bovine free, enteric coated, vegetable capsule made entirely of vegetable gum (agar agar) and a derivative of cellulose made from plant fiber. There is an enormous amount of clinical research supporting this probiotic.

Boswellian serrata at the dose of 900mg was found to reduce the symptoms associated with both Crohn's and ulcerative colitis in a small clinical trial.

Curcumin supplementation has been shown to result in a reduction in myeloperoxidase activity, a reduction in the number of infiltrating neutrophils, as well as a reduced expression of IL-1 in IBD patients. Dose range is 650mg to 1300mg three times per day.

Pure sources of EPA and DHA, which have been shown to reduce inflammation in the gastrointestinal tract, might be better tolerated in some cases if enteric coated. Dose range is usually 2 to 9 grams daily.

Mixed tocopherol vitamin E should be used as part of an antioxidant program at the dose of 400 IU soft gels twice per day with meals.

Folate is an important nutrient that is normally lacking in people with inflammatory bowel disease due to depletion by medications, poor intestinal health, and malabsorption, and it must be supplemented. Common dosages are 1 to 5 mg daily.

Herbal preparations containing *Taraxacum officinale*, *Hypericum perforatum*, *Melissa officinalis*, *Calendula officinalis*, and *Foeniculum vulgare* may be beneficial for IBD. A small study on 24 patients with colitis revealed a complete resolution in pain and diarrhea in 23 patients after 15 days.

Quercetin has been found to counteract glutathione depletion, and reduce adhesions and surface damage in colonic tissue in the rat model of induced colitis. Standard dose in IBD is 500mg, three times daily.

In clinical research, methylation, which plays an important role in sulfide detoxification of colonocytes, may be enhanced with methyl donor supplementation. Research focusing on L-methionine, and a very stable form of SAM-e (S-adenosylmethionine 1,4 butane disulfonate) may have therapeutic value in ulcerative colitis. Many patients with IBD also have hyperhomocysteinemia, which is an indication of inadequate methylation.

DHEA is usually very low in patients with IBD, partially because DHEA levels are usually suppressed in inflammatory conditions, and as a casualty of steroid therapy.

Interestingly, melatonin reduced symptoms of IBD in animal research, by acting as an assistant to the transportation of electrolytes across cell membranes, and as an antispasmodic. In an in vitro study, large doses of melatonin inhibited TNF α induced mucosal addressin cell adhesion molecule, which is believed to be involved in inflammation associated with IBD. Keep in mind that much like serotonin, levels of melatonin in the gastrointestinal tract greatly exceed those that are in the brain.

Phosphatidylcholine has been used to prevent stricture formation of colonic tissue in animal studies. Phosphatidylinositol seems to exhibit similar effects. In an animal study, PI, just like PC, resulted in significant mucosal recovery and decreased permeability of gut tissue in rats with acetic acid induced colitis.

Compounds that may be beneficial in IBD but require more study include bromelain, sterols and sterolins, transfer factors, ginkgo biloba (by inhibition of platelet-activating factor, which mediates mucosal inflammation), Peumus boldus, N-acetyl-glucosamine, aloe polysaccharide extract, white fish peptides, and butyric acid enemas.

Nutritional intravenous therapy is essential for the IBD patient. Formulations should be calculated for osmolarity to assure patient comfort and tolerance. Vitamin C should be part of the formula since this is the preferred way to administer this nutrient in the IBD patient. Following an IV with a separate glutathione drip will help reduce the ROS burden in the IBD patient.

Psychological Impact of Crohn's Disease

According to a survey of people with Crohn's disease titled *Voices of Crohn's*, 60 percent of people with Crohn's, between the ages of 18 and 34, have been hospitalized within the last two years, and more than half have required surgery within the past five years. Nevertheless, more than half of the people surveyed

still find that their employers, families and friends underestimate the effect of the disease on their daily lives.

The survey was conducted by Manhattan Research, a marketing information and services firm, on behalf of Crohn's & Colitis Foundation of America (CCFA) and the Digestive Disease National Coalition (DDNC), and was sponsored by Centocor, Inc. It revealed the impact of the symptoms of Crohn's, including unpredictable and persistent diarrhea, fever and severe abdominal pain, on the physical, social and emotional well being of people with the disease. A sub-analysis of those surveyed focused specifically on the adult segment of Generation Y (ages 18 to 27), as well as family relationships and workplace issues, and provides new and comprehensive insight into the debilitating nature of Crohn's disease.

Voices of Crohn's was designed to increase general understanding of the life-altering nature of Crohn's disease. Through raised awareness about Crohn's disease, people with Crohn's may be able to lead more comfortable and fulfilling lives. For more information about the study results, visit www.voicesofcrohns.com.

In summary, many patients reported that it took years to obtain a proper diagnosis, and that they had to visit more than one physician, in some cases more than five physicians. Due to the life altering effects of Crohn's disease work productivity, relationships (including the fear of starting one), and family all suffer.

References:

Miranda C. E. Lomer, Rory S. J. Harvey, Stephan M. Evans, et al, "Efficacy and tolerability of a low microparticle diet in a double blind, randomized, pilot study in Crohn's disease." *European Journal of Gastroenterology and Hepatology* 2001, 13:101-106.

