International Foundation for
Gastrointestinal Disorders

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Symposium Report (250)

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Report from the 9th International Symposium on Functional Gastrointestinal Disorders

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The 9th International Symposium on Functional GI Disorders took place April 8–10, 2011 in Milwaukee, Wisconsin. The meeting was jointly sponsored by the University of Wisconsin School of Medicine and Public Health Office of Continuing Professional Development in Medicine and Public Health, and the International Foundation for Gastrointestinal Disorders (IFFGD).

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By: Spencer D. Dorn, M.D., M.P.H., M.H.A., Vice Chief, UNC Center for Functional GI and Motility Disorders and Assistant Professor, Division of Gastroenterology and Hepatology, University of North Carolina at Chapel Hill, Chapel Hill, NC

The 9th International Symposium on Functional GI Disorders took place April 8–10, 2011 in Milwaukee, Wisconsin. The multi-disciplinary, CME accredited meeting was jointly sponsored by the University of Wisconsin School of Medicine and Public Health Office of Continuing Professional Development in Medicine and Public Health, and the International Foundation for Gastrointestinal Disorders (IFFGD).

More than 325 persons from 23 countries attended, including clinicians, researchers, industry leaders, patient advocates, and government health regulators. Over the course of three days, experts in functional GI and motility disorders presented state-of-the-art information on a variety of related topics in plenary sessions, mini symposia, and small group workshops. Interactive sessions and networking opportunities produced stimulating discussions, lively exchange of ideas, and collaborative opportunities.

The summary that follows highlights and provides an overview of some of the important aspects of the plenary sessions.

Friday April 8

Introductory Comments

Nancy Norton; Stephen James, M.D.; Lin Chang, M.D.

Nancy Norton, President of the IFFGD discussed the IFFGD's continued mission to inform, assist, and support people affected by gastrointestinal disorders. Throughout its 20 year history, the IFFGD has worked with the multiple stakeholders to broaden understanding about GI disorders and support research. Ms. Norton observed how this meeting demonstrates the importance and significance that functional GI and motility disorders have in the field of medicine internationally. This biennial meeting originated in 1995 and it is gratifying that IFFGD has been able to continue to provide a forum to promote advancing knowledge and discussion in a field that impacts so many patients' lives. This is made possible by the participants and the generous support from corporations who all contribute to the overall success of the program. Special thanks acknowledged the following supporters:

- Forest Laboratories, Inc
- Ironwood Pharmaceuticals
- The Procter & Gamble Company
- Takeda Pharmaceuticals North America
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- Prometheus Laboratories
- Salix Pharmaceuticals

Stephen James, M.D., Director of the Division of Digestive Diseases and Nutrition at NIH, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), discussed the ways in which NIH helps support research into functional GI and motility disorders. In 2010, NIDDK provided over $1.6 billion in total research support. Some of this funding specifically targeted functional GI and motility disorder research, including grants to support investigator initiated projects, the Gastroparesis Clinical Research Consortium, the UCLA Center for Neurovisceral Research, as well as patient information and awareness campaigns. Regarding the 2011 financial year, Dr. James commented that funding levels are difficult to predict.

Lin Chang, M.D., UCLA, led a moving tribute to our friend and colleague Vanessa Ameen, M.D., whose unexpected, sudden death several months ago was a deep loss to our community.

Clinical Approach

Moderator: Douglas A. Drossman, M.D.; Panel: Ami D. Sperber, M.D., MSPH; Jan Tack, M.D., Ph.D.; Douglas A. Drossman, M.D..

Ami Sperber, Ben-Gurion University of the Negev, discussed **Epidemiological Studies in Functional GI Disorders: Issues and Findings**. As an example, he examined the often stated irritable bowel syndrome (IBS) prevalence estimate of 10–20%. These estimates are based on early studies conducted in the US, Western Europe, and Australia, though more recent studies from Asia and Latin America have yielded similar findings. The wide ranges of IBS prevalence reflects either true worldwide variation or underlying study methodological limitations, including:

- the absence of a diagnostic gold standard;
- use of different symptom based criteria;
- use of different surveys, including some that were not officially translated or validated;
- differences in how the survey was administered;

- cultural differences in symptom reporting (e.g., there is no term for bloating in Spanish);
- survey samples that may not be representative of the overall population; and
- inclusion of respondents who use certain medications which may affect GI symptoms.

