From Rome to Los Angeles -- The Rome III Criteria for the Functional GI Disorders
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Background and Context
Functional gastrointestinal problems (FGIDs) have turned out to be generally extra broadly accepted as reliable diagnostic circumstances worthy of scientific consideration and scientific investigation.[1] These situations are very prevalent throughout the world and remain a problem for clinicians and research scientists, among others.

- The Rome Foundation has taken on the challenge of establishing symptom-based diagnostic standards for these FGIDs due to a present lack of diagnostic biologic markers.
- The latest modification of the criteria, the Rome III criteria, was recently completed and presented at a symposium at this year's Digestive Diseases Week (DDW) meeting.

A collection of shows got by the Rome Foundation Board members on the symposium and included the muse and rationale of the Rome III course of and a evaluation of the Rome III diagnostic standards for functional gastroduodenal issues, functional bowel disorders, and for the group of disorders previously referred to as useful biliary disorders.

Classification and responses of the Rome III process have been additionally mentioned and included validation of the criteria and growth of a diagnostic questionnaire, generalizability of the factors for clinicians, and new developments in the design of therapy trials.

Introduction
The road to Rome continued its journey by touring west to Los Angeles, California, in May 2006 to unveil the newly established Rome III standards for FGIDs at this year's DDW meeting.[2] The Rome Foundation contains over one hundred international FGID experts who served on various committees and helped develop standardized diagnostic standards for 28 adult and 16 pediatric FGIDs.

The imaginative and prescient of the Rome Foundation is to boost the medical recognition and legitimization of FGIDs and to develop a greater scientific understanding of the pathophysiologic mechanisms so as to optimize treatment.

- Substantial progress has been remodeled lately years, and thus the diagnostic criteria, the understanding of its pathophysiologic mechanisms, and pointers for therapy for these FGIDs have been updated.
- The Rome III standards have been revised from the Rome II standards and are largely based on findings from printed literature.
- The criteria shall be printed in a full-length e-book model and in addition in a condensed model on this year's April edition of Gastroenterology.

This work not only consists of the Rome III diagnostic standards for the varied FGIDs, but also incorporates detailed evaluations of the literature on a considerable vary of topics pertaining to FGIDs, including epidemiology, pathophysiology, diagnostic testing, and remedy. The DDW symposium was chaired by Douglas Drossman, MD, who is President of the Rome Foundation.

Featured lectures on the Rome III standards, questionnaire growth, applicability to patients, and design of therapy trials were presented by the opposite Rome Foundation Board members. The Functional GI
Disorders and Rome III Process

Dr. Drossman opened the symposium and laid the inspiration for the entire Rome III improvement course of and the rationale for the factors.

He mentioned factors that contribute to the rationale for growing standards for FGIDs, which include the truth that symptoms aren’t defined primarily by abnormal motility but are outlined by multiple factors similar to motility disturbances, visceral hypersensitivity, irritation and mucosal immune dysfunction, brain-gut dysfunction, and early life and psychosocial components.

Standardized and widely accepted standards additionally present epidemiologic support by defining symptom-based subgroups and demonstrating related frequencies throughout completely different populations.

The Rome standards have additionally supplied diagnostic requirements for both scientific trials and scientific cares and have therapy implications. However, there are issues and limitations that have been mentioned.

The main adjustments instituted in the Rome III course of embody (1) revision of time-frame requirement to fulfill diagnostic standards, (2) adjustments in classification standards (eg, rumination is now one of the practical gastroduodenal problems, and practical abdominal pain syndrome [FAPS] is now a separate category and never a functional bowel disorder), (3) addition of pediatric classes (ie, Neonatal/Toddler and Child/Adolescent), (4) functional dyspepsia as a single dysfunction has been de-emphasized for research, (5) IBS bowel habit subgroup use primarily of stool consistency to determine IBS bowel behavior subgroups (eg, diarrhea or constipation predominance), and (6) more restrictive standards for gallbladder and sphincter of Oddi dysfunction. Future plans for the Rome Foundation include international educational packages, assist for validation research, partnering with regulatory agencies, working team initiatives (eg, pointers for brain imaging and pointers for severity in FGID working teams), and diversification of construction.

