



PRESIDENT'S REPORT

Douglas A. Drossman, MD
President, Rome Foundation
Senior Editor, Rome III Book

It is again a pleasure to send you our biannual newsletter an update on the Rome Foundation's activities. There has been considerable growth and some new initiatives which I am pleased to present.

In our effort to stay connected to the field, thanks to Michele Pickard our administrator, we have set up a program for "Associates of Rome" and to date we have 54 associates from 22 countries. These individuals, most of whom are in academic positions in their countries are afforded closer communication with Rome Foundation activities, discounts on functions and educational products and open access to our newsletters and other materials.

We continue to grow our association with the American Gastroenterological Association. This includes a co-marketing arrangement to provide some of our educational products and a collaboration on several learning initiatives for AGA members. Perhaps one of the more exciting one is to develop a 1½ day communication skills workshop designed to manage difficult clinical scenarios and to enhance the patient-physician relationship in caring for patients with FGIDs.

We have also expanded our translations of educational materials into many languages and have begun several global educational and research programs. Dr. Ami Sperber (Israel) has taken forwarded our efforts to provide international availability for our questionnaires and criteria and currently there are over 16 translations completed or underway, and our Rome III book is now published in Chinese, Japanese and Spanish. Our publication of the Rome Foundation Algorithms for Common GI Symptoms in the *American Journal of Gastroenterology* in April, was replicated thanks to the efforts of Dr. Max Schmulson (Mexico) into Spanish and published in the *Mexican Journal of Gastroenterology* this past November.

With regard to global education, the Rome Foundation sought collaboration in association with the World Gastroenterology Organisation (WGO) produced a multi-national conference on cross-cultural research and care in IBS. **"IBS – The Global Perspective" which was held at the Pfister Hotel in Milwaukee, WI on April 6-7** just prior to the IFFGD International Conference on Functional GI disorders. This conference provided the venue for understanding IBS from a multinational and multi-cultural perspective. This information will continue to be of interest to academicians, clinicians, industry representatives and regulatory agencies. Representatives from the FDA, EMEA and the Japan

Regulatory Agency attended; we are hopeful that this meeting will spur interest in the development of standards for multi-national research, just as the Foundation has provided guidance for diagnostic criteria and endpoints and outcomes in clinical trials. The presentations and supplementary material will soon be available on our website (www.theromefoundation.org). Of course we continue to hold educational programs at United European Gastroenterology Week (UEGW) and at venues in Eastern Europe, Latin American and Asia. Most recently the **Asian Working Team for Functional GI Disorders** (Kok Ann Gwee MD, PhD – Singapore, Chair, William E. Whitehead PhD – USA, Co-Chair) with representatives from 6 Asian countries convened at the Asian Neurogastroenterology and Motility Association in Beijing to begin a multi-national survey of the prevalence of FGIDs in the clinical setting. This information will be used to help develop or modify existing criteria that will be of value to studies involving the Asian community.

Our Working Teams remain active and **The Role of Intestinal Microbiota in Functional GI Disorders** (Magnus Simren MD – Sweden, Chair; Giovanni Barbara PhD – Italy, Co-Chair) is more than halfway through the process and expect to submit their review of the field and recommendations for research later this year. After a 2 year hiatus to complete additional research, the **Severity in IBS** (Doug Drossman MD – USA, Chair; Lin Chang MD – USA Co-Chair) has completed their work and the manuscript is currently under review. Two new important working teams under development include one on **Food and Diet** (William Chey MD – USA, and Jan Tack, MD, PhD – Belgium, Co-Chairs) and another on **Multi-National Cross Cultural Research in the FGIDs** (Ami Sperber MD – Israel, Chair). The information provided by these committees will be well timed for the Rome IV committees to use in their work on building the new chapters.

Lin Chang, MD (USA) continues to chair our educational activities and possibly the highlight this year will be the **4th Annual Rome Foundation – AGA Institute Lecture** at DDW. We will have two speakers for this session to be held on Sunday, May 8 from 10:30 – noon in Room E 451B in the Chicago convention Center. Both speakers are from Columbia University in NYC, and they will be presenting on the brain and gut aspects of neurogenesis. Tarique Perera MD will speak on "The Role of Neurogenesis in the Brain" and Michael D. Gershon MD will discuss "The Role of Neurogenesis in the Enteric Nervous System" as related to the Functional GI Disorders.

Our research program under the direction of Bill Whitehead, PhD (USA), has finalized the selection of our **Rome Foundation**

continued on page 2

continued from page 1

Research Award and our **Ray Clouse Prize for the Best Research in the FGIDs** along with a new award, the **Ray Clouse Award for Paper Most Cited in Functional GI and Motility Disorders**. The awards will be presented at our annual reception at DDW on Saturday evening at 6 PM in Chicago.

The most exciting news to report is that the Rome IV process has just begun. An editorial board will be in place by DDW in May and there will be several new and exciting initiatives that will help carry the field of FGIDs forward.

- Publication will be delayed to 2015-2016. This will permit the use of support committees that will be charged to provide new information that will help the Rome IV committees in their work. The committees will include those doing systematic reviews and meta-analyses, working on cross-cultural aspects of the FGIDs, and looking at the application of the information in primary care and others.
- We plan to focus more on online access to the information by computer or iPad. For a subscription, individuals will be able to free text search for information or download chapters or the entire book. Of course hard copies of the book and a journal supplement containing abridged information will be available as usual.
- In keeping with our efforts to disseminate information globally we will work to provide simultaneous translation of the chapter material at the time of or soon after publication of Rome IV
- The content will be expanded to include more information on Women's Health, biomarkers and global aspects of research and patient care
- We also plan to develop products derived from this content that is more portable. This will include pocket information on the criteria, a primary care version and products for use by our sponsors.
- Finally, we recognize that the diagnostic criteria while helpful for recruitment into research studies, do not fully capture the spectrum of the patient within the clinical context. Accordingly we plan to develop a multi-dimensional clinical profile classification in addition to the diagnostic criteria, which will encompass aspects of severity and disability, level of physiological dysfunction and psychosocial co-morbidity.

Our mission: **"To improve the lives of people with functional GI disorders"** and our three goals, to: **"promote clinical recognition and legitimization of the functional GI disorders"**, **"develop a scientific understanding of their pathophysiological mechanisms"** and **"optimize clinical management for patients with FGIDs"** continue to drive all activities. We are grateful for our 14 industry sponsors and look forward to working with you to advance the field of FGIDs.

