FUNCTIONAL DISORDERS

ROME IV CRITERIA AND DIAGNOSTIC QUESTIONNAIRE

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Functional gastrointestinal disorders (FGIDs), the most common diagnoses in gastroenterology, are recognized by morphologic and physiological abnormalities that often occur in combination including motility disturbance, visceral hypersensitivity, altered mucosal and immune function, altered gut microbiota, and altered CNS processing.
Research on these FGIDS is based on using specific diagnostic criteria. The Rome Foundation has played a pivotal role in creating diagnostic criteria, thus operationalizing the dissemination of new knowledge in the field of FGIDs. Rome IV is a compendium of the knowledge accumulated since Rome III was published 10 years ago.
It improves upon Rome III by: (1) updating the basic and clinical literature; (2) offering new information on gut microenvironment, gut–brain interactions, pharmacogenomics, biopsychosocial, gender and cross-cultural understandings of FGIDs; (3) reduces the use of imprecise and occasionally stigmatizing terms when possible; (4) uses updated diagnostic algorithms; and (5) incorporates information on the patient illness experience, and physiological subgroups or biomarkers that might lead to more targeted treatment.
This introductory article sets the stage for the remaining 17 articles that follow and offers a historical overview of the FGID field, differentiates FGIDs from motility and structural disorders, discusses the changes from Rome III, reviews the Rome committee process, provides a biopsychosocial pathophysiological conceptualization of FGIDs, and offers an approach to patient care.
- It emphasizes recent advances in our understanding of the enteric nervous system, sensory physiology underlying pain, and stress signaling pathways. There is also a focus on neuroimmunne signaling and intestinal barrier function, given the recent evidence implicating the microbiome, diet, and mucosal immune activation in FGIDs.
The fundamental gastrointestinal functions include **motility, sensation, absorption, secretion, digestion, and intestinal barrier function**. Digestion of food and absorption of nutrients normally occurs without conscious perception. Symptoms of FGIDS often are triggered by meal intake, suggesting abnormalities in the physiological processes are involved in the generation of symptoms.
Genetic mechanisms associated with visceral pain and motor functions in health and FGIDS are reviewed. Understanding the basis for digestive tract functions is essential to understand dysfunctions in FGIDS.
For decades, interactions between the enteric neuromuscular apparatus and the CNS have served as the primary focus of pathophysiological research in the FGIDS. The accumulation of patient reports, as well as clinical observations, has belatedly led to an interest in the role of various luminal factors and their interactions with each other and the host in FGIDS.
Most prominent among these factors has been the role of **food**. As a consequence, although not always evidence-based, dietary interventions are enjoying a renaissance in IBS management. Not surprisingly, given its exploration in many disease states, the **gut microbiota** has also been studied in functional gastrointestinal disorders; data remain inconclusive.
Likewise, there is also a considerable body of experimental and some clinical data to link the pathogenesis of functional gastrointestinal disorders to disturbances in **epithelial barrier integrity**, abnormal **enteroendocrine signaling**, and **immune activation**.

**THE INTESTINAL MICROENVIRONMENT AND FGID**
medications commonly used for the treatment of patients with FGIDS. Specifically, we review the animal models that have been validated for the study of drug effects on sensation and motility; the preclinical pharmacology, pharmacokinetics, and toxicology usually required for introduction of new drugs; the biomarkers that are validated for studies of sensation and motility end points with experimental medications in humans; the pharmacogenomics applied to these medications and their relevance to the FGIDs; and the agents that are applied or have potential for the treatment of FGIDs, including psychopharmacologic drugs.
Patients with FGIDs often experience distress, reduced quality of life, a perceived lack of validation, and an unsatisfactory experience with health care providers.
consideration of important factors that impact FGIDs, such as gender, age, society, and the patient’s perspective. Although the majority of FGIDs, including globus, rumination syndrome, IBS, bloating, constipation, functional abdominal pain, sphincter of Oddi dyskinesia, pelvic floor dysfunction, and extraintestinal manifestations, are more prevalent in women than in men, functional chest pain, dyspepsia, vomiting, and anorectal pain do not appear to vary by gender.
Studies have suggested **sex differences in somatic**, but not visceral, pain perception, motility, and central processing of visceral pain; although further research is required in autonomic nervous system dysfunction, genetics, and immunologic/microbiome. However, a greater clinical response to 5-HT\textsubscript{3} antagonists but not 5-HT\textsubscript{4} agonists has been reported in women compared with men.
Cross-cultural factors are important in FGIDs. In the setting of FGIDs, the aims of this review were as follows: (1) to engender interest in global aspects; (2) to gain a clearer understanding of culture, race, and ethnicity, and their effect on patient care and research; (3) to facilitate cross-cultural clinical and research competency; and (4) to improve and foster the quality and conduct of cross-cultural, multinational research.
Cultural variables inevitably are present in the physician–patient context. **Food and diets**, which differ among cultural groups, are perceived globally as related to or blamed for symptoms. From an individual perspective, biological aspects, such as **genetics, the microbiome, environmental hygiene, cytokines, and the nervous system**, which are affected by cultural differences, all are relevant.
a general framework for understanding FGIDs from a biopsychosocial perspective. More specifically, we provide an overview of the recent research on how the complex interactions of environmental, psychological, and biological factors contribute to the development and maintenance of FGIDs.