Criteria Development

A Paradigm Shift for Functional Gastroduodenal Disorders

Nicholas J. Talley, MD, PhD, mentioned how dyspepsia was defined as "pain or discomfort centered within the upper abdomen" by the Rome I and II standards. This old definition was discarded in Rome III as a result of there is no single symptom current in all patients with useful dyspepsia (FD), as a outcome of considerable variation in symptom patterns exists between patients, and because despite Rome II recommendations, studies nonetheless include heartburn and acid regurgitation as "dyspepsia."

- [6-8] Dyspepsia is often polysymptomatic, with 99% of sufferers reporting more than 2 symptoms, over 80% reporting greater than 5 signs, and fewer than 0.1% reporting 1 symptom.
- These signs include upper belly ache, heartburn, and acid regurgitation, amongst others. [9] FD is often referred to as pain or discomfort centered in the upper stomach with no proof of organic disease likely to clarify symptoms.

The Rome III committee decided that the Rome III standards had been restricted for a quantity of reasons: (1) a scarcity of proof that subdividing FD by predominant symptom is helpful in figuring out pathophysiology because of low sensitivity and specificity; (2) they have been based mostly largely on expert opinion; and (3) an element evaluation on signs suggests that there’s a meal-related syndrome not accounted for by Rome II.
Therefore, the Rome III committee beneficial the next pragmatic definition: Dyspepsia is defined because the presence of 1 or extra dyspepsia signs which are thought of to originate from the gastroduodenal area, within the absence of any organic, systemic, or metabolic disease that's likely to clarify the symptoms.[12] These signs are listed in Table 1. Thus, the oppositesymptoms that were listed in Rome II no longer fall underneath the FD umbrella.

The committee concluded that the "umbrella term" FD had restricted utility and that on the idea of the obtainable evidence, a meal-related grouping and pain-related grouping seem to symbolize FD as a end result of they are associated with distinct symptom groups and pathophysiologic mechanisms. Thesesubgroups are known as epigastric ache syndrome (EPS) and postprandial misery syndrome (PDS).

The Rome III definitions for these 2 syndromes are listed in Tables 2 and 3. These newsyndromes were defined however stay to be validated and ought to be used for analysis functionally and not for clinical follow at this time. Clinicians are advised to use the definition of FDs as a end result of remedy research have utilized this definition (and not these of EPS and PDA) in the trials.

Another vital change from the Rome II criteria was that the Rome III committee recognized that patients might meet standards for FD (and EPS or PDA) and have coexistent heartburn or IBS. On the idea of professional opinion, heartburn doesn't exclude a diagnosis of FD if dyspepsia persists despite a trial of sufficient acid suppression.

Coexisting IBS has been provento haven't any main impression on symptom sample or putative pathophysiologic mechanisms in FD.

Fullness and early satiety represent a clear group distinct from nausea and vomiting. There are 2 distinct situations that at the second are recognized syndromes in adults and have been outlined with Rome III criteria: cyclic vomiting syndrome (CVS) and persistent idiopathic nausea (CIN) -- these are separate from FD on the idea of issue evaluation and medical opinion (Tables four and 5).

The New Rome III Criteria for Functional Bowel Disorders and IBS SubgroupsNext, Robin Spiller, MD, mentioned how functional bowel disorders comprise the followingsituations: irritable bowel syndrome (IBS), useful bloating, practical constipation, functional diarrhea, and unspecified useful bowel dysfunction.

The main changes instituted from Rome II to Rome III criteria are: (1) introduction of a frequency threshold of signs needed to meet standards (ie, three or more days per 30 days in the last 3 months; (2) length of signs (reduced to more than 6 months) earlier than one can make a agency prognosis; and (3) refining the subtyping of IBS.

The Rome III diagnostic criteria for IBS are proven in Table 6. The Rome II committee subclassified IBS on the premise of expert opinion and attempted to incorporate stool frequency, stool form, and defecation symptoms. However, because of its complexity and an absence of an evidence-based strategy, the subclassification was revised to be primarily based solely on stool consistency, which has been supported by current research.

Subclassification of IBS is essential because it would probably be related to completely different therapy selections and pathophysiologic mechanisms.
The proposed new subtyping based mostly on stool consistency alone is IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS blended type (IBS-M), and IBS unsubtyped (IBS-U). Patients with IBS-M have both exhausting and unfastened stools over periods of hours or days, whereas IBS sufferers with alternating bowel habits change subtype over intervals of weeks and months.