PLANNING FOR ROME IV

The Rome Foundation is beginning to plan for *Rome IV*. This will be an update of knowledge of the functional GI disorders with the inclusion of new diagnostic criteria. There are several new features that are worth noting. First, careful attention is being paid to produce the most needed information for this publication. A planning committee will select the Editorial board and make recommendations for the publication content. The editorial board will have an active role in selecting the committee chairs, coordinating the publication, and each board member will serve as a liaison with one or two chapter committees to be sure there is consistency in the work effort across chapters. Standards for selecting chapter committee members will be based on academic credibility will be maintained.

Another new feature will be a delay in the publication date. While in the past the publication sequence from Rome I, to II to III had been 6 years, it is expected that the Rome IV will be published late 2015 or early 2016, about 10 years after the Rome III book in 2006. The main reason is to allow enough time for new data to accumulate that will be used by the Rome IV chapter committees. In addition there will be several "support committees" activated to facilitate the provision of new knowledge that will be made available for the chapter committees to use in their work. This will include many of the existing and newly developed working teams on severity, intestinal microflora, cross-cultural aspects (Asian working team) and food and nutrition. In addition we expect to set up a committee of experts to do meta-analyses for the committees, as well as a committee to make recommendations for multi-national research. As a result the chapters to come out for Rome IV will have new information to help in their recommendations.

We are also looking to improve the distribution of this new knowledge. Rome IV will be accessible electronically by text searching or downloading of sections, chapters or the entire book, in addition to hard copy availability. We plan to have simultaneous translation of the book into several languages at the time of publication or soon thereafter. Ceciel Rooker, managing editor and public relations director will be working with the committees to produce "deliverables" that can be distributed by sponsors to clinicians. This may include smaller brochures or information cards for example of the criteria that can fit in a lab coat. Finally, we plan to have multiple "launches" at major GI meetings in the US and with the help of our International Liaison Committee at major international conferences.

We are hopeful that Rome IV will be a welcome addition to investigators, clinicians, regulatory agencies and our industry sponsors. Stay tuned.

Douglas A. Drossman, MD
Senior Editor

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OUR MISSION IS:
“TO IMPROVE THE LIVES OF PEOPLE WITH FUNCTIONAL GI DISORDERS.”

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TABLE OF CONTENTS

PROGRAM AND PROJECT UPDATES

PRESIDENTS REPORT.....	1
EDUCATION REPORT.....	4
WELCOME NEW EXECUTIVE DIRECTOR.....	4
ROME TRANSLATION PROJECT.....	5
ROME FOUNDATION RESEARCH PROGRAM.....	6
ROME FOUNDATION WORKING TEAM.....	10
ASSOCIATES OF ROME.....	11

MEETING AND EVENTS

MEET THE EXPERTS AT UEGW 2011.....	12
IBS - THE GLOBAL PERSPECTIVE.....	13
ROME FOUNDATION/AGA LECTURESHP AT DDW 2011.....	14

ANNOUNCEMENTS

IFFGD UPDATE.....	15
ROME FOUNDATION LEGAL COUNSEL.....	17
ROME AND AGA COLLABORATION.....	18
ROME CRITERIA REFERENCE LIST.....	19



ROME FOUNDATION EDUCATIONAL PROGRAM

LIN CHANG, MD

CHAIR, EDUCATION COMMITTEE

Education

There are both continuing and new educational programs that the Rome Foundation has been working on. These include the Rome educational slide sets on FGIDs, the annual Rome-AGA lectureship at Digestive Diseases Week (DDW), and a Best of DDW FGID abstract webcast.

Rome educational slide sets

The *Computer-Based Learning Program* includes state-of-the-art slides that brings to life information from the Rome III book on FGIDs. This educational program is endorsed by AGA Institute. The slide set includes a wide range of information that spans from epidemiology to pathophysiology to treatment. A number of animations, videos and conceptual slides help to communicate ideas that may otherwise seem difficult to convey. Notes and legends for every slide give a description of the slide with key references.

Fourth Annual Rome-AGA lectureship at the DDW

Two faculty members from Columbia University, Dr. Tarique Perera and Dr. Michael Gershon, will lecture at the Fourth Annual Rome-AGA lectureship at this year's DDW meeting on *The Role*

of Neurogenesis in the Brain and Gut and its Implications for Functional GI and Motility Disorders. Dr. Perera is an Assistant Professor in Clinical Psychiatry will discuss the suppression of neurogenesis in the brain, specifically the hippocampus, and its role in increasing the vulnerability to developing depression. Dr. Perera's work has important implications for functional gastrointestinal disorders (FGIDs) because of their overlap with depression and that antidepressants, which restore and stimulate neurogenesis, are frequently used to treat FGIDs. Dr. Gershon is an internationally renowned scientist who has studied microcircuits within the enteric nervous system and their regulation of motor, secretory and absorptive functions within the GI tract and their relevance in functional and motility GI disorders. The Rome-AGA lectureship will take place on Sunday, May 8, 2011 at 10:30am.

Best of DDW webcast

Rome Foundation Board members will review and discuss the best abstracts on FGIDs from this year's DDW. Working with the GI Health Foundation on this educational endeavor, this information will be broadcast on a webcast that will be available for viewing soon after the meeting.



WELCOME WILLIAM ("WINK") HILLIARD JR.
EXECUTIVE DIRECTOR ROME FOUNDATION

We are grateful to Mr. George Degnon and Ms. Kathy Haynes of Degnon and Associates for their 15 years of service and support to the Rome Foundation. As of January 1, the business operations have moved from Degnon Associates to Hilliard Associates in Raleigh, NC. Mr. William ("Wink") Hilliard Jr. will then continue as Executive Director of the Rome Foundation and will handle all the day to day activities. Mr. Hilliard is a graduate of the University of North Carolina in Chapel Hill and held an academic position in Corporate and Divisional Strategic Planning. His experience has involved the management of several medical organizations

including the NC Society of Anesthesiologists, the NC Society of Internal Medicine, and the NC College of Emergency Physicians. He has extensive experience in meeting management and the provision of financial services including portfolio management. Mr. Hilliard will represent the Foundation in its many activities, coordinate sponsor related contracts, financial reports, fund raising and distribution of our books and educational products. He can be reached at P.O. Box 6524, Raleigh, NC 27628. Phone: 919-787-5859, Fax: 919-900-7646, email: whilliard@theromefoundation.org.



