

IBS DAYS

New insights for a better management of irritable bowel syndrome

May 17 - 19, 2018

Royal Carlton Hotel - Bologna, Italy
Congress Chair: Giovanni Barbara

Abstract Book



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UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI SCIENZE MEDICHE E CHIRURGICHE



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Jan Tack, *Belgium*
Umberto Volta, *Italy*
Julian Walters, *UK*

Opening Ceremony - Thursday May 17th

Royal Carlton Hotel

18.00 **Welcome**

Giovanni Barbara and **Vincenzo Stanghellini**, *University of Bologna*

Antonino Rotolo, *Prorector, University of Bologna*

Fabrizio De Ponti, *President, School of Medicine, University of Bologna*

Antonella Messori, *General Director, St. Orsola-Malpighi Hospital, Bologna*

Pierluigi Viale, *Director, Department of Medical and Surgical Sciences, University of Bologna*

Gilberto Poggioli, *Chief of Surgery of Alimentary Tract, Department of Digestive Diseases, St. Orsola-Malpighi Hospital, Bologna*

18.30 **Lecture**

Discovering Bologna. The secret charme of a city

Anna Ottani Cavina, *Emeritus Professor of History of Art, University of Bologna*

19.30 **Cocktail**

Program - Friday May 18th

Royal Carlton Hotel

07.00 **Registration**

08.00 **Program Overview**

Giovanni Barbara (Italy)

Session I - Clinical Practice

Chairs: Douglas Drossman (USA), Vincenzo Stanghellini (Italy)

08.30 **The Global Burden of IBS**

Jan Tack (Belgium)

08.55 **History and Impact of the Rome Foundation and Rome IV and its Future in GI Health Care**

Douglas Drossman (USA)

09.20 **How to Use the Rome IV Criteria in Clinical Practice**

Fermin Mearin (Spain)

09.45 **What Is Important to Know About Bowel Habit**

Enrico Corazziari (Italy)

10.10 ***Coffee Break***

Session II - Clinical Phenotype

Chairs: Jan Tack (Belgium), Guido Basilisco (Italy)

10.40 **When and How to Exclude an Organic Disease**

Alexander Ford (UK)

11.05 **Why is Gender So Important in IBS**

Lin Chang (USA)

11.30 **Tandem Talk on Gas-Bloating**

All in the Diaphragm

Fernando Azpiroz (Spain)

All in the Gut

Maura Corsetti (UK)

12.20 **Usefulness of Clinical and Laboratory Biomarkers**
Magnus Simren (Sweden)

12.45 **Lunch Break**

13.00 - 14.00
BIOCURE SATELLITE SYMPOSIUM
IBS Treatment and “Targeted” Probiotics: What’s New?
Supported by: Biocure-Groupe PiLeJe
Giove Room

Session III – Clinical Phenotype

Chairs: Stephen Collins (Canada), Gabrio Bassotti (Italy)

14.15 **How to Improve the Patient-Physician Relationship**
Douglas Drossman (USA)

14.45 **IBS in Primary Care**
Pali Hungin (UK)

15.10 **Overlapping Functional GI Disorders**
Kok Ann Gwee (Singapore)

15.35 **Tandem Talk on Genetic Factors**
The Basic Scientist View
Mauro D’Amato (Spain)
The Clinician Perspective
Michael Camilleri (USA)

16.25 **Coffee Break**

Session IV – ‘Hot Off the Press’

Chairs: Massimo Bellini (Italy), Roberto De Giorgio (Italy)

16.45 **Mucosal Barrier and Permeability**
Maria Raffaella Barbaro (Italy)

17.10 **Intestinal Fungal Dysbiosis Is Associated With Visceral Hypersensitivity in Patients With IBS and Rats**
Wouter de Jonge (The Netherlands)

- 17.25 **Volatile Organic Compounds in Feces Associate With Response to Dietary Intervention in Patients With IBS**
Megan Rossi (UK)
- 17.40 **Distinct Abnormalities of Small Bowel and Regional Colonic Volumes in Subtypes of IBS Revealed by MRI**
Ching Lam (UK)
- 17.55 ***Adjourn***
- 19.30 ***Social Dinner***

Program - Saturday May 19th

Royal Carlton Hotel

Session V – Microenvironment and Gut-Brain Axis

Chairs: Jordi Serra (Spain), Patrizia Brigidi (Italy)

08.30 **Gut Microbiota: What is New**

Antonio Gasbarrini (Italy)

08.55 **The Microbiota Gut Brain Axis in the IBS**

Stephen Collins (Canada)

09.20 **IBS / Tropical Sprue Overlap**

Uday Ghoshal (India)

09.45 **Neuro-Immune Interactions: Clinical and Therapeutic Perspectives**

Guy Boeckstaens (Belgium)

10.10 **The Biopsychosocial Model of FGIDs**

Paul Enck (Germany)

10.35 ***Coffee Break***

Session VI – Dietary Factors

Chairs: Rosario Cuomo (Italy), Umberto Volta (Italy)

11.05 **IBS, Dietary Factors and Gut Microbiome:
The Non-Celiac Gluten Sensitivity Paradigm**

Alessio Fasano (USA)

11.30 **FODMAPs**

Robin Spiller (UK)

11.55 **Probiotics**

Cesare Cremon (Italy)

12.20 **Clinical Effect of Probiotic Mixture on Gut-Specific Anxiety and HRQoL**

Jordi Serra (Spain)

Sponsored by Mayoly

12.40	Kiwifruit for IBS-C: Effect on Symptoms and Microbiota Juliet Ansell (New Zealand) <i>Sponsored by Zespri</i>
13.00	Lunch Break
	Session VII – Clinical Management Chairs: Franco Bazzoli (Italy), Giuseppe Chiarioni (Italy)
14.00	Diagnosis and Management of Bile Acid Diarrhea Julian Walters (UK)
14.25	Microbiota Directed Therapies Carmelo Scarpignato (Italy)
14.50	Management of Abdominal Pain Jan Tack (Belgium)
15.15	New Therapeutic Perspectives Michael Camilleri (USA)
15.40	CME Questionnaire
16.00	Concluding Remarks Giovanni Barbara (Italy)



Congress Chair

Giovanni Barbara
Italy

Giovanni Barbara graduated Summa cum Laude in Medicine at the University of Bologna, Italy. He subsequently qualified in Internal Medicine and then in Gastroenterology at the same University. He was trained partly in London, UK and completed a three years post-doctoral research fellowship in neuro-immunology at McMaster University in Canada. Currently he is involved in clinical gastroenterology diagnostic and therapeutic endoscopy, teaching and research at the Departments of Medical and Surgical Sciences and Digestive Diseases of the University of Bologna.

Professor Barbara's main research interest relate to basic and clinical aspects of functional gastrointestinal disorders, neurogastroenterology, gut inflammation and microbiota. He has authored numerous indexed peer-reviewed articles and reviews on these topics, published in various biomedical journals, including Gastroenterology, Gut, Journal of Clinical Investigation and Trends in Pharmacological Science. He is, or has been, a member of the Editorial Board of Gut, American Journal of Gastroenterology, Neurogastroenterology and Motility the American Journal of Physiology and other international scientific Journals.

Professor Barbara has received numerous national and international awards including the Master Award in Gastroenterology from the American Gastroenterological Association. He is Member of the Board of Directors of the Rome Foundation and President of the European Society of Neurogastroenterology and Motility (ESNM).



Scientific Committee Chair

Vincenzo Stanghellini
Italy

Vincenzo Stanghellini is Professor of Internal Medicine at the Department of Medical and Surgical Sciences, University of Bologna and St.Orsola-Malpighi Hospital Bologna, Italy.

PRESENT POSITION: Vincenzo Stanghellini is Specialist at Internal Medicine and Gastroenterology, Professor of Medicine at the University of Bologna, and Chair of Internal Medicine at the Department of Internal Medicine and Gastroenterology of the University Hospital St. Orsola – Malpighi of Bologna.