**Stool kind is predicated on the Bristol stool scale that categorizes stool kind and correlates best with colon transit occasions**

Stability and association with other options, such as visceral sensitivity and response to remedy, stay to be decided. Functional Gallbladder and Functional Sphincter of Oddi Disorders

Enrico Corazziari, MD, subsequent mentioned that the principle change is that this group of issues isn't any longer referred to as functional biliary problems; it has been renamed in accordance with the area the placethe abnormality actually happens.

This group of circumstances has been updated to practical gallbladder dysfunction, useful biliary sphincter of Oddi disorder, and useful pancreatic sphincter of Oddi dysfunction. These circumstances are not defined by structural abnormalities (eg, gallstones).

The definition of biliary-like pain was developed by consensus: (1) pain positioned within the epigastrium and/or right upper quadrant; (2) recurrent signs occurring at different intervals (not daily); and (3) episodes lasting 30 minutes or extra; ache builds up to a steady stage, and is average to extreme enough to interrupt the affected person's day by day activities or lead to an emergency division go to.

There are also supportive symptoms, such as that the ache might current with 1 or more of the following: (a) associated nausea and vomiting; (b) radiating to the again and/or right infrasubscapular area; and (c) inflicting one to awaken from sleep in the midst of the night time. Consensus-recommended Rome III algorithm for practical gallbladder dysfunction and useful sphincter of Oddi disorder were additionally mentioned.

**Challenges and Responses**

Rome III Diagnostic Questionnaire -- Development and Validation

William Whitehead, PhD, discussed the targets of the questionnaire development and validation course of which were: (1) to develop a questionnaire that incorporates the Rome III standards as an assist to prognosis; (2) insure that questions are comprehensible; and (3) validate the questionnaire and the standards by comparing to diagnoses made by clinicians.

- Novel to the Rome course of, questionnaire was developed and validated via a multistep process using the expertise of the Rome committee, working groups, and multicenter research websites.
- A main innovation of Rome III is the development of an ordinal scale with individual frequency thresholds.
- One of the goals was to ensure that frequency thresholds of signs had the best sensitivity and specificity for abdominal ache in IBS, which was discovered to be 2-3 days per thirty days with a sensitivity of 71% and specificity of 88%.

The Rome III diagnostic questionnaire's reliability and specificity are excellent and sensitivity is sweet. However, further testing is needed for different FGIDs. Applicability of Rome III Criteria for Clinical Practice

W. Grant Thompson, MD, mentioned the problems and questions faced by clinicians associated
with trying to use revealed trial and survey data to clinical follow, specifically therapy selection for their sufferers.

**Questionnaires help within the diagnosis, and also choose topics for scientific trials and survey populations.**

Optimally, they want to be inclusive so that all sufferers with this situation are encompassed. However, algorithms and inclusion and exclusion standards utilized in questionnaire research can have an effect on the outcomes. Cutoffs of severity and frequency scales are necessary and can decide who is included. Exclusions are additionally essential because sufferers with the signs of the situation may be excluded relying on the standards requirements.

When reviewing scientific treatment trial data, it is important that the clinician ask the following questions to determine whether or not the information are relevant to his/her affected person: (1) Was the questionnaire altered? (2) What was the purpose of the study? (3) How was the research inhabitants selected? and (4) Can the proof from that trial or survey apply to my patient?

**Update on Design of Treatment Trials**

Next, Michel Delvaux, MD PhD, addressed the design of trials to evaluate the efficacy of latest therapies for FGIDs, emphasizing trials in IBS and dyspepsia as a result of most research has been undertaken in these circumstances. Design of remedy trials is extremely necessary in evaluating the efficacy of remedy and in making use of knowledge to clinical care.

- Optimal design must be placebo-controlled, double-blind, parallel group, and randomized to therapy allocation.
- However, there are challenges in designing medical trials in FGIDs.
- These embody high placebo response rate, fluctuating symptoms, heterogeneous and complicated mechanisms, avoiding bias, contamination by over-the-counter remedies or drugs for different circumstances, and avoiding hurt given that FGIDs aren’t thought-about life-threatening conditions.

