



International Foundation for Functional Gastrointestinal Disorders

IFFGD

P.O. Box 170864

Milwaukee, WI 53217-8076

Phone: 414-964-1799

Toll Free: 888-964-2001

Fax: 414-964-7176

Internet: www.iffgd.org

Symposium Report (199)

© Copyright 2006 by the International Foundation for Functional Gastrointestinal Disorders

Report on the 6th International Symposium for Functional Gastrointestinal Disorders

The 6th International Symposium on Functional Gastrointestinal Disorders was hosted by IFFGD on April 7–10, 2005. The biennial meeting was jointly sponsored by the Office of Continuing Medical Education, University of Wisconsin Medical School and the International Foundation for Functional Gastrointestinal Disorders (IFFGD) in cooperation with the Functional Brain-Gut Research Group (FBG). The program, a culmination of two years planning was both stimulating and informative. In fact, our knowledge of the functional gastrointestinal (GI) disorders continues to evolve, and these symposia are in many ways a barometer of the many changes occurring in the field.

Nearly 400 persons from around the world attended representing a variety of health care disciplines. Over 80 experts in the field of functional GI disorders presented their work in general sessions, multiple symposia directed toward specialties, and mini-workshops. The attendees included gastroenterologists, other medical physicians, nurses, physician assistants, lab technicians, and related allied health personnel, as well as representatives from the U.S. National Institutes of Health (NIH), the U.S. Food and Drug Administration (FDA), and the pharmaceutical and medical device industry. The summary that follows highlights several of the important aspects presented in the general sessions, including:

- Are Some Persons More Likely Than Others to get a Functional GI Disorder
- Treating the Patient with a Functional GI Disorder
- Gut Function in the Functional Gastrointestinal Disorders
- What is the Brain-Gut Interaction – Can it Influence Symptoms
- Treatment of IBS and other Functional GI Disorders
- Diagnostic Approach to the Functional GI Disorders
- What is New on the Horizon
- Delivery of Health Care to Patients

Opinions expressed are an author's own and not necessarily those of IFFGD. IFFGD does not guarantee or endorse any product in this publication, nor any claim made by an author and disclaims all liability relating thereto.

The information in this article is in no way intended to replace the knowledge or diagnosis of your doctor. We advise seeing a physician whenever a health problem arises requiring an expert's care

IFFGD is a nonprofit corporation. For more information, or permission to reprint this article, write to IFFGD, PO Box 170864, Milwaukee, WI 53217. Toll free: 888-964-1799. Phone: 414-964-1799. Fax: 414-964-7176. Visit our web site at: www.iffgd.org

Report on the 6th International Symposium on Functional Gastrointestinal Disorders

By: Douglas A. Drossman, M.D., Symposium Chair, and William F. Norton, IFFGD

Introductory Comments

Nancy Norton, President of IFFGD welcomed the participants and discussed the needs of individuals affected by functional gastrointestinal disorders. She described the mission of IFFGD and the efforts of the foundation to respond to these needs. In addition to the educational efforts of the foundation, this includes encouraging federal support for research, and working with investigatory and regulatory groups as well as with medical organizations and industry to help advance the field.

Stephen James MD, Director of the Division of Digestive Diseases and Nutrition at NIDDK, the National Institute of Diabetes and Digestive and Kidney Diseases, of the National Institutes of Health discussed ways in which NIH helps support research in the functional GI and motility disorders. This includes new initiatives with requests for applications for research grants, support for new Centers of research, and support for small grants. Notably, Nancy Norton has been a member of the NIDDK Advisory Council.

George Longstreth MD, President of the Functional Brain-Gut Research Group (FBG), thanked IFFGD for their efforts and addressed the areas where the two organizations have partnered over a 14-year period. The FBG is a professional organization that supports, promotes and advances multidisciplinary research and education into various aspects of brain-gut interactions.

Are Some Persons More Likely Than Others to get a Functional GI Disorder?

Epidemiology is an area of study that looks at what factors influence the incidence, causes, and distribution of diseases within groups of people. Sociocultural influence, race, gender, and ethnicity may all play a role. Genetics, which looks at how particular traits may be passed from one generation to the next through heredity, is another area of study through which we can understand who gets a particular condition and why. By understanding who, why, and under what circumstances some people get a disorder, we may better understand how to control or treat the condition.