EXPERIENCE: Research Fellow (1981-1983) and Visiting Professor (1983-1985) at the Gastrointestinal Unit of the Mayo Clinic, Rochester, Minnesota.

RESEARCH INTEREST: Leading a successful group of investigators, his main research interests are represented by the pathophysiology of functional disorders of the GI tract, as well as diagnosis and treatment of functional digestive syndromes.

AWARDS and HONORS: The Master Award for Sustained Achievement in Digestive Sciences of the American Gastroenterological Association (2009).

PUBLICATIONS: author of over 250 scientific publications on peer review journals.

MEMBERSHIPS: United European Gastroenterological Federation (UEGF); European Society of Neurogastroenterology and Motility (former member of the Steering Committee); American Gastroenterological Association (AGA); Italian Society of Internal Medicine (SIMI) (past-President of the Regional Committee), Italian Society of Gastroenterology (SIGE); Italian Group for the Study of Gastrointestinal Motility (GISMAD) (past-President); International Foundation for Functional Gastrointestinal Disorders (IFFGD), (member of the Advisory Board). He is also Associate Editor, member of the Editorial Board referee for many peer-review journals.

Faculty



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Discovering Bologna The secret charm of a city

Anna Ottani Cavina
Italy

Professor Emeritus of Art History
University of Bologna, Italy
Adjunct Professor of Italian Art History
The Johns Hopkins University SAIS Europe

Background and Education

Founding member and former director of the Federico Zeri Foundation; member of the scientific committee Fondazione Musei Civici di Venezia; served as distinguished visiting professor of art history at Columbia University and visiting professor at Brown University; visiting fellow at the Yale Center for British Art; senior visiting fellow and later (2014) Edmond J. Safra Visiting Professor at the Center for Advanced Study in the Visual Arts, National Gallery of Art, Washington D.C.

Member of the Istituto Veneto di Scienze Lettere e Arti; Ph. D. University of Rome.

Recipient of the Chevalier (1996) and Officier (2011) dans l'ordre des Arts et des Lettres; Chevalier dans l'ordre de la Légion d'honneur in 2001.

Publications:

Carlo Saraceni e la cultura caravaggesca (1968); On the Theme of Landscape: Elsheimer and Galileo (1976); La pittura del Seicento (1977); l'Età neoclassica 1780-1820, catalogo della mostra (1979); Il settecento e l'antico (1982); I paesaggi della ragione (Einaudi 1994), awarded the "Premio Morassi per la Storia dell'Arte;" Felice Giani e la cultura di fine Settecento (2 vol., Milano 1999) awarded the "Premio Salimbeni per la storia dell'Arte 2000; Il diario di Thomas Jones (Milan, 2003); Geometrics of Silence, Columbia University Press (2004); Les Paysages de la Raison, Actes Sud (2005); Prospettiva Zeri (2009); Terre senz'ombra (Adelphi 2013; Il Falso specchio della realtà (2017).

Organization and direction of several important exhibitions: "Paysages d'Italie. Les peintres du plein air" (Paris, Grand Palais 2001) ; Montagna. Arte, scienza (MART 2003); Granet de Rome à Paris. Le plein air romantique (Académie de France, 2009); Federico Zeri. Dietro l'immagine (2009). John Ruskin. Le Pietre di Venezia (Venezia, Palazzo Ducale, 2018).

Regular contributor to the cultural interest pages of the daily La Repubblica newspaper.

Abstract

The presentation is going to be a sort of welcome to the participants to the congress in Bologna, mainly to those who never had the pleasure of visiting the town.

Bologna is a town to be explored with great care.

It's not a town of monuments and isolated masterpieces, spectacular at first glance.

Its charm is mostly the very special urban texture, the networks of its streets, the medieval heart of the city, the many towers built between 11th and 13th century.

The long parade of the porticoes, nominated as Unesco "world heritage site", make Bologna unique, creating scenographic images, lights and shadows, deep architectural perspectives.

Built in brick, with its colorful appearance, Bologna has a high cultural and scientific tradition due to the Studio, the ancient University founded in 1088.



The Global Burden of IBS

Jan Tack
Belgium

Jan Tack, M.D., Ph.D.
Translational Research Center for Gastrointestinal Disorders (TARGID)
University of Leuven
Leuven, Belgium

Professor Jan Tack is currently a Head of Clinic in the Department of Gastroenterology, a Professor in Internal Medicine and Chairman of the Department of Clinical and Experimental Medicine at the University of Leuven, Belgium, and a principal researcher in TARGID (the Translational Research Center for Gastrointestinal Disorders) at the University of Leuven. He graduated summa cum laude in 1987 from the University of Leuven and specialised in internal medicine and gastroenterology at the same institution. A research fellow at the Department of Physiology at the Ohio State University, Columbus, Ohio, USA, from 1989 to 1990, he has been conducting research at Leuven University since 1990.

Professor Tack's scientific interest focuses on neurogastroenterology and motility, and includes diverse topics such as the pathophysiology and management of gastrointestinal functional and motor disorders, the physiology and pharmacology of the enteric nervous system, gastrointestinal hormones and the control of satiation and food intake. He has published more than 580 articles and 40 book chapters on various aspects of scientific and clinical gastroenterology.

Abstract

The irritable bowel syndrome (IBS) is a highly prevalent disorder and a major cause of visits to general practitioners and specialists. Several recent and ongoing studies have been conducted to establish the burden associated with IBS to the individual, his or her family, the healthcare system and society. Epidemiological studies are available from many countries and regions, and have been summarized in 2 review articles. However, these analyses suffer from heterogeneous approaches in terms of selection of the surveyed population, questionnaires used and criteria used to define IBS. Currently ongoing is the Rome IV epidemiology study, which surveys 76000

patients in 34 countries around the globe. Once finalized, this effort will provide the most detailed and most up-to-date knowledge of IBS prevalence.

The impact of IBS has also been addressed in many studies using heterogeneous populations and approaches. The “IBS Global Impact Reports 2017 and 2018” summarized current facts and gaps in our knowledge on the impact of IBS. IBS puts considerable strain on healthcare resources which is still likely to be under-estimated due to under-diagnosis. Indeed, it has been estimated to take more than 4 years before a formal diagnosis of IBS is made. Quality of life reductions are major and can be explained by the chronic nature of IBS, the delays in diagnosis, the lack of effective treatment approaches and the lifestyle implications associated with IBS. The impact of IBS on the spouse or partner also lacks systematic studies. People with IBS are twice as likely to take time off work than those without IBS, and greater IBS symptom severity leads to lower productivity. These reports also uncovered a substantial hidden cost of IBS, paid by the patients themselves.

The findings led to a number of calls to action, including the need to develop a set of simple diagnosis and management guidelines for daily practice, with effective communications between patients and healthcare providers, a choice to direct of healthcare resources towards patients with more severe symptoms, and the need to uncover the hidden costs and consequences of IBS.

References

1. Lovell and Ford. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol*. 2012 Jul;10(7):712-721
2. Sperber et al. The global prevalence of IBS in adults remains elusive due to the heterogeneity of studies: a Rome Foundation working team literature review. *Gut*. 2017 Jun;66(6):1075-1082.
3. Corsetti, Sabaté, Freemantle, Tack. IBS Global Impact Report 2017.
4. Corsetti, Tack, Attara, Sewell. IBS Global Impact Report 2018.



History and Impact of the Rome Foundation and Rome IV and its Future in GI Health Care

Douglas A. Drossman
USA

President, Drossman Center for the Education and Practice of Biopsychosocial Care LLC
President, Drossman Consulting LLC
President, Rome Foundation
Professor Emeritus of Medicine and Psychiatry,
University of North Carolina School of Medicine, USA
Former Co-Director, UNC Center for Functional GI and Motility Disorders

Dr. Drossman received his M.D. degree at Albert Einstein College of Medicine and subspecialized in biopsychosocial (psychosomatic) medicine and Gastroenterology. He is a Fellow of the American College of Physicians, a Master of the American College of Gastroenterology, on the Board of Directors of the International Foundation for Functional GI Disorders (IFFGD) (www.iffgd.org), and Past-President of the American Psychosomatic Society (1997).

