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EVOLUTION OF AN IDEA

FROM FUNCTIONAL GI DISORDERS
TO DISORDERS OF
GUT-BRAIN INTERACTION

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Dr. Doug Drossman has been instrumental in developing the current conceptual basis of what used to be called “functional bowel disorders,” now known as “disorders of gut-brain interaction” (DGBI). This interview in the ACG MAGAZINE “Discoverers” Series tracks his intellectual journey from just trying to understand his patients’ complaints to the development of a criteria-based diagnosis system which has led to a flowering of our understanding and ability to treat these disorders. – Dr. Lawrence Schiller

Q1. Thanks for agreeing to reminisce about your career and the development of ideas that we now take for granted. How did you get interested in gastroenterology as a career choice?

I chose gastroenterology because it met my need to combine medicine’s technical aspects with a strong focus on the patient. It is a blending of science and art. In that regard, it is different from other medical subspecialties. For example, with cardiology, pulmonary disease, and nephrology, clinicians can rely on cardiac catheterization, lung physiology, or kidney function tests to understand how well the specific organs function, which determines how the patient is doing and the management. But those techniques almost exclude any interaction with the patient in decision making.

In contrast, GI illnesses and diseases are more complex; there are no numbers or calculations of organ function to explain why the patient has abdominal pain or nausea. So, traditional physician and patient expectations to test, diagnose, and treat aren’t always successful. Gastroenterology looks at the person and his or her symptoms in the context of daily functioning, life stress, quality of life, and coping style. Optimal patient diagnosis and management require human interaction through history, physical examination, and a patient-centered care model. Of course, we also need imaging methods and endoscopy for many of our patients, but it all comes back to the patient and patient communication.

Furthermore, gastroenterology science involves brain-gut interactions, and that has always appealed to me. We need to understand how serotonin, norepinephrine, or endorphins/opioids neurotransmitters and their receptors and inflammatory mediators affect gastrointestinal and brain function. Particularly for the DGBI (formerly functional GI disorders), all GI symptoms are a derivative of brain and gut interactions, and it is their dysregulation that leads to these disorders. So, this also met my need to address brain-gut interactions and the biopsychosocial aspects of GI illness.

How endoscopic, pathological, or physiological (motility) findings affect GI function and symptoms also appealed to me. People may not be aware that I was an interventional endoscopist until the last decade and I edited a GI procedure manual. I thought it fascinating to learn to what extent observable disease-specific, structural abnormalities related to patient illness, and ill health experience. Correlations between structure and even GI physiological disturbances and symptoms are far lower than many realize. Patients with active ulcerative colitis or Crohn’s disease may have severe disease on endoscopy yet have minimal GI symptoms. Conversely, patients with

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IBD may have minimal mucosal disease after treatment yet have continuing severe pain and diarrhea; we now call that IBD-IBS. Even the relation between physiological testing such as delayed gastric emptying or colonic motility and GI symptoms is low. These discrepancies posed a challenge to me and eventually led me to focus on the biopsychosocial aspects of GI illness and disease.

Q2. What led you to seek additional training in the biopsychosocial aspects of medicine at the University of Rochester?

When I was in medical school, I wasn't sure if I wanted to go into medicine or psychiatry. I enjoyed learning about human behavior and the role of psychosocial factors in GI illness. I chose a medical residency because my priority was to take care of patients as a medical doctor. When I was a medical resident at the University of North Carolina and later an internist at an Air Force hospital during the Vietnam era, I learned that many of the medical symptoms that patients described were unrelated to the X-rays and laboratory findings. I believed that something was missing in understanding and treating patients and considered integrating psychosocial learning into GI practice. I heard about George Engel in Rochester, NY, who soon became my mentor, and joined his program as a fellow before going into gastroenterology. Dr. Engel coined the term Biopsychosocial Model which became the driving force of my career. He was an internist and psychoanalyst who set up a training program to teach what was then called psychosomatic medicine.

