

## History of Functional Disorders

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### THE PAST

#### *HISTORICAL PRECEDENTS*

Historians and physicians have documented the presence of Functional GI disorders throughout recorded human history. However, until recently, limited attention has been granted to these disorders due to the lack of identifiable pathology and the absence of a conceptual framework to understand and categorize them. Systematic investigation of functional GI disorders did not begin until the middle of the 20th century, and prior to this time, only occasional reports of functional GI symptoms were published, the first appearing only 200 years ago.

Over the past 25 years, scientific attention to understanding and properly caring for patients with functional GI disorders has grown progressively. With the understanding comes the rationale for use of medications directed at intestinal receptors as well as psychopharmacological, behavioral, and psychological forms of treatment. Additionally, there has been an increase in the rate of scientific publications and greater media exposure to the public through television, radio, and Internet.

To understand the historical classification of these disorders, two differing theories relating to the interaction between the mind and body should be considered.

- ◇ Holism: a theory built upon the foundation that the mind and body are integrated and utterly inseparable.
  
- ◇ Dualism: a theory that proposes a separation between the mind and the body.



Greek philosophers Plato, Aristotle, and Hippocrates first proposed the principle of holism about 3,000 years ago, and later in the 12th century; Jewish physician and philosopher Maimonides reexamined this philosophy. Based on holism, the study of medical disease must take into account the whole person rather than merely the diseased part. However, societal concepts of illness and disease drastically shifted when European philosopher Rene Descartes offered the divergent theory of dualism in the 17th century. Prior to the notion of dualism, the church discouraged human dissection on the

premise that the spirit resided in the body. The acceptance of dualism paved the way for the emergence of scientific investigation and new medical discoveries by lifting the prohibition of human dissection. This shift in medical thought was congruent with the societal changes of the 17th century: the shift towards a separation in church and state.

## **IMPLICATIONS FOR FUNCTIONAL GI DISORDERS**

Based on the concept of dualism, disease was now understood in terms of structural abnormalities. Therefore, the validity of a disease rested with the observation of morphological abnormalities. Medical conditions occurring in the absence of such morphological abnormalities and symptoms were not considered legitimate, and were often viewed as psychiatric, consistent with the concept of dualism. The concept of dualism had other effects with regard to treatment.

For example, this would include all the functional GI disorders and other somatic syndromes, such as fibromyalgia. Until the latter part of the 20th century, a medical illness was considered amenable to scientific inquiry and treatment. However, patients with psychiatric disorders were interred in insane asylums and considered to no longer be treatable by medical physicians.

Unfortunately this concept leads to a clinical dilemma. Specific diseases explain only about 10% of medical illnesses seen by physicians. Furthermore, people with structural (i.e. organic) diagnosis such as inflammatory bowel disease or cancer show considerable variation in their symptom presentation and clinical behavior. Gastroenterologists (as well as other health care practitioners) are all too familiar with the poor correlation between structural findings on endoscopy and their patient's symptoms.

Although efforts to find morphological or even motility etiologies for functional GI disorders in the latter part of the 20th century were unsuccessful, the assumption that functional GI disorders must be psychiatric has developed and has permeated current thinking. However, in the face of current scientific research, this is being seriously challenged. Studies have shown that persons with irritable bowel syndrome who do not seek health care are psychologically much like healthy subjects.

## **THE PRESENT**

### **CONCEPTUAL BASES FOR THE STUDY OF FUNCTIONAL GI DISORDERS**

The recent acceptance of functional GI disorders as legitimate medical entities is based on the following three developments:

- ◇ The concept of the Biopsychosocial model of illness and disease
- ◇ The development of new investigative methods for studying disease
- ◇ The development of the Rome Criteria

#### **Biopsychosocial Model**

In 1977, the publication of the concept of the Biopsychosocial model by George Engel, and its later demonstration specifically for gastrointestinal disorders, marked an important change in thinking.

A biopsychosocial model of illness and disease provides the needed framework to understand, categorize, and treat common GI symptoms. These symptoms are the integrated product of altered motility, enhanced visceral sensitivity, and brain-gut dysregulation and often are influenced by psychosocial factors. Figure 1 illustrates the proposed relationship between psychosocial and physiological factors with functional GI symptoms and the clinical outcome.

Early in life, genetics and environmental influences (family attitudes toward bowel training or illness in general, major loss or abuse history or exposure to infection) may affect one's psychosocial development (susceptibility to life stress, psychological state, coping skills, social support) or the development of gut dysfunction (abnormal motility or visceral hypersensitivity).

Additionally, the presence and nature of a functional GI disorder is determined by the interaction of psychosocial factors and altered physiology via the brain-gut axis. In other words, one individual afflicted with a bowel disorder but with no psychosocial disturbances, good coping skills and adequate social support may have less severe symptoms and not seek medical care.