Moving forward, Dr. Sperber suggests we conduct epidemiological studies using the same methods at the same time in different countries. Along these lines, the Rome Foundation has formed a Multinational Cross-Cultural Research Team, an Asian Working Team, and a group of Latin American Collaborators.

Jan Tack, University Hospital Gasthuisberg, Belgium, presented a concise, yet comprehensive overview of the **Pathophysiology of Functional GI Disorders**. Dr. Tack used functional dyspepsia as a paradigm for a schema that integrates both central and peripheral mechanisms. Patients with functional GI disorders, upon eating often exhibit abnormal GI motility (both impaired accommodation and gastric emptying abnormalities) which, in turn, activates mechanoreceptors. Likewise, changes in luminal contents lead to chemoreceptors activation, which in functional dyspepsia patients may be exaggerated due to increased epithelial permeability from low grade inflammation.

Combined, activation of mechano- and chemoreceptors triggers afferent nerves to send signals to the central nervous system. Once received, the central nervous system often fails to appropriately inhibit pain signals. Consequently, individuals with functional GI disorders perceive increased pain. Furthermore, those with somatization tend to report more symptoms, and those with certain psychological traits, notably anxiety, often exhibit exaggerated illness behaviors. In sum, functional GI disorder pathophysiology is "a complex process with abnormalities at every possible level."

Douglas Drossman, University of North Carolina at Chapel Hill, presented an **Integrated Understanding of Functional GI Disorders**. He started by discussing how modern Western society's tendency to separate mind and body has negatively affected functional GI disorder research and patient care. This tendency can be traced back to Rene Descartes, who conveniently separated mind and body in order to allow for anatomical dissections (which at the time were prohibited by the church). Centuries later, the result is a biomedical model which fails to appreciate the distinctions and relationships between "disease" (defined as externally verifiable evidence of a pathological state) and "illness" (defined as the patient's perception of ill health). Consequently, "non-disease" based disorders, such as functional GI disorders, are considered by some as less important and sometimes illegitimate.

Dr. Drossman argued for a more integrated biopsychosocial approach that recognizes the bidirectional relationship between disease and illness, along with the potential influences of biological, environmental, and psychosocial factors. He then took a quick tour of novel functional GI disorder topics, including our current understanding of biological mechanisms (including the potential role of genetics, mucosal inflammation, serotonin metabolism, and central nervous system pain processing) and psychological factors (including the importance of coping skills on clinical outcome). He briefly discussed diagnostic challenges, including the role of the Rome Clinical Algorithms (discussed in more detail below) as well as candidate biomarkers, before concluding on treatment, including the role of placebos, the FODMAP Diet, antidepressants, and psychotherapy.

Hot Topics

Co-Moderators: Gary Mawe, Ph.D. and Robin Spiller, M.D., F.R.C.P.; Panel: Erwin G. Zoetendal, Ph.D.; Tarique D. Perera, M.D.; Anthony J. Lembo, M.D.

Erwin Zoetendal, Wageningen University, The Netherlands, gave an overview of the **Microbiome**, the vast microbial community of the GI tract. The microbiome is "huge," weighing 500 grams and outnumbering human host cells by a factor of ten. However, identifying the specific species and their various functions is quite difficult, especially because only 20% of microbiome species can be cultured. Therefore, the microbiome is quantified by classical and newer high throughput approaches to analyze 16S ribosomal RNA, a phylogenetic marker present in every microbial cell.

Studies using this approach suggest that the human gut microbiome consists of a stable core of organisms (most notably *Bacteroides*, *Firmicutes*, and *Actinobacter*) that remains relatively unchanged over time, as well as a non-core population that tends to vary. Between individuals there is both significant overlap and variability in the types of microbial organisms that populate the gut.