My growing concern about the disconnect between symptoms and medical findings drew me to his program. Also, he was considered a master medical interviewer. I recall him diagnosing what was later confirmed to be a thalamic tumor of the brain based on the quality of the pain that the patient-reported; I guess he preceded by decades the TV doctor "House." My learning with him allowed me to develop and expand my interview skills to improve my ability to acquire even subtle medical and biopsychosocial data. It also helped me to understand the patient's inner world and illness experience entirely

differently. I believed that this training would add a unique perspective to my training in gastroenterology.

Q3. What did physicians use to make a diagnosis of IBS before the Manning Criteria were published in 1978?

The simple answer is that there was no unified approach to making a diagnosis of IBS other than to exclude other diseases and rely on the physician's experience. To fully answer this question, let me bring in a bit of history about how IBS and the other functional GI disorders evolved. At the turn of the 19th-century, abdominal pain, diarrhea, nausea, or vomiting were considered merely collections of symptoms. From the 1950s well into the 1980s, gastroenterology was dominated by attention to structural disorders, like peptic ulcers, GI tumors, diverticulitis, pancreatic disease, and inflammatory bowel disease. They were easy to diagnose using imaging methods like X-rays and, later, endoscopies. Yet these structural diagnoses applied to only about half of the patients seen in GI clinics. The other half having symptoms not diagnosed by imaging studies were called "functional." These functional symptoms were attributed to the GI tract's abnormal movements and were considered motility disorders. Motility testing helped diagnose motility disorders such as gastroparesis, achalasia, sphincter of Oddi dysfunction, dyssynergic defecation, etc. However, motility testing did not diagnose the common GI symptoms like pain, bloating, or nausea and, furthermore, this type of testing was not readily available in clinical practice.

So, before 1978, a diagnosis of IBS was made by exclusion of other problems. But diagnosing by exclusion was not cost-effective because there were no guidelines to help decide what studies to do, and there was no limit to the number of tests that could be ordered. The Manning study was a breakthrough because it opened the door to making a positive diagnosis. The authors tested whether collections

of GI symptoms might distinguish patients with IBS from organic disease (e.g., IBD, diverticular disease, etc.). Their findings showed that clusters of symptoms could lead to a diagnosis when physiological testing or endoscopy was negative. This study was a precursor to the Rome criteria.

Q4. How did the initial Rome criteria for IBS and other functional GI diagnoses come to be?

In the late 1970's and early 1980's, I was part of a small group of gastroenterologists and scientists including W. Grant Thompson, MD (Canada), William Whitehead, Ph.D. (USA), Nicholas Talley, MD, MPH, (Australia), Ken Heaton, MD (UK), and Enrico Corazzari, MD (Italy), who believed that the disorders called "functional" were not well-understood nor well-conceptualized. As a result, they were treated as "second class" to the structurally-based GI diagnoses. We believed that creating a classification system for the functional GI disorders would "put them on the map," so to speak. Then patients could be identified and studied scientifically—and, in the process, be legitimized.

At the time, we were all conducting clinical and epidemiological research to characterize GI symptoms and see if they had diagnostic value. The Manning Criteria was the first of several publications we did that followed into the 1980s. In 1987, Dr. Aldo Torsoli, of the International Congress of Gastroenterology (Roma '88), created a working team of five GI experts researching this area. We worked by a Delphi approach: a consensus of experts made clinical recommendations for diagnosis and treatment when there was inadequate scientific evidence. The team included W. Grant Thompson (Canada, chair), myself (USA), Wolfgang Kruis (Germany), Ken Heaton (UK), and Gerhard Dotevall (Sweden). This team created the first consensus document that established diagnostic criteria for IBS. The work was presented at Roma '88 and published in 1989 (Thompson,

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WG, *et al.*, Irritable Bowel Syndrome: Guidelines for the diagnosis. *Gastroenterology International* 1989; 2:92-95).