Differences have been noted in the proportion of individuals with functional GI disorders around the globe.

However, this may relate more to the criteria used in studies than true differences in the number of people with the conditions. Efforts are underway, through a group of experts called the Rome Committees, to establish one set of standard definitions that can be used by all researchers (the Rome Criteria).

As the criteria used to define each functional GI disorder has changed over the past decades, the measured prevalences have changed as well. Despite these past limitations in determining the true prevalence, we do know that these disorders are extremely common. For example, irritable bowel syndrome (IBS) has a prevalence of 200/100,000 person years, which is 20 times that of inflammatory bowel disease. There is considerable overlap and shifting of categories across the functional GI disorders. Most are more common in women, and tend to decrease with age. Ultimately they pose a significant global health care burden.

The female to male prevalence of the functional GI disorders is more equal in childhood; they become more frequent in women after adolescence. The reasons are not clear, but some notable differences between men and women include:

- Women are more likely to recall and report GI symptoms
- Women perceive bodily pain at lower thresholds and report more discomfort. This may relate to their having greater perception or responsiveness within the gut (heightened visceral sensitivity)
- There is greater activation in women within regions of the brain which amplify the component of pain related to feelings and emotion
- There are greater changes in motility that relate to the menstrual cycle
- Women experience more co-existing disorders
- There are gender differences in response to drugs

Ethnic differences in health care use and symptom reporting have also been noted.

Childhood factors and intergenerational influences may also play a role. Children of parents with IBS tend to have higher rates of health care utilization. This relates in part to increased heritability (the influence of our genetic

makeup) within families as well as to influences arising from the family environment.

Increased sensitization is noted in both the gut and in the brain of patients with IBS. This is likely to be influenced by genetics as well as environmental factors. Several genes are being studied. Genetic variants effect hormonal reactivity to stress. Certain genotypes – that is the genetic makeup of an individual – may be associated with more emotional reactions and possibly some changes in bowel habit, though this is debated in the scientific literature. Investigation of the effects that genetic makeup of individuals has on IBS is difficult to study because of the genetic variability within populations that exists as well as gender and cultural differences.

Treating the Patient with a Functional GI Disorder

The practice of medicine involves both art and science. The functional gastrointestinal (GI) disorders, perhaps more than any other GI disease, present as an interwoven combination of both illness (the patient's experience of ill health within the context of lived experiences) and disease (objective signs of disease). Separation of the biological and mechanical concept of disease from the lived experience of illness is a relic of the past. Rather, they must be understood from an integrated, or biopsychosocial, perspective. In this point of view the disease, and the individual patient's personality and social construct are considered in combination. To do this requires that a rapport, an understanding relationship, be established between the patient and the doctor or health care provider. The physician must not only listen but *hear* the information expressed by the patient. The patient must be placed at the center of the diagnostic and therapeutic process, and the mind-body connection explained and understood.

Some of the major research advances that support the integrated or biopsychosocial approach include:

- Genetic and early environmental influences on the functional GI disorders
- The role of neurotransmitter and neurohormonal signaling in intestinal/enteric function
- The use of animal models
- Newer research relating to altered neuroimmune function, cytokine (cell molecules involved in the immune system response) activation, and brain-gut interactions
- Demonstration of post-infectious IBS as a brain-gut disorder
- The role of brain imaging in understanding the modulation of visceral pain

Effective communication – the physician-patient relationship – is an important part of effective long-term

management of a functional GI disorder. The patient interview by the health care provider is the most frequently practiced procedure, accounting for about 150,000 interviews in a clinician's lifetime. However, the average visit is now too brief, and this has led to the decline of the humanistic approach to patient care. Impaired communication with the patient is the overarching problem for patient dissatisfaction with care.

Therapeutic Value of the Medical Interview – Biases among health professionals toward care of patients with functional GI disorders are ever present. One study confirmed that physicians differ from patients in their perception of the seriousness of patient complaints, their degree of disability, and the reasonableness of late night phone calls. These differences were much more attributed to patients with functional, rather than organic, GI disorders.

Evidence supports that doctors asking patients about what they understand about the illness, their concerns, and the impact of their illness, as well as demonstrating empathy leads to reduced patient anxiety and improved symptoms. Similarly, patients who are allowed to express themselves fully (feelings, opinions, information) have improved health status and symptom resolution.