The specific functions of the gut microbiome are studied using metagenomic techniques. Applying these techniques on ileostomy effluent samples, Dr. Zoetendal has determined that small bowel microbial species are involved in simple carbohydrate utilization, primary transport systems, cofactor synthesis, and pyruvate dissipation pathways.

Tarique Perera, Columbia Medical Center, discussed **Neuroplasticity and Neurogenesis**. Contrary to long held dogma that the brain ceases to generate new neurons

following birth, the human brain has the capability of forming new neurons. In fact, neurogenesis is likely essential to healthy brain function.

In animal studies neurogenesis is suppressed by factors that predispose to depression and anxiety (e.g., early life stress and alcohol abuse), and stimulated by factors that improve mood (e.g., exercise and antidepressant medications). At a cellular level, this process involves BDNF (a growth factor that stimulates stem cells to become neurons) and BCL-2 (a protein that prevents cellular apoptosis).

Neurogenesis appears especially important in the anterior hippocampus, a region of the brain involved in storing contextual memories. In the context of stress, genetically vulnerable individuals may fail to develop new neurons in this region. Consequently, their emotions may become uncoupled from external context, leading to mood disorders, including depression and anxiety.

Anthony Lembo, Harvard Medical School, gave an overview of the powerful **Placebo Response**. The placebo response consists of many components, including the natural history of illness (both spontaneous remission and regression to the mean) and the "placebo effect," which itself includes reporting bias, measurement artifact, as well as the effects of co-interventions, observation (Hawthorne Effect), rituals, and patient-practitioner interactions.

In 2001 a *New England Journal of Medicine* meta-analysis questioned whether there really was a placebo effect. Since then, several studies conducted in patients with IBS by Dr. Lembo and his colleagues suggest that in IBS the placebo response is quite powerful. The first study compared IBS patients who underwent acupuncture delivered in the context of an augmented patient-practitioner relationship, acupuncture delivered in the context of a limited patient-practitioner relationship, and those in a no treatment wait list. They found that at 3 and 6 week follow-up, outcomes (using four global endpoints) were best for those in the augmented relationship acupuncture, intermediate for those in the limited relationship acupuncture, and worst for those in the no treatment wait list control.

A more recent study ("Placebo without Deception") compared a non-treatment control group to a group that received daily placebo. Interestingly, those in the placebo group were told that they were getting a placebo (i.e., an inert sugar pill) and that the placebo effect is powerful. After four weeks those in the placebo group had superior outcomes to those on the wait list. In summary, the placebo response is a powerful phenomenon. More research is needed to understand it, and to learn how to effectively harness it in clinical practice.

Clinical Application #1

Moderator: Stephen J. Vanner, M.D., M.Sc., F.R.C.P.; Panel: Robin Spiller, M.D., F.R.C.P.; Max J. Schmulson, M.D.; Douglas A. Drossman, M.D.; William D. Chey, M.D., A.G.A.F., F.A.C.G.; Jan Tack, M.D., Ph.D.; André J.P.M. Smout, M.D., Ph.D.; William E. Whitehead, Ph.D.

Robin Spiller, University Hospital, Nottingham, discussed **Validation of the Rome Criteria**. The Rome Criteria must be validated in order to confirm that they accurately distinguish between those with and without a functional GI disorder, such as IBS. This is accomplished by assessing the criteria's performance characteristics, including their sensitivity (proportion of individuals with IBS who are appropriately classified as such), specificity (proportion of individuals without IBS who are appropriately classified as such), positive predictive values (the proportion of individuals who meet criteria who actually have IBS), and negative predictive value (the proportion of individuals who do not meet criteria who do not have IBS). However, because these latter characteristics are strongly influenced by pre-test probability (i.e., the baseline prevalence of a functional GI disorder), likelihood ratios may be more useful for validation purposes. A negative likelihood ratio represents the amount that the odds of IBS are lowered if criteria are not met. Conversely, a positive likelihood ratio represents the amount that the odds of IBS are increased if criteria are met.