ROME TRANSLATION PROJECT - UPDATE

AMI D. SPERBER, MD, MSPH

CHAIR, ROME FOUNDATION
TRANSLATION PROJECT

The increasing interest in research in IBS and other functional gastrointestinal disorders (FGIDs) and the growing sophistication of communication technology make cross-cultural, multinational research a feasible endeavor. Collaborative multinational, cross-cultural studies in FGIDs, using appropriate research methodology, can make a significant contribution to the understanding of FGIDs and to patient care.

In addition, pharmaceutical companies are increasingly conducting trials of new drugs in numerous countries around the world.

The conduct of multinational research successfully requires an infrastructure of study instruments validly translated into the languages of the study populations.

"The Rome Translation Project", headed by Dr. Ami Sperber, was established to oversee the translation of all relevant Rome Foundation material, in particular the Rome III book, the Rome III diagnostic questionnaire, and the Rome clinical algorithms. The diagnostic questionnaire and criteria, in its approved language versions, will be available for use in epidemiologic studies and clinical trials.

LANGUAGE	ALL ADULT MODULES *	ADULT FD MODULE STAND-ALONE	ADULT IBS MODULE STAND-ALONE	PEDIATRIC	ALARM QUESTIONS	PSYCHOSOCIAL ALARM QUESTIONNAIRE
ARABIC	TO BE STARTED					
CHINESE	YES	INCLUDED IN "ALL ADULT MODULE"	INCLUDED IN "ALL ADULT MODULE"	YES	YES	YES
DUTCH	NO	NO	YES	YES		
FRENCH	IN PROGRESS				IN PROGRESS	IN PROGRESS
GERMAN	YES			YES	YES	IN PROGRESS
HEBREW	YES	INCLUDED IN "ALL ADULT MODULE"	INCLUDED IN "ALL ADULT MODULE"		YES	YES
ITALIAN	YES	INCLUDED IN "ALL ADULT MODULE"	INCLUDED IN "ALL ADULT MODULE"		YES	
JAPANESE	YES	INCLUDED IN "ALL ADULT MODULE"	INCLUDED IN "ALL ADULT MODULE"	YES	YES	YES
KOREAN	YES	INCLUDED IN "ALL ADULT MODULE"	INCLUDED IN "ALL ADULT MODULE"			
MALAY-BAHASA	NO	YES	YES		YES	YES
NORWEGIAN	NO		IN PROGRESS	YES		
PORTUGUESE		YES	TO BE STARTED			
SPANISH	YES	INCLUDED IN "ALL ADULT MODULE"	INCLUDED IN "ALL ADULT MODULE"	YES	YES	YES
THAI	NO			IN PROGRESS		

The challenge of cross-cultural translation is to adapt an instrument so that it retains the meaning and intent of the original instrument (the source language) and is culturally relevant and comprehensible in the target language. Thus, the aim is to achieve a "cultural" rather than a "literal" translation into a target language.

The project has developed official guidelines for translation of these materials that must be followed before Rome Foundation approval is granted. The guidelines are available for download at the Rome Translations Project website: www.theromefoundation.org/translations/guidelines.cfm. More complete information on the translation project can be found at its homepage at: www.theromefoundation.org/translations/. The project will both monitor translation initiated by others and initiate translations itself. Approval is required for all uses of translated versions of the Rome material including research and education.

Approved language versions of the Rome questionnaires will be available free of charge for academicians conducting independent studies that are not funded by pharmaceutical companies or

other commercial interests. A request can be placed through the translation project website. In commercially funded studies a fee will be charged for the use of translated questionnaires. In all events a licensing agreement will be signed with the Rome Foundation before the translated version is provided to the investigator. Dr. John Kellow will be in charge of licensing and fee arrangements.

The following table details available language versions as of the moment. This is an ongoing project with an ever-increasing number of available, validated translations.

**All adult modules includes Functional Dyspepsia (FD) module, IBS module, Alarm questions, and psychosocial alarm questionnaire.*



ROME FOUNDATION RESEARCH PROGRAM

WILLIAM E. WHITEHEAD, PHD

CHAIR, RESEARCH COMMITTEE

ROME FOUNDATION RESEARCH AWARD

The Rome Foundation provides a \$50,000 research grant each year to a young investigator. Preference is given to applications that (1) test the validity and/or utility of the Rome III diagnostic criteria, (2) assess the epidemiology of functional GI and motility disorders, or (3) advance knowledge of outcome assessment or trial design for FGID treatment trials. The applications receive an NIH-style review by an independent review committee. This year the review committee was chaired by Dr. Brooks Cash, Professor of Medicine at the Uniformed Services University for the Health Sciences and Chief of Medicine at Walter Reed Army Medical Center.

RAY CLOUSE PRIZE FOR THE BEST RESEARCH ARTICLE ON FUNCTIONAL GASTROINTESTINAL AND MOTILITY DISORDERS 2010

In 2008 the Rome Foundation created an award in memory of Ray E. Clouse, MD, a gastroenterologist and scholar at Washington University School of Medicine and a devoted member of the Rome Foundation. This award recognizes the author of the best original research paper published in the functional gastrointestinal and motility disorders for the calendar year preceding each DDW. While many papers are nominated by the Board of the Rome Foundation, anyone may submit a nomination by briefly describing how the paper will impact the field of functional gastroenterology and motility along with a pdf of the paper. Rome Foundation board members are ineligible. The best paper is selected by a vote of the Rome Foundation board.

RAY CLOUSE PRIZE FOR THE MOST CITED ARTICLE IN FUNCTIONAL GASTROINTESTINAL AND MOTILITY DISORDERS 2009

This year a new prize has been created to provide an award for the most cited original research article in functional GI and motility disorders for the year 2009. Papers by members of the Board of the Rome Foundation are not eligible. The two-year lag between the year of publication and the year the award is made reflects the fact that citations of a paper are usually delayed by approximately one year; by choosing a two year lag, the Rome Foundation sought to avoid disadvantaging papers published late in the calendar year. The most cited paper is identified by the Web of Science search engine.



ROME FOUNDATION RESEARCH GRANT AWARD 2011 WINNER – LARS AGRÉUS MD, PHD

Lars Agréus MD, PhD

*Professor and Chair
Center for Family and Community Medicine
Department of Neurobiology, Care Sciences and Society
Karolinska Institutet/Stockholm County Council*

Lars Agréus has been a professor of family medicine since 2007. The focus of his research is gastroenterology in primary care. Since September 2009, he has been head of the Center for Family and Community Medicine at Karolinska Institutet, Stockholm, Sweden.