Effective methods of physician interviewing that would improve the physician and patient relationship include:

- Active listening
- Identifying the patient's priorities
- Providing empathy – technology is not a substitute for caring and compassion
- Validating the patient's feelings
- Not overreacting
- Educating
- Providing reassurance
- Mutually developing a treatment plan
- Helping the patient to identify areas where he or she can take personal responsibility
- Setting realistic goals and limits

Gut Function in the Functional Gastrointestinal Disorders

Both sensory and motor function (motility) frequently appear to be altered in patients with functional GI disorders. Many patients exhibit an increased or exaggerated response to stimuli (hypersensitivity), which means they sense or perceive pain or discomfort more easily, or at lower levels, than is considered normal. Abnormal contractions of the muscles in the gastrointestinal tract (intestinal dysmotility) are also often observed. Are there factors that make some people more likely than others to experience sensory or motor dysfunction? Are there factors that trigger the

development of sensory and motor (sensorimotor) dysfunction? Our understanding of these factors is rapidly increasing and research interest ongoing.

Neuroplasticity relates to the ability of the brain and nervous system to learn, grow, and change to conditions. Neuroplasticity is affected by life experiences, gender, age, injury, and genetic makeup. It is important for learning but can be detrimental with regard to chronic pain conditions. Here, pain may beget more pain (“windup”). Repetitive exposures to painful stimuli in early life can alter physiology and behavior and can profoundly affect the neural processing of sensory information from the gut. Thus early life factors may potentially provoke the development of visceral hypersensitivity (exaggerated perception or responsiveness within the gut) along the brain-gut axis.

Humans have evolved a close association with certain disease producing organisms (pathogens), such as bacteria or viruses, leading to immune “tolerance” where there is low grade inflammation in the gut. Inflammation is a normal immune response by the body in reaction to tissue damage such as caused by injury or infection. Some bacteria can be associated with anti-inflammatory production that decrease inflammation by activating anti-inflammatory substances within immune cells (cytokines), while other bacteria can be associated with more inflammatory cytokine production. However, if this system gets out of balance, there may be increased or destructive immune responses. For example, with IBS with diarrhea a low grade inflammatory response can contribute to the disorder. With post-infectious IBS, in particular, there is loss of the “good” bacteria (commensals) with increased mucosal inflammation, activation of anti-inflammatory substances, and increased small bowel permeability to bacteria. Probiotics may have a role in improving these symptoms by reversing the inflammatory immune state, by introducing the “good” bacteria.

New investigative techniques, such as animal studies, are producing a testable hypothesis about underlying disease mechanisms and developing therapeutic targets for treatment of the functional GI and motility disorders. Improvements in brain imaging methods increasingly will play a role in understanding the processing of pain and other sensory signals, and possibly in defining subgroups of patients for treatment. However, we are still early in developing standards for these assessments, and that is much needed.

What is the Brain-Gut Interaction? Can it Influence Symptoms?

The central nervous system and the gastrointestinal tract are linked. Information continuously flows back and forth within a network called the “brain-gut axis.” These interrelated feedback circuits can influence brain processes and bowel functions. Normally, these interactions occur without conscious awareness in most healthy people. But in persons with functional GI disorders, these interactions may be consciously perceived and may play a role in symptom generation, such as feelings of pain or discomfort. Three systems are involved in this dialogue:

- 1) The normal stress response system that helps the body adapt to change and ensure survival
- 2) The signaling system (serotonin) within the gut
- 3) The brain, which perceives and responds to gut signals.

The Stress Response System – Adverse experiences in life combined with certain genetic abnormalities may lead to distinct traits or characteristics that manifest as a stress-related disorder. This may be processed in a person through a system in the body that controls reactions to stress (the hypothalamic-pituitary-adrenal, or HPA, axis). In response to a stressor, the HPA axis stimulates or inhibits the release of various hormones, in particular cortisol, into the blood. This then stimulates systems essential to self-preservation, such as heightened vigilance or fear, as well as effecting regulation of the body’s immune response.

Corticotropin-releasing factor (CRF) is a stress hormone that may be an important factor in mediating a relationship between stress and functional GI disorders. CRF has effects on pain sensitivity and colonic motility; drugs that inhibit the actions of CRF (antagonists) eliminate the enhanced colonic response to stress as seen with irritable bowel syndrome (IBS).

