

# *Proper Nutrition*

How Better Health Begins



SEACURE®

## History and Clinical Applications of a Promising New Protein Supplement

by Peter Barry Chowka® and Patricia Fahey

In 1995, Dr. James Sensenig, a naturopathic physician practicing in Hamden, Connecticut, was visited by a 22-year-old college student with severe ulcerative colitis. His condition was typical of the problem faced by millions of Americans currently suffering with inflammatory bowel disease: multiple episodes of diarrhea each day, accompanied by painful cramping with blood and mucus in the stool. Not surprisingly, the patient had previously been treated with a wide range of state-of-the-art conventional drugs, which either exacerbated his symptoms or offered only minimal, temporary palliation. After a month on Sensenig's natural treatment protocol, which included dietary modification, nutritional supplements, and homeopathy, the young man also failed to show significant and sustained improvement.

A remarkable breakthrough in the student's condition occurred, however, when Sensenig decided to add a new, highly assimilable protein supplement to his diet. After just two weeks on this unique formulation (*SEACURE*® — a naturally derived, concentrated fish protein), the young man had no more pain, no more diarrhea or loose stools, and was able to discontinue the cortisone and prednisone he had been taking. Under Sensenig's care, he continued on Seacure and has remained symptom-free.

As it turns out, Sensenig's amazing clinical experience with the healing power of Seacure is not unique. From Oregon, Dr. Tom Kruzel, another leading naturopathic physician, reports similar results

when he adds the peptide-based product to the treatment regimens of patients with severe digestive disorders, including colitis and proctitis. In Maine, Christiane Northrup, MD has documented numerous case histories of patients who recovered rapidly when Seacure was used to treat irritable bowel syndrome, malabsorption problems, upset stomach, diarrhea, heartburn, and Crohn's disease. As a graduate of Dartmouth Medical School and a former president of the American Holistic Medical Association, Northrup is an acclaimed author and an assistant clinical professor at the University of Vermont School of Medicine.

Interestingly, Seacure's clinical value appears to extend well beyond serious diseases of the digestive tract. In California and Pennsylvania, Drs. Paul Lynn and Jeff Marrongelle have successfully utilized Seacure as a primary therapy for patients suffering with pressure ulcers and other types of chronic wounds, immune deficiency, chronic fatigue syndrome, and malnutrition associated with cancer chemotherapy. In just over two years since the encapsulized supplement was made commercially available, naturopathic physicians, medical doctors, chiropractic physicians, and other clinicians throughout the country have collected an enormous body of data which offers provocative evidence of Seacure's ability to alleviate a broad range of serious and previously intractable chronic degenerative diseases.

Seacure's clinical efficacy may be based on its chemical composi-

tion and easy digestibility. It is made from fresh, lean, white fish harvested from the deep, cold waters of the North Pacific. Fish has long been recognized by physicians and nutritionists as an unsurpassed form of dietary protein with an amino acid profile equivalent to meat and superior to milk and soy. But unlike meat, whole milk, and eggs, fish is low in salt, cholesterol, and saturated fats, while it is high in essential omega-3 fatty acids, the kinds that are good for the heart.

Once harvested, the fish flesh is transformed into the highly absorbable protein powder through a proprietary bio-conversion process. A unique microorganism culture is used to break down the white fish protein into its constituent peptides and amino acids. Unlike the chemical methods typically used to produce other types of protein supplements, this gentle and completely natural bio-conversion process effectively preserves the nutritional value of the fish protein. The resulting fish concentrate is almost 100% assimilable by the body.

### Origins of a Novel Protein Supplement

The innovative process used to produce Seacure today was originally developed in the 1960s as the result of a humanitarian project to relieve world hunger. At the time, scientists and food technologists from many nations joined forces in an ambitious effort to address the global food crisis. They viewed protein deficiency as the most serious aspect of world hunger and agreed that the use of bountiful and under-

utilized ocean fish offered the best and most affordable solution. Yet there was a very significant technical problem which first needed to be resolved. Low cost and effective means needed to be developed for the removal of water and oil from the fish so that the protein could be easily stored and transported. Thus began the well known fish protein concentrate (FPC) programs.

Most FPC research teams worldwide focused on physical and chemical procedures to concentrate the fish protein. But these processes only succeeded in creating denatured, intact protein concentrates. In contrast, one team discovered a biological approach which fermented large protein fragments into smaller, undenatured protein fragments (peptides) and simple amino acids. This approach had a great advantage since malnourished people (especially babies), often lack the enzymatic strength to digest intact protein.

By the 1970s, the team had perfected its fermentation or bio-conversion process. In subsequent years the hydrolyzed fish protein was tested in a massive nutritional study with over 3,000 premature and dystrophic (malnourished) babies. The results were extremely favorable. Malnourished and low birth-weight babies gained weight and achieved normal growth rates, while those with symptoms related to premature birth, such as edema and respiratory insufficiency, experienced rapid recoveries.

During the study, the clinicians noted that infants fed the pre-digested fish protein exhibited a range of additional — and unexpected — health improvements. For example, cases of acute and chronic diarrhea and blood-based immune disorders suddenly cleared up. When the fish

concentrate was fed to babies with milk intolerance and other serious food allergies, they were soon able to tolerate normal diets. These strikingly positive clinical outcomes attracted the attention of numerous other physicians and researchers. As a result, the fish protein was ultimately tested by over 100 leading physicians and surgeons on more than 100,000 patients, both adults and children. It proved to be very beneficial in promoting tissue regeneration with hard-to-heal wounds (fistulas, abscesses, lesions, pressure ulcers, and necrotic tissue) and when used for enteric feeding in post-operative patients.

Despite the exciting nature of these discoveries, developed nations, for a variety of economic and political reasons, lost interest in world hunger. One reason was that fish prices rose sharply by the 1970s, and politicians refused to support new technologies for worldwide feeding in the absence of inexpensive raw material. Fortunately, however, there was an American scientist who recognized the vital significance of the biological FPC achievement.

The scientist was Dr. Donald Snyder. As a technical advisor to the Kennedy Administration, the director of the U.S. Department of the Interior's Fisheries Research Laboratory, and a professor at the University of Maryland at College Park, Snyder directed the U.S. involvement in the FPC project. Early on he assumed a proactive role by seeking ways to effectively integrate solutions and expedite the process. For instance, Snyder arranged for the U.S. National Academy of Sciences to host meetings in Washington so that the 30 research teams from around the world could meet regularly to

exchange ideas on effective preparation of fish protein for supplementation purposes. It was Snyder who had set the project's parameters of providing an FPC to the world's hungry, "at levels they need, in a form they can use, and at a price they can afford."

Few people in the U.S. understood the potential of fish protein better than Snyder, and he was eager to see the laboratory research translated into real-world solutions. But the U.S. Food & Drug Administration (FDA) had other ideas. The agency opposed the concept of using whole fish as a food supplement because the use of any whole animal includes parts which are considered "filthy" or "unfit for human consumption" by the FDA. If the whole fish could not be used, the low-cost aspect of FPC would be lost. Frustrated, Snyder, with the support of President John F. Kennedy's Secretary of the Interior Stewart Udall, transformed his own FPC research program into a vast data collection machine designed to overcome the FDA's objections. An eight-year, \$40 million battle ensued. In the end, Snyder's team won the tug-of-war with the FDA, but by then policy makers worldwide had almost completely lost interest in world feeding.

Snyder recognized that biologically-derived fish protein had another important role: It could be introduced to health-conscious consumers in the U.S. and elsewhere. If it could gain acceptance in the commercial marketplace, it might one day be revived as the basis of a world hunger project. The developer of the process died in 1979 and Snyder's hopes faded as time passed. Perhaps the discovery would be buried with the discoverer. But by the early 1990s, Snyder was

able to arouse enough interest in the U.S. to prevent the loss of the technology and form Proper Nutrition, Inc., a corporate entity which would purchase the culture and know-how from the developer's heir.

### **Provocative Research on Peptide Activity**

Proteins are of primary importance in all cellular, tissue, organ, and bodily structures and functions. They are giant molecules comprised of large chains of amino acids, which are linked end-to-end through chemical connections known as "peptide bonds." During digestion, proteins are first broken down into oligopeptides, which are then digested into smaller peptides (tripeptides or dipeptides), and free amino acids. Once protein digestion is complete, the resulting small peptides and free amino acids are suitable for absorption by the intestinal mucosa and delivered to the liver and other body cells, where they become involved in numerous essential metabolic activities.