Professor Agréus began his research career in 1987 at the Department of Family Medicine, Uppsala University, Sweden. In 1993, he defended his doctoral dissertation, "The Abdominal Symptom Study." He spent a postdoctoral year at the University of Sydney in Australia studying associations between the quality of doctors' consultations and the outcome of dyspepsia. Subsequently, he served as a senior lecturer in family medicine at Uppsala University. In 2000, he accepted a position as a senior lecturer and researcher at the Center for Family and Community Medicine in Stockholm.

For the past decade, Professor Agréus has focused on population-based endoscopy studies. During this time, he has developed an international network of collaborators from the fields of gastroenterology, pathology, microbiology, genetics, and psychoneuroimmunology. An example of their work is the Kalixanda Study, an upper endoscopy study that included endoscopies with biopsies, blood tests,

and supplementary questionnaires in a random sample of 1001 adults. The Kalixanda Study has resulted in three PhD dissertations and 19 scientific publications so far; follow-up is still underway. Professor Agréus and his research group have also completed a colonoscopy study that included 746 randomly selected adult volunteers. The first articles about this study are in the pipeline for publication.

Professor Agréus has published approximately 60 scientific articles, reviews, and editorials in peer-reviewed journals and has contributed abstracts to or given lectures at numerous scientific meetings in the field of gastroenterology. He has been on the board of the European Society for Primary Care since its establishment in 1996 and now serves as the society's president. Professor Agréus is a member of the Swedish Gastrointestinal Society and the Swedish Primary Care Society, and is a fellow of the American Gastrointestinal Association.

Lars Agréus is also a dedicated rural general practitioner. He has served the same rural district since 1981, and is a member of both national and international rural medicine societies.

Functional dyspepsia and functional heartburn: Natural history of symptoms in the general population and validity of Rome III upper gastrointestinal diagnostic criteria

Abstract

Background: Functional gastrointestinal disorders (FGIDs) are common and usually life-long conditions that affect quality of life. Symptoms may fluctuate over time. However, only a minority of people with symptoms seek health care. A better understanding of the long-term natural history of FGIDs requires population-based studies with years or even decades of follow-up. Moreover, Rome III definitions of upper FGIDs have become the diagnostic standard but have never been validated by esophagogastroduodenoscopy (EGD) in non-patients.

Aims: First, to study the natural history of FGIDs, especially functional heartburn (FH) and functional dyspepsia (FD) over 23 years. Second, to validate the Rome III criteria for upper FGIDs using EGD with biopsies to rule out organic causes. To achieve these aims, we will use true population-based data with a high participation rate and robust non-response data not biased by healthcare-seeking behavior.

Methods: The study builds on a series of postal surveys of abdominal/gastrointestinal symptoms in the same adult random population sample ($n \cong 1400$) in the municipality of Östhammar, Sweden, conducted in 1988, 1989, 1995, and (in a subsample) in 1996, using the validated Abdominal Symptom Questionnaire (ASQ). Residents of the municipality ≥ 20 years and born on the 3rd, 12th, or 24th of each month plus surviving members of the original study population who have moved elsewhere in Sweden will be mailed a further ASQ in spring 2011. Responders to the spring survey aged 20 to 80 years will be invited to endoscopy with biopsies in fall 2011. At the EGD visit, participants ($n \cong 800$) will provide medical history; respond to the Rome III questionnaire, the ASQ, and other questionnaires; and provide a blood sample for biomarker analysis. Non-response studies will be performed for each study step.



Ray E. Clouse, MD

The Rome Foundation established an award in memory of Ray E. Clouse, MD a gastroenterologist and scholar at Washington University School of Medicine and a devoted member of the Rome Foundation. Ray's academic career spanned 27 years of research, teachings and writings that has left an indelible mark in the field of functional GI and motility disorders and of gastroenterology in general.

This year, the Rome Foundation is pleased to offer three awards, two for The Ray Clouse Prize for the Best Research Article on Functional GI and Motility Disorders, 2010, and a third, new award entitled The Ray Clouse Prize for the Most Cited Article on Functional GI and Motility Disorders 2009. The Best Research Article prizes are being awarded to Tamira K. Klooker MD for her paper, "The mast cell stabilizer ketotifen decreases visceral hypersensitivity and improves intestinal symptoms in patients with irritable bowel syndrome" and to QiQi Zhou MD, PhD for her paper, "MicroRNA-29a regulates intestinal membrane permeability in patients with irritable bowel syndrome." The Most Cited Article prize is being awarded to Siobhain M. O'Mahony, PhD for her paper, "Early life stress alters behavior, immunity, and microbiota in rats: implications for irritable bowel syndrome and psychiatric illnesses."

RAY CLOUSE PRIZE FOR THE MOST CITED ARTICLE IN FUNCTIONAL GASTROINTESTINAL AND MOTILITY DISORDERS, 2009



Siobhain M. O'Mahony, PhD (award recipient)

with coauthors: Marchesi JR, Codling C, Ceolho AM, Quigley EM, Cryan JF, Dinan TG

Early life stress alters behavior, immunity, and microbiota in rats: implications for irritable bowel syndrome and psychiatric illnesses. Biol Psychiatry 2009;65:263-7.

BACKGROUND: Adverse early life events are associated with a maladaptive stress response system and might increase the vulnerability to disease in later life. Several disorders have been associated with early life stress, ranging from depression to irritable bowel syndrome. This makes the identification of the neurobiological substrates that are affected by adverse experiences in early life invaluable.

METHODS: The purpose of this study was to assess the effect of early life stress on the brain-gut axis. Male rat pups were stressed by separating them from their mothers for 3 hours daily between postnatal days 2-12. The control group was left undisturbed with their mothers. Behavior, immune response, stress sensitivity, visceral sensation, and fecal microbiota were analyzed.

RESULTS: The early life stress increased the number of fecal boli in response to a novel stress. Plasma corticosterone was increased in the maternally separated animals. An increase in the systemic immune response was noted in the stressed animals after an in vitro lipopolysaccharide challenge. Increased visceral sensation was seen in the stressed group. There was an alteration of the fecal microbiota when compared with the control group.

CONCLUSIONS: These results show that this form of early life stress results in an altered brain-gut axis and is therefore an important model for investigating potential mechanistic insights into stress-related disorders including depression and IBS.

RAY CLOUSE PRIZE FOR THE BEST RESEARCH ARTICLE ON FUNCTIONAL GASTROINTESTINAL AND MOTILITY DISORDERS, 2010

This year two outstanding papers were chosen for this award



Tamira K Klooker, MD (award recipient)

with coauthors: Braak B, Koopman KE, Welting O, Wouters MM, van der Heide S, Schemann M, Bischoff SC, van den Wijngaard RM, Boeckstaens GE.