The Signaling System – The gut based serotonin system is an important component in the brain-gut dialogue, and this is an important area of investigation because of its therapeutic implications in treating patients. Serotonin is a neurotransmitter, a chemical that acts on the nervous system to help transmit messages. Most of serotonin in the body resides in the bowel wall within enterochromaffin (EC) cells lining the gut and nerve cell bodies. There are different types of serotonin that are called receptor subtypes, identified as “5-HT” followed by a number. The serotonin found in the gut consists mainly of 5-HT₃ and 5-HT₄ subtypes.

Serotonin is released from the enterochromaffin cells and acts on receptors on the nerves within the bowel wall.

These nerves may be part of the nervous system which resides completely within the bowel wall, known as the enteric nervous system, or may be nerves that transmit painful and non-painful information by projecting from the bowel to the spinal cord and brain. Activation of these nerves by serotonin leads to the release of other neurotransmitters and through their actions, it plays a major role in gut motility, secretion, and sensation.

Patients with post-infectious IBS (or IBS with diarrhea) have increased EC cells, and the process (reuptake) in which serotonin, after transmitting its message, is taken up again by nerve endings, broken down, and inactivated is blunted. This leads to an increased serotonin effect, which may enable IBS symptoms. This has clinical implications for drugs that inhibit the effect of serotonin (5-HT₃ antagonists) in IBS with diarrhea. Conversely, in patients with IBS with constipation, drugs that enhance the effect of serotonin (5-HT₄ agonists) can be helpful.

The Brain – There are various ways in which the brain can effect the perception of pain arising in the gut. The circuitry for visceral pain rises from the gut to a part of the spinal cord that receives information from the body's organs and tissue (the dorsal horn), and then to an area of the brain involved with perception of the intensity of stimulus involved with processing pain (the posterior insula) and also to another area of the brain that is associated with the emotional and cognitive aspects of pain (the anterior cingulate cortex).

Once registered as pain, there is a descending inhibitory system within the brain, which attempts to restore homeostasis. A clinically relevant factor is that attention and distraction can modulate this system via interacting circuits that inhibit the noxious response. These interacting circuits can affect perception of pain and be associated with feelings of distress, or conversely, can modulate and reduce the pain experience.

Treatment of IBS and other Functional GI Disorders

Currently, there is no single consistently successful treatment approach for patients with IBS. Because IBS is typically a chronic, or long-term, condition the goals of therapy typically focus on reassurance that some other disorder is not causing symptoms, education on how to manage the condition, and symptom improvement rather than cure.

Most patients with IBS have mild symptoms that minimally interfere with daily life. Up to 25% have more severe symptoms that significantly impair daily life and about 5% have severe and incapacitating symptoms where referral to a multi-specialty treatment center is required.

Traditional Treatments in IBS – Traditional management strategies often include dietary modifications, such as: a) Avoiding carbohydrate overload or intolerance; b) Avoiding fatty foods and caffeine; and c) Avoiding overeating or an overly restrictive diet. Fiber intake can help with constipation, but the data do not support its role for pain or diarrhea, and bran may in fact increase bloating and abdominal pain. Laxatives, though commonly used are understudied with regard to IBS with constipation. Loperamide (e.g., Imodium, Loperacap) is favored over other opiates because it does not cross the blood brain barrier, and it may also increase resting anal sphincter tone, possibly reducing incontinence. Antispasmodics to ease spasms or cramping have shown some benefit in European studies but the studies were methodologically flawed. Prokinetics that promote motility, like cisapride and domperidone, have been used, but there is no clear benefit from well designed studies.

Newer Medications – Newer receptor acting agents for IBS are available or under investigation. Tegaserod, a 5-HT₄ partial agonist was shown to have beneficial effects on bowel function and abdominal pain in a recent Cochrane review. Renzapride showed some improvement in adequate relief and loosening of stool in a phase IIb study. Alosetron, a 5-HT₃ antagonist was effective for IBS with diarrhea in women, and brain imaging shows increased brain activity in areas that suggest an effect on enhancing central down-regulation of signals from the gut to the brain. A recent paper shows it may also be helpful for men. Several other medications are under investigation to reduce pain, diminish motility and visceral hypersensitivity, help with constipation, and promote motility and anti-inflammatory effects. Further studies in larger trials are needed for these newer agents to determine their precise role in IBS.