With this background in place, Dr. Spiller then discussed that individual symptoms are not sensitive or specific enough to reliably diagnose IBS. Diagnostic yield is improved by combining symptoms to create a "syndrome." The original symptom criteria were proposed by Manning and colleagues. The "Manning Criteria" was later supplanted by the Rome Criteria. Currently in its third iteration, only Rome I Criteria have been assessed in validation studies. The results of these studies suggest that in a clinical setting when the Rome I criteria for IBS are combined with red flags it performs moderately well. Further work is needed to assess the validity of Rome III.

Max Schmulson, Experimental Hospital General de México, provided an overview of **Rome Clinical Algorithms in Functional GI Disorders**. Historically, the Rome Criteria have been widely utilized in clinical research, but have been underused in clinical practice. Accordingly, the Rome Foundation sought to increase the clinical applicability of the Rome Criteria by creating a set of diagnostic/therapeutic algorithms that aim to place the functional GI disorders in clinical context, help clinicians recognize the disorders, and assist them in making

functional GI disorder diagnoses using symptom based criteria.

Thus far algorithms have been created for 15 symptom patterns (e.g., recurrent abdominal pain with disordered bowel habit). They are available through an *American Journal of Gastroenterology* publication and online via the Rome Website (www.romecriteria.org). Currently the algorithms are being translated into other languages. Further work is needed to assess validity.

Douglas Drossman, UNC Chapel Hill, considered the use of **Centrally Acting Agents**, including psychotropic medications and various forms of psychotherapy. Multiple lines of evidence support the use of centrally acting therapies for functional GI disorders, including:

- a high prevalence of psychological distress;
- enhanced gut reactivity to stress;
- cognitive bias as a factor affecting symptom reporting;
- brain-gut dysfunction as a key pathophysiologic mechanism; and
- evidence of benefit from clinical trials.

Unfortunately, many clinicians are not experienced prescribing these therapies and, due to associated stigma, many patients are hesitant to take them. Dr. Drossman therefore suggests that clinicians properly educate patients about the use of these therapies and jointly negotiate a treatment plan with them.

Once prescribed, physicians should initially stay in close touch with their patients, and if side effects develop they should assess whether these are true side effects. If side effects are intolerant clinicians should reduce the dosage or switch to another agent within the same class.

Finally, Dr. Drossman discussed particular psychotropic agents, including:

- mirtazapine (useful for nausea, anorexia, and weight loss);
- busiprone (useful for anxiety and possibly dyspepsia);
- atypical antipsychotics (useful for reducing anxiety, treating insomnia, and some analgesic benefits);
- selective serotonin reuptake inhibitors (good for mood though provide little analgesia); and
- tricyclic antidepressants and serotonin norepinephrine reuptake inhibitors (stronger analgesic properties).

More advanced practitioners may consider "augmentation therapy," which involves combining low dosages of two or more agents to maximize effectiveness and minimize side effects.

William Chey, University of Michigan Health System, surveyed **Emerging Therapies for IBS**. Existing therapies are 40–60% effective, or roughly 10–20% more effective than placebo. Yet developing effective and safe therapies is quite challenging, in part due to the heterogeneity of IBS (both in terms of pathophysiology and presentation), the consistently high placebo response rate, a low tolerance for adverse events, and controversy over appropriate trial endpoints.

Over the next five years, Dr. Chey predicts therapies will remain empiric based upon clinical phenotype. Several potentially promising agents are in the pipeline, including:

- Linaclotide (a guanylate cyclase C agonist that in two large, well designed studies benefited global and individual IBS symptoms);
- Chenodeoxycholate (a bile salt that accelerates colonic transit, though often causes abdominal cramping);
- A3309 (a selective ileal bile acid transport inhibitor which may treat constipation);
- DDP-733 (a 5-HT_3 agonist proven effective in Phase II trials for IBS global symptoms); and
- Rifaxamin (a non-absorbable antibiotic that when administered for two weeks improved primary and secondary outcomes for up to 12 weeks).