Dr. Drossman has founded multiple organizations to advance patient-centered education and treatment of IBS:

- UNC Center for Functional Gastrointestinal and Motility Disorders, founder
- The Rome Foundation, founder, chair and Senior Editor of the Rome I, II, III, and IV textbooks. (www.theromefoundation.org)
- Drossman Center for the Education and Practice of Biopsychosocial Care, founder. Physicians are trained in relationship-centered biopsychosocial care with emphasis on communication skills and enhancing the patient-doctor relationship. (www.drossmancenter.com)

In his gastroenterology practice, Dr. Drossman receives referrals nationally to consult or manage the care of difficult-to-diagnose and -treat patients with functional gastrointestinal and motility disorders. (www.drossmangastroenterology.com)

Dr. Drossman has written over 500 articles and book chapters, serves on six editorial and advisory boards, was Associate Editor of the journal *Gastroenterology* and was the *Gastroenterology*

Section Editor of the Merck Manual for 17 years.

His research relates to the clinical, epidemiological, psychosocial and treatment aspects of gastrointestinal disorders, and he has been principal investigator in several federally-funded epidemiological, outcomes, and abuse grants, including brain imaging in IBS. Dr. Drossman is the recipient of many research awards including:

- American College of Gastroenterology (ACG) David Sun Award (2012)
- American Journal of Gastroenterology Lectureship (2011)
- American Gastroenterological Association (AGA) Mentors Research Scholar Award (2007)
- AGA Joseph B. Kirsner – Fiterman Award in Clinical Research (2005)
- Janssen Award for Clinical Research (1999)

His work relates to the biopsychosocial aspects of patient care and Dr. Drossman has produced articles and videotapes on medical interviewing and the patient-doctor relationship. He also facilitates workshops and communication skills training programs and has received numerous awards, both as an educator and practitioner:

- ACG David Sun Lecture Award (2012)
- AGA Distinguished Educator Award (2004)
- Annual "Who's Who," "Patient Choice," and "Best Doctors" citations over the past 15 years.
- "Best Gastroenterologist" in Women's Health (2008)
- "Best Gastroenterologist" in Men's Health (2007)
- Featured as one of 12 gastroenterologists in the book "Best Gastroenterology Practices" (2007)

Abstract

Functional gastrointestinal disorders (FGIDs) now called Disorders of Gut Brain Interaction¹ are recognized by morphologic and physiological abnormalities that occur in combination including motility disturbance, visceral hypersensitivity, altered mucosal and immune function, altered gut microbiota, and altered central nervous system processing. The Rome Foundation has for over 25 years played a pivotal role in many aspects of the development of our field including the evidence that led to this new definition. This presentation will review how and why the Rome Foundation began, the factors leading to the organization's directives and impact on the field of disorders of gut-brain interaction.

The foundation began late early 1990's when diagnosis of IBS and FGIDs were done by exclusion. Research on motility which was dominant at the time was not sufficient to explain GI pain and clinical trials were flawed by lack of adequate inclusion criteria: "Not a single IBS treatment trial reported to date has used an adequate operational definition of IBS"². To fill that gap, the concept of a classification system using symptom-based criteria was developed, based on the consensus of experts (Delphi approach). These criteria provided the substrate for the

development and sustenance of our field and this is related to: 1) standardization of inclusion criteria for clinical trials, 2) validation by clinical, epidemiological and factor analytic studies, 3) recognition by international regulatory agencies, 4) support by pharmaceutical industry, 5) development of a data pool of patients with FGIDs using these criteria by investigators which encouraged further research and ultimately, 6) fostering the concept of gut-brain interactions, neurogastroenterology and neuromodulators and ultimately, 7) legitimization of these disorders as “real”.¹

The Foundation has evolved in its functions. It began by heralding the development of the criteria by consensus and then succeeded to modify them based on scientific evidence with Rome II, III and IV. Beginning with the publication of a single book we have since created a vast range of educational products tailored to clinicians as well as scientists. This includes research questionnaires, diagnostic algorithms, the multi-dimensional clinical program concept, slide programs and most recently the interactive clinical decision toolkit, an intelligent software learning method. We began with books in and have now gone digital to meet the needs of younger audiences and more advanced learning methods. We disseminate this knowledge globally and foster education programs including symposia, webinars and other live and digital presentations to reach not only gastroenterologists but also primary care, mental health, pediatric and mid level providers. We sponsor and support young investigators through our mentoring program and mental health providers through our Foundation’s Psychogastroenterology section. Further information on our educational materials is available on our website: www.theromefoundation.org

Finally, for the future, we have identified a new need: “To create an international academic and research initiative to advance scientific understanding of the disorders of gut-brain interaction”. Over the next several years, with the support of our sponsors we will have in place the Rome Foundation Research Institute which will serve as an international clearinghouse for investigators and industry in the development, administration and analysis of clinical research for the disorders of gut brain interaction. We believe the future looks good for research, education and clinical care for our patients and look forward to continuing in that process.

References

1. Drossman DA. Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. *Gastroenterol* 2016;150:1262-1279.
2. Klein KB. Controlled treatment trials in the irritable bowel syndrome: a critique. *Gastroenterol* 1988;95:232-241.



How to Use the Rome IV Criteria in Clinical Practice

Fermín Mearin
Spain

Institute of Functional and Motor Digestive Disorders
Centro Médico Teknon, Barcelona, Spain

Dr. Fermín Mearin is Director of the Department of Gastroenterology, Teknon Medical Center in Barcelona. He studied Medicine and Surgery at the Faculty of Medicine, Autonomous University of Madrid. He specialized in Gastroenterology at the Hospital de la Princesa in Madrid and completed his training at the Mayo Clinic, Rochester, Minnesota, USA. Dr. Mearin has specific research interests in GI motility, visceral perception and functional digestive disorders. Past President of the Spanish Association of Gastroenterology (2008-2012). Current Director of the National Course of GI Residents (AEG). He is also a member of the International Foundation for Functional Gastrointestinal Disorders as well as part of Rome III committee. Currently is the chairman of the Rome IV Functional Bowel Disorders Committee. He has authored more than 300 scientific publications, and has imparted lectures and teaches courses in Spain and abroad.

Abstract

There are a number of reasons to establish a quick and accurate diagnosis of IBS: to relieve patient uncertainty; to avoid adverse effects of unnecessary medications or treatments; to avoid unnecessary diagnostic procedures and surgery; to conserve limited healthcare resources; and, of course, to initiate the most appropriate treatment. However, making the diagnosis of IBS remains challenging because it is clinically heterogeneous, no biological marker to detect it exists, many other diseases share the same clinical manifestations and it is often difficult for both physicians and patients to accept the uncertainty of a symptom-based diagnosis.

Different diagnostic criteria have been developed during the last four decades but, so far, none have proved to be an ideal method of accurately diagnosing IBS. Just as importantly, physicians are frequently unaware of published guidelines or consciously ignore these diagnostic criteria. Most clinicians still believe IBS is a diagnosis of exclusion and not a positive diagnosis based on history, physical examination, use of published diagnostic criteria, and the absence of alarm features.

Although these points may generate despair in many providers, clinicians should not give up hope on the diagnosis and treatment of IBS. Although not perfect (and no diagnostic criteria are), the Rome IV criteria can be used to make a presumptive diagnosis and allow the initiation of therapy based on the predominant symptom. During this session, the key considerations for making a practical diagnosis of IBS using Rome IV criteria will be discussed as well as the areas for improvement of IBS diagnosis.

1. Mearin F, Lacy BE. Diagnostic criteria in IBS: useful or not? *Neurogastroenterol Motil* 2012; 24: 791-801.
2. Lacy BE, Mearin F, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel Disorders. *Gastroenterology* 2016; 150: 1393-407.
3. Mearin F, Ciriza C, Mínguez M, Rey E, Mascort JJ, Peña E, Cañones P, Judez J. Guía de Práctica Clínica: Síndrome de Intestino irritable y estreñimiento funcional en adultos. *Rev Esp Enf Dig* 2016; 108: 332-63.