BIOPSYCHOSOCIAL ASPECTS: HOW CENTRAL AND ENVIRONMENTAL PROCESSES CONTRIBUTE TO THE DEVELOPMENT AND EXPRESSION OF FGIDS
- listen to your patients: ask the right questions & use symptom questionnair
- characterize the phenotype of disorder
- only performe diagnostic tests (R/O Structural or Motility form)
- therapy; pharmacotherapy & dietary & psychososial & behaviourl approach.

DIAGNOSTIC FGIDS
were developed to screen for FGIDS, serve as inclusion criteria in clinical trials, and support epidemiologic surveys. Separate questionnaires were developed for adults, children and adolescents, and infants and toddlers.
Sensitivity was 62.7% for IBS, 54.7% for F-Dyspepsia, and 32.2% for F-Constipation. Specificity, assessed in a population sample of 5931 adults, was 97.1% for IBS, 93.3% for FD, and 93.6% for FC. Excess overlap among IBS, FC, and FD was a major contributor to reduced diagnostic sensitivity, and when overlap of IBS with FC was permitted, sensitivity for FC diagnosis increased to 73.2%.
All questions were understandable to at least 90% of individuals, and Rome IV diagnoses were reproducible in three-fourths of patients after 1 month. Validation of the pediatric questionnaires is ongoing.
This report defines criteria and reviews the epidemiology, pathophysiology, and management of the following common anorectal disorders: **fecal incontinence (FI)**, **functional anorectal pain**, and **functional defecation disorders**.
FI is defined as the recurrent uncontrolled passage of fecal material for at least 3 months. The clinical features of FI are useful for guiding diagnostic testing and therapy. Anorectal manometry and imaging are useful for evaluating anal and pelvic floor structure and function. **Education, antidiarrheals, and biofeedback therapy** are the mainstay of management; **surgery** may be useful in refractory cases.
Functional anorectal pain syndromes are defined by clinical features and categorized into 3 subtypes. In **proctalgia fugax**, the pain is typically fleeting and lasts for seconds to minutes. In **levator ani syndrome and unspecified anorectal pain**, the pain lasts more than 30 minutes, but in levator ani syndrome there is puborectalis tenderness.
Functional defecation disorders are defined by ≥2 symptoms of chronic constipation or IBS with constipation, and with ≥2 features of impaired evacuation, that is, abnormal evacuation pattern on manometry, abnormal balloon expulsion test, or impaired rectal evacuation by imaging. It includes 2 subtypes: **dyssynergic defecation** and **inadequate defecatory propulsion**. Pelvic floor biofeedback therapy is effective for treating levator ani syndrome and defecatory disorders.
- Fecal incontinency not responding to conservative management.
- Constipation with Dyssnergic Defication
- Possible levatore ani syndrome failing other therapies
The concept that motor disorders of the gallbladder, cystic duct, and sphincter of Oddi can cause painful syndromes is attractive and popular, at least in the United States.

However, the results of commonly performed ablative treatments (eg, cholecystectomy and sphincterotomy) are not uniformly good.
The predictive value of tests that are often used to diagnose dysfunction (eg, dynamic gallbladder scintigraphy and sphincter manometry) is controversial. Evaluation and management of these patients is made difficult by the fluctuating symptoms and the placebo effect of invasive interventions. A recent stringent study has shown that sphincterotomy is no better than sham treatment in patients with post-cholecystectomy pain and little or no objective abnormalities on investigation, so that the old concept of sphincter of Oddi dysfunction type III is discarded.
ERCP approaches are no longer appropriate in that context. There is a pressing need for similar prospective studies to provide better guidance for clinicians dealing with these patients. We need to clarify the indications for cholecystectomy in patients with functional gallbladder disorder and the relevance of sphincter dysfunction in patients with some evidence for biliary obstruction (previously sphincter of Oddi dysfunction type II, now called “functional biliary sphincter disorder”) and with idiopathic acute recurrent pancreatitis.