The mast cell stabilizer ketotifen decreases visceral hypersensitivity and improves intestinal symptoms in patients with irritable bowel syndrome. Gut 2010;59:1213-21.

BACKGROUND: Mast cell activation is thought to be involved in visceral hypersensitivity, one of the main characteristics of the irritable bowel syndrome (IBS). A study was therefore undertaken to investigate the effect of the mast cell stabiliser ketotifen on rectal sensitivity and symptoms in patients with IBS.

METHODS: 60 patients with IBS underwent a barostat study to assess rectal sensitivity before and after 8 weeks of treatment. After the initial barostat, patients were randomised to receive ketotifen or placebo. IBS symptoms and health-related quality of life were scored. In addition, mast cells were quantified and spontaneous release of tryptase and histamine was determined in rectal biopsies and compared with biopsies from 22 age- and gender-matched healthy volunteers.

RESULTS: Ketotifen but not placebo increased the threshold for discomfort in patients with IBS with visceral hypersensitivity. This effect was not observed in normosensitive patients with IBS. Ketotifen significantly decreased abdominal pain and other IBS symptoms and improved quality of life. The number of mast cells in rectal biopsies and spontaneous release of tryptase were lower in patients with IBS than in healthy volunteers. Spontaneous release of histamine was mostly undetectable but was slightly increased in patients with IBS compared with healthy volunteers. Histamine and tryptase release were not altered by ketotifen.

CONCLUSIONS: This study shows that ketotifen increases the threshold for discomfort in patients with IBS with visceral hypersensitivity, reduces IBS symptoms and improves health-related quality of life. Whether this effect is secondary to the mast cell stabilising properties of ketotifen or H(1) receptor antagonism remains to be further investigated. Trial Registration Number NTR39, ISRCTN22504486.



QiQi Zhou, MD, PhD (award recipient)

with coauthors: Souba WW, Croce CM, Verne GN

MicroRNA-29a regulates intestinal membrane permeability in patients with irritable bowel syndrome. Gut 2010;59:775-84.

BACKGROUND: The molecular mechanisms underlying the pathophysiology of irritable bowel syndrome (IBS) are poorly understood. One mechanism may involve increased intestinal permeability that is reversed with glutamine supplementation. Our goal was to evaluate the expression of glutamine synthetase and its complementary miRNA in blood microvesicles and gut tissues of IBS patients with increased intestinal membrane permeability.

METHODS: We evaluated 19 diarrhoea-predominant IBS patients and 10 controls for intestinal membrane permeability using the lactulose/mannitol method. miRNA expression was evaluated in blood microvesicles and gut tissue. To further confirm the relationship between miRNA and glutamine synthetase expression, cell culture experiments were conducted. Glutamine synthetase was also evaluated in the gut tissues of patients.

RESULTS: A subset of patients with IBS (8/19, 42%) had increased intestinal membrane permeability and decreased glutamine synthetase expression compared to patients with IBS normal membrane permeability, and to controls. Expression of miR-29a was increased in blood microvesicles, small bowel and colon tissues of IBS patients with increased intestinal membrane permeability. Increased intestinal permeability was modulated by miR-29a which has a complementary site in the 3'-UTR of the GLUL gene.

CONCLUSIONS: The results support the conclusion that GLUL regulates intestinal membrane permeability and miR-29a regulates both GLUL and intestinal membrane permeability. The data suggests that miR-29a effects on intestinal membrane permeability may be due to its regulation of GLUL. Targeting this signalling pathway could lead to a new therapeutic approach to the treatment of patients with IBS, especially because small molecules that mimic or inhibit miRNA-based mechanisms are readily available.



ROME FOUNDATION WORKING TEAM COMMITTEE

THE ROLE OF THE INTESTINAL MICROBIOTA IN
FUNCTIONAL GASTROINTESTINAL DISORDERS – MARCH 2011

MAGNUS SIMRÉN, MD, PHD
CHAIR

The group was formed during the spring 2010 and had a start-up telephone conference in May 2010, where the aims of the working team were clarified and an outline for the publications was discussed. This outline was thereafter modified and finalized via e-mails in June 2010. The group members volunteered for the different tasks and a number of groups within the working team were formed based on the expertise of the members. The work was divided between the members and a timeline was decided (updated timeline, see below). Part of the members met at a face-to-face meeting in Boston at the International Neurogastroenterology and Motility meeting in August 2010, and those who were not able attend participated via telephone. During the autumn/winter 2010/2011, the different chapters for the manuscript, as outlined below, have been prepared, and a first draft manuscript is currently being prepared. This will be discussed and finalized at a face-to-face meeting of the Working Team Group the day after Digestive Disease Week in Chicago. Thereafter, an internal review process within the team, as well as within the Rome Foundation, will be performed and the goal is to have a manuscript to submit to a major gastroenterology journal early autumn 2011. Moreover, during this years UEGW in Stockholm, two lectures, based on the work of this Working Team Group will be given at a two-days symposium within the congress, entitled “Today’s science; tomorrow’s medicine: Role of bacteria in health and disease”.

Objectives:

- To critically review the existing literature on the role of gut microbiota in functional GI disorders (FGIDs), with focus on clinical and translational aspects.
- Based on the literature search, provide recommendations how to implement the current knowledge into clinical practice, in order to improve the health of our patients.
- Give recommendations for future work in order to improve the current knowledge on the role of gut microbiota in functional GI disorders.
- Produce an extensive background document including all the relevant references and information of relevance, as well as a clinically useful, review, submitted to one of the major scientific journals in our field.

MEMBERS OF THE WORKING TEAM

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ASSOCIATES OF ROME

Membership in the Associates of Rome program has more than doubled since the last newsletter! There are now 54 Associates including gastroenterologists, pediatricians, primary care physicians, and psychotherapists. Joining is easy (and free), just visit www.theromefoundation.org/join_mailing/assoc_rome.cfm. Benefits include a discount on Rome products and conferences, the bi-annual printed newsletter and quarterly e-newsletter, Rome pin, and a Certificate of Association. Several Associates were recently able to register at a discounted rate for the IBS – A Global Perspective Conference, held in Milwaukee, Wisconsin.

The program best serves health care professionals and investigators. Patients are welcome to join, but may also want to consider contacting IFFGD (International Foundation for Functional Gastrointestinal Disorders, www.iffgd.org) for more patient-centered information about life with GI disorders.