Conventional scientific wisdom has long held that peptides, unlike amino acids, cannot be absorbed directly into the human intestine, and in turn exert little if any direct influence on physiological processes. In recent years, however, researchers have come to know that smaller peptides may be absorbed directly into the gut, and may in fact have a high degree of bioactivity. In his book *Nutrition and Critical Care*, Gary P. Zaloga, MD, contends that peptides are a highly absorbable form of protein. According to Zaloga, research has shown that "more than 70% of amino acids which appear in portal blood are in the peptide fraction." Zaloga and others believe that these peptide fragments have potent biological

activity with a strong influence on digestive, immune, hormonal, and neurological functions.

Another researcher who has been actively investigating peptides for the past seven years is Pamela Roberts, MD, a physician with the Bowman Gray School of Medicine at Wake Forest University. During a presentation at the 11th Annual Convention of the American Association of Naturopathic Physicians in Bellevue, WA, in September 1996, Roberts said, "I believe that the therapeutic uses of dietary peptides offer exciting potential in many clinical areas and that the areas which need to be focused on first, according to the available data, are immune function and modulation of the immune response, modulation of gut integrity, wound healing, and effects on the heart and kidney."

Although Roberts is not connected with Proper Nutrition, Inc. nor with Seacure, there are many striking parallels between her experimental work and the clinical observations made by numerous physicians who utilize dietary peptides in their practices. For example, when Roberts and her associates added peptide formulations to the diets of hospitalized patients in intensive care units, the patients experienced less diarrhea. Other research teams have also analyzed the nutritional status of critical care patients given peptide-based diets versus intact protein-based diets. Patients given the peptide formulations were able to manufacture their own bodily protein more rapidly than those who received intact proteins — a key indication that peptides are highly assimilable.

At the naturopathic conference, Roberts also reported on a series of provocative studies that she and her

colleagues conducted with laboratory animals. In an experiment designed to study growth rates, the researchers found that rats fed peptide-based diets grew faster and gained more weight than rats fed either intact protein formulas or amino-acid formulas.

The researchers designed other studies to test wound healing and immune responses in these animals. When rats with abdominal wounds received peptide diets, they healed at a faster rate (a statistically significant improvement) compared with rats fed amino acid-based diets. Peptides were also shown to enhance immune responses (measured by the activity of red blood cells) and survival time in rats exposed to lethal doses of toxic substances.

### **Clinical Success with Chronic GI Disorders**

Among the increasing number of clinicians around the country who have used Seacure is Bruce Shelton, MD, who employs the product as a first line treatment in patients with all types of gastrointestinal disorders, including diverticulitis, ulcerative colitis, and the weakened digestive functioning frequently seen in elderly or immune compromised individuals. A graduate of New York Medical College and a Diplomate of the British Institute of Homeopathy, Shelton currently practices as a homeopathic family physician in Arizona. He also utilizes dietary modification and nutritional supplementation.

Like many other clinicians, Shelton sees a large number of patients with chronic GI disorders. One example is a 49-year-old man who had suffered for a decade with ulcerative colitis. The patient had all the usual symptoms of the disease:

abdominal cramps, pain, rectal bleeding, and diarrhea. For almost a year, Shelton treated the man with vitamins, minerals, and homeopathic remedies, but there was little improvement. When he tried Seacure, the colitis cleared up completely. Shelton is convinced that it was the Seacure that made the difference, since the fish protein concentrate was the only new addition to the patient's regimen at the time he experienced dramatic improvement in bowel function.

Tom Kruzel, ND is a nationally known naturopathic physician who served for three years (1993-96) as president of the American Association of Naturopathic Physicians. In his clinical practice in Gresham, OR, Kruzel attends to a wide variety of patients with serious digestive disorders. In late 1996, he treated a seven-year-old boy who presented with esophageal varices, ascites, Crohn's disease, neurofibromatosis, and malabsorption syndrome. The child had previously been scheduled for a liver transplant which was cancelled after the diagnosis of neurofibromatosis was made.

Kruzel prescribed various homeopathic remedies as well as herbal medications for the boy's liver and Crohn's disease. To raise the child's chronically low serum albumin, Kruzel prescribed Seacure 500 mg, four capsules BID. The boy's liver enzymes returned to normal, his chronic diarrhea resolved, the ascites diminished, he grew 1/2 to 3/4 inches, and he gained five pounds. Kruzel plans to keep the child on Seacure until his serum albumin levels stabilize and his liver is better able to regulate them.

As a chiropractic physician, clinical nutritionist, and director of a bio-nutritional medical facility in Schuylkill Haven, PA, Jeff

Marrongelle, DC, was one of the first clinicians in the country to use Seacure. During the past four years he has prescribed the supplement to hundreds of patients who have presented with many different types of chronic diseases.

Recently, Marrongelle was visited by a 57-year-old female with a case history of previous hepatitis and a confirmed ten-year-old diagnosis of Babesiosis. The woman had a severe case of acute jaundice brought on by non-viral hepatitis. Lab values on bilirubin (33.5 on initial examination) and liver enzymes were extremely critical.

Marrongelle prescribed three liquid herbal formulas from Nestmann Company in Germany, along with lactobacillus acidophilus and Seacure (twenty 500 mg capsules per day). Blood tests were repeated every ten days during a six week period. Interestingly, the patient's bilirubin level fell to 2.7 and her liver enzymes returned to normal, while both red and white blood counts returned to within normal ranges. All signs of the woman's jaundice disappeared, and her albumin and serum protein levels, which had been abnormally low, increased to within normal limits.

A much more common gastric disturbance that Marrongelle often treats is Irritable Bowel Syndrome (IBS). A typical case history is that of a 66-year-old female, positively diagnosed with IBS. Five months prior to starting treatment, the woman's symptoms included pain in the lower abdomen, constipation alternating with diarrhea, nausea, poor appetite, and a weight loss of fifteen pounds during the previous five months. Marrongelle prescribed homeopathic detoxification, herbal digestive enzymes, and probiotic support, along with Seacure

equalling about 3.8 grams per day of mixed amino acids, including 600 mg of L-glutamine. After eight weeks, all of the patient's original symptoms were downgraded to "1" on a scale of "1" to "10" (where "10" represents the most severe symptoms). The patient continued taking the same dosage of Seacure for an additional eight weeks, at which time all diarrhea, constipation, and nausea ceased and her appetite returned to normal.

### **Protein Calorie Malnutrition: A Widespread Clinical Problem**

For decades, clinical nutritionists have focused extensively on the use of vitamins and minerals (micronutrients), along with herbs and, in recent years, phytochemicals (naturally occurring chemicals found in food). Yet, these elements actually represent a very small fraction of a person's total dietary intake. Meanwhile, the macronutrients proteins, carbohydrates, and fats which comprise the lion's share of any given diet, have often been overlooked or de-emphasized.

In recent years, however, many clinicians have started to focus increased attention on the vital role of macronutrients. There is growing interest in both quantitative and qualitative considerations. For example, what is the ideal intake of, or balance among, proteins, carbohydrates, and fats? Or, are there "good" fats as well as "bad" fats? Some researchers are also suggesting now that certain well established beliefs about healthy eating may be fundamentally flawed. For instance, is a high carbohydrate, low fat diet really optimal? And what about protein — just how important is this nutrient? Additionally, what are the best sources of protein and what factors affect its digestibility?

The effective use of dietary protein is becoming a high priority in the clinical practice of many physicians. Without a doubt, protein is the most basic of nutrients. Yet, protein calorie malnutrition is an extremely common, if underdiagnosed, occurrence, affecting virtually every segment of the population — young and old, rich and poor, vegetarian and meat eater alike. Clinical nutritionist and researcher Marrongelle offers this perspective on the problem: “Of prime importance to practitioners is an awareness of how many people they see who are ambulatory [who] are in critical need of protein calories — actually *have* protein calorie malnutrition.” Marrongelle believes that a majority of people with almost any kind of health disorder have impaired digestion — primarily an inability to break down and assimilate protein and its components. He says, “Most of the people we see who are ill are compromised in their absorption of amino acids, peptides, and protein, and have starved themselves of protein.”

In his clinical practice, Marrongelle sees 400 to 500 new patients each year. He uses Seacure to treat most of them, including people with diabetes, chronic wounds, and GI disorders; geriatric patients with weakened digestion and muscle wasting; patients undergoing cancer chemotherapy; and people scheduled for surgery. In Marrongelle’s view, Seacure provides an ideal nutritional foundation or “baseline feeding program” to which clinicians can add more targeted or subtle therapies — including herbs, homeopathy, or specific vitamins and minerals. He is convinced that Seacure is superior to other types of protein supplements, because of its source, method of

preparation, and absorbability. In contrast, milk or casein-based protein supplements can be difficult to digest, Marrongelle notes, especially for pediatric patients, while soy-based proteins are contraindicated for many people because they produce phytoestrogens.