GALLBLADDER AND SPHINCTER OF ODDI DISORDERS
Centrally mediated abdominal pain syndrome, formerly known as functional abdominal pain syndrome, can be distinguished from other FGIDS by its strong central component and relative independence from motility disturbances.
Centrally mediated abdominal pain syndrome is a result of central sensitization with disinhibition of pain signals rather than increased peripheral afferent excitability.
A newly described condition, narcotic bowel syndrome/opioid-induced gastrointestinal hyperalgesia, is characterized by the paradoxical development of, or increases in, abdominal pain associated with continuous or increasing dosages of opioids. Patients only have relief when opioids are withdrawn.
We define both conditions in the context of epidemiology, pathophysiology, clinical evaluation, and treatment, emphasizing the importance of a physician–patient relationship in all aspects of care.
Functional bowel disorders are highly prevalent disorders found worldwide. These disorders have the potential to affect all members of society, regardless of age, sex, race, creed, color, or socioeconomic status.
Improving our understanding of FBD is critical, as they impose a **negative economic impact** to the global health care system in addition to **reducing quality of life**. Research in the basic and clinical sciences during the past decade has produced new information on the **epidemiology, etiology, pathophysiology, diagnosis, and treatment of FBDs**. These important findings created a need to revise the Rome III criteria for FBDs, last published in 2006.
This article classifies the FBDs into 5 distinct categories: **IBS**, **functional constipation**, **functional diarrhea**, **functional abdominal bloating/distention**, and unspecified FBD.

- a new sixth category, **opioid-induced constipation**, which is distinct from FBDs.
Each disorder will first be defined, followed by sections on epidemiology, rationale for changes from prior criteria, clinical evaluation, physiologic features, psychosocial features, and treatment. It is the hope of this committee that this new information will assist both clinicians and researchers in the decade to come.
Symptoms that can be attributed to the gastroduodenal region represent one of the main subgroups among FGIDS. A slightly modified classification into the following 4 categories is proposed:

GASTRODUODENAL DISORDERS
(1) **functional dyspepsia**, characterized by 1 or more of the following: postprandial fullness, early satiation, epigastric pain, and epigastric burning, which are unexplained after a routine clinical evaluation; and includes 2 subcategories: postprandial distress syndrome that is characterized by meal-induced dyspeptic symptoms and epigastric pain syndrome that does not occur exclusively postprandially; the 2 subgroups can overlap;
(2) **belching disorders**, defined as audible escapes of air from the esophagus or the stomach, are classified into 2 subcategories, depending on the origin of the refluxed gas as detected by intraluminal impedance measurement belching: *gastric and supragastric* belch
(3) **nausea and vomiting** disorders, which include 3 subcategories: chronic nausea and vomiting syndrome; cyclic vomiting syndrome; and cannabinoid hyperemesis syndrome.
(4) rumination syndrome.
DIAPHRAGMATIC BREATHING RETRAINING

Indications:
- Rumination syndrome
- Urgency/fear of accidental bowel leakage
- A core feature of most psychological therapies for FGIDS, such as hypnosis, mindfulness
- Keep hand on chest motionless with taking deep inspirations and expirations using abdominal muscles.
- Target abdominal wall contraction, believed to be a precipitating event, especially during a meal when symptoms are anticipated.
Functional esophageal disorders consist of a disease category that presents with esophageal symptoms (heartburn, chest pain, dysphagia, globus) that are not explained by mechanical obstruction (stricture, tumor, eosinophilic esophagitis), major motor disorders (achalasia, esophagogastric junction outflow obstruction, absent contractility, distal esophageal spasm, jackhammer esophagus), or GERD.
Although mechanisms responsible are unclear, it is theorized that **visceral hypersensitivity and hypervigilance** play an important role in symptom generation, in the context of normal or borderline function.
Treatments directed at improving borderline motor dysfunction or reducing reflux burden to subnormal levels have limited success in symptom improvement. In contrast, strategies focused on modulating peripheral triggering and central perception are mechanistically viable and clinically meaningful.
- IBS
- Centrally mediated abdominal pain syndrome
- Functional esophageal disorders including reflux hypersensitivity
- *tried method; hypnotherapy & cognitive-behavior therapy & interpersonal psychotherapy

PSYCHOTHERAPY