Many publications on other functional GI disorders like functional dyspepsia, functional heartburn, or post-cholecystectomy biliary pain were starting to appear during this time. However, there was no viable way to characterize and diagnose these disorders systematically. The next step was to bring our group together to establish guidelines for diagnosing all these disorders.

To this end, we convened another working team and created 23 diagnoses that were categorized by location or domain: esophageal, gastroduodenal, bowel, biliary, and anorectal. Within each domain, there were several diagnoses. Each had a definition and diagnostic assessment, including the new symptom-based criteria (Drossman DA, *et al.*, Identification of Sub-groups of Functional Gastrointestinal Disorders. *Gastroenterology International* 1990;3:159-172).

We used this publication as a template to expand upon the knowledge by creating additional working teams for each domain and published the findings over the next several years. We also created a working team to make recommendations on designing treatment trials. Finally, we used all the criteria to publish the first nationwide epidemiological study of 10,000 US Householders (Drossman, DA, *et al.*, US Householder Survey of Functional Gastrointestinal Disorders. *Dig Dis Sci* 1993;38:1560-1580). We then compiled these documents into a book (Drossman (ed) *et al.*, *The Functional Gastrointestinal Disorders: Diagnosis, Pathophysiology, and Treatment*. 1994; Little Brown and Company, Boston, pp. 1-370), which, retrospectively, is considered to be Rome I. This was the beginning of the Rome Foundation

» WATCH: romedross.video/origins

Q5. What was the impact of the initial

Rome criteria on research in IBS?

The use of symptom-based diagnostic criteria changed the way doctors diagnosed these patients, and investigators incorporated these criteria into epidemiological and clinical studies. Symptom-based criteria offered a new conceptual framework to study disorders not related to structural or motility disturbances (see Figure 1). It also legitimized these disorders and created a framework for clinical and biopsychosocial research; this countered dualistic thinking which ineffectively categorized all disorders as being “organic” or “psychosomatic.”

Initially, however, and into the early 1990s the Rome classification system and its criteria were not well accepted by investigators. Understandably, this new classification was based on empiric wisdom, not scientific validation studies. Many thought that there was a lack of evidence to support the criteria because there were no structural or physiological correlations or measurement methods to legitimize them. Then the Food and Drug Administration (FDA) and other regulatory agencies saw the value of these criteria and recommended their use for clinical research on patients. The criteria were then adopted by pharmaceutical companies to use in clinical trials. Subsequently, more and more studies were done, and this established a database of patients to use in future validation studies for the criteria, which ensued in the coming years.

Q6. How have the subsequent revisions of the Rome criteria improved their utility?

The criteria were never meant to be “etched in stone.” The Rome Foundation Board believed that the diagnostic criteria would change as new scientific data emerged. The revisions of the criteria occurred with subsequent publications from Rome I (1994) to Rome II (2000), Rome III (2006), Rome IV (2016), and may occur for Rome V scheduled for 2026. Surprisingly, the criteria have not changed very much over the

	Organic Disorder	Motility Gut-Brain	DGBI (Functional GI)
Primary Domain	Organic morphology	Organ function	Illness experience
Criterion	Pathology (disease)	Altered Motility	Symptoms
Measurements	<ul style="list-style-type: none"> • Histology • Pathology • Endoscopy • Radiology 	<ul style="list-style-type: none"> • Motility • Visceral sensitivity 	<ul style="list-style-type: none"> • Motility • Visceral sensitivity • Symptom criteria (Rome) • Psychosocial
Treatment Options	<ul style="list-style-type: none"> • Medications • Surgery • Ther. endoscopy 	<ul style="list-style-type: none"> • Pro / anti-kinetics • Surgery • Pacing / Stimulator 	<ul style="list-style-type: none"> • Pro / anti-kinetics • Antinociceptives • Antidepressants • Behavioral
Examples	<ul style="list-style-type: none"> • Esophagitis • Peptic Ulcer • IBD • Colon Cancer 	<ul style="list-style-type: none"> • Diffuse esophageal spasm • Gastroparesis • Pseudo-obstruction • Colonic inertia 	<ul style="list-style-type: none"> • Esophageal chest pain • Functional dyspepsia • IBS • Functional abdominal pain

Figure 1.

years, but when criteria are changed, scientific data is required to justify the change. While the Rome I criteria were developed by consensus, each subsequent Rome iteration became more evidence-based.