The examine design should clearly outline the FGID to be handled, the subgroups, and inclusion and exclusion standards (eg, sex, symptom severity, comorbidities, concurrent medications). Some unresolved points concern the period of the remedy intervention (eg, four vs 12 weeks), frequency of treatment (eg, day by day vs on-demand), and problem blinding the intervention (eg, psychotherapy, hypnotherapy, sphincterotomy, or remedy with predictable results or facet effects). There are major and secondary outcome measures.

These will likely depend on the mechanism of action of the therapeutic modality. Secondary outcomes are essential for determining the efficacy of the remedy on particular person signs or nongastrointestinal outcomes, similar to health-related high quality of life. A definition of a responder is a 2-dimensional consequence, the amplitude of the response of the treatment, and the period of the response over the treatment interval.

**There is a steady spectrum of response from full relief 100 percent of the time to some relief for a short length of time.**
We at present do not know the brink for a clinically significant treatment effect. In summary, the Rome course of has facilitated methodologic advances that have been essential over the last 2 a long time. However, various study designs want further validation, and outcome measures are the critical problem and deserve additional analysis.

Conclusion

The Rome course of has been devoted to providing education, legitimization, and validation for the numerous FGIDs affecting the pediatric and grownup populations.

The Rome III committees have just lately supplied up to date reviews on the essential science, physiologic mechanisms, psychosocial, epidemiologic, diagnostic, and therapy aspects of those disorders. A new Rome III classification system for FGIDs has been established with the inclusion of symptom-based criteria for medical investigation and apply.

An evidence-based strategy was taken; nevertheless, in areas the place this kind of information was missing, consensus opinion was employed. A number of issues nonetheless continue to challenge healthcare suppliers, analysis scientists, regulatory companies, and business, and these remain a aim of the Rome Foundation to sort out sooner or later in the evolving process of unraveling the complexities surrounding FGIDs.

Table 1.

Rome III Diagnostic Criteria for Functional Dyspepsia

Functional Dyspepsia

At least 3 months, with onset no less than 6 months beforehand, of 1 or more of the next:

- Bothersome postprandial fullness
- Early satiation
- Epigastric pain
- Epigastric burning
- No evidence of structural illness (including at higher endoscopy) that's likely to clarify the signs

Table 2.

Rome III Diagnostic Criteria for Epigastric Pain Syndrome

Epigastric Pain Syndrome

At least 3 months, with onset at least 6 months previously, with ALL of the following:

- Pain and burning that's:
  - intermittent
  - localized to the epigastrium of at least average severity, a minimum of once per week,
  - and NOT: 1. generalized or localized to different abdominal or chest regions
    2. relieved by defecation or flatulence
    3. fulfilling criteria for gallbladder or sphincter of Oddi problems

Table 3.

Rome III Diagnostic Criteria for Postprandial Distress Syndrome

Postprandial Distress Syndrome

At least 3 months, with onset no less than 6 months beforehand, of 1 or more of the next:

- Bothersome postprandial fullness
  1. occurring after ordinary-sized meals
  2. a minimum of a number of times every week

Or

- Early satiation
  1. that forestalls finishing a daily meal
  2. and happens at least several occasions a week

Table 4. Rome III Diagnostic Criteria for Cyclic Vomiting Syndrome

Cyclic Vomiting Syndrome

At least 3 months, with onset no much less than 6 months beforehand of:

- Stereotypical episodes of vomiting concerning onset (acute) and length (less than 1 week)
- three or more discrete episodes in the prior year
• Absence of nausea and vomiting between episodes

Supportive criteria: History of migraine headaches or a family historical past of migraine complications

Table 5.

Rome III Diagnostic Criteria for Chronic Idiopathic Nausea

Chronic Idiopathic Nausea

At least three months, with onset at least 6 months previously, of:

• Bothersome nausea, occurring at least several occasions per week in the final 3 months
• Not normally associated with vomiting
• Absence of abnormalities at higher endoscopy or metabolic illness that explains the nausea

Separate from FD (factor analyses)

Table 6.

Rome III Diagnostic Criteria for Irritable Bowel Syndrome

Irritable Bowel Syndrome

At least three months, with onset at least 6 months beforehand of recurrent belly pain or discomfort** associated with 2 or more of the following:

• Improvement with defecation; and/or
• Onset associated with a change in frequency of stool; and/or
• Onset related to a change in form (appearance) of stool**

Discomfort means an uncomfortable sensation not described as pain.

References


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