Over the next 5–10 years Dr. Chey predicts novel agents that attack multiple targets, including gut microbiota, inflammation, HPA axis, non-narcotic analgesics, and cannabinoids. Finally, Dr. Chey optimistically looked forward to a future when biomarkers are used to subgroup patients by pathophysiology (rather than symptoms alone) so that they can be treated more specifically.

Jan Tack, University Hospital Gasthuisberg, discussed the **Application of Upper GI Physiologic Testing to Functional GI and Motility Disorders**. Physiologic testing is useful to help explain symptoms, give specific diagnoses, determine treatment choices, and predict long-term outcomes. Numerous testing options are available.

For the esophagus this includes impedance-pH monitoring, which Dr. Tack finds most helpful for patients who have persistent GERD symptoms despite anti-acid therapies. While this test allows detection of non-acid reflux, evidence for treating this condition with surgery and/or baclofen is quite limited. Next, high resolution esophageal manometry provides far more detail than conventional manometry on esophageal motor function. In fact, since the advent of this technology many new entities have been recognized and characterized within the new "Chicago

Classification." Nonetheless, it is again unclear whether this additional information actually improves outcome.

Moving down to the stomach, Dr. Tack discussed gastric scintigraphy (the "old workhorse"), as well as a new approach to measuring gastric emptying through a breath test. Results from both techniques closely correlate and Dr. Tack finds both acceptable for studying gastric emptying.

Finally, the newest modality is the "Smart Pill," which combines information on pH, temperature, and pressure to measure transit time in the stomach, small bowel, and colon.

André JPM Smout, University Medical Center, The Netherlands, considered the **Application of Lower GI Physiologic Testing to Functional GI and Motility Disorders**. As with the upper GI tract, lower GI tract motility can also be assessed several ways. The ANMS lists seven indications for gastroduodenojejunal manometry, though Dr. Smout thinks this is most useful for diagnosing chronic intestinal pseudo obstruction. His enthusiasm about using the test to differentiate between intestinal myopathy and neuropathy has been tempered by a recent study that showed poor correlation between findings on manometry and histopathology.

SmartPill, scintigraphy, and breath testing can all measure small bowel transit time, though Dr. Smout questions the value of doing so. Colonic transit can be easily assessed using radio-opaque markers followed by x-ray or by SmartPill. However, colonic transit is slowed in not only "slow transit constipation," but also many patients with pelvic floor dyssenergia and some with IBS.

Dr. Smout was most sanguine when discussing anorectal manometry, a test which can be used to rule out Hirschsprung's disease, assess sphincter function (in cases of incontinence) and diagnose pelvic floor dyssynergia (though he prefers defecography for this purpose).

In sum, "there is a multitude of tests…though review of the literature reveals that there are many uncertainties about [their] diagnostic value."

William Whitehead, University of North Carolina at Chapel Hill, concluded the session by discussing **Biofeedback for Pelvic Floor Disorders**. This technique has been successfully used to treat fecal incontinence, constipation, and rectal pain. For fecal incontinence, patients should first be treated conservatively with education, medications to normalize stool consistency, and pelvic floor exercises. Those who do not respond to these measures may undergo biofeedback, though clinical trial results are conflicting, perhaps due to varied protocols. In one trial, 77% of patients randomized to biofeedback experienced adequate relief (compared to 41% randomized to pelvic floor exercises alone).
For constipation due to dyssynergic defecation the results are more consistent: 80% of adults treated with biofeedback experience major improvement (compared to 22% of those treated with laxatives alone). However, children do not respond as well as adults do.

Finally, a recently conducted randomized controlled trial showed that biofeedback is quite useful for patients with levator ani syndrome who also report pain with traction on digital exam (87% of biofeedback-treated patients reported adequate relief compared to 45% of those treated with electrogalvanic stimulation and 22% treated with massage).