Psychological and Behavioral Treatments – In some cases, patients are not satisfied with their medical treatments and behavioral treatments may have overarching effects on helping manage and adapt to their symptoms. After reviewing the existing literature, there are four treatments that have been studied rigorously enough to show meaningful results: 1) Cognitive behavioral therapy (CBT); 2) Hypnosis; 3) Interpersonal psychotherapy; and 4) Biofeedback. In one large multicenter trial CBT showed a 70% response compared to patient education. Hypnosis has shown benefit in several studies. Hypnotherapy was of benefit for IBS as well, and hypnosis and CBT have been shown beneficial for functional dyspepsia. In general, these methods are successful, though the data are not available to determine which is more effective in which subgroups of patients. This decision needs to be based on patient preference and available resources. Finally, anorectal biofeedback may be

of value for some patients with fecal incontinence or constipation (pelvic floor dyssynergia).

Psychopharmacological Treatments – An evolving concept involving the use of antidepressants in IBS is that they may be targeting something besides depression. In fact, depression does not predict a response to antidepressants in IBS. This is supported by the fact that IBS patients are twice as likely to have other non-GI somatic disorders, and possibly these agents help centrally to reduce the sensitivity to bodily symptoms as well as having other effects. Other evidence shows that in treatment trials antidepressants (low-dose tricyclics for example) are not treating psychiatric disturbance but have some other effect that leads to improvement in symptom reporting.

Diagnostic Approach to the Functional GI Disorders

A positive diagnosis of a functional GI disorder is important. The symptoms of functional GI disorders are neither inconsequential nor unworthy of medical attention. Diagnosis identifies conditions that are as real as structural diseases. Furthermore, diagnosis helps to promote a productive doctor-patient relationship. There is an increasing body of scientific evidence about the nature and prevalence of the functional GI disorders, as well as appropriate testing and treatment. The Rome Foundation and the IFFGD are among those that have led the movement within the medical community to legitimize the functional GI disorders, and diagnosis has an essential role. No longer should a patient with a functional disorder leave a doctor's office without a diagnosis, or the feeling that the physician thinks, "It is all in his or her head."

The Rome Foundation is an international organization that classifies the functional gastrointestinal disorders and by using the best evidence establishes criteria for their diagnosis. Known as the "Rome Criteria" they provide a system for identifying the many functional gastrointestinal disorders based on symptoms.

Criteria are needed for defining and diagnosing the functional gastrointestinal disorders because there is no consensus on the pathophysiology of these disorders. Clinicians need a system to organize their knowledge around conditions and to select diagnostic methods and treatments. Additionally, investigators need a standardized group to study. The criteria for IBS is supported by at least one well designed study that showed a positive predictive value of 98% when Rome Criteria are used. The use of these criteria is also supported by factor analysis of population study data. The use of "red flags" or "alarm signs" (i.e., identification of easy to obtain data like blood

in the stool, or a family history of cancer or inflammatory bowel disease, which are suggestive of another disease) can help the physician in the decision to do additional testing to exclude other diseases. Overall, symptom criteria are needed and when used by trained personnel they have adequate validity and reliability.

There are no reproducible or reliable markers for functional GI disorders, since these disorders have varied and atypical presentations. A "marker" is a clearly identifiable characteristic – such as would show up in a blood test or x-ray, for example – that would support a diagnosis. It is noteworthy that most diagnostic studies to exclude other diseases for IBS have a pretest probability that is no different than the general population, the one exception possibly being celiac sprue. As such clinical judgment must prevail over any diagnostic algorithm (i.e., predetermined, step-by-step procedure). The American College of Gastroenterology (ACG) diagnostic guidelines recommend that tests are not indicated in IBS without alarm features. In general, celiac screening is needed, colorectal cancer screening requires colonoscopy for patients over age 50, and a diagnosis of functional dyspepsia requires an upper endoscopy to test for and exclude organic gastrointestinal disease, such as GERD or ulcer. This has to be balanced with the fact that many patients expect that testing be done.

What is New on the Horizon?

Some of the newer innovations in the field are of interest to practitioners, investigators, regulatory agencies, health economists, and industry as well as to patients.