WELCOME ASSOCIATES OF ROME

Shahab Abid, PhD <i>Pakistan</i>	Lillian Ethapemi <i>England</i>	Mildret Quisbert <i>Bolivia</i>
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Mohammed Butt <i>Qatar</i>	Shengxi Han, MD <i>China</i>	Rosa Soares, MD <i>Brazil</i>
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Thomas DuHamel, PhD <i>USA</i>	Sabrina Nery, MD <i>Brazil</i>	Wei Wei, PhD <i>China</i>
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Gulin Erdemir, MD <i>Turkey</i>	Tatjana Puc Kous, MD <i>Slovenia</i>	Lee Yeong Yeh, MD <i>Malaysia</i>

Meet the experts

How I manage a patient with a difficult case of...

- **Food Allergy** with *Javier Santos*
- **IBS in IBD** with *Magnus Simrén*
- **Postfundoplication Dysphagia** with *André Smout*

Chairmen: *Robin Spiller*
Fernando Azpiroz



Date: Mon. Oct 24th
Time: 5:30-6:30 pm
Location: Room K24; Stockholmsmässan



October 22 – 26, 2011 // Stockholm, Sweden
Stockholm Exhibition & Congress Center



IBS – THE GLOBAL PERSPECTIVE CONFERENCE

MILWAUKEE, WISCONSIN
APRIL 6-7, 2011



The Rome Foundation and the World Gastroenterology Association convened an international symposium on “IBS – The Global Perspective” that took place on April 6-7, 2011 in Milwaukee, Wisconsin.

The primary aim of the symposium was to bring together an international group of clinicians, scientists and researchers with an interest in IBS and other functional GI disorders to foster greater awareness of the multi-national, cross-cultural aspects of IBS, and update existing knowledge on similarities and differences at a global level. In terms of clinical practice the focus was on greater awareness of the complexity of working in a multicultural clinic, and the development clinical skills to function successfully in that milieu. This included awareness of patient and physician explanatory models of illness and their cultural associations. In terms of research the focus was on improving the quality of multinational clinical trials and research, and establish international research networks.

The participants heard talks from a spectrum of speakers that included gastroenterologists from around the world, and medical anthropologists and psychiatrists who provided insights from perspectives that are not usually represented in meetings of gastroenterologists. There were two

workshops, one on cross-cultural clinical competence and the second on cross-cultural research competence. In the first, the participants witnessed and participated in role-play simulating real-life cross-cultural clinical situations.

The conference also had a session with regulatory agency representatives from the United States (FDA), Europe (EMA) and Japan. This session focused on the conduct of multinational clinical trials including developing culturally appropriate study instruments and patient-reported outcomes (PROs).

The participants in this meeting expressed their feeling that it was unique and stimulating with an excellent faculty. There was a feeling that it could energize the functional GI community to develop new initiatives on an international scale.

As one outcome of this meeting the Rome Foundation has established a working team on multinational, cross-cultural research with a mandate to develop guidelines for future research projects, to foster international research networks, and to plan and implement a global study on IBS epidemiology.

SPECIAL THANKS TO OUR CONFERENCE SPONSORS

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THE FOURTH ANNUAL ROME FOUNDATION — AGA INSTITUTE LECTURESHIP AT DIGESTIVE DISEASE WEEK 2011

SUNDAY MAY 8, 2011
10:30 - 12:00
E 451 B LAKESIDE LEVEL 4
MC CORMICK PLACE, CHICAGO, IL

The Rome Foundation and the American Gastroenterological Association (AGA) were pleased to announce their 4th annual lectureship at Digestive Diseases Week (DDW). The lectureship is designed to address broad aspects of health care that are relevant to digestive diseases and the functional GI disorders.

Learning Objectives:

1. To discuss the suppression of neurogenesis in the hippocampus in depression and the potential restoration with antidepressants
2. To review neurogenesis of enteric nerves and their role in gut function
3. To explain the relevance of neurogenesis in the central and enteric nervous systems to functional GI and motility disorders

AGENDA



The Role of Neurogenesis in the Brain

with Tarique Perera, MD
Columbia University



The Role of Neurogenesis in the Enteric Nervous System and its implications for Functional GI and Motility disorders

with Michael D. Gershon, MD
Columbia University



May 7-10, 2011
MCCORMICK PLACE
CHICAGO, IL

DIGESTIVE DISEASE WEEK BOOTH 2354

The Rome Foundation encourages all members and sponsors to visit our booth at DDW. This year we are proud to offer the Diagnostic Algorithms for Common Gastrointestinal Symptoms on CD-ROM. We will also be offering copies of the Rome III book, published in 2006, as well as the Computer-Based Learning Program and Understanding the Irritable Gut, by W. Grant Thompson, MD. New this year will be details about our latest program – Associates of Rome. A listing of benefits of this initiative and enrollment forms will be available at our booth. There will also be many handouts and other research materials available. Be sure to visit us at booth 2354!!



PATIENT PERSPECTIVE:

AN UPDATE FROM THE INTERNATIONAL FOUNDATION FOR FUNCTIONAL GASTROINTESTINAL DISORDERS (IFFGD)

DANE CHRISTIANSEN
DEVELOPMENT COORDINATOR

2011 marks IFFGD's 20th year of service to the functional gastrointestinal and motility disorders (FGIMDs) community. Over the past two decades, much progress has been made through efforts to advocate, raise awareness, and advance research into FGIMDs. We are humbled and sincerely grateful to all who have participated in these efforts.

To honor the dedication of our volunteers and apply their contributions to maximum effect, IFFGD has launched a bold new initiative known as the Digestive Health Alliance™ or DHA. This grassroots network will provide affected individuals in towns and cities across America with the tools they need to take action in support of the field. In this regard, DHA activities will focus on advocating on Capitol Hill, raising awareness, and donating or fundraising for research.

Advocacy

IFFGD and DHA grassroots advocates continue to conduct outreach to Members of Congress in support of a Legislative Agenda that stresses increasing the federal commitment to FGIMDs research and improving patient care. Since the 112th Congress convened in January of this year, meaningful progress has been made in the following areas:

- Defending federal funding for the National Institutes of Health (NIH) and working to secure a funding increase to bring the agency's overall level of support to \$35 billion in Fiscal Year 2012.
- Introduction and passage of a bill initially drafted by IFFGD to bolster support for critical research activities and open new avenues of research support, the Functional Gastrointestinal and Motility Disorders Research Enhancement Act.
- Including "functional gastrointestinal disorders" on the annual list of conditions deemed eligible for study through the Department of Defense's Peer-Reviewed Medical Research Program.
- Passage of a bipartisan bill to increase financial support for pediatric research networks through NIH, the Pediatric Research Consortium Establishment Act (H.R. 1080).