What Is Important To Know About Bowel Habit

Enrico Corazziari
Italy

Enrico Corazziari, MD
Senior Consultant, Department of Gastroenterology
Istituto Clinico Humanitas, Rozzano. Italy

Professor of Gastroenterology. Senior Consultant, Department of Gastroenterology, Clinical Institute Humanitas, Viale A Manzoni ,Rozzano , Italy - University Teacher, Medical Doctor; Full Professor of Gastroenterology (2000-2016); Head UOC Gastroenterologia A (2004-2016) - Director Postgraduate Specialization School of Gastroenterology (2007-2016) Head UOC S.S. Fisiopatologia Digestiva (2001-2004) Professorship 2000; Researcher 1981; Gastroenterology Specialization 1980; Internal Medicine Specialization 1975. Graduation in Medicine and Surgery 1970.

Abstract

Knowledge of bowel habit is important for diagnosis and treatment of Irritable Bowel Syndrome (IBS) patients.

IBS diagnosis is made in the presence of recurrent abdominal pain on average at least 1 day/week in the last three months, related to defecation and associated with a change in frequency and/or in form of stool.

Of the different aspects of bowel habit, the proportion of days with altered stool form alone is indicated by the Rome IV diagnostic criteria as the most valuable tool to subtype IBS patients according to the Bristol Stool Form Scale (BSFS) into three categories: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS with a mixed pattern (IBS-M). Unclassified (IBS-U) patients do not match the Rome IV criteria of the predominant bowel habit of the above three IBS subtypes. These four IBS subtypes and other intestinal functional disorders, also characterized by bowel habit alterations, functional diarrhea and functional constipation, share several common pathophysiological features, belong to the same clinical spectrum, and may transition from one phenotype to another.

Knowledge of bowel habit is important for IBS treatment, being the therapy mainly targeted to the IBS subtype. Treatment, however, can be challenging in patients with variable or poorly defined bowel habit such as IBS-M and IBS-U.

Rome IV. Functional Gastrointestinal Disorders. Fourth Ed-Vol II. Publisher The Rome Foundation, Raleigh. NC, 2016



When and How to Exclude an Organic Disease

Alexander C. Ford
UK

Leeds Institute of Biomedical and Clinical Sciences
University of Leeds, UK

Alex Ford is currently a Professor and Honorary Consultant Gastroenterologist at St. James's University Hospital, Leeds, UK. During his registrar training he conducted a 2-year period of research funded by the Medical Research Council, obtaining an MD from Leeds University. Work from his thesis was used to inform the National Institute for Health and Clinical Excellence's guidelines for the management of dyspepsia in the UK.

From October 2007 to September 2008 he completed a post-doctoral fellowship in the Gastroenterology Division of McMaster University Medical Centre, Hamilton, Ontario, Canada. During this time he conducted a series of systematic reviews and meta-analyses to inform the American College of Gastroenterology's monograph for the management of irritable bowel syndrome. He updated this work in 2014, and was the first author on the latest version of the monograph published in The American Journal of Gastroenterology in August 2014.

He is an Associate Editor for Alimentary Pharmacology and Therapeutics handling papers dealing with the functional gastrointestinal disorders, and a member of the international editorial boards of Alimentary Pharmacology and Therapeutics, The American Journal of Gastroenterology, and Clinical Gastroenterology and Hepatology. He has published over 280 peer-reviewed articles and book chapters, including original scientific papers in JAMA, BMJ, Gastroenterology, Gut, Archives of Internal Medicine, and The American Journal of Gastroenterology. His h-index on Web of Science is 46, and his papers have been cited over 7000 times in total.

Abstract

Irritable bowel syndrome (IBS) is a chronic functional bowel disorder with a relapsing and remitting natural history. The condition is characterised by abdominal pain in association with abnormal stool form or frequency. The condition is meant to be diagnosed on clinical grounds alone, using symptom-based criteria, a so-called “positive” diagnosis. This avoids injudicious use of invasive investigations, which may be costly, anxiety-provoking, and lead to increased consultation behaviour and a refusal to accept a diagnosis of IBS. However, the gastrointestinal (GI) tract has a limited repertoire of symptoms. There may therefore be concerns of a missed organic diagnosis among patients presenting with abdominal pain and a change in bowel habit, who meet criteria for IBS. This presentation will discuss the accuracy of a positive diagnostic strategy for IBS, as well as the potential organic diseases that may masquerade as IBS, presenting with similar symptoms. When diagnosing a functional disorder, such as IBS, the rate of missed organic disease needs to be as low as possible. The optimal diagnostic test should therefore have a low false positive rate (i.e. people with organic disease incorrectly classified as having IBS), and therefore specificity needs to be maximised. Unfortunately, symptom-based diagnostic criteria perform poorly, to date, in predicting a diagnosis of IBS among unselected patients presenting with lower GI symptoms. Sensitivities of the Manning criteria and various iterations of the Rome criteria range between 62% and 96% in a large cross-sectional survey in Canada¹, but specificities were between 71% and 82%. Incorporating items from the clinical history and a limited diagnostic evaluation, such as the presence of nocturnal passage of stools, normal full blood count, and C-reactive protein, and mood scores, appeared to improve the performance of the Rome III criteria in one study², with sensitivities ranging from 17.5% to 51%, and specificities in excess of 95% with each of these modifications. The Rome IV criteria have yet to be independently validated. As a result of the modest performance of symptom-based criteria, there may be concerns on the part of the responsible physician that an organic disease has been missed. Reviewing the literature suggests that some organic conditions are more common in people with symptoms meeting criteria for IBS. A recent systematic review and meta-analysis demonstrated that biopsy-proven coeliac disease was 4.5 times more likely among individuals with IBS-type symptoms, compared with healthy controls without IBS-type symptoms³. Bile acid diarrhoea may also mimic IBS-type symptoms, and another systematic review demonstrated that >25% of patients with IBS with diarrhoea may have evidence of moderate or severe BAD on SeHCAT scanning⁴. However, there is little evidence that pancreatic insufficiency, colorectal cancer, or inflammatory bowel disease (including microscopic colitis) will be missed in patients presenting with IBS-type symptoms⁵⁻⁷. In addition, a randomised controlled trial of exhaustive investigation among patients with suspected IBS, compared with a positive diagnostic strategy, demonstrated no differences in subsequent GI symptoms, quality of life, or patient satisfaction between the two arms of the trial, and costs were significantly higher in the exhaustive investigation arm⁸. Judicious use of a limited panel of investigations in

IBS to exclude coeliac disease and BAD appears warranted, but more exhaustive investigation to exclude other organic diseases is not supported by current evidence.

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Why Is Gender So Important in IBS?

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Lin Chang, MD, is a Professor of Medicine and Vice-Chief of the Vatche and Tamar Manoukian Division of Digestive Diseases, Department of Medicine at the David Geffen School of Medicine at UCLA. She serves as the Co-Director of the G. Oppenheimer Center for Neurobiology of Stress and Resilience at the David Geffen School of Medicine at UCLA. She is also Program Director of the UCLA Gastroenterology Fellowship Program. Dr. Chang's clinical expertise is in functional gastrointestinal disorders. She is a NIH funded investigator studying brain-gut interactions underlying irritable bowel syndrome (IBS). Specifically, her research is focused on the pathophysiology of IBS related to stress, early life adversity, sex differences, genetic and epigenetic factors, and gut microbiome and the treatment of IBS.