Another having similar symptoms but with coexistent psychosocial disturbance, high life stress, or poor coping skills may frequent his physician's office and have generally poor outcome.

## **DEVELOPMENT OF NEW INVESTIGATIVE METHODS**

The second concurrent process has been the expansion and refinement of investigative methods that allow the study of functional GI disorders in terms of biological, cultural, and psychosocial (i.e. brain) influences. These developments include:

1. the improvement of motility assessment,
2. the standardization of the barostat to measure visceral sensitivity,
3. the enhancement of psychometric instruments to determine psychosocial influences,
4. the introduction of brain imaging (PET, fMRI) to determine CNS contribution to symptoms, and
5. the molecular investigation of brain-gut peptides, which provide insight into how these symptoms become manifest.

In less than ten years, these methods have produced new knowledge of the underlying pathophysiological features that characterize the age-old symptoms we now define as functional GI disorders.

## **ROME CRITERIA**

The Rome Criteria is an international effort to characterize and classify the functional GI disorders using a symptom-based classification system. This approach that has its precedents with classification systems in psychiatry and rheumatology. The rationale for such a system is based on the premise that patients with functional GI complaints consistently report symptoms that breed true in their clinical features, yet cannot be classified by any existing structural, physiological or biochemical substrate. The Rome Criteria was built upon the Manning Criteria, which was developed from discriminate function analysis of GI patients. The decision to develop diagnostic criteria by international consensus was introduced as part of a larger effort to address issues within gastroenterology that are not easily resolved by usual scientific inquiry or literary review. By 1992, several committees had met to discuss the criteria, which ultimately resulted in the publishing of many articles in *Gastroenterology International* and a book detailing the criteria titled "The Functional Gastrointestinal Disorders (Rome I)".

Elaboration of the Rome I criteria led to a second edition of the Rome criteria (titled Rome II) in 2000 as well as the publication of a supplement to the journal *Gut* in 1999. Recently the Rome Coordinating Committee has met to begin Rome III, expected to be published in 2006. To learn more about the Rome Committees and to see a summary of the Rome II book: go to [www.romecriteria.com](http://www.romecriteria.com).

## **PRESENT PATHOPHYSIOLOGICAL OBSERVATIONS**

Despite differences among the functional gastrointestinal disorders, in location and symptom features, common characteristics are shared with regard to:

- ◇ motor and sensory physiology,
- ◇ central nervous system relationships,
- ◇ approach to patient care.

What follows are the general observations and guidelines.

## **MOTILITY**

In healthy subjects, stress can increase motility in the esophagus, stomach, small and large intestine and colon. Abnormal motility can generate a variety of GI symptoms including vomiting, diarrhea, constipation, acute abdominal pain, and fecal incontinence. Functional GI patients have even greater increased motility in response to stressors in comparison to normal subjects. While abnormal motility plays a vital role in understanding many of the functional GI disorders and their symptoms, it is not sufficient to explain reports of chronic or recurrent abdominal pain.

## **VISCERAL HYPERSENSITIVITY**

Visceral hypersensitivity helps to account for disorders associated with chronic or recurrent pain, which are not well correlated with changes in gastrointestinal motility, and in some cases, where motility disturbances do not exist. Patients suffering from visceral hypersensitivity have a lower pain threshold with balloon distension of the bowel or have increased sensitivity to even normal intestinal function. Additionally, there may be an increased or unusual area of somatic referral of visceral pain. Recently it has been concluded that visceral hypersensitivity may be induced in response to rectal or colonic distension in normal subjects, and to a greater degree, in persons with IBS. Therefore, it is possible that the pain of functional GI disorders may relate to sensitization resulting from chronic abnormal motor hyperactivity, GI infection, or trauma/injury to the viscera.

## **BRAIN-GUT AXIS**

The concept of brain-gut interactions brings together observations relating to motility and visceral hypersensitivity and their modulation by psychosocial factors. By integrating intestinal and CNS central nervous system activity, the brain-gut axis explains the symptoms relating to functional GI disorders. In other words, senses such as vision and smell, as well as enteroceptive information (i.e. emotion and thought) have the capability to affect gastrointestinal sensation, motility, secretion, and inflammation. Conversely, viscerotropic effects reciprocally affect central pain perception, mood, and behavior. For example, spontaneously induced contractions of the colon in rats leads to activation of the locus coeruleus in the pons, an area closely connected to pain and emotional centers in the brain. Jointly, the increased arousal or anxiety is associated with a decrease in the frequency of MMC activity of the small bowel possibly mediated by stress hormones in the brain. Based on these observations, it is no longer rational to try to discriminate whether physiological or psychological factors produce pain or other bowel symptoms. Instead, the Functional GI disorders are understood in terms of dysregulation of brain-gut function, and the task is to determine to what degree each is remediable. Therefore, a treatment approach consistent with the concept of brain-gut dysfunction may focus on the neuropeptides and receptors that are present in both enteric and central nervous systems.