To further advance our legislative priorities, IFFGD will be hosting its Capitol Hill Advocacy Day at the Phoenix Park Hotel in Washington, DC on Tuesday, June 14th and Wednesday, June 15th, 2011. This event is open to patients, physicians, and anyone who wants to make a difference; it is also free of charge so please contact us and make your plans to attend today.

Research & Awareness

Through the Digestive Health Alliance many individuals have already begun conducting volunteer-led fundraisers, such as walk-a-thons and letter writing campaigns to bolster the IFFGD's research fund and raise awareness of FGIMDs. The Foundation will also be expanding our efforts in these areas by hosting a benefit regatta at the Kenosha Yacht Club in Kenosha, WI on August 20th, 2011. In addition to the boat races, this event will feature a beach party cook-out with live entertainment and special guests.

IFFGD continues to provide support for a children's FGIMD research initiative, and peer-reviewed research awards. Through the Digestive Health Alliance, we are looking forward to securing additional funds and expanding both of these programs.

As the flagship event of our continuous effort to advance scientific understanding of FGIMDs, the 9th International Symposium on Functional Gastrointestinal Disorders was held on April 8–10, 2011 at the Pfister Hotel in Milwaukee, WI. The meeting was once again jointly sponsored by the University of Wisconsin School of Medicine and Public Health, Office of Continuing Professional Development, and IFFGD. Participation in this event continues to grow and reflect a growing interest in the field. Given the success of this year's event, we are already looking forward to the next Symposium in 2013, and we hope you are too!



The Rome Foundation Proudly Presents



the latest educational resources for all health care professionals and patients concerned with functional gastrointestinal disorders (FGIDs)



The Diagnostic Algorithms for Common Gastrointestinal Symptoms are now available on CD-ROM.

Be sure to get your copy at the Rome booth (#2354) at DDW in Chicago.

The Rome Foundation is committed to develop and support research and education to help people with Functional GI Disorders.

Learn more about any of our educational materials at:
www.theromefoundation.org



PLEASE VISIT OUR ROME FOUNDATION BOOTH #2354 AT DDW IN CHICAGO



RANDALL D. AVRAM

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We are pleased to introduce Randall D. Avram as our Counsel for the Rome Foundation. In this capacity he will advise the President and Board on issues relating to personnel and Business related issues.

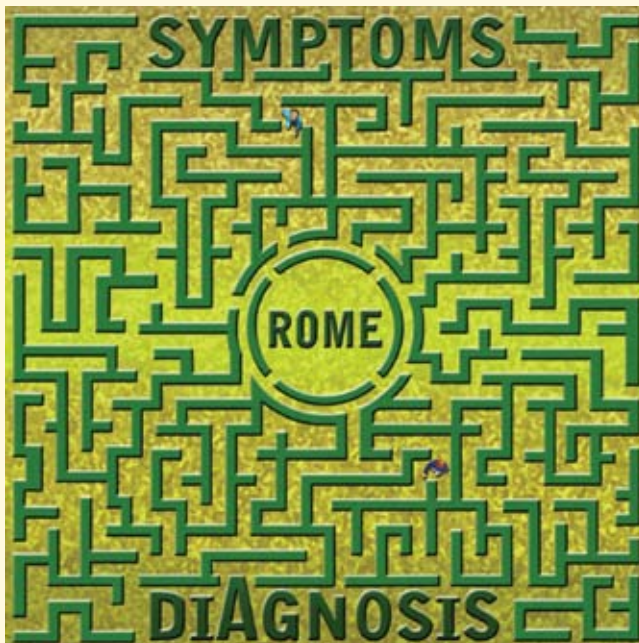
Randall D. Avram is a partner in the multinational, multipractice law firm of Kilpatrick Townsend & Stockton LLP (Kilpatrick Townsend). Kilpatrick Townsend serves clients in the areas of intellectual property, business and finance, construction and infrastructure, government, litigation and labor and employment from 18 offices in California, Colorado, District of Columbia, Georgia, New York, North

Carolina, Washington, Sweden, Dubai, Japan and Taipei.

Randy concentrates his time in labor and employment law and is chairman of the Labor and Employment Department. Randy has been named Best Lawyer in America(r) and as Top 100 Lawyers by "North Carolina Magazine."

Since joining us, Randy has helped us develop an effective copyright and licensing Policy and has advised us on business relations relative to our sponsors and personnel. We are most grateful for his interest in helping us.

ALGORITHM PUBLICATION AND ACCESS



The Rome Foundation Diagnostic Algorithms for Common Gastrointestinal Symptoms are now available via the following:

- A CD-ROM of all 15 Algorithms is now available and will be given out at all Rome Foundation booths.
- The interactive webpage on the Rome Foundation website will now contain all 15 Diagnostic Algorithms.
- A Spanish version of the Algorithms was published in November 2010 in the Mexican Journal of Gastroenterology.
- For free download as a PDF from our website and the AJG website, www.nature.com/ajg/index.html.



ROME AND AGA FORGE COLLABORATION

DIANNE BACH

SENIOR VICE PRESIDENT
AGA INSTITUTE

Our mutually beneficial educational collaboration with the Rome Foundation continues. To recap, we are excited to conduct our fifth joint lecture series at DDW to shine a spotlight on the importance of research, clinical education and physician-patient communications related to functional GI disorders. This year our lecture will take place on Sunday, May 8, from 10:30am to 12 noon in Room E451A of the Convention Center and will feature Tarique Perera, MD, assistant professor in clinical psychiatry, and Michael D. Gershon, MD, professor of pathology and cell biology, to provide a comprehensive overview of The Role of Neurogenesis in the Brain and Gut and its Implications for Functional GI and Motility Disorders. Both internationally renowned experts teach at Columbia University in New York. We've had stellar turn out for these lectures so I hope you can mark it on your schedule to attend.

We will also continue providing marketing support for two Rome created educational activities—the Rome III book and the Computer Based Learning Program. I hope you have seen our colorful advertisements in Gastroenterology, Clinical Gastroenterology and Hepatology and in GI and Hepatology News. We want AGA members to be aware of and purchase these valuable resources at a nice discount!

A new and exciting joint activity is starting to take shape thanks to some preliminary educational support for Forest Laboratories, Inc. It is a unique communication skills workshop designed to improve the dialogue between physicians and patients that have functional GI disorders. In order to launch this workshop, we have asked for additional educational support from other sources and are awaiting a response. If our industry friends are reading this and want to learn more, please don't hesitate to contact me (dbach@gastro.org) or Dr. Doug Drossman for further details and how you can help.

