

The Launching of Rome III

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On Tuesday, May 23, 2006, Rome III was officially launched as part of an American Gastroenterological Association (AGA) sponsored symposium at Digestive Disease Week (DDW). It is a pleasure to present a summary of the major features and recommendations of the Rome III launching, the culmination of five years of work. This article provides summary information that can be viewed in more detail in the 13th issue of *Gastroenterology* (released in May 2006 and now available on the Rome III website – www.romecriteria.org), and it precedes the publication of the Rome III book to be released in late-summer 2006.

Publications

Gastroenterology Rome III Edition. The 13th edition of *Gastroenterology* is devoted entirely to Rome III. This issue contains 16 articles from 14 committees, each comprised of up to seven international experts. The introductory article sets the stage for what is to come and conceptualizes these functional disorders within a biopsychosocial context. The content-related articles that follow include new ones on Gender, Age, Society Culture, and the Patient, and Pharmacological and Pharmacokinetics. They also include revised articles from the Rome II edition -- Basic Science, Physiology, Psychosocial Factors, and Design of Treatment Trials. These are followed by the seven criteria-related articles (as compared to five in Rome II) -- Esophageal, Gastroduodenal, Gall Bladder/Biliary, Bowel, Functional Abdominal Pain, Anorectal, and Pediatrics GI: Neonate/Toddler and Child Adolescent. The increase in criteria-related articles relates to the Functional Abdominal Pain committee being split off from the Bowel committee, and the Pediatric committee being expanded to two committees. The final article of the issue -- "The Road to Rome" by Grant Thompson -- traces the history of the Rome committee work.

Rome III book. The book contains over 1000 pages and will provide more comprehensive information than the *Gastroenterology* issue, including more graphics and hundreds of references in each chapter. In addition, there is a 17th chapter written by Bill Whitehead that provides the validation data for the adult questionnaire. One of the highlights of the book is the set of appendices which now contain: (a) the new validated adult and pediatric Rome III questionnaires for diagnosis and their scoring algorithms; (b) "red flag" questions to help exclude other diseases; (c) a set of psychological "red flag" questions to alert the clinician when mental health referral is suggested or urgently required; (d) a comparison table of Rome II and Rome III diagnostic criteria presented side by side, where the proximity of the two sets of criteria may assist clinical or industry investigators to reconcile differences in clinical trials; and (e) glossary, listing of the referees, and photo gallery of the contributors.

The Rome III Classification

To understand what is new in the criteria for Rome III it would help to review the classification system as shown in Table 1. The Functional GI Disorders (FGIDs) are classified into six major domains for adults: -- Esophageal (category A), Gastroduodenal (category B), Bowel (category C), Functional Abdominal Pain Syndrome (category D), Biliary (category E), and Anorectal (category F). The pediatric system is classified first by age range -- Neonate/Toddler (category G) and Child/Adolescent (category H) -- and then by symptom pattern or area of symptom location. Each domain contains several disorders, each with relatively specific clinical features. Therefore, the functional bowel disorders (category C) include irritable bowel syndrome (C1), functional bloating (C2), functional constipation (C3) and functional diarrhea (C4), which anatomically are attributed to the small bowel, colon and rectum. While symptoms (e.g., diarrhea, constipation, bloating, pain) may overlap across these disorders, IBS (C1) is more specifically defined as pain associated with change in bowel habit, which is distinct from functional diarrhea

(C4) characterized by loose stools and no pain or functional bloating (C2) where there is no change in bowel habit. Each condition also has different diagnostic and treatment approaches.

The symptoms of the FGIDs relate to combinations of several known physiological determinants - increased motor reactivity, enhanced visceral hypersensitivity, altered mucosal immune and inflammatory function (which includes changes in bacterial flora), and altered CNS-enteric nervous system (ENS) regulation (as influenced by psychosocial and sociocultural factors and exposures). For example, fecal incontinence (category F1) may primarily be a disorder of motor function, while Functional Abdominal Pain Syndrome (category D) is primarily understood as amplified central perception of normal visceral input. IBS (Category C1) is more complex and results from a combination of dysmotility, visceral hypersensitivity, mucosal immune dysregulation, alterations of bacterial flora, and CNS-ENS dysregulation. The contribution of these factors may differ across different individuals or within the same individual over time. Thus, the clinical value of separating the functional GI symptoms into discrete conditions as shown in Table 1 is that they can be diagnosed reliably and treated more specifically.

Changes from Rome II to Rome III

The Rome III process is a conservative one, with efforts to not make changes unless there is good evidence to do so. In that regard, the process is also a dynamic one that is responsive new scientific data as it emerges. The following is a summary of the changes in criteria and other recommendations along with their justification.

1. *Time frame change for FGIDs.* The time frame for a diagnosis now originates at 6 months prior to clinical presentation and diagnosis and must be currently active (i.e., meet criteria) for 3 months. This time frame is less restrictive than Rome II (12 weeks of symptoms over 12 months) and is easier to understand in a questionnaire or for research and clinical practice.
2. *Changes in classification categories.*
 - a. *Rumination syndrome has moved from being a functional esophageal (category A) to a functional gastroduodenal disorder (category B).* This reflects the evidence that symptoms originate from pressures generated in the stomach and abdominal musculature.
 - b. *Removal of functional abdominal pain syndrome (FAPS) from functional bowel disorders (category C) into its own category (category D).* This is based on the growing evidence that FAPS relates more to CNS amplification of normal regulatory visceral signals rather than functional abnormalities *per se* within the GI tract. The committee members selected for this new category included psychologists, psychiatrists and gastroenterologists involved in brain gut interactions.
 - c. *Creation of two pediatric categories.* The Rome II category of Childhood Functional GI Disorders is now classified as Childhood Functional GI Disorders: Neonate/Toddler (category G) and Childhood Functional GI Disorders: Child/Adolescent (category H). This reflects the different clinical conditions existing between the two categories relating to the growth and development of the child.
3. *Criteria changes.*
 - a. *Functional Dyspepsia.* For Rome III, functional dyspepsia is de-emphasized as an entity for research due to its symptom heterogeneity. Instead, the gastroduodenal committee has recommended using an umbrella term -- "dyspepsia symptom complex" -- which is subclassified into two conditions that may overlap: (a) *Postprandial Distress Syndrome*, and (b) *Epigastric Pain Syndrome*. Although similar to the dysmotility-like and ulcer-like dyspepsia of Rome II, there now are several items for the criteria derived from factor analytic