The utility of the criteria also has increased through their globalization. Over the years, the Rome books and criteria were translated into Spanish, Portuguese, Italian, and Chinese. This increases the opportunity to study these disorders from a cross-cultural basis. Under the direction of Dr. Ami Sperber, the Rome IV criteria were used to study the prevalence and phenotypic features for the DGBIs in over 70,000 subjects in 33 countries (Sperber A, *et al.*, Worldwide Prevalence and Burden of FGIDs, Results of the Rome Foundation Global Study. *Gastroenterology* 2020 romedross. video/GlobalStudy). The utility of the criteria has also increased through the Rome Foundation's educational efforts in publishing diagnostic algorithms and the development of the Multi-Dimensional Clinical Program (MDCP) to standardize treatment approaches. There is also an intelligent software program incorporating the diagnostic algorithms and MDCP called the GI Genius (romeonline.org).

Q7. How should clinicians utilize the

Rome criteria in their practices?

It may come as a surprise to many that the Rome criteria were designed for clinical trials, not for clinical practice. As a result, the criteria's preciseness can lead to discrepancies when experienced clinicians diagnose these disorders and find they do not meet the Rome criteria exactly. This is best highlighted for IBS when comparing Rome III to Rome IV criteria. Epidemiological studies show that the frequency of IBS using Rome IV is about half that of Rome III. What has changed, though, is not the true prevalence, but the number of patients meeting the more stringent criteria. Rome III requires the frequency of symptoms to be at least three times a month, and Rome IV requires symptoms to be present at least once a week, which explains the discrepancy. It turns out that Rome IV identifies a more severe population that may be more amenable to clinical trials. However, clinicians will diagnose patients who don't meet frequency criteria, but clinically still have this diagnosis qualitatively. In other words, the pattern of abdominal pain relieved or made worse with defecation and associated with diarrhea or constipation symptoms still clinically support the diagnosis. So, in clinical practice, the criteria can be used as a guide to making a diagnosis. Milder cases may not meet the research criteria, but these patients can still be given a "form fruste" diagnosis and be

treated appropriately. While it is too early to say with certainty, I believe that we may develop both clinical and research criteria for Rome V.

Q8. Recently, "Functional Bowel Disorders" have been relabeled as "Disorders of Brain-Gut Interaction." How does that alter our conception of these disorders?

In the 1980's, I surveyed the AGA membership and asked the definition of a functional bowel disorder. The most common response was that there was "nothing found," and of course, this often prompted doctors to do more tests. The second most common response was that it was a psychiatric disorder. Only about 5% thought that the definition meant a disorder of the functioning of the GI tract. While this last definition could be considered acceptable, the other two were not helpful to patients or doctors. Moreover, the term can be regarded as stigmatizing. After much discussion, the Rome Foundation Board and Rome IV Chapter Committee chairs decided to change the name to Disorders of Gut-Brain Interaction because it eliminates the stigma and is scientifically based. We understand these disorders as related to dysregulation of the gut-brain axis manifest by any combination of 1) motility disturbance, 2) visceral hypersensitivity, 3) altered mucosal and immune function, 4) altered microbiota, and 5) altered CNS processing. The Rome Foundation has increased the use of this term in our publications and educational programs, and we see it being used more and more in research papers and teaching. We know that patients find it more acceptable, and doctors are beginning to feel more comfortable using it.