Gotschall, Elaine, Breaking The Vicious Cycle: Intestinal Health Through Diet, The Kirkin Press, 1994, Canada.

Valhouny, G. and Kritchevsky, D., Dietary Fiber in Health and Disease, Plenum Press, New York, NY, 1982.

Schwartz, George, R. In Bad Taste: The MSG Symptom Complex, Pellum Press, New York, 2000.

Probiotics beneficial for Crohn's disease Townsend Letter for Doctors and Patients, Nov, 2001
Alan R. Gaby

J Pediatr Gastroenterol Nutr. 2000 Oct; 31(4):453-7. Is lactobacillus GG helpful in children with Crohn's disease? Results of a preliminary, open-label study.

Fukuda M, Kanauchi O, Araki Y, et al. Prebiotic treatment of experimental colitis with germinated barley foodstuff: A comparison with probiotic or antibiotic treatment. *Int J Mol Med* 2002;9:65-70.

Guslandi M, et al. *Saccharomyces boulardii* in maintenance treatment of Crohn's disease. *Dig Dis Sci* 2000;45:1462-1464.

Gupta P, et al. Is Lactobacillus GG helpful in children with Crohn's disease? Results of a preliminary, open-label study. *J Pediatr Gastroenterol Nutr* 2000;31:453-457.

Triadafilopoulos G, Hallstone AK. Acute abdomen as the first presentation of pseudomembranous colitis. *Gastroenterology* 1991; 101:685-91.

Jacobs NF Jr. Antibiotic-induced diarrhea and pseudomembranous colitis. *Postgrad Med* 1994; 95:111-20.

Peterson LR, Kelly PJ. The role of the clinical microbiology laboratory in the management of *Clostridium difficile*-associated diarrhea *Infect Dis Clin North Am* 1993; 7:277-93.

Fekety R, Shah AB. Diagnosis and treatment of *Clostridium difficile* colitis. *JAMA* 1993; 269:71-5.

Anand A, Bashey B, Mir T, Glatt AK. Epidemiology, clinical manifestations, and outcome of *Clostridium difficile*-associated diarrhea *Am J Gastroenterol* 1994; 89:519-23.

Brown CH, Ferrante WA, Davis WD. Toxic dilatation of the colon complicating pseudomembranous enterocolitis. *Am J Dig Dis* 1968; 13:813-21.

Agnifili A, Gola P, Marino M, Ibi I, Carducci G, Verزارo R, Bernardinis G. The role of timing in the treatment of pseudomembranous colitis, a case complicated by toxic megacolon. *Hepatogastroenterology* 1994; 41:394-6.

Burke GW, Wilson ME, Mehrez IO. Absence of diarrhea in toxic megacolon complicating *Clostridium difficile* pseudomembranous colitis *Am J Gastroenterol* 1988; 83:304-7.

Cone JB, Wetzel W. Toxic megacolon secondary to pseudomembranous colitis. *Dis Colon Rectum* 1982; 25:478-82.

Boland GW, Lee MJ, Cats AM, Gaa JA, Saini S, Mueller PR. Antibiotic-induced diarrhea specificity of abdominal CT for the diagnosis of *Clostridium difficile* disease. *Radiology* 1994; 191:103-6.

Drapkin MS, Worthington MG, Chang TW, Razvi SA. *Clostridium difficile* colitis mimicking acute peritonitis. *Arch Surg* 1985; 120:1321-2.

Morris JG, Shay DK, Hebden JN, McCarter RJ, Perdue BE, Jarvis W, et al. Enterococcus resistant to multiple antimicrobial agents, including vancomycin: establishment of endemicity in a university medical center. *Ann Intern Med* 1995; 123:250-9.

Morris LL, Villalba MR, Glover JL. Management of pseudomembranous colitis. *Am Surg* 1994; 60:548-52.

Olson MM, Shanholtzer CJ, Lee JT, Gerding DN. Ten years of prospective *Clostridium difficile*-associated disease surveillance and treatment at the Minneapolis VA Medical Center, 1982-1991. *Infect Control Hosp Epidemiol* 1994; 15:371-81.

Ignazio Castagliuolo, Martin F. Riegler, Leyla Valenick, J. Thomas LaMont, and Charalabos Pothoulakis. *Saccharomyces boulardii* Protease Inhibits the Effects of *Clostridium difficile* Toxins A and B in Human Colonic Mucosa. *Infect Immun.* 1999 January; 67(1): 302–307.

Ecker JA, Williams RG, McKittrick JE, Failing RM. Pseudomembranous enterocolitis-an unwelcome gastrointestinal complication of antibiotic therapy. *Am J Gastroenterol* 1970; 54:214-28.

Trinchieri A, Lizzano R, Castelnuovo C, Zanetti G, Pisani E, Urinary patterns of patients with renal stones associated with chronic inflammatory bowel disease, *Gut*, 2004.

Akoban AK. Glutamine Supplementation and Intestinal Permeability in Crohn's Disease. *J Parenter Enteral Nutr* 200; 24:196.

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