## **THE ROLE FOR PSYCHOLOGICAL FACTORS**

Although psychological factors do not define these disorders and are not required for diagnosis, they are important modulators of the patient's experience and ultimately, the clinical outcome.

Research on the psychosocial aspects of patients with functional GI disorders yields three general observations:

- ◇ Psychological stress exacerbates gastrointestinal symptoms in patients with functional GI disorders and can even produce symptoms in healthy patients (but to a lesser degree).

- ◇ Psychological disturbances modify the experience of illness and illness behaviors such as health seeking. For example, a history of major psychological trauma (e.g. sexual or physical abuse) is more common among patients seen in referral centers than in primary care and is associated with a more severe disorder and a poorer clinical outcome. Additionally, psychological trauma may increase painreporting tendency.
- ◇ Having a functional GI disorder has psychological consequences in terms of one's general well-being, daily functional status, concerns relating to control over symptoms, and future implications of the illness (e.g. functioning at work and home).

## **APPROACH TO TREATMENT**

The approach to treatment for all functional GI disorders is founded on a therapeutic physician-patient relationship. The basis for implementing a strong physician-patient relationship is supported by evidence that patients with functional GI disorders have anywhere from a 30 to 80% placebo response rate regardless of treatment.

Because functional GI disorders are chronic, it is important to determine the immediate reasons behind each visit, after which treatment can be based on severity and nature of symptoms, physiological and psychosocial determinants of the patient's illness behavior, and the degree of functional impairment. These factors can separate patients into mild, moderate, and severe categories.

### **Patients with mild symptoms:**

- ◇ usually seen in primary care,
- ◇ do not have major impairment in function or psychological disturbance and
- ◇ can maintain normal activity.

These patients have concerns about their condition but do not need to make many visits to their physician. Regarding treatment, these patients require education about their disorder and its symptoms as well as information regarding a proper diet and the kinds of medication that can have adverse effects.

### **Patients with moderate symptoms:**

- ◇ seen in both primary and secondary care facilities and
- ◇ experience intermittent disruptions in activity on account of their symptoms.
- ◇ may identify a close relationship between symptoms and inciting events such as stress, travel, or dietary indiscretion.

For these patients, symptom monitoring to record time, severity, and presence of associated factors can help to identify inciting factors and give the patient a sense of control over the disorder. Additionally, pharmacotherapy directed at specific symptoms, particularly those that impair daily function, can be helpful, as can psychological treatments (relaxation, hypnosis, cognitive-behavioral therapy, and combination treatments) in reducing anxiety and encouraging health promoting behaviors.

### **Patients with severe symptoms:**

- ◇ have trouble functioning daily,
- ◇ find their disorder to be disabling and debilitating in nearly every facet of life,
- ◇ have a high frequency of associated psychological difficulties,
- ◇ make frequent visits to their physicians , and

- ◇ may hope for a magical cure.

In these cases a long-term physician-patient relationship, which sets realistic treatment goals (such as improved quality of life rather than elimination of all pain) is necessary. The focus for these patients needs to shift from treating a disease to coping with a chronic disorder, where much of the responsibility is placed on the patient, himself. Furthermore, antidepressants have proven useful to control pain and alleviate associated depressive symptoms.

### THE FUTURE

Future studies will identify pathophysiological subgroups, each having its own set of determinants and treatment. Examples are as follows:

- ◇ Some patients will develop their disorders or exacerbate symptoms via sensitization of afferent transmission from infection, enhanced motility, or trauma to the gut. They may respond to the newly developing neurotransmitter blocking agents.
- ◇ Patients with more painful and severe symptoms may prove to have "abnormal perception of normal gut function" rather than abnormal function. This dysfunction in the central regulation of incoming visceral signs may be remedied with a psychopharmacological treatment approach.
- ◇ The symptoms of some patients could be attributed to genetic factors, which result in abnormalities in central reactivity to stress, in which case genetic manipulation strategies would prove beneficial.
- ◇ Early learning within the familial structure and socio-cultural influences has been demonstrated to affect symptom perception and illness behavior. Future studies are also likely to identify psychological and behavioral interventions that are targeted for this subgroup.

While it is likely that there are potent new treatments that will follow our growing pathophysiological knowledge of these disorders, it is unlikely that they will replace some of the fundamental clinical principles:

- ◇ active listening,
- ◇ careful decision making,
- ◇ an effective patient-physician relationship, and
- ◇ patient centered biopsychosocial plan of care.