Saturday April 9

Clinical Application #2

Moderator: Lin Chang, M.D.; Panel: Albena Halpert, M.D.; Stine Störsrud, Ph.D.; Carlo Di Lorenzo, M.D., Douglas A. Drossman, M.D.

Albena Halpert, Boston University Medical Center, discussed **Maximizing the Physician-Patient Relationship**. The physician-patient relationship is a sacred, fundamental aspect of medical care. Still, in a recent survey most patients with IBS reported unmet expectations and only 17% felt their physician was helpful and reassuring.

Contrary to common belief, patients do not necessarily want more time with their physician, rather they seek clinicians who listen, validate their symptoms, and express empathy. Dr. Halpert recommends physicians improve communication with their patients by working to build rapport with them, setting a collaborative agenda up-front, and acknowledging social and emotional cues. In return, improved communication and a therapeutic relationship can pay major dividends, including making visits more efficient, enhancing patient and clinician satisfaction, bolstering adherence to treatment, and improving health outcomes.

Magnus Simren, MD was unable to attend the meeting so his colleague, Stine Störsrud, Sahlgrenska University Hospital, Göteborg, Sweden, presented **Food and IBS**. The majority of IBS patients (particularly females and those with anxiety) recognize a relationship between food intake and GI symptoms. Food may trigger IBS symptoms due to:

- exaggerated sensorimotor responses to nutrients;
- food allergy (which is debatable) and/or hypersensitivity (which may be mediated by non-IgE immunoglobulins); and

- carbohydrate malabsorption.

Although patients with IBS are *not* more likely to malabsorb lactose or fructose, they may be more hypersensitive to the effects of malabsorption.

The presentation concluded with a discussion of FODMAPs, a group of poorly absorbed, osmotically active, fermentable substances. A FODMAP free diet may be beneficial, though confirmatory studies are needed. In sum, food related symptoms are common and may be a result of multiple, poorly understood mechanisms that likely differ between patients.

Carlo Di Lorenzo, The Ohio State University, discussed **Functional GI Disorders: From Children to Adults**. Over the past decades a number of studies have tracked long-term outcomes of children with functional GI disorders. In sum, these studies suggest that children with these disorders have an increased likelihood of gastrointestinal and psychological symptoms later on in life. Interestingly, modifying how parents respond to their children's pain reports may improve outcomes. While hypnotherapy appears to improve short-term outcomes, the role of probiotics and antidepressants remains unclear.

Douglas Drossman, UNC Chapel Hill, concluded the session with a presentation on **Narcotic Bowel Syndrome**. In the US, prescription narcotic use is widespread and increasing. Unlike opioid bowel dysfunction, which is characterized primarily by constipation and nausea, in narcotic bowel syndrome pain is the dominant symptom.

Affected patients are typically started on narcotics to treat abdominal pain (secondary to both functional GI Disorders and 'organic' conditions, such as Crohn's disease), though chronic use over time paradoxically worsens their pain. One possible mechanism is chronic opioid induced activation of glia toll-like receptors, which thereby triggers the release of inflammatory cytokines, which, in turn, increases neuronal excitability.

Dr. Drossman discussed his group's work on a detoxification protocol, which proved effective over the short-term, though unfortunately the majority of detoxified patients resumed use of these drugs within 6-weeks on average.

Sunday April 10

Ami Sperber, Ben-Gurion University of the Negev, summarized the recent Rome-World Gastroenterology Organization sponsored conference **IBS Global Perspective**. The major message of the meeting was that in both clinical and research fields we must become more cognizant of the multi-national, multi-ethnic, and multi-cultural nature of our increasingly connected world. Presenters from around the world discussed various topics, including: Are there real differences in IBS around the world? (short answer: there appears to be, though further research is needed). How are explanatory models affected by cultural factors? (short answer: cultural identity and beliefs influence functional GI disorders, and should be considered, though we must avoid creating stereotypes that may not apply to all individuals within a group). And how can we improve multi-national drug trials? (short answer: by attending to factors that vary by culture, including language, literacy, numeracy, and culture). To these ends, The Rome Foundation has established a working team on cross cultural research, is working with regulatory agencies on multi-national trials, and is promoting international functional GI disorder research networks.