Dr. Chang is the recipient of the Janssen Award in Gastroenterology for Basic or Clinical Research and the AGA Distinguished Clinician Award. She is a member of the Rome Foundation Board of Directors, Chair of the Rome Advisory Council, and was a member of the Rome IV Editorial Board and Functional Bowel Disorders Committee. Dr. Chang previously served as President of the American Neurogastroenterology and Motility Society (ANMS). She is Associate Editor of Clinical Gastroenterology and Hepatology. She is a fellow of the American Gastroenterological Association (AGA) and was recently selected to be Clinical Research Councilor of the AGA Governing Board. She is also a fellow of the American College of Gastroenterology. Dr. Chang is a member of the FDA GI Drug Advisory Committee and the NIH Clinical, Integrative, Molecular Gastroenterology (CIMG) Study Section. She has authored more than 115 original research articles, 55 review articles, and 20 book chapters on her specialty interests.

Abstract

Epidemiological studies indicate sex-related differences among functional gastrointestinal disorders (FGIDs) including irritable bowel syndrome (IBS). A meta-analysis of 80 studies that included 260,960 subjects identified a IBS prevalence rate of 11.2%. In both the general population and IBS patients, women were more likely to report predominantly constipation-related symptoms including abdominal distension, bloating, straining, and hard stools than men. In contrast, men with IBS were significantly more likely to report the diarrhea-related symptoms of loose/watery stools and increased stool frequency than women with IBS. There is also evidence of gender differences in treatment response. However, the mechanisms by which females exhibit an increased vulnerability for development of IBS remains incompletely understood. Sex is an important biological variable (SABV) in the study of many chronic diseases including IBS as it can impact reproducibility, generalizability, and effectiveness of treatment responses. Evidence of sex and gender related differences in IBS include: 1) Amplification of symptoms during the late luteal and early menses phases coincident with falling estrogen and progesterone levels, 2) Similar or increased visceral perception in women with IBS compared to men with IBS and healthy women, 3) Slower colonic transit in women, 4) Men with IBS have greater cardiosympathetic and lower vagal tone at baseline and in response to visceral stimulation than women with IBS, 5) IBS is associated with a dysregulated hypothalamic-pituitary-adrenal (HPA) axis and there are divergent responses in men and women with IBS, 6) Morphologic and functional brain differences exist in men and women with IBS, 7) IBS women have lower colonic mucosal expression of cytokine IL-10 and numbers of CD+3 and CD+8 T cells but higher number of mast cells, 8) Sex differences in intestinal permeability exist in IBS, and 9) IBS therapeutic agents alosetron and lubiprostone appear to have a more robust efficacy in IBS women compared to men. Greater attention needs to be placed on recruiting similar numbers of men and women in human studies and studying SABV in pathophysiologic, diagnostic and treatment studies. A better understanding of the role of SABV in the pathophysiology of IBS could lead to novel therapeutic strategies tailored to the distinct sex related pathophysiologic mechanisms underlying IBS.

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Tandem Talk on Gas-Bloating. All in the Diaphragm

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Abstract

Abdominal bloating, distension and flatulence are frequently reported in relation to flatulogenic meals, but the mechanism by which gas produces symptoms is not clear. In most cases the rate of gas production, as well as the volume of intestinal gas, are within the normal range¹. In this context, bloating and flatulence may be related to gut hypersensitivity. On the other hand, visible abdominal distension seems a behavioral response, featuring a diaphragmatic contraction and descent with anterior wall protrusion². Indeed, abdominal distension can be corrected by abdomino-phrenic EMG-guided biofeedback. However, why these patients acquire this abnormal behavior remains unknown. Likewise, the factors that trigger the episodes of abdominal distension have not been identified, but conceivably, perception of bloating sensation may play a role. Diets low in flatulogenic residues decrease gas production and improve symptoms, but in the long run such restrictive diets may have deleterious effects on intestinal microbiota. Other studies showed that prebiotics influence the composition of microbiota and have a beneficial effect of on bloating and distension. Proper pathophysiological diagnosis seems important for the management of these patients.

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Tandem Talk on gas-bloating: All in the Gut

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Maura Corsetti graduated in Medicine and obtained her Specialization (2000) and PhD (2004) at the Università degli Studi di Milano in Italy. She is currently Associate Professor of Gastroenterology in the NIHR Nottingham BRC, Nottingham University Hospitals and the University of Nottingham, Nottingham Digestive Diseases Centre, UK and Associate Editor of Neurogastroenterology and Motility. Her main research interest is the role of gut motility in the pathophysiology of functional bowel disorders applying the high-resolution manometry.

Abstract

Abdominal bloating is a relevant and poorly understood symptom, frequently reported in many functional disorders, including IBS (1). Despite its clinical importance, its pathophysiology and treatment is unclear. Many studies have demonstrated that the problem does not seem to be the gut gas content but rather abnormal responses to gas. Recent reports have indeed demonstrated that the ingestion of meal with different composition determine the production of the same quantity of gas in the gut of healthy subjects and IBS patients (2). However IBS patients report more symptoms than healthy controls (2). Some authors have reported the presence of abnormal control of abdominal muscle activity in IBS patients (3). However some data indicate that patients complaining of bloating have impaired transit and tolerance of intestinal gas loads (4,5). This lecture will revise the evidences about the possible role of gut-related factors in the pathophysiology of bloating and in particular of the altered GI motor response to intraluminal gas.

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Usefulness of Clinical and Laboratory Biomarkers

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Doctor Magnus Simrén graduated from medical school, University of Gothenburg in 1991, and afterwards completed his internship and fellowship in internal medicine at the County Hospital of Lidköping. From 1998 to 1999, Doctor Simrén completed his fellowship in gastroenterology at Sahlgrenska University Hospital, and has been working as a specialist physician in gastroenterology at Sahlgrenska University Hospital since 1999. He defended his thesis entitled Irritable Bowel Syndrome. Pathophysiological and clinical aspects in 2001. He was a post-doctoral research fellow at the University of Leuven, Belgium, in 2002. Between 2011 and 2016, Dr. Simrén had a Senior Research position at the Swedish Research Council and the University of Gothenburg in Molecular Gastroenterology. He was visiting research scientist at the Center for Functional GI and Motility Disorders, University of North Carolina (UNC), Chapel Hill, NC, United States 2015-2016, and currently holds a position as Adjunct professor of Medicine at UNC School of Medicine (2017-). Since 2013 he has a combined position as Professor of Gastroenterology at the University of Gothenburg, and Senior Consultant at the Sahlgrenska University Hospital in Gothenburg, Sweden.

Doctor Simrén is head of the Neurogastroenterology Unit at Sahlgrenska University Hospital. His main research areas are the pathogenesis and pathophysiology of functional GI disorders, as well as the treatment of these. He has published more than 240 original articles and also written book chapters on GI motility diseases and functional GI disorders, and is currently supervisor for nineteen PhD students and five post-docs. Doctor Simrén has been the President of the Scandinavian Association for Gastrointestinal Motility (SAGIM), and Scientific Secretary to the Swedish Society of Gastroenterology, and served as council member for several international

organizations. He has been the chair of the United European Gastroenterology (UEG) Scientific Committee 2013-2017, and is currently the UEG Secretary General (2018-2021), and a member of the UEG council (2013-2021). Professor Simrén has also been working as Deputy Editor and Associate Editor of Gut, and as the Clinical Editor of Neurogastroenterology and Motility. He is also on the Rome Foundation Board of Directors since 2011. 2010-2012 he led the Rome Foundation Working Team, "Intestinal microbiota in Functional Bowel Disorders 2010-2012, and was on the Rome IV committees for Functional Bowel Disorders and Centrally Mediated Disorders of GI Pain. Dr Simren is the Research Director of the Rome Foundation Research Institute (RFRI) 2017.