Q9. How should we explain these disorders to our patients?

I believe that the change in terminology to DGBI makes it easier to explain these disorders. No other organ system is as hardwired to the brain as the gut; this is the brain-gut axis. In the



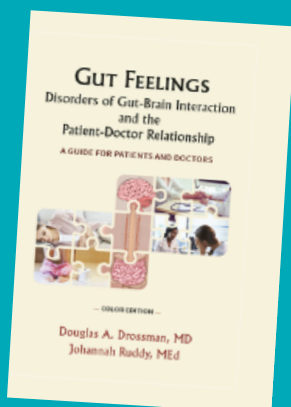
Ms. Johannah Ruddy and Dr. Drossman have now co-authored a book: "*Gut Feelings: Disorders of Gut-Brain Interaction and the Patient-Doctor Relationship. A Guide for Patients and Doctors*" that promotes a model where patients and doctors collaborate (romedross.video/GutFeelingsWebsite).

Part 1 offers a conceptual understanding of the DGBIs and the biopsychosocial model

Part 2 is a compendium of all 33 DGBIs and includes pathophysiology, diagnosis, and treatment

Part 3 teaches methods for doctors and patients to improve communication

Part 4 is a guide for doctors to optimize the patient-doctor relationship by implementing shared responsibility. Both authors hope that this book will help make the patient-doctor relationship more meaningful for both parties.



Johannah Ruddy, M.Ed., and Douglas A. Drossman, MD, MACG

embryo, nerve cells from the developing brain send down nerves to populate the GI tract to become the enteric nervous system. We can tell our patients that the GI symptoms are a product of nerve signals generated in the gut that go to the brain and the brain signals' reciprocal effects going to the gut to regulate them. The brain-gut axis is usually in harmony, but with the DGBIs, symptom-perception or gut function may be dysregulated. So, for example, abdominal pain could be due to dysmotility or visceral hypersensitivity, but there may also be a failure of the brain to downregulate these signals and this can be enabled by stress. Dysregulation of the brain-gut axis can apply not only to pain but to other GI symptoms, including nausea, vomiting, diarrhea, etc. The Rome Foundation has produced a card to demonstrate this concept to patients. It contains an image of the brain-gut axis with a written explanation and a video for a demonstration: <http://romedross.video/B-GAxisCard>. There is also a series of brief video discussions on the pathophysiology, diagnosis, and treatments of the DGBIs on the Rome website: <https://theromefoundation.org/patient-educational-q-a/>

Q10. One of the new initiatives for you and the Rome Foundation is to teach ways to improve the patient-doctor relationship. What made you decide to do this, and how are you doing it?

During my fellowship with George Engel, I became trained in advanced interview and communication techniques. I learned of its value to make a better diagnosis and solidify the patient-doctor relationship. I also learned from the teachings of Carl Rogers, and a group called the American Academy of Physician and Patient (now called the Academy of Communication in Healthcare) about patient-centered care. This concept was later promoted in 2001 by the Institute of Medicine. Subsequently, I started teaching these methods when I lectured at GI and medical programs. This led to the founding of the Center for Education and Practice of Biopsychosocial Care (DrossmanCare). We created videos on communication skills teaching and did workshops and symposia at national and international programs.

Two years ago, I started collaborating

with a patient advocate, Johannah Ruddy, M.Ed., who is also the Executive Director of the Rome Foundation. She joined me in our educational programs, bringing in the patient's perspective which was enlightening for the attendees. We then created a collaboration between DrossmanCare and the Rome Foundation and created a multimodal curriculum to teach communication skills to optimize the patient-doctor relationship. Since then, we have successfully produced educational lectures and workshops at GI and medical programs, workshops, symposia, Train the Trainer programs, visiting scholars programs, and several peer-reviewed publications: <https://romedross.video/2kfU3Dd>. The ACG has used these services at its FGID School where I have run workshops at several of the meetings.