“Seacure gives patients a base to work with,” says Marrongelle. “In almost all of our cases where there is gastrointestinal dysfunction, which is most of them, we use a combination of Seacure, a probiotic (a high quality lactobacillus combination), and proteolytic enzymes. We shift the bowel ecology to become more efficient. We are finding that the immune response begins in the gut and dysbiosis is the biggest compromise the patient can have: poor digestion, leaky gut syndrome, poor elimination, poor assimilation — they’re all part of the picture of ill health.”

Clinical researcher Jeffrey Moss, DDS, CCN, concurs with Marrongelle and other investigators about the widespread nature of protein calorie malnutrition and the limitations of conventional nutritional approaches in combatting chronic illnesses. Moss says, “Many would have us believe that the answer to all nutritional challenges is to consume vitamin and mineral supplements in high enough quantities. But in my fifteen years of clinical experience, I have never seen a chronically ill patient gain optimal health solely from such an approach. I believe that proper protein nutrition may be the missing link in some of the most vexing, difficult patients.”

#### **A Wealth of Clinical Applications**

In September 1996, Lana Barr, a 52-year-old female, was diagnosed with advanced, metastacized breast

cancer. Her naturopathic physician agreed with her oncologist and surgeon that she should undergo four months of chemotherapy to shrink the primary tumor so that a lumpectomy, rather than a mastectomy, would suffice.

On March 17, 1997, Barr wrote, “I began very toxic doses of Adrimycin and Cytosin in October of 1996. The first dose of chemo caused nausea, severe vomiting, severe diarrhea, loss of energy, loss of hair, and very dark circles around my eyes. By the second dose of chemo (four weeks later) I had been taking Seacure (6 tablets per day) for well over three weeks. This time there was no vomiting, very little nausea, an increase in energy, the diarrhea stopped, my bowels became normal, and the black circles around my eyes lightened. I continued to feel stronger and had much more energy.”

“I was able to continue working, my immune system was good, and, unlike most chemo patients, my white blood cell count stayed normal and consistent. This continued month after month with each chemo treatment. There was a two week period when I ran out of Seacure and I began to feel very weak, and very tired, and I started to feel ill. I ordered some more Seacure, and again I bounced back to good health.”

Many cancer patients report similar positive experiences with Seacure, while numerous clinicians consider it to be an indispensable nutritional supplement for a wide range of critical care situations.

James Sensenig, ND uses Seacure to treat wasting syndrome in people with AIDS and cancer. He believes that it is very useful in stabilizing or reversing weight loss, and in alleviating the fatigue and

leukopenia (low white blood cell counts) that typically accompany chemotherapy.

Jackie Haught, LAc is a New York City-based acupuncturist who sees a number of people with AIDS. Many of her patients are also undergoing various forms of toxic chemotherapy for conditions such as Kaposi's Sarcoma. They too suffer from the malabsorption, irritable bowel syndrome, weight loss, and muscle wasting so frequently seen in cancer patients. Haught reports, "Every client who has tried Seacure has experienced some benefit, including weight gain, increased energy, and improved digestion."

Jeff Marrongelle points out that chemotherapy is very detrimental to the GI system, and that 40% of cancer patients actually die of protein calorie malnutrition: They starve to death because of the lack of absorptive ability. Marrongelle and his colleagues place all of their cancer patients on a double dose of Seacure, at least 12 capsules per day.

Seacure has also been shown to be highly effective in promoting the healing of chronic wounds and in assisting recovery from surgeries, traumatic injuries, and even birth defects.

Marrongelle states, "We strongly recommend to all our patients who are having any type of surgery a pre- and post-surgical regimen that includes 12 to 20 capsules per day of Seacure. Their hospital stay, wound repair, post surgical sepsis — all those things in clinical obser-

vations have been decreased in people who have used Seacure as opposed to people who haven't. They're the first ones out of the hospital, the first ones out of rehab, and they get a better recovery with fewer complications."

Paul Lynn, MD is a holistically-oriented physician and the Medical Director of the San Francisco Preventive Medical Group. Lynn was visited by a woman in her early 60s with severe diabetes and a non-healing ulcer on her foot. She had tried many types of conventional treatments as well as chelation therapy, but nothing worked. Lynn used other approaches which are known to stimulate wound healing, such as high doses of Vitamin C and natural hormone replacement. But these therapies, too, had no discernible impact, and the woman was facing amputation of her foot.

Lynn then decided to prescribe Seacure and started the patient on 16 capsules per day. Over a period of ten weeks, he reports, her foot ulcer gradually diminished and then cleared up completely. As he considers the timing of the various therapies that were used, Lynn is convinced that it was Seacure which ultimately made the positive difference in the woman's condition. She has remained on a maintenance dosage of 3 Seacure capsules twice a day, and her foot ulcer has not returned.

Many physicians report similar results with the use of Seacure to treat chronic non-healing wounds.

For example, Tom Kruzel consulted with a 78-year old female who presented with an ulceration of the right ankle due to stasis and varicosities. The condition had persisted for two years and was causing significant pain and discomfort. Prior attempts to promote healing through leg wrappings and medicated dermal patches had failed to produce any positive changes.

Kruzel started the patient on a daily dose of homeopathic Lachesis 30c, along with Seacure, 500 mg., two capsules TID. Within two weeks the lesion had reduced to approximately 50% of its original size, and the constant weeping of serosanguenous fluid stopped. The patient was maintained on Seacure at the same dosage for 8 weeks until the lesion completely resolved. Now, more than two years later, there has been no recurrence.

Jeff Marrongelle's most dramatic case involved an 8 year old boy with a colostomy and serious birth dysfunctions, including blindness, no speech or cognitive ability, and virtually no ambulation. Marrongelle and his colleagues were surprised to learn that previous clinicians had never addressed the child's diet. They placed the boy on a ketogenic (low carbohydrate) diet along with Seacure. Amazingly, in about 45 days he started to talk and could for the first time communicate and respond to questions, despite the fact that he had never before spoken in his life. He also achieved better ambulation.

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# Symptom Reduction in Irritable Bowel Syndrome with Pre-Digested Fish Protein Supplement

by Carol Englender, MD

## Abstract

An outcome-based study on 13 patients, nine females and four males, with Irritable Bowel Syndrome (IBS) was conducted, as a first step in a comprehensive research program, to determine the symptom-mediating effectiveness of a commercially available pre-digested protein supplement (60% peptides:40% amino acids) made from the flesh of deep-ocean white fish. Responses on patient questionnaires concerning specific IBS symptoms and related health symptoms were evaluated at 30 and 60 days. Results show that the predigested fish protein supplement was effective in mediating IBS symptoms for eight of the 13 participants at 30 days and 12 of 13 participants at 60 days, and in improving general health in 11 of the 13 participants at both 30 and 60 days.

**Key Words:** Irritable Bowel Syndrome, IBS, pre-digested protein, white fish protein, peptides.

## Introduction

Irritable Bowel Syndrome (IBS) is considered a functional gastrointestinal disorder. The pathophysiology of the condition is poorly understood, but abnormal gastric motility, altered visceral sensitivity, and psychological factors may contribute to the etiology, severity, or perception of the disease. Although a variety of approaches to symptom assessment are available, the primary focus of diagnostic categorization of IBS by primary care physicians is the determination of the presence or absence of specific symptoms.<sup>1,2</sup> IBS is characterized by diarrhea sometimes alternating with constipation, abdominal pain often relieved by defecation, nausea, gas, bloating, and cramping. Certain symptoms of poor health such as loss of weight, loss of energy, and depression are also often seen with IBS. Up to 20% of the U.S. population experiences symptoms consistent with IBS, while only 10-20% of these seek medical intervention.<sup>3</sup> Nonetheless, IBS accounts for up to 50% of all referrals to gastroenterology clinics and is a leading cause of loss of work time.<sup>4,5</sup> Both men and women experience IBS, but women are more than twice as likely to seek medical attention.<sup>6</sup> The majority of diagnoses are made in both men and women between the ages of 15 and 40 years,<sup>5</sup> and occurrence in the US is consistent among varying ethnic groups.<sup>7,8</sup> IBS affects not only the quality of life and the individual economic status of the sufferers, but also the economy in general.<sup>9-11</sup>

Hundreds of observations by numerous medical personnel note that the symptoms of IBS, as well as of Crohn's disease and ulcerative colitis are significantly mediated by the administration of a commercially available, pre-digested protein supplement produced from the flesh of deep-ocean white fish.<sup>12</sup> This dietary supplement is unique in that 70% of its protein content is composed of small-chain peptides and free amino acids in a ratio of 60:40.<sup>13</sup>

Although the empirical data on the basis of sheer numbers might be regarded as conclusive, definitive data is nevertheless considered necessary to add validity to the observations. Accordingly and as a first step in a comprehensive research program, a self-assessment, 30/60-day outcome-based study was conducted in which patients diagnosed with IBS consumed

three grams per day of the pre-digested fish protein supplement over a period of 60 days.