studies and physiological support instead of being based on the single symptom of epigastric discomfort or pain. Further studies will be needed to validate this change.

- b. *More restrictive criteria for functional disorders of the gallbladder and Sphincter of Oddi.* One of the more complex and controversial areas of the FGIDs relates to the diagnosis and treatment of patients with functional gallbladder and biliary tract disorders. In part, this relates to the low prevalence of these disorders relative to other FGIDs, making these conditions difficult to study, as well as the iatrogenic risk associated with diagnosing non-life threatening conditions with invasive assessments like ERCP and Sphincter of Oddi manometry, or treating them with unnecessary surgery or endoscopic sphincterotomy. Accordingly, Rome III has developed more specific criteria features and exclusions for symptom-based diagnosis. In doing so, the criteria reduce the patient population who then require invasive studies -- like ERCP and manometry -- to confirm the diagnosis and initiate treatment.
- c. *Revision of IBS subtyping.* The Rome II subtype classification for IBS with constipation (IBS-C) and IBS with diarrhea (IBS-D) has been difficult to use in clinical practice. Furthermore, it is unclear how to classify patients who may not meet criteria for these two subtypes, yet still have IBS. In Rome III, the classification has been simplified so that diarrhea, constipation and mixed subtypes are based on the single classification of stool consistency (which can be determined by the Bristol Stool Scale Form). This criterion has a physiological linkage to intestinal transit rather than defecation difficulties. However, clinicians and investigators may also use the bowel Rome II subtyping scheme for IBS-D and IBS-C.

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Table 1. Rome III Functional Gastrointestinal Disorders

- A. Functional Esophageal Disorders
 - [A1. Functional Heartburn](#)
 - [A2. Functional Chest Pain of Presumed Esophageal Origin](#)
 - [A3. Functional Dysphagia](#)
 - [A4. Globus](#)

- [B. Functional Gastroduodenal Disorders](#)
 - [B1. Functional Dyspepsia](#)
 - [B1a: Postprandial Distress Syndrome \(PDS\)](#)
 - [B1b: Epigastric Pain Syndrome \(EPS\)](#)
 - [B2: Belching Disorders](#)
 - [B2a: Aerophagia](#)
 - [B2b: Unspecified excessive belching](#)
 - [B3: Nausea and Vomiting Disorders](#)
 - [B3a: Chronic Idiopathic Nausea \(CIN\)](#)
 - [B3b: Functional vomiting](#)
 - [B3c: Cyclic Vomiting Syndrome \(CVS\)](#)
 - [B4: Rumination Syndrome in Adults](#)

- [C. Functional Bowel Disorders](#)
 - [C1. Irritable Bowel Syndrome](#)
 - [C2. Functional Bloating](#)
 - [C3. Functional Constipation](#)
 - [C4. Functional Diarrhea](#)
 - [C5. Unspecified Functional Bowel Disorder](#)

- [D. Functional Abdominal Pain Syndrome \(FAPS\)](#)

- [E. Functional Gallbladder and Sphincter of Oddi Disorders](#)
 - [E1. Functional Gallbladder disorder](#)
 - [E2. Functional Biliary SO disorder](#)
 - [E3. Functional Pancreatic SO disorder](#)

- [F. Functional Anorectal Disorders](#)
 - [F1: Functional Fecal Incontinence](#)
 - [F2: Functional Anorectal Pain](#)
 - [F2a: Chronic Proctalgia](#)
 - [F2a1. Levator Ani Syndrome](#)
 - [F2a2. Unspecified Functional Anorectal Pain](#)
 - [F2b: Proctalgia Fugax](#)
 - [F3: Functional Defecation Disorders](#)
 - [F3a Dyssynergic Defecation](#)
 - [F3b Inadequate Defecatory Propulsion](#)

- G. Childhood Functional GI Disorders: Neonate/Toddler
 - G1. Infant Regurgitation
 - G2. Infant Rumination Syndrome
 - G3. Cyclic Vomiting Syndrome
 - G4. Infant Colic
 - G5. Functional Diarrhea
 - G6. Infant Dyschezia
 - G7. Functional Constipation

H. Childhood Functional GI Disorders: Child/Adolescent

H1. Vomiting and Aerophagia

H1a. Adolescent Rumination Syndrome

H1b. Cyclic Vomiting Syndrome

H1c. Aerophagia

H2. Abdominal Pain-related FGIDs

H2a. Functional Dyspepsia

H2b. Irritable Bowel Syndrome

H2c. Abdominal Migraine

H2d. Childhood Functional Abdominal Pain

H2d1. Childhood Functional Abdominal Pain Syndrome

H3. Constipation and Incontinence

H3a. Functional Constipation

H3b. Non-Retentive Fecal Incontinence