As a member of the Rome Foundation Advisory Board, I have truly enjoyed my friendship with the leaders and the staff of the Rome Foundation and look forward to continuing to grow our relationship in 2011-12 and beyond.



AGAINSTITUTE
AGA Education, Practice and Research

WE ARE PLEASED TO PROVIDE FOR YOU IN THIS AND FUTURE ISSUES ARTICLES THAT HAVE BEEN PUBLISHED THAT HIGHLIGHT THE ROME CRITERIA.

1: Hellström PM, Saito YA, Bytzer P, Tack J, Mueller-Lissner S, Chang L. Characteristics of Acute Pain Attacks in Patients With Irritable Bowel Syndrome Meeting Rome III Criteria. *Am J Gastroenterol*. 2011 Mar 29. [Epub ahead of print] PubMed PMID: 21448146.

2: Van Oudenhove L, Holvoet L, Vandenberghe J, Vos R, Tack J. Do we have an alternative for the Rome III gastroduodenal symptom-based subgroups in functional gastroduodenal disorders? A cluster analysis approach. *Neurogastroenterol Motil*. 2011 Mar 30. doi: 10.1111/j.1365-2982.2011.01703.x. [Epub ahead of print] PubMed PMID: 21447145.

3: Tam YH, Chan KW, To KF, Cheung ST, Mou JW, Pang KK, Wong YS, Sihoe JD, Lee KH. Impact of Pediatric Rome III Criteria of Functional Dyspepsia on the Diagnostic Yield of Upper Endoscopy and Predictors for a Positive Endoscopic Finding. *J Pediatr Gastroenterol Nutr*. 2011 Apr;52(4):387-91. PubMed PMID: 21415670.

4: Savarino E, Marabotto E, Zentilin P, Frazzoni M, Sammito G, Bonfanti D, Sconfienza L, Assandri L, Gemignani L, Malesci A, Savarino V. The added value of impedance-pH monitoring to Rome III criteria in distinguishing functional heartburn from non-erosive reflux disease. *Dig Liver Dis*. 2011 Mar 2. [Epub ahead of print] PubMed PMID: 21376679.

5: Abid S, Siddiqui S, Jafri W. Discriminant value of Rome III questionnaire in dyspeptic patients. *Saudi J Gastroenterol*. 2011 Mar-Apr;17(2):129-33. PubMed PMID: 21372351.

6: Ohara S, Kawano T, Kusano M, Kouzu T. Survey on the prevalence of GERD and FD based on the Montreal definition and the Rome III criteria among patients presenting with epigastric symptoms in Japan. *J Gastroenterol*. 2011 Feb 26. [Epub ahead of print] PubMed PMID: 21359521.

7: Reisswitz PS, Mazzoleni LE, Sander GB, Francisconi CF. Portuguese validation of the Rome III diagnostic questionnaire for functional dyspepsia. *Arq Gastroenterol*. 2010 Dec;47(4):354-60. PubMed PMID: 21225145.

8: Czyzewski DI, Lane MM, Weidler EM, Williams AE, Swank PR, Shulman RJ. The interpretation of Rome III criteria and method of assessment affect the irritable bowel syndrome classification of children. *Aliment Pharmacol Ther*. 2011 Feb;33(3):403-11. doi: 10.1111/j.1365-2036.2010.04535.x. Epub 2010 Dec 8. PubMed PMID: 21138454.

9: Stanghellini V, Frisoni C. Editorial: Reflux, dyspepsia, and Rome III (or Rome IV?). *Am J Gastroenterol*. 2010 Dec;105(12):2632-4. PubMed PMID: 21131930.

10: Hsu YC, Liou JM, Yang TH, Hsu WL, Lin HJ, Wu HT, Lin JT, Wang HP, Wu MS. Proton pump inhibitor versus prokinetic therapy in patients with functional dyspepsia: is therapeutic response predicted by Rome III subgroups? *J Gastroenterol*. 2011 Feb;46(2):183-90. Epub 2010 Oct 19. PubMed PMID: 20957498.

11: Xiao YL, Peng S, Tao J, Wang AJ, Lin JK, Hu PJ, Chen MH. Prevalence and symptom pattern of pathologic esophageal acid reflux in patients with functional dyspepsia based on the Rome III criteria. *Am J Gastroenterol*. 2010 Dec;105(12):2626-31. Epub 2010 Sep 7. PubMed PMID: 20823838.

12: Chogle A, Dhroove G, Sztainberg M, Di Lorenzo C, Saps M. How reliable are the Rome III criteria for the assessment of functional gastrointestinal disorders in children? *Am J Gastroenterol*. 2010 Dec;105(12):2697-701. Epub 2010 Aug 31. PubMed PMID: 20808296.

13: Devanarayana NM, Adhikari C, Pannala W, Rajindrajith S. Prevalence of functional gastrointestinal diseases in a cohort of Sri Lankan adolescents: comparison between Rome II and Rome III criteria. *J Trop Pediatr*. 2011 Feb;57(1):34-9. Epub 2010 Jun 4. PubMed PMID: 20525779.

ABOUT THE ROME FOUNDATION

The Rome Foundation is an independent not for profit 501(c) 3 organization that provides support for activities designed to create scientific data and educational information to assist in the diagnosis and treatment of functional gastrointestinal disorders (FGIDs). Our mission is to improve the lives of people with functional GI disorders.

Over the last 20 years, the Rome organization has sought to legitimize and update our knowledge of the FGIDs. This has been accomplished by bringing together scientists and clinicians from around the world to classify and critically appraise the science of gastrointestinal function and dysfunction. This knowledge permits clinical scientists to make recommendations for diagnosis and treatment that can be applied in research and clinical practice.

The Rome Foundation is committed to the continuous development, legitimization and preservation of the field of FGIDs through science-based activities. We are inclusive and collaborative, patient-centered, innovative and open to new ideas.

The goals of the Rome Foundation are to:

- Promote clinical recognition and legitimization of the functional GI disorders
- Develop a scientific understanding of their pathophysiological mechanisms
- Optimize clinical management for patients with FGIDs



VISIT US ON
THE WEB AT

www.theromefoundation.org

ROME BOARD OF DIRECTORS



From left to right: (Front row): Nicholas Talley, John Kellow, Doug Drossman, William Whitehead, Lin Chang; (Back row): Jan Tack, Enrico Corazzari, Fernando Azpiroz, Robin Spiller, William D. Chey

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