## Methodology

### Recruitment

Patients diagnosed with IBS were invited to become study participants in a 30/60-day outcome-based clinical study employing questionnaires to evaluate results. The purpose of the study, they were told, was to determine whether a natural dietary protein supplement made from white fish fillets would be beneficial in alleviating symptoms associated with their condition. They were not informed of the anecdotal evidence suggesting that the supplement was effective. The participants were then asked to sign an agreement of study participation involving self-assessment.

Selected subjects for this study, a total of 13, were recruited over a period of just under two years. Each subject received a complete medical work-up that included a history, a physical examination, and a comprehensive blood analysis to detect or rule out organic disease. Using symptom-based criteria referenced earlier, all subjects were diagnosed as having IBS. The participants included nine females ranging in age from 21 to 61 (mean age 39.1) and four males ranging in age from 31 to 45 (mean age 37.5). This distribution of females to males, nine to four respectively, represents roughly that found in the general population with IBS.<sup>7</sup>

Most subjects had been taking medication before having been selected as participants in this study. Two were on Prilosec (a gastric acid pump inhibitor), one on Prednisone (a corticosteroid, anti-inflammatory), one on Methotrexate (an immunosuppressive), one on Voltaren (an anti-inflammatory), one on Lomotil (an anti-diarrheal), one on Zoloft (an anti-depressant), one on Axid (an acid blocker), and two on Sporonox (an anti-fungal). Some participants were on more than one of these medications. There seemed to be no consistency in prescriptions related to symptoms. Some of the participants reported having been on dietary supplements: three on multiple vitamins, two on probiotics, one on glutamine, and one on flaxseed oil. All subjects on medications and supplements had been on them for at least 60 days before starting this study. Symptoms reported by the participants were thus present while they were on these medications and supplements. These medications and supplements were continued throughout the course of the study to maintain a steady state.

Interviews with study participants indicated that medications and supplements had been ineffective. Accordingly, all significant positive changes in symptoms that might occur as a result of this study should be due to the predigested fish protein concentrate under test.

### Pre-digested Fish Protein Concentrate

The concentrated pre-digested fish protein was prepared from the flesh of deep-ocean white fish (*Merluccius productus*) caught in the Pacific Ocean off the coast of the State of

# Protein Supplement

Washington. The process employed to manufacture the concentrate is known generally as an enzymatic-fermentation technology. The technology is described as a controlled, self-regulating, aerobic process using a unique (patent pending) marine proteolytic micro-organism.<sup>14</sup> During the fermentation process, all pathogens and those viruses having previously been tested are destroyed, and spoilage organisms are minimized.<sup>15</sup>

As a result of the fermentation approximately 70% of the protein is reduced to 60% peptides and 40% amino acids.<sup>13</sup> After a low heat treatment, the ferment is concentrated by spray drying into a powder, 80% protein (N X 6.25). Only water is removed and some volatiles escape. The concentrate contains 3.5% fish oils, 70% of which are polyunsaturated, and 30% of which are omega-3 fatty acids.<sup>16</sup> The concentrate also contains low levels of phospholipids.<sup>13</sup> The concentrate (a powder), 500mg, is encapsulated in Size 0 gelatin capsules in which form it is consumed. Hazard Analysis Critical Control Points (HACCP) procedures are employed throughout the processing operation.<sup>12</sup>

The protein of the concentrate is approximately 98% digestible and nearly 100% utilized.<sup>13,17</sup> Various chemical and biological tests performed on the concentrate have shown the protein to be of superior quality reflecting the amino acid profile in the protein of the raw material. Accordingly, and as recommended by the National Academy of Sciences, the concentrate may function as a supplement to diets deficient in protein.<sup>18</sup> The concentrate was also shown in previous research to be effective in mediating symptoms associated with protein-deficiency diseases.<sup>13</sup>

The study participants were instructed to take two (2) capsules before each meal on an empty stomach for a total of six (6) capsules daily.

## Questionnaires

### Preliminary Questionnaire

The preliminary questionnaire, after a series of background questions, asked the following questions:

- How long have you been experiencing intestinal problems?  
Number of months \_\_\_\_\_ Number of years \_\_\_\_\_
- How long have you been under medical supervision for your intestinal problems?  
Number of months \_\_\_\_\_ Number of years \_\_\_\_\_
- Has your doctor diagnosed your condition as Crohn's, ulcerative colitis, irritable bowel syndrome, or some other specific problem?  
No \_\_\_\_\_ Yes \_\_\_\_\_ Which? \_\_\_\_\_
- What medications has your doctor prescribed for you?
- Do you take any medication other than what has been prescribed? (Include here complementary products such as digestive enzymes or probiotics. Also include pain medication such as aspirin or Tylenol.)

A listing of 14 symptoms followed with a choice of degree of severity for each symptom: mild, intermediate, and severe (see Table 1).

The first seven symptoms on Table 1 are those related directly to IBS. The next seven symptoms are those related to general health conditions often associated with IBS. The relationship between the IBS and health symptoms was not indicated on the questionnaire. All 14 symptoms were combined into one section for logistical reasons. Separating the questions might also have confused the respondents.

Two questions were asked about the subject's general health:

- Other than intestinal problems, how is your general health?  
Good \_\_\_\_\_ Fair \_\_\_\_\_ Poor \_\_\_\_\_

Are you experiencing any other medical problems?  
No \_\_\_\_\_ Yes \_\_\_\_\_ What are they? \_\_\_\_\_

And two questions were asked related to emotional considerations:

- How do you consider your life?  
Fairly calm \_\_\_ Moderately stressful \_\_\_ Very stressful \_\_\_
- Do you have a tendency to worry excessively?  
No \_\_\_\_\_ Yes \_\_\_\_\_

### Intermediate Questionnaire (30 days)

After a series of questions, including those on dosage, other medications, and compliance in taking the fish protein concentrate, a question was posed on general health:

- Has your general health improved since you began taking the protein supplement?  
Yes \_\_\_\_\_ No \_\_\_\_\_

A question on their IBS condition was also asked:

- In general, have the symptoms of your intestinal problem diminished since you began taking the fish supplement?  
Yes \_\_\_\_\_ No \_\_\_\_\_

The participant was then presented with the same seven IBS symptoms and the same seven health symptoms as seen on Table 1 with a "Yes" or "No" choice and then asked whether the "Yes" symptoms had disappeared, had lessened, had remained the same, or had worsened. The IBS symptoms are shown here as examples:

Original Symptoms	Yes	No	Disappeared	Lessened	Same	Worsened
Diarrhea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Constipation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Abdominal pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nausea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Gas	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bloating	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cramping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

### Final Questionnaire (60 days)

After some general background follow-up questions, the combined listing of the seven IBS and seven health symptoms with choices as indicated above was offered again as was the one question on general health and the one question on intestinal symptoms.

### Ratings

Two methods of ratings were employed in evaluating results obtained in this study. The first is based on a symptoms-only tabulation as reported by the participants. Such a method of presentation provides a quick visual means of determining the effectiveness and degree of effectiveness (or noneffectiveness) of the fish supplement in alleviating each experienced symptom.



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The second is based on a score applied to the total number of IBS and related health symptoms reported by each patient. This scoring method permits conclusions to be reached regarding the degree of effectiveness of the pre-digested fish supplement and permits comparison of results between 30 and 60 days.

## Tabulation of IBS and Related Health Symptoms

A compilation was made of the number of symptoms reported and the severity of each symptom for both the seven IBS and seven health symptoms followed by a compilation of whether these reported symptoms had disappeared, had become less, had remained the same, or had worsened at both the 30-day and 60-day period.

## Scoring of IBS and Related Health Symptoms

The Intermediate and Final Questionnaires were reviewed as to whether each experienced IBS symptom such as diarrhea and abdominal pain and each related health symptom such as loss of weight, loss of energy, and depression had disappeared, had lessened, had remained the same, or had worsened. Numerical values were given to each response.