Abstract

IBS is characterized by abdominal pain associated with abnormal bowel habits, and defined by diagnostic criteria, currently the Rome IV version. By definition, standard clinical routine investigations are normal. The search for biomarkers to define IBS, rather than basing the diagnosis on a combination of symptoms, is ongoing. There are several candidate biomarkers that have been evaluated based on the current knowledge about the pathophysiology of IBS. However, so far none of the candidate biomarkers are present in all IBS patients, and can in most cases only modestly discriminate IBS from health or from other GI diseases. However, the candidate biomarkers may be of relevance for subgroups of IBS patients, and are therefore of potential value to phenotype IBS patients in research studies. Some of the most widely accepted pathophysiological factors in IBS are altered GI motility and visceral hypersensitivity, and 25-60% of IBS patients demonstrate different types of GI sensorimotor abnormalities, and these are associated with some of the key symptoms in IBS. Measurement of oroanal transit time and rectal balloon distensions are the most widely available tests to assess lower GI sensorimotor function, and therefore possible to include in large scale IBS studies. Moreover, a substantial proportion of IBS patients lose bile acids into the colon and different measures of the function of the enterohepatic circulation, such as 75SeHCAIT test, s-C4, or s-FGF19 can be used to define relevant subgroups of IBS patients with a specific clinical phenotype. More recent data also suggest that there may be promising serum, faecal and colonic mucosal biomarkers for IBS, and of these circulating anti-CdtB and anti-vinculin antibodies, faecal granins, faecal volatile organic metabolites, colonic immune cells and tight junctions seem to be the most promising candidates. Also novel endoscopic techniques to identify gut barrier dysfunction seem promising. Furthermore, using psychologic questionnaire data ("psychomarkers") may also be used to identify relevant subgroups of IBS patients alone or in combination with a panel of serum biomarkers, and can therefore be seen as valuable phenotyping tools and/or potential biomarkers.

Conclusion: Use of biomarkers, function testing and "psychomarkers" seem to be of relevance for defining phenotypically distinct subgroups of IBS patients, and therefore valuable in large-scale IBS research studies. Currently the usefulness of some of these biomarkers in clinical practice is under evaluation.



How to Improve the Patient-Physician Relationship

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Dr. Drossman received his M.D. degree at Albert Einstein College of Medicine and subspecialized in biopsychosocial (psychosomatic) medicine and Gastroenterology. He is a Fellow of the American College of Physicians, a Master of the American College of Gastroenterology, on the Board of Directors of the International Foundation for Functional GI Disorders (IFFGD) (www.iffgd.org), and Past-President of the American Psychosomatic Society (1997).

Dr. Drossman has founded multiple organizations to advance patient-centered education and treatment of IBS:

- UNC Center for Functional Gastrointestinal and Motility Disorders, founder
- The Rome Foundation, founder, chair and Senior Editor of the Rome I, II, III, and IV textbooks. (www.theromefoundation.org)
- Drossman Center for the Education and Practice of Biopsychosocial Care, founder. Physicians are trained in relationship-centered biopsychosocial care with emphasis on communication skills and enhancing the patient-doctor relationship. (www.drossmancenter.com)

In his gastroenterology practice, Dr. Drossman receives referrals nationally to consult or manage the care of difficult-to-diagnose and -treat patients with functional gastrointestinal and motility disorders. (www.drossmangastroenterology.com)

Dr. Drossman has written over 500 articles and book chapters, serves on six editorial and advisory boards, was Associate Editor of the journal *Gastroenterology* and was the *Gastroenterology*

Section Editor of the Merck Manual for 17 years.

His research relates to the clinical, epidemiological, psychosocial and treatment aspects of gastrointestinal disorders, and he has been principal investigator in several federally-funded epidemiological, outcomes, and abuse grants, including brain imaging in IBS. Dr. Drossman is the recipient of many research awards including:

- American College of Gastroenterology (ACG) David Sun Award (2012)
- American Journal of Gastroenterology Lectureship (2011)
- American Gastroenterological Association (AGA) Mentors Research Scholar Award (2007)
- AGA Joseph B. Kirsner – Fiterman Award in Clinical Research (2005)
- Janssen Award for Clinical Research (1999)

His work relates to the biopsychosocial aspects of patient care and Dr. Drossman has produced articles and videotapes on medical interviewing and the patient-doctor relationship. He also facilitates workshops and communication skills training programs and has received numerous awards, both as an educator and practitioner:

- ACG David Sun Lecture Award (2012)
- AGA Distinguished Educator Award (2004)
- Annual "Who's Who," "Patient Choice," and "Best Doctors" citations over the past 15 years.
- "Best Gastroenterologist" in Women's Health (2008)
- "Best Gastroenterologist" in Men's Health (2007)
- Featured as one of 12 gastroenterologists in the book "Best Gastroenterology Practices" (2007)

Abstract

This presentation will address important features that will help clinicians improve their communication skills in the care of patients with functional GI disorders (FGIDs)¹. One might question why is it important to learn these skills given our modern technology that influence diagnosis and treatment of these disorders. We diagnose and manage patients by ordering increasingly expensive and often unnecessary tests that lead to increased health care costs, and this is particularly true for the FGIDs. We are no longer comfortable with our clinical judgment and diagnostic skills and because we approach human illness from a dualistic (i.e., organic vs. functional) perspective we often feel compelled to "rule out organic disease". Patients also share these views. The evidence shows that in this reality, doctors and patients are dissatisfied, health care costs go up and there is a widening gap in the level of engagement between physician and patient leading to mutual dissatisfaction and a competitive rather than collaborative level of care.

In this presentation we will review the essential elements that can be learned and used by clinicians to increase patient and physician satisfaction, help establish a realistic set of goals,

improve patient adherence to treatment, negotiate treatment and improve clinical outcomes regardless of the disorder or treatment modality. We will also discuss effective ways to recommend neuromodulators for treatment² Using case examples, and video with interactive discussion we will discuss ways to obtain more relevant clinical information to improve diagnosis and treatment. We will also demonstrate both verbal and nonverbal methods to provide empathy reassurance and validation. Finally, we will also help the attendee identify the barriers to good communication and offer methods to help reduce those barriers. This is a session on the process of care: "It is not what you do but how you do it that makes the difference".

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IBS in Primary Care

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Professor Hungin graduated from Newcastle Medical School, UK and became a GP as well as working part time in hospital gastroenterology. He came to academic life late completing his doctorate at the old age of 46 and was appointed Professor of General Practice at Durham University. He became their Founding Dean of Medicine and the Head of School from 2002 to 2014, building a department that included undergraduate medicine, pharmacy, the medical humanities, and health policy and services research. He is currently Professor in the Faculty of Medical Sciences at Newcastle University.

His research interests are centred on the earlier diagnosis of long term conditions and barriers to evidence-based implementation. He has served with the Italian Medicines Agency (AIFA) as a grants referee and with the Central Research Ethics Group of Unilever plc, the National Institute for Health Research (UK), the UK Medicines and Healthcare Regulatory Agency and the Scientific Committee of the UEGF. He is a founder member of the UK and European Primary Care Societies for Gastroenterology, Chair of the Rome Foundation's primary care committee and co-author of the Rome IV book on functional disorders for non-gastroenterologists.

Pali's current work is centred the evolving role of the doctor in a fast moving world and this was the subject of his Presidency of the British Medical Association during 2016-17.

Abstract

In most healthcare systems the first point of contact and the ongoing management of IBS lies in primary care. GPs are encouraged to make a positive diagnosis but in reality the situation is very variable.

A systematic review (29 studies) revealed that relatively few primary care physicians (PCPs) were aware of (2–36%; 8 studies) or used (0–21%; 6 studies) formal diagnostic criteria for IBS although most could recognise the key symptoms of abdominal pain, bloating and disturbed defaecation. A minority of PCPs (7–32%; one study of six European countries) preferred to refer

patients to a specialist before making an IBS diagnosis, and few patients (4–23%; three studies, two UK, one US) were referred to a gastroenterologist. Most PCPs were unsure about IBS causes and treatment effectiveness, leading to varied therapeutic approaches and broad but frequent use of diagnostic tests. Diagnostic tests, including colon investigations, were more common in older patients (5 studies, four European, one US).

It has to be accepted that whilst there has been much emphasis about the desirability of an initial positive diagnosis of IBS this is not universally accepted by GPs. Most GPs do make a presumptive IBS diagnosis from the start but they still tend to use additional tests. Although an early, positive diagnosis has advantages in avoiding unnecessary investigations and costs, until formal diagnostic criteria are conclusively shown to sufficiently exclude organic disease, bowel investigations, such as colonoscopy, will continue to be important to GPs. Similarly, uncertainties about the effectiveness of treatments leads to a variety of approaches, not necessarily symptom targeted or evidence-based.