Genetics

Moderator: William Whitehead, Ph.D.; Panel: William Maixner, Ph.D., D.D.S.; Nicholas J. Talley, M.D., Ph.D.; Yuri A. Saito-Loftus, M.D., M.P.H.

William Maixner, University of North Carolina Chapel Hill, provided an overview of **Pharmacogenetics and Phenotypes**. The current drug development model has not been particularly fruitful, in part because animal models may not apply well to human pain. Dr. Maixner described a novel, genetic-based approach that may more quickly yield a greater number of therapeutic agents.

First, a well characterized human cohort is identified. Next, genetic analyses are used to identify specific genetic polymorphisms. The molecular pathways associated with these genetic polymorphisms are then identified. Subsequently, animal models are used to modify these pathways and develop therapeutic compounds. Finally, these compounds are brought back to humans for testing. Dr. Maixner presented three "vignettes" from his own research on temporomandibular joint disorder to show this paradigm in action.

Nicholas Talley, Mayo Clinic, Jacksonville, continued with a discussion of **Genetics and Functional GI Disorders 2011**. Overall, Dr. Talley believes that the extant published genetic literature is deficient because most associations are spurious (i.e., false positives) and have not been confirmed. Nonetheless, he believes there are some real associations between genes and functional GI disorders, including polymorphisms in the gene that encodes GNbeta3 protein with functional dyspepsia, genes that encode certain proteins involved in epithelial cell barrier function and innate immune response with post-infectious IBS, and genes that encode sodium channels with IBS-diarrhea subtype. Dr. Talley believes that, although genetic studies may help us better understand

functional GI disorders and develop new treatments, higher quality studies conducted within larger populations are sorely needed.

Yuri Saito-Loftus, Mayo Clinic, Rochester, concluded the conference with an overview of **Genetic Epidemiology**. Specific genetic and environmental factors likely interact to produce the sensorimotor abnormalities that underlie functional GI disorders. The great challenge is sorting through vast genetic variation to identify the particular genes that may contribute to the disorders. Genetic epidemiology can help us sort things out.

Overall, more than 100 genetic variants and 60 genes have been studied. Dr. Saito believes "it is conceivable that there are different genetic markers that may be responsible for IBS." Moving ahead, she suggests we refine the IBS phenotype and use a combination of methods, including linkage studies, genome wide association studies, candidate gene studies, and studies that examine gene-gene and gene-environment interactions.

More Information from the Symposium

The brief summaries above cover plenary presentations at the Symposium. Missing are the presentations at the Mini Symposia and Workshops that took place at the meeting.

IFFGD has available a limited number of Syllabus material covering the Plenary sessions, Mini Symposia, and Workshops. This information can be purchased for $75 plus shipping; to order, contact IFFGD by email at **iffgd@iffgd.org** or phone at **414-964-1799**.

Mini Symposia topics include:

- Biomarkers
- Challenging Cases at the Referral Centers
- Treatment of Pediatric Functional GI Disorders
- Intestinal Permeability and Visceral Hypersensitivity
- Overlapping Conditions
- Upper GI Dysfunction
- Clinical Trial Design – Patient Reported Outcomes
- Cross Cultural
- Microbiota in Functional GI Disorders
- Parent-Child-Physician Interaction

Workshop topics include:

- Interview Techniques and Communication Skills
- Brain-Gut Modulation of GI Symptoms
- Serotonin
- Psychological Assessment: Pearls for the Clinician at the Bedside
- Fecal Incontinence
- Brain Imaging
- Basic Principles of Neurophysiology for the Clinician
- Constipation in a Hospitalized Patient: New Tools, New Objectives
- Functional Biliary Disorders
- Enteric Regulation
- What's New in Esophageal Disorders?
- Cognitive-Behavioral Therapy and Self Management Approaches