A value of plus 10 (+10) was given to a symptom that had disappeared, a plus five (+5) to a symptom that had lessened, a zero (0) to a symptom that had remained the same, and a minus 10 (-10) to a symptom that had worsened. Totals were then calculated and divided by the number of symptoms

reported. For instance, if five symptoms were reported and four of these symptoms lessened and one became worse, the total would be +20 - 10 = 10. And 10 divided by 5 would yield a score of 2. Theoretically the best score would be +10 whereas the poorest score would be -10 no matter the number of symptoms reported.

No credit was given or taken away for the number of symptoms acknowledged on the reporting form nor was the severity of the symptoms weighted. The results of the seven IBS symptoms and the seven health symptoms are reported separately.

Responses to the question on general health and to the question on symptoms of intestinal problems on the questionnaire, although considered very important, are not numerically rated. Results are discussed, however. Blood profiles were conducted on all participants to rule out organic disease.<sup>19</sup>

No other correlations were made because the number of observations are considered too limited to be conclusive.

## Results

### Overall IBS and Health Status

In response to the questions on the Intermediate and Final Questionnaires, at 30 days all but three of the participants thought their intestinal symptoms had diminished; and at 60 days all participants responded positively with either a "yes" (11 participants) or "more or less" (two participants) response.

As to the questions on their general health, at 30 days all but two of the participants thought that their general health had improved. At 60 days one of the 30-day "no" responses changed to a "yes," one of the 30-day "no" responses remained a "no," and one of the 30-day "yes" responses changed to a "no." Overall, 11 gave positive responses at both 30 and 60 days.

Blood chemistries, not reported, showed no evidence of organic disease.

### Symptoms Tabulation

#### IBS Symptoms

The number of IBS symptoms reported, the severity of grouped symptoms, the 30-day and 60-day results showing whether symptoms had disappeared, had lessened, had remained the same, or had become worse are shown on Table 2.

Of the 62 total symptoms reported by the 13 participants, 28 (45%) were considered mild, 26 (42%) were considered of intermediate severity, and eight (13%) were considered severe.

**Table 1:**  
Listing and severity index of IBS and related health symptoms

Which of the following symptoms do you experience with your intestinal problem? Please also indicate degree of severity.

	No	Yes	Mild	Intermediate	Severe
Diarrhea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Constipation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Abdominal pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nausea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Gas	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bloating	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cramping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Heartburn	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fever	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Chills	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Loss of energy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Loss of appetite	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weight loss	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Depression	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Table 2: The number and severity of IBS symptoms and the 30-day and 60-day outcome of the symptoms.**

Symptoms	No*	Severity of Symptoms			30-Day Results				60-Day Results			
		Mild	Inter**	Severe	Dis***	Less	Same	Worse	Dis***	Less	Same	Worse
Diarrhea	10	5	4	1	4	5	1		6	4		
Constipation	8	4	3	1	3	3	2		5	3		
Abdominal Pain	9	3	6	1	4	3	2		4	4	1	
Nausea	6	5	1		6				6			
Gas	11	4	5	2	3	5	3		4	6		1
Bloating	10	4	3	3	2	5	3		2	6	2	
Cramping	8	4	4		3	4	1		3	5		
<b>Total</b>	<b>62</b>	<b>28</b>	<b>26</b>	<b>8</b>	<b>25</b>	<b>25</b>	<b>12</b>	<b>0</b>	<b>30</b>	<b>28</b>	<b>3</b>	<b>1</b>

\*NO = Number Reported \*\*INTER = Intermediate \*\*\*DIS = Disappeared

# Protein Supplement

The 30-day results show that of the 62 reported symptoms, regardless of their severity, 25 (40%) had disappeared, 25 (40%) had lessened and 12 (11%) had remained the same. The 60 day results show that the number of symptoms that had disappeared was 30 (48%), and the number that had lessened was 28 (45%), an improvement over 30 days. But most notably, only three symptoms (5%) remained the same, down from the 12 that had remained the same for the 30-day period. One symptom, however, was reported as worse.

## Related Health Symptoms

The number of related health symptoms reported, the severity of the grouped symptoms, the 30-day and 60-day results showing the outcome of the symptoms are shown on Table 3.

Of the 26 symptoms reported on the preliminary questionnaire, 14 (54%) were reported as mild, 10 (38%) reported as intermediate, and two (8%) as severe. The 30-day results, (only 23 symptoms were reported) indicate that 11 (48%) had disappeared, 11 (48%) had lessened, none had remained the same and one had turned worse. At 60 days, of 22 reported symptoms, 14 (68%) had disappeared, six (27%) had lessened, none had remained the same and the one symptom denoted as a severe depression had worsened.

The limited data permits no other correlations, but note that all participants reporting a loss of energy and appetite as well as a weight loss reported that these symptoms had disappeared or had become less. Of the five who reported depression symptoms, three reported that they had disappeared, one that they had become less, and one that they had worsened.

## Symptoms Scoring

### IBS Symptoms

The results of scoring IBS symptoms are seen on Table 4.

The average score for the IBS symptoms for the 30-day period was +5.9. Eight of the 13 participants scored +5 or above and of these, six of these scored above +7. These high scores (high scores arbitrarily determined to be a +5 or above) suggest that the fish supplement was highly effective for the majority of participants within the period of 30 days. Five of the participants scored low positive scores for the 30-day period ranging from +2.5 to +3.3, but no participants scored zero or below (a score of zero is ineffective).

The average score for the IBS symptoms for the 60-day period was +7.4, a jump of +1.5 from the 30-day scores. Twelve of the participants scored above +5 and seven of these scored above +7. Four of the five low scores for 30 days reached above a +5 score at 60 days, while one low score remained unchanged. Three participants lost all symptoms (+10) during the study.

## Related Health Symptoms

The results of scoring the related health symptoms are shown on Table 5.

The average score for the secondary symptoms for the 30day period was +6.8, and for the 60-day period was +8.0. One of the low scores for the 30-day period jumped to a perfect score at 60 days. The other changed from a negative score to zero (ineffective) at 60 days, that same participant reporting a low score with the IBS symptoms.

## Discussion

Data presented here support the numerous observations by medical personnel and patients alike that the pre-digested white fish protein does indeed significantly mediate the symptoms of IBS and improve general health often poor because of IBS. The mechanism for effectiveness of the predigested fish protein is not known, but may concern the peptide and amino acid content of the supplement as discussed below.

A feature of the dietary supplement used in this study is the nature of the unique enzymatic fermentation process,

which yields small peptides in addition to the normally expected amino acids.<sup>20</sup> From a strict nutritional viewpoint, the biological value of pep tides exceeds that of intact protein, which, in turn, exceeds that of amino acids.<sup>21</sup> Nitrogen retention is significantly higher in patients with intestinal disorders who are receiving peptide-based diets as compared with amino acid based diets.<sup>22</sup> Accordingly, it might be expected that a good nutritional response from peptides would aid in improving general health. However, many small peptides from dietary protein have been shown to have biological activity in excess of their nutritional value.<sup>23</sup>

Allergies, diabetes, infectious diseases, neurodegenerative diseases, cardiovascular problems, and cancer all show the potential to yield to peptide based-treatments.<sup>24</sup> Perhaps more pertinent to the issue in this paper, we find that peptides function at the gut level. For instance, met-enkephalin, a pentapeptide, modulates immune reaction.<sup>25</sup> Arginine-glycineaspartic acid forms a component of the cell attachment sites for microbes, and this peptide has been used to antagonize the adherence of *Candida albicans* to subendothelial binding sites.<sup>25</sup> Some small peptides have also been shown to modulate bowel permeability.<sup>26</sup> Further, amino acids are known to possess biological activity in addition to their nutritive value. Glutamine for instance, a component of the pre-digested fish concentrate, is important for the maintenance of GI integrity,<sup>27</sup> and arginine enhances wound healing.<sup>28</sup>

**Table 3: The number and severity of related health symptoms and the 30-day and 60-day outcome of the symptoms.**

Symptoms	No*	Severity of Symptoms			30-Day Results				60-Day Results			
		Mild	Inter**	Severe	Dis***	Less	Same	Worse	Dis***	Less	Same	Worse
Heartburn	3		2	1								
Fever												
Chills	1	1				1			1			
Loss of Energy	7	3	4		3	4			4	3		
Loss of Appetite	7	4	3		4	3			5	1		
Weight Loss	3	2	1		2	1			2	1		
Depression	5	4		1	2	2		1	3	1		1
<b>Total</b>	<b>26</b>	<b>14</b>	<b>10</b>	<b>2</b>	<b>11</b>	<b>11</b>		<b>1</b>	<b>15</b>	<b>6</b>		<b>1</b>

\*NO = Number Reported \*\*INTER = Intermediate \*\*\*DIS = Disappeared

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It is not known whether or to what extent the action of the fermentation process described results in the elaboration of different, perhaps unique, peptides than normally would be expected employing specific isolated enzymes such as trypsin and chymotrypsin that cleave protein at well-defined sites. This question is under study. Nor is it known whether differences would be found with the fermentation process using different sources of protein raw material, soy for instance, or even different sources offish other than the white fish. These aspects are also scheduled for study. It is known, however, that the parent protein used in nutritional formulas can alter physiologic and metabolic function. For instance, the immune response of mice fed lactalbumin hydrolysates is significantly greater than that of mice fed casein hydrolysates.<sup>29</sup>

Controlled studies on the pre-digested fish supplement are underway to define its effectiveness in mediating hyperpermeability (leaky gut syndrome) and in preventing bacterial translocation. Controlled studies on the effectiveness of the supplement for Crohn's disease and ulcerative colitis are to begin shortly.