It also has to be accepted that the Rome criteria have minimal impact in primary care. Patients are increasingly empowered by Internet information and they frequently use supermarket and OTC products and seek alternative remedies and practitioners. Some are determined to manage their own therapies, seeking tests and drugs that the PCP might not normally use. National guidelines continue to be either all-encompassing or over-specific – as an example, there has been an explosion in the use of FODMAP diets in the UK, with most PCPs having no real understanding of their indication or effects. Equally, whilst probiotics have been shown to be limited in their application they remain popular with IBS sufferers. Importantly, PCPs recognise the associations between the various functional disorders, are experienced in the whole person approach and are comfortable with psychological approaches, both with drugs and the interactional therapies.

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Overlapping Functional GI Disorders

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Kok-Ann Gwee is Adjunct Associate Professor of Medicine at the National University of Singapore. He obtained his medical degree from National University of Singapore, and his PhD from University of Sheffield for his thesis on post-infectious IBS. His research includes epidemiology and Asian socio-cultural perspectives of GI diseases, and the roles of inflammation, gut microbes, probiotics, sleep disturbance and psychological factors in FGID. He is a past president of the Asian Neurogastroenterology & Motility Association, and chaired the Rome-Asian Working Team.

Abstract

Overlap is common among the various FGID syndromes, and possibly, more common than the pure forms. [Siah TH. Gut 2017] Subjects with overlapping symptoms have poorer QOL, and are more likely to seek medical attention. [Aziz I. Am J Gastroenterol 2018] This overlap is also a predictor of greater symptom severity and dissatisfaction with treatment. [Matsuzaki J. Neurogastroenterol Motil 2012] [Xiong LS. J Gastroenterol Hepatol 2017] Studies of post-infection cohorts report the development of FD-IBS overlap syndromes. [Wensaas KA Neurogastroenterol Motil 2016] suggesting a common aetiopathogenesis. In Asia, spice has been reported to trigger burning sensations in association with IBS in addition to dyspepsia. [Gonlachanvit S 2009] Current diagnostic and treatment algorithms do not cater to this real world situation.



Tandem Talk on Genetic Factors: The Basic Scientist View

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Mauro D'Amato investigates how genetic variations predispose to gastrointestinal (GI) disease. Through computational and genetic approaches, his team strive to identify causative genes and the mechanisms by which they affect risk to inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), and other GI conditions. They also study how human genes influence gut microbiota composition, and the dysregulation of this interaction in human disease. Their ultimate goal is a translational application for improved therapeutic precision in gastroenterology. Mauro D'Amato is an IKERBASQUE Research Professor, and Head of the Gastrointestinal Genetics Unit at the BioDonostia Health Research Institute in San Sebastian, Spain. He formed in Rome at the University "La Sapienza" and the National Research Council. Later, first as a postdoctoral fellow and then as senior researcher, Mauro worked at the Wellcome Trust Center for Human Genetics in Oxford UK, and the Karolinska Institutet in Stockholm Sweden, where he currently holds a Visiting Professor chair in Gastrointestinal Genetics. Mauro has published more than 130 articles in the area, conceived and coordinates the bellygenes initiative on the genetics of IBS (www.bellygenes.org), and has established large international collaboration that constitutes an excellent platform for the development of junior scientists and clinical researchers.

Abstract

A hereditary component of irritable bowel syndrome (IBS) has been demonstrated in family and twin studies. However, gene studies in IBS so far have been mainly limited to candidate genes in small sample sets of cases and controls, and no unequivocal IBS risk locus has been identified. Our group has pioneered IBS genetic research in the past few years, identified a few risk genes and variants, and recently proposed the use of large population-based biobanks and cohorts for the study of IBS predisposition.

This translated into the bellygenes initiative we coordinate, which is a multi-national project supported by the European Biobanking and Biomolecular Resources Research Infrastructure – Large Prospective Cohorts (bbmri-lpc), aiming to study IBS and genotype in a target population exceeding 800,000 Europeans (www.bellygenes.org). Through GWAS studies and their meta-analyses, we make use of genotype data in relation to a series of IBS definitions and classifications, spanning questionnaire data for the Rome Criteria and self-reported diagnoses, linkage to medical records using the International Classification of Diseases (ICD) system, and clinical diagnoses from tertiary centres with expertise in IBS. The initial results of this large-scale efforts are communicated and discussed.



Tandem Talk on Genetic Factors: The Clinician Perspective

Michael Camilleri
USA

Michael Camilleri, M.D.

Clinical Enteric Neuroscience Translational and Epidemiological Research (C.E.N.T.E.R.) Program

Mayo Clinic, Rochester, Minnesota, USA

Michael Camilleri, M.D., is a consultant in the Division of Gastroenterology and Hepatology in the Department of Internal Medicine at Mayo Clinic in Rochester, Minnesota. He was recognized with the Atherton and Winifred W. Bean Professorship in 2001 and as a Mayo Distinguished Investigator in 2008. He currently serves as Executive Dean for the Department of Development. He holds the ranks of Professor of Medicine, Pharmacology, and Physiology at Mayo Clinic College of Medicine. He joined the staff of Mayo Clinic in 1990.

Dr. Camilleri received his M.D. degree from University of Malta Medical School and completed residency at St. Luke's University Hospital in Malta. He pursued fellowships in research and internal medicine and gastroenterology at Hammersmith Hospital at the University of London, England. He completed fellowships at Mayo Graduate School in both research and clinical studies in gastroenterology.

Dr. Camilleri's research interests include clinical enteric neurosciences, gut neurohormonal control, obesity, irritable bowel syndrome, and pharmacology and pharmacogenomics. He is principal investigator and co-investigator on research funded by the National Institute of Diabetes and Digestive and Kidney Diseases. He has published extensively in high-impact scientific journals such as New England Journal of Medicine, Gastroenterology, American Journal of Physiology, Neurogastroenterology and Motility, Gut, and American Journal of Gastroenterology.

Throughout his training and career, Dr. Camilleri has received numerous awards and honors, including the 2012 Ismar Boas Medal from the German Society of Digestive and Metabolic Disease, the 2012 American Gastroenterological Association Distinguished Mentor Award, the Janssen Research Award, the Joseph B. Kirsner Award from the American Gastroenterological Association, and is listed in "Best Doctors in America" for GI and GI motility.

Dr. Camilleri also participates in educational and mentorship activities at Mayo Clinic and has mentored many national and international postdoctoral fellows and scientists. He is a faculty member in the Clinical Research Training Program and has full faculty privileges in Clinical and Translational Science at Mayo Graduate School. Dr. Camilleri maintains an active clinical practice in gastroenterology at Mayo Clinic, specializing in gastroenterology motility disorders, gastroparesis and functional GI disorders.

Dr. Camilleri is currently President of the American Gastroenterological Association Institute. He has served as Chair of the Food and Drug Administration's Gastrointestinal Drugs Advisory Committee and as a member of study sections of National Institutes of Health.

Abstract

The objectives of this presentation are to review:

- Genetic associations with IBS: To extend on Dr. Mauro D'Amato's presentation, examples will be based on genetic association with intermediate phenotypes: immune activation, barrier function and transit
- Genetic causation of "IBS" phenotype with examples of patients with sporadic or familial megacolon, familial watery diarrhea, and unusual presentations of constipation
- Pharmacogenetics and drug metabolism, particularly in relation to central neuromodulators and the role of CYP450 metabolism (CYP2D6, 3A4)
- Pharmacogenetics in IBS treatment with examples on the variation in response to alosetron on colonic transit and symptomatic responses to tegaserod
- Will precision medicine impact public health in FGIDs? A brief discussion of expectations, deliverables, pitfalls and the current state of genomic testing

The conclusions from this discussion are that clinicians need to characterize the phenotype well and check for unusual manifestations that may suggest a genetic component in the disease presentation (e.g. dilated bowel, history from childhood, DPS at young age); unstructured genetic screening has had little impact in GI diseases to date; to check CYP2D6, 3A4 is appropriate when prescribing central neuromodulators and, generally, the impact of precision medicine is still awaited.