Measuring Quality of Life – Health related quality of life (HRQOL) may be defined as a multi-dimensional measure that captures information from biological, psychological, and social function. The rationale for its study relates to the fact that physiological outcomes don't capture the patient's experience of illness, and HRQOL are more relevant as an outcome measure for disorders associated with chronic illness. There are both generic (e.g., SF-36, SIP) and disease-targeted (e.g., IBS-QOL, IBSQOL) instruments, which have an overall score and then subcomponents or domains. IBS patients have poorer HRQOL than many other medical conditions including GERD and depression, and it is similar to Type I diabetes and end stage renal disease. This type of measurement is also important because effects on quality of life are often not recognized or addressed by health care providers, and recognizing these effects may strengthen the physician-patient relationship.

Complimentary and Alternative Medicine (CAM) – The role of the U.S. National Center for Complementary and Alternative Medicine (NCCAM-NIH) is to look at both

alternative (i.e., outside the conventional realm of medical practice) and complementary (i.e., methods used in addition to conventional treatments) interventions, and determine their scientific validity. In a recent U.S. national health interview it was found that 36% of patients use CAM (40% with IBS), and 61% use prayer, natural products, deep breathing, meditation, and chiropractic. The use of these methods correlates with lower satisfaction with the care, less belief in conventional doctor explanations, and poorer health related quality of life (HRQOL). Thus it is important to understand not only the values of CAM treatments, but also what it is about conventional medicine that is not working for patients.

New Directions for Drug Development – Well designed treatment trials have shown benefit for centrally (central nervous system) targeted agents over peripheral, gut-acting agents. Examples include the antidepressants and behavioral treatments like cognitive behavioral therapy, and even alosetron, the 5-HT₃ antagonist that has central as well as peripheral effects. In contrast, anticholinergic and other antispasmodic drugs, cholecystokinin (CCK) antagonists, and peripheral kappa agonists have not shown benefit.

Progress in developing effective drug treatments for functional GI disorders has been hindered because there is no disease model that describes the actual process of why people have symptoms. In IBS for example, while a series of gut abnormalities have been described (ranging from alterations in motility, secretion, immune activation to bacterial flora) no single one of these findings has been demonstrated to have a direct relationship to the characteristic symptom complex of chronic abdominal pain or discomfort associated with altered bowel habits. It may be that there are subgroups of patients with differing processes underlying their IBS symptoms. Identifying and targeting specific IBS subgroups with correspondingly specific treatments may in future result in improved results.

Recent developments provide a better understanding of the interactions between stress, pain, and emotions. This offers new opportunities for the development of therapeutic agents for IBS and other functional disorders. This new approach is supported by data related to activation of the central stress system, and by neuroimaging to look at activity within the brain, which is beginning to disclose the neural circuitries underlying pain modulation, autonomic function, and emotion regulation. A more effective future approach would be to look at drugs that more selectively choose targets aimed at different levels of the central nervous system and thus re-establish altered homeostasis.

What is Stress?

Stress is the term used to describe the neurophysiological and subjective response to stimuli. In contrast to the common interpretation of the term "stress" as a psychological phenomenon, it should be understood as any real or perceived disturbance of an organism's homeostasis, or state of harmony or balance. Stress may disrupt the function of nerve and even immune cells in the GI tract and in the brain. The **central stress system** involves the release of chemical stress mediators in the brain, which in turn orchestrate an integrated autonomic, behavioral, neuroendocrine, and pain modulatory response. This biological response in turn will alter the way the brain and the viscera (internal organs such as the gut/intestines) interact, and this altered brain-gut interaction can result in worsening of symptoms in functional GI disorders. For example, stress can increase GI symptoms by changing how the brain controls unwanted and painful sensation.

Probiotics – The gut normally maintains a delicate balance of bacteria, which plays a role in intestinal homeostasis. Alterations in the number, distribution, and composition of these bacteria may disrupt this balance. With IBS, the environment within the intestines may be involved with bacterial overgrowth, exposure to foreign substances (antigens), and carbohydrate maldigestion. This can lead to increased gas, short chain fatty acids, and bile salts, all of which can exacerbate symptoms. Probiotics ("good" bacteria) are defined as live organisms that in adequate amounts can exert a health benefit.

Theoretically, probiotics could help improve IBS symptoms by suppressing inflammation, altering the form or composition of stool, reducing flatus/gas production, and competing with pathogens in the gut. One small double-blind, placebo-controlled study demonstrated a significant benefit, in terms of pain relief and other symptoms improvement, among IBS patients randomized to a *bifidobacterium* strain, but not a *lactobacillus* strain. These findings need to be confirmed in a larger trial. Not all probiotics are the same and they need to be studied individually; the ideal probiotics strain has yet to be identified.