**Table 4: Scores of IBS symptoms**

Patient Number	Age	Sex	Term [Years]	Number Reported	Symptoms 30 Days	Scores 60 Days
1	34	M	3	6	6.7	6.7
2	39	F	14	6	2.5	5.0
3	50	F	25	4	10	8.0
4	42	F	.5	2	5.0	10
5	38	F	15	7	10	10
6	61	F	.9	3	3.3	8.3
7	26	F	.8	7	2.9	2.9
8	45	M	35	2	7.5	10
9	26	F	2	6	3.3	5.8
10	39	F	5	5	7.0	9.0
11	31	F	.6	3	3.3	6.7
12	40	M	18	5	8.0	8.0
13	31	M	10	5	7.0	6.0
<b>Total</b>					<b>76.5</b>	<b>96.4</b>
<b>Mean</b>					<b>5.9</b>	<b>7.4</b>

**Table 5: Scores of related health symptoms**

Patient Number	Age	Sex	Term [Years]	Number Reported	Symptoms 30 Days	Scores 60 Days
1	34	M	3	4	6.3	7.5
2	39	F	14	3	8.3	6.7
3	50	F	25	1	5.0	10
4	42	F	.5	1	10	10
5	38	F	15	2	10	10
6	61	F	.9	2	2.5	10
7	26	F	.8	3	-3.3	0
8	45	M	35	4	6.3	10
9	26	F	2	3	6.7	6.7
10	39	F	5	2	10	10
11	31	F	.6	4	10	10
12	40	M	18	4	8.8	7.5
13	31	M	10	2	7.5	5.0
<b>Total</b>					<b>88.1</b>	<b>103.4</b>
<b>Mean</b>					<b>6.8</b>	<b>8.0</b>

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The protein supplement used in the study is Seacure™, a product manufactured by Proper Nutrition.

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# Making sense of Leaky Gut, IBS, and IBD

By Trent W. Nichols, MD, and Barry W. Ritz, BS

By now, we've all heard that intestinal health is the foundation of overall well being. That fact is clear. The intestinal lining is responsible for absorbing nutrients from the foods that we eat and serves as our most important immune barrier, protecting us from potential allergens in undigested foods, as well as microbiological and chemical threats. But sorting through the terminology and the countless catalog pages and store aisles of intestinal health products and digestive aids can be confusing and overwhelming. We're not all gastroenterologists (gut doctors), but it seems a brief discussion on leaky gut, irritable bowel syndrome, and inflammatory bowel disease, as well as how to best support intestinal health in all of these conditions or in a preventive manner, is in order.

In general, the intestinal lining serves two distinct functions: nutrient absorption and immune defense. The gut not only facilitates the digestion and absorption of nutrients from the food we eat, but it also acts as a physical barrier to microbes or undigested food particles that serve as potential allergens, so they don't go beyond the gut environment and get into the blood stream through the process of translocation. Normal absorption occurs in two ways. First, cells that line the gut, called enterocytes, selectively absorb nutrients on the side facing the inside of our GI tracts. The nutrients pass through the cells and exit the side of the cells facing the circulatory system's blood and lymph, sometimes altered or bound to carrier proteins. This is called a transcellular process (through the cells). Our intestinal linings also have tiny porous openings between the cells called tight junctions that allow small nutrients, like many minerals, to pass between the cells and enter the circulatory system directly. This is called a paracellular process (between the cells). If the pore-like structures become damaged and open too wide, toxins and undigested food particles from the gut can flood into the bloodstream causing dozens of ailments. This movement of unwanted substances through the tight junctions is what we call leaky gut.

Leaky gut is a surprisingly common problem with widespread effects. Food allergens and toxins that leak through are carried by the blood to the liver and eventually affect systems throughout the body by aggravating inflammation in the joints, expressing toxins in skin disorders, triggering food sensitivities, and causing "brain fog" or hyperactivity. Managing leaky gut is preventive medicine at its finest. Reducing this toxic load on the liver and body can prevent illness or improve its outcome. Resolving leaky gut can produce very real benefits to total health.

Leaky gut is associated with a wide range of general symptoms, such as fatigue, fevers of unknown origin, abdominal pain, bloating, diarrhea, feelings of toxicity, memory problems, difficulty concentrating, and poor tolerance to exercise. Leaky gut can cause:

- Attention deficit disorders
- Symptoms resembling autism
- Chronic and rheumatoid arthritis
- Chronic fatigue syndrome
- Eczema
- Food allergies and intolerances
- Inflammatory bowel disease
- Irritable bowel syndrome

- Joint and collagen problems
- Compromised liver function
- Malnutrition
- Multiple chemical sensitivities
- Psoriasis
- Symptoms like schizophrenia
- Skin disorders

Leaky gut can also be *caused by* any number of different conditions that cause inflammation (infection), severe trauma (bums or surgery), or many medications (NSAIDs), as well as:

- Aging
- AIDS with diarrhea/HIV
- Alcoholism
- Cancer
- Celiac disease
- Chemotherapy
- Crohn's disease
- Cystic fibrosis
- Giardia and other parasites
- Chronic hepatitis
- Intensive illnesses
- Malnutrition
- Pancreatitis
- Psoriasis
- Radiation therapy
- Rheumatoid arthritis
- Shock or anaphylaxis
- Toxic shock syndrome
- Ulcerative colitis

## IBS and IBD

Both irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) are associated with leaky gut syndrome. Irritable bowel syndrome is a disorder of intestinal function. The condition occurs in the small intestine, colon, or both. It can be characterized by abdominal discomfort, pain, bloating, mucus in the stools, and irregular bowel habits. IBS is typically a gut motility problem, either constipation or diarrhea, or an alteration between these two extremes. It may also involve low-grade inflammation that is not detected in evaluations, but plagues the patient (termed sub-clinical inflammation). The cause of IBS is not well understood, and IBS is something of a catch-all term. While not considered the cause, stress may exacerbate existing irritable bowel symptoms. Traditional GI tests are necessary to rule out diseases such as cancer, ulcerative colitis, or Crohn's, but diagnosis of IBS is based entirely on symptoms. Two FDA-approved prescription medications are available for the treatment of IBS, both limited in use to women only. The first medication for IBS, Lotronex® (alosteron hydrochloride), was approved in 2000, withdrawn the same year for adverse events, and then re-released in 2002 under restricted conditions of use, including specific use in women with severe diarrhea-predominant IBS. Zelnorm™ (tegaserod maleate) was approved in 2002 for the short-term treatment of women whose primary symptom is constipation.

Inflammatory bowel disease is a chronic inflammatory condition divided into two types depending on the location of the inflammation. Ulcerative colitis affects the colon, but just the lining. Crohn's disease can affect all layers of the intestine and even the entire length of the GI tract from mouth to anus. Again, the cause of IBD is not entirely

understood, but autoimmune conditions and allergies, lack of blood supply to the area, abnormal bacterial overgrowth (often related to the overuse of antibiotics), and heredity all seem to play a role. Current medical therapy consists of anti-inflammatory drugs such as corticosteroids (Prednisone), Azulfidine, or mesalamine, and immunosuppressives like 6-mercaptopurine, Imuran, methotrexate, or cyclosporine. All of these medications have been shown to be effective, but long-term use is often complicated by serious side effects. The relation between leaky gut and Crohn's disease is better established than between leaky gut and either ulcerative colitis or IBS.