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Mucosal Barrier and Permeability

Maria Raffaella Barbaro
Italy

Maria Raffaella Barbaro, PhD
Department of Medical and Surgical Sciences
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Dr. Maria Raffaella Barbaro graduated Summa cum Laude in Biological Sciences in 2008 from the University of Bologna, Italy. She obtained her PhD in Molecular and Cellular Biology in 2012 and she qualified in Clinical Pathology in 2017. During her PhD program, she spent a period in Paris, at the CEA-Saclay, where she focused on electron paramagnetic resonance and reactive oxygen species. Since 2012, she has been working as research fellow in the Laboratory of Gastrointestinal and Functional Exploration at St. Orsola-Malpighi Hospital- University of Bologna with the team of Prof. Stanghellini and Prof. Barbara. Her research interests include functional gastrointestinal diseases, particularly IBS, intestinal permeability, neurogastroenterology and immunity. She is a co-author of papers in high impact journals and among the awards she received, there is a Certificate of Recognition for Young Scientific Accomplishment as an Early Stage Investigator (DDW2015).

Abstract

The intestinal barrier is the most extended interface between the human body and the environment. It is essential for the passage of ions and molecules crucial for body homeostasis and to avoid the translocation of harmful microbial factors. According to the “leaky gut” hypothesis, increased intestinal permeability may enhance the passage of luminal particles (e.g., bacteria, antigens, toxins) through the mucosal layer of the gut leading to the abnormal activation of the immune system which consequently would influence the function of enteric nerves.

Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder, with a prevalence of 10-25% in the general population. Although its pathophysiology is still incompletely known, a role for intestinal barrier has been proposed on the basis of several studies demonstrating enhanced intestinal permeability both in the colon and small bowel of patients with IBS and its implication in symptom development. Tight junctions (TJ) are a multiprotein complex essential for the regulation of paracellular permeability and increasing evidence show alterations in their expression and localization in the colonic mucosa of patients with IBS. In my talk, I will discuss the key findings regarding the role of intestinal barrier in the pathophysiology of IBS.



Intestinal Fungal Dysbiosis Is Associated With Visceral Hypersensitivity in Patients With IBS and Rats

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The Netherlands

Professor at the Dept. of Surgery
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Professor Wouter de Jonge received his doctoral training at University of Utrecht, and Columbia University, and received his Phd in 2001 (Medicine, University of Amsterdam and Maastricht). He took up postdoctoral positions at the AMC in Amsterdam (prof Guy Boeckstaens) and Oxford University (prof Siamon Gordon). He chairs the gastro-intestinal research group (www.gut-research.com) at the AMC since 2013 and holds a part time W2 professorship at the Dept of Surgery at the University of Bonn, Germany.

He is interested in gastrointestinal physiology, nutrition, and the function of neural networks within the gastrointestinal tract, in particular in relation to the mechanisms involved in functional bowel disorders (IBS), and chronic inflammation of the GI tract (IBD, EoE). His research has translational nature and involves basic as well as clinical studies. His work is funded via national Science Foundation grants (NWO-Vidi-STW), EU FP7 and Horizon2020 grants, Marie Curie IEF (Oxford), Health Holland TKI topsector grants, and multiple public private partnership grants. He is currently coordinating a Marie Curie industrial training network (EpiMac; www.epimac.eu) aimed at understanding epigenetic marks that shape differentiation of inflammatory cells. He is working with the Galvani Bioelectronics network consortium since 2014 and currently leading a large-scale project on the development of Bioelectronic medicine for IBD.

He served on the board of the scientific committees a.o. national trust for Gastro Intestinal and Liver Diseases, and is founder of the spin off company Gut-research Services (<http://gut-research-services.com>) aimed to facilitate industry collaborations in the field of gastro intestinal diseases.

Abstract

Activation of nociceptive sensory pathways in IBS has been linked to bacterial dysbiosis, but the mycobiome (i.e. fungal microbiome) was excluded from investigations so far. Recent evidence indicate that immune recognition of intestinal fungi through the resident innate immune system can play a role in inflammatory bowel disease (Leonardi et al, Science 2018; Iliev et al, Nat Rev Immunol 2017). Similarly, we have established earlier that fungal dysbiosis is seen in a cohort of IBS patients and in an animal model for IBS. Using Internal Transcribed Spacer 1 (ITS)-based meta-barcoding, we established altered gut mycobiota in hypersensitive IBS patients compared to normally sensitive healthy individuals. Mycobiome dysbiosis was also observed in the rat model of maternal separation and, in maternally separated rats, blocking fungal recognition via Dectin-1/Syk signaling reversed post-stress visceral hypersensitivity. Treatment of hypersensitive rats with fungicide and fecal transplantation studies further demonstrated a causal association of mycobiome dysbiosis to visceral hypersensitivity. Taken together, these results suggest that host recognition of a dysbiotic intestinal mycobiome is critical to elicit stress-induced visceral hypersensitivity common in IBS (Botschuijver et al. Gastroenterology, 2017).



Volatile Organic Compounds in Feces Associate With Response to Dietary Intervention in Patients With IBS

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**Authors contributed equal parts to this research*

Megan is a Registered Dietitian (RD) with a PhD in gut health from the Faculty of Medicine and Biomedical Sciences at the University of Queensland, Australia. Megan's PhD was recognised for its contribution to science receiving the Dean's Award for excellence.

Megan leads research at King's College London investigating nutrition-based therapies in gastrointestinal (GI) health, including pre- & probiotics, dietary fibres, the low FODMAP diet and food additives. Megan was the recipient of the 2017 British Medical Journal Open Gastroenterology prize 'Best clinical science abstract for oral presentation' and the British Nutrition Foundation 'Drummond Pump Priming Award'. Megan also leads a GI dietetic clinic and is working with food industry to support research translation.

Abstract

Background & Aims: Dietary interventions are effective in management of patients with irritable bowel syndrome (IBS), although responses vary.¹ We investigated whether fecal levels of volatile organic compounds (VOCs) associate with response to dietary interventions in patients with IBS.

Methods: Adults who fulfilled the Rome III criteria for IBS were recruited to a 2x2 factorial

randomized controlled trial². Patients were randomly assigned to a group counselled to follow a diet low in fructans, galacto-oligosaccharides, lactose, fructose, and polyols (low-FODMAP diet, n=46) or a group that received placebo dietary advice (sham diet, n=47) for 4 weeks. Patients from each group were also given either a multi-strain probiotic or placebo supplement. Response was defined as a reduction of 50 points or more on the validated IBS symptom scoring system. Fecal samples were collected from participants at baseline and end of the 4-week study period; VOCs were analyzed by a gas-chromatography sensor device.³ VOC profiles were determined using a pipeline involving wavelet transformation followed by feature selection based on random forest. A partial least squares classifier was constructed to classify VOC profiles by response and accuracies were determined using 10-fold cross-validation.

Results: Data from 93 patients who completed the study (63 female) were used in the final analysis. More patients responded to the low-FODMAP diet (37/46, 80%) than the sham diet (21/47, 45%) ($P<.001$), but there was no difference in response between patients given the probiotic (31/49, 63%) vs the placebo (27/44, 61%) ($P=0.850$), with no interaction between the diet and supplement interventions. At baseline, VOC profiles contained 15 features that classified response to the low-FODMAP diet with a mean accuracy of 97% (95% CI, 96%–99%) and 10 features that classified response to probiotic with a mean accuracy of 89% (95% CI, 86%–92%). End of treatment models achieved similar predictive powers and accuracies.

Conclusion: Faecal VOC profiling is a low cost, non-invasive tool that may help predict response to dietary intervention in IBS patients as well as shedding