Delivery of Health Care to Patients

Are changes needed that affect our health care delivery system? Regrettably, less than 1% of the U.S. NIDDK-NIH budget goes to functional GI disorder research. Yet the costs of these disorders are considerable not only in terms of direct costs to the health care system, but also

indirect costs (productivity, work absenteeism) as well as intangible costs (pain and impaired health related quality of life). IBS is the most common functional GI disorder. The U.S. Householder study by Drossman identified indirect costs in terms of work absenteeism of 13.4 days in IBS vs. 4.9 days for the control group. An estimated \$20.2 billion is spent annually on IBS in terms of indirect costs and estimates of annual direct costs range from \$2.0 to 10.0 billion. Other studies show that 27% are unemployed due to illness with functional GI disorders. The message is clear – these are conditions that have serious consequences on our health and economy and need to be treated more effectively.

Conclusion

In addition to the general sessions at the Symposium, there were a large variety of workshops and mini-symposia on the design of treatment trials, interview techniques, case study sessions, psychological testing and treatment, brain imaging, GI physiology sessions, basic aspects of the brain-gut axis, alternative-integrative medicine, and pediatric disorders. IFFGD gave Research Awards to six clinical and basic investigators; Dr. Allen Spiegel, then director of NIDDK presented the awards to the recipients.

From the time when IFFGD initiated this Symposium in 1995 we have seen the field of functional gastrointestinal disorders expand as our scientists and clinicians remain committed to understanding the pathophysiology of these disorders and strive to identify better diagnostic measures and treatment options. The amount of education that surrounds these disorders has broadened in scope and the level of public discourse has increased.

We see messages every day in print, on television, or on the Internet about hundreds of over the counter or self-help remedies for individual symptoms like diarrhea, constipation, gas, bloating and pain that accompany functional GI disorders. These messages would have us believe the answers are at hand. While some people are being helped by a variety of treatment options, many others are not.

These disorders affect not only those who suffer with chronic symptoms, but also their families and others in the community at large. We can measure the economic costs of healthcare utilization and lost productivity. We can measure the social costs with quality of life surveys. But we can never measure the cost of lost individual potential.

The work being done by the participants in this Symposium is essential to the individual, the patient who continues to strive for some kind of normalcy in their life and the lives of their families. Through these efforts, there is hope for the future.

We are grateful to all those who participated in and who helped organize the meeting. Preparations for the 7th International Symposium on Functional GI Disorders planned for April 2007 are underway.

Information incorporated into this article was drawn from presentations at the Symposium by the following individuals.

Elie Al-Chaer, MD
Michael Camilleri, MD
Brooks D. Cash MD
William D. Chey, MD
Margaret Chesney, PhD
Ray E. Clouse, MD
Nicholas E. Diamante, MD
Douglas A. Drossman, MD
Richard Frankel, PhD
Shin Fukudo, MD
David Grundy, PhD
Christine Heim, PhD
Margaret Heitkemper, PhD
John E. Kellow, MD
Rona Levy, PhD
G. Richard Locke III, MD
Emeran A. Mayer, MD
Nancy J. Norton, IFFGD
Olafur Palsson, PsyD
P. Jay Pasricha, MD
Charlene Prather, MD
Eamonn M.M. Quigley, MD
Brennan M.R. Spiegel, MD
Robin Spiller, MD
W. Grant Thompson, MD
William E. Whitehead, PhD

A complete description of the programs and list of the faculty is available on-line: www.iffgd.org/images/FGID_brochure2005.pdf

Symposium Support

We gratefully acknowledge the unrestricted educational grants from the supporters of the Symposium:

Principal Supporters

Ethicon Endo-Surgery, Inc., A Johnson & Johnson Company
GlaxoSmithKline
Novartis Pharmaceuticals Corporation
Solvay Pharmaceuticals, Inc.

Other

Chugai Pharma USA, LLC

Exhibitors

Ethicon Endo-Surgery & Its Inscope Division
Functional Brain-Gut Research Group
Genova Diagnostics
GlaxoSmithKline
Medtronic
Novartis Pharmaceuticals
QuinTron Instrument Company
SmartPill Diagnostic, Inc.
Solvay Pharmaceuticals
T.L. Recordings Limited
UNC Center for Functional GI & Motility Disorders