### Testing for Leaky Gut

Well-established diagnostic tools like colonoscopy or sigmoidoscopy are necessary to rule out serious disease, like chronic inflammation or cancer. Several functional tests can provide additional insight. The comprehensive digestive stool analysis (CDSA) is a simple stool test that gives some twenty different measures, including fat absorption, bacteria and yeast in the colon, and the level of bacterial by-products (both good and bad). Food allergy testing will identify foods that should be eliminated from the diet in order to break the cycle of inflammation. The intestinal permeability test involves the consumption of a solution of two non-metabolized sugars, lactulose (different from lactose) and mannitol, followed by urine analysis. This test can give an indication of leakiness *between* the cells of the intestinal lining, as well as altered absorption *through* the cells. Look for a doctor who will order these functional tests for you or contact the laboratories directly for assistance (see resources).

### Nutrients that heal a leaky gut

In addition to removing food and chemical allergens from diet and environment (seek information on the elimination diet), as well as reducing stress that might trigger intestinal distress (there are a variety of mind-body techniques), there are a number of nutrients and supplements that can help heal a leaky gut:

- The most impressive addition to my treatment protocol is a dietary peptide supplement from hydrolyzed white fish. The product is manufactured by Proper Nutrition, Inc., and is available as Seacure®. Bioactive peptides act locally on the gut lining as healing factors and may increase protein synthesis. My success with this product led me to design a clinical study on the use of peptides from fish in reducing leaky gut and associated symptoms of IBD. I recently presented the results to the American College of Gastroenterology and plan to continue study in this area.
- Another source of peptides is bovine colostrum that also supplies valuable immune factors. If food allergies are present, consider a form that is lactose-free and casein-free.

- The amino acid L-glutamine is considered the primary energy source of the healing intestinal cell.
- Zinc is essential for growth and wound healing, particularly in cells that turn over rapidly, like those of the intestinal lining.
- Vitamin A is necessary for the maintenance of GI tract integrity, as well as the production of secretory IgA, an antibody that protects the gut lining.
- Antioxidants, like NAC (N-acetyl cysteine) for example, are necessary to reduce oxidative stress to the gut lining. NAC is a synthetic amino acid that helps to replenish glutathione, a very important cellular antioxidant.
- Short-chain fatty acids, the butyrates, are important for the lower portion of the GI tract, particularly the colon.
- Soothing herbs, like DGL (deglycyrrhizinated licorice), and herbs with anti-inflammatory properties, like boswellia and peppermint, can promote healing. There are many useful herbs.

All of these supplements work to promote intestinal healing. Specific treatment depends on the particular case, as leaky gut is associated with so many different underlying causes. For example, inflammatory bowel conditions can lead to the malabsorption of specific nutrients that may also have to be addressed.

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For more information regarding the healing power of peptides or reprints of Dr. Nichols' study on leaky gut, contact Proper Nutrition (800-555-8868).

Resources:

*Optimal Digestion*, Edited by Trent W. Nichols, MD, and Nancy Faass, MSW, MPH  
 Proper Nutrition, Inc. [www.propernutrition.com](http://www.propernutrition.com) 800-555-8868

[www.ibsgroup.org](http://www.ibsgroup.org)

[www.fda.gov](http://www.fda.gov)

Great Smokies Diagnostic Laboratories [www.gsdl.com](http://www.gsdl.com) 800-522-4762

Doctor's Data, Inc. (laboratory) [www.doctorsdata.com](http://www.doctorsdata.com) 800-328-7197

MetaMetrix Laboratory (food allergy testing) 770-446-5483

# PRELIMINARY REPORTS: IMPROVEMENT IN MUCOSAL INTEGRITY AND GI SYMPTOMS IN IBD AND HIV WITH HYDROLYZED WHITE FISH

Trent W. Nichols, MD, Paul D. Thomas, DO, John DelRossi, MPAS, PA, Angie Angstadt, BS, and Barry W. Ritz, BS

## ABSTRACT

*Dietary peptides are known to have biological importance beyond their nutritive value as protein, influencing structural, immune, and gastrointestinal functions. Protein balance studies performed in patients with inflammatory bowel disease (IBD) indicate better nitrogen balance with peptide-based diets than with whole food diets, which are in turn better than amino acid-based diets. However, no studies have examined the use of supplemental peptides in improving gut epithelial permeability and associated symptom relief. In a preliminary investigation, supplementation with a dietary bioactive peptide supplement prepared from hydrolyzed white fish was studied in two distinct populations in separate trials. In the first study, 15 IBD patients assessed to have gut mucosal hyperpermeability by a urine test utilizing lactulose and mannitol ratios were given either 3g per day of the fish peptide supplement or a placebo for 6 weeks, followed by a second permeability test and symptom assessment scoring. Results with the IBD patients taking the supplement showed a trend towards improvement in both intestinal permeability and symptom assessment versus controls. We then hypothesized that if GI symptoms resulting from current recommended HIV therapy are associated with a similar inflammatory mechanism, as suggested, these patients would also respond favorably to the peptide supplementation. Accordingly, a second population of 23 HIV-infected males experiencing GI side effects on highly active antiretroviral therapy (HAART) were given either 3g per day of the fish peptide supplement or a placebo for 5 months, with symptoms assessed before and after the treatment period. In the HIV patients, the number of GI symptoms collectively reported as decreased in the supplement group was significantly greater than the number of symptoms collectively reported as decreased in the control group. These bioactive peptides appear to have a possible dual function in HIV patients: controlling intestinal permeability that may result*

*from long-term use of HAART and reducing GI symptoms, which may result in increased HAART compliance and improved treatment outcome.*

## BACKGROUND

Inflammatory bowel disease (IBD) is a chronic inflammatory condition generally categorized as either ulcerative colitis (UC) or Crohn's disease, based on established disease criteria and the location of the inflammation. Recommended medical treatment includes corticosteroid therapy, as well as nutritional interventions, such as elemental peptide diets and micronutrient supplementation.<sup>1</sup> Up to 85% of patients hospitalized with IBD have protein-energy malnutrition, which can inhibit response to therapy and limit wound and fistula healing.<sup>2,3</sup> Nutritional therapy for IBD has traditionally consisted of elemental or oligopeptide diets with the theory of "putting the gut at rest," while supplementing with easily digestible, hypoallergenic nutrients.<sup>4</sup> Oligomeric (small-chain peptides or hydrolyzed protein) supplementation is preferred over monomeric (free amino acid) or polymeric (whole protein) supplementation, based on evidence of increased biological value (in starved rats)<sup>5</sup> and increased nitrogen balance in Crohn's patients.<sup>6</sup> Glutamine-supplemented polymeric diets have demonstrated no benefit in Crohn's disease.<sup>7</sup> Specific nutrients believed to benefit patients with IBD include fish oils, which provide anti-inflammatory omega-3 fatty acids that are shown to reduce the rate of relapse frequency in IBD;<sup>8</sup> short-chain fatty acids, like butyrate;<sup>9</sup> and other trophic factors, such as dietary peptides.<sup>10</sup> Bioactive dietary peptides act locally on the mucosal

barrier, as well as cross into the systemic circulation.

Seacure, used in both trials, is a commercially available hydrolyzed fish protein supplement (manufactured by Proper Nutrition, Inc.) that provides peptides and amino acids, predominantly glutamine, in an approximate ratio of 60:40.

Both DC and Crohn's disease are associated with intestinal epithelial hyperpermeability, although the evidence is more established for the latter.<sup>11</sup> Successful treatment of Crohn's with elemental diets is demonstrated by a reduction in intestinal permeability (IP), and normal IP in IBD patients has prognostic implications and may predict well-being.<sup>12</sup>

When properly used in HIV management, highly active antiretroviral therapy (HAART) can prevent opportunistic infections (OIs), maintain weight, improve viral counts, delay the progression to AIDS, and extend life.<sup>13,14</sup> However, GI complaints, such as diarrhea, affect an estimated 50-70% of HIV patients on HAART.<sup>15,16</sup> Such events can limit compliance to HAART, which leads to sub-therapeutic drug levels, viral mutations against HAART agents, and failure to achieve or maintain viral suppression.<sup>17</sup> The management of GI issues in HIV patients on HAART relates to quality of life and may play a role in compliance with medications and treatment outcome.

A relationship appears to exist between HIV and the health of the GI tract, including increased intestinal permeability, impaired gut-associated immune function, and oxidative stress,<sup>18</sup> although the particular inflammatory and functional changes in HIV-related intestinal disease remain unclear.<sup>19</sup>

## MATERIALS AND METHODS

### Study 1: IBD

The study design was randomized, double-blind, and placebo-controlled, with final evaluation at the end of 6 weeks of treatment. The treatment group (n=7) received a fish peptide supplement, while the placebo group (n=8) received a barley placebo, 2 x 500 mg capsules three times daily. The study population consisted of adult patients with Crohn's disease or DC who had been on the same dose of mesalamine, sulfasalazine, or prednisone for at least 3 months, or had not taken prednisone for at least 14 days.

Intestinal barrier function has implications for the etiology and pathogenesis of IBD, and tests of intestinal permeability are useful in screening, assessing treatment, and predicting the prognosis.<sup>20,21</sup> IP is most commonly assessed by differential urinary excretion of lactulose and mannitol.<sup>12</sup> Lactulose is a larger molecule than mannitol, such that a relative increase in the presence of lactulose signifies hyperpermeability. Successful treatment of IBD is matched by a significant reduction in the lactulose:mannitol ratio, indicative of improved permeability.<sup>22</sup> Testing was conducted by Great Smokies Diagnostic Laboratories, Asheville, NC.

Disease severity was assessed using the Crohn's Disease Activity Index,<sup>23</sup> and each patient completed before and after global symptom assessments. According to practice guidelines developed under the auspices of the American College of Gastroenterology patient and clinician global assessments correlate well to IBD activity for use in clinical research.<sup>24</sup>

IP and symptom scores were analyzed for treatment and control subjects separately by T-tests. A P-value of <0.05 was required for statistical significance. In order to standardize starting points and analyze test patients against control patients, percent changes in scores were calculated [% change = (score1-score2)/score1x100%], with analysis by ANOVA.

### Study 2: HIV

The site for the study was a large urban private medical practice with approximately 400 HIV-positive patients. Thirty-two patients were selected over a 2-month period, based on the following inclusion criteria: HIV-positive, ability to provide informed consent, ability to adhere to daily supplement regimen, life expectancy of at least 6 months, age greater than 18 years, absence of any OIs, compliance with uninterrupted HAART for at least 6 months, and viral load of less than 50 copies/mL; and the following exclusion criteria: female gender, life expectancy of less than 6 months, opportunistic malignancy requiring systematic chemotherapy within 30 days of study entry, the presence of any OIs, or concurrent use or prior use of anabolic agents/appetite stimulants/corticosteroids within 30 days of study entry.

The outcome-based study design was randomized, double-blind, and placebo-controlled. Patients were evaluated monthly for a total study duration of 5 months. The treatment group (n=18) received the fish peptide supplement, while the placebo group (n=14) received the barley placebo, 2 x 500 mg capsules three times daily. Patient questionnaires and clinician interviews were used to assess changes in intestinal symptoms and quality-of-life issues, while routine blood testing was used to identify any changes in disease status. The use of questionnaires for evaluating quality-of-life issues related to HAART and nutritional support has been documented.<sup>25</sup> Interviews and blood tests were conducted monthly. Statistical analysis was performed using T-tests, assuming normal distributions and equal variances. A P-value of <0.05 was required for statistical significance.

## RESULTS

### Study 1: IBD

We observed a trend toward improvement in both IP (Figure 1, p=0.07) and symptom scores (not shown) in patients receiving fish peptides, although results failed to

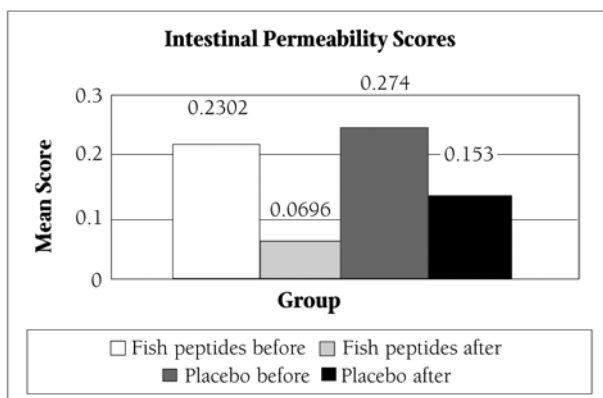
reach statistical significance. No such trend toward improvement in IP was identified in control patients ( $p=0.41$ ). The percent changes were 76% improvement in patients receiving fish peptides and 32 % improvement in controls (Figure 2), again not statistically significant but indicative of a trend towards increased improvement in patients receiving fish peptides versus control patients.

### Study 2: HIV

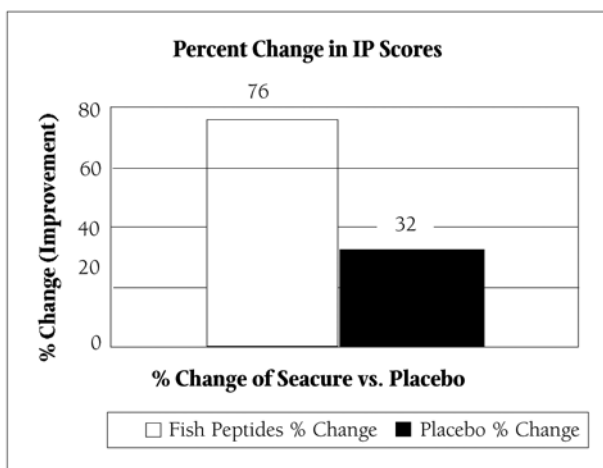
The mean age of patients was 43.9 years (00-64). Five patients in the fish peptides group were lost to follow-up, one patient withdrew from the study prior to completion, and one patient died from Hepatitis B 2 months into the study. Two patients in the placebo group withdrew prior to completion. Twenty-three patients completed the study (test  $n=11$ , control

$n=12$ ) and were used for data analysis. Blood profiles were monitored, and remained stable for all patients.

As seen in Table 1, there was no difference between the 2 study groups in the number of patients reporting symptoms at baseline ( $p=0.911$ ). At 5 months (Table 2), the number of symptoms collectively reported as decreased in the fish peptides group was significantly greater than the number of symptoms collectively reported as decreased in the control group ( $p=0.0479$ ). Further, all 11 patients receiving fish peptides, and 2 of 12 patients receiving placebo, felt better overall.



**FIGURE 1**  
**INTESTINAL PERMEABILITY SCORES BEFORE AND AFTER 6 WEEKS OF SUPPLEMENTATION WITH FISH PEPTIDES OR PLACEBO**



**FIGURE 2**  
**PERCENT CHANGE IN INTESTINAL PERMEABILITY SCORES AFTER 6 WEEKS OF SUPPLEMENTATION WITH FISH PEPTIDES OR CONTROL**

**TABLE 1**  
**ANALYSIS OF STUDY RESULTS—BASED ON 11 PATIENTS IN FISH PEPTIDE GROUP AND 12 PATIENTS IN PLACEBO GROUP AT THE START OF THE STUDY**

Symptom	Number of Fish peptide patients reporting symptom at baseline	Number of Placebo patients reporting symptom at baseline
Diarrhea	7	7
Nausea	4	4
Constipation	2	2
Bloating	7	6
Fatigue	9	9
MEAN	5.8±2.8	5.6±2.7

**TABLE 2**  
**ANALYSIS OF STUDY RESULTS—BASED ON 11 PATIENTS IN FISH PEPTIDE GROUP AND 12 PATIENTS IN PLACEBO GROUP AT THE END OF THE 5-MONTH STUDY**

Symptom	Number of Fish peptide patients reporting a decrease in symptom at 5 months	Number of Placebo patients reporting a decrease in symptom at 5 months
Diarrhea	7	2
Nausea	3	1
Constipation	0	0
Bloating	5	1
Fatigue	4	1
MEAN	3.8±2.6*	1.0±0.71

\* $p=0.0479$

## DISCUSSION

We observed a trend (not significant) towards improvement in IP and symptoms in IBD patients, as well as a significant decrease in total GI symptoms in HIV-positive males on HAART when supplemented with the fish peptides. We were limited by a small sample size, which may have been responsible for the failure to reach significance in IP testing. In the first study, we also observed that patients clearly identified by standard measures as having IBD did not always exhibit abnormal IP scores, making it difficult to recruit a suitable number of subjects. As a result, HIV patients evaluated in the second study were not assessed for changes in IP, greatly limiting our ability to draw clear conclusions.

Clinicians must recognize that, to the patient, the GI effects of HAART are like a disease unto themselves. The management of GI issues in HIV treatment may relate not only to quality of life, but also to HAART compliance, and thus contribute to viral suppression and extend life. Supplementation with these fish peptides may control IBD-like intestinal permeability that results from long-term HAART use, and appears to reduce the GI side effects of HAART, which may result in increased compliance and improved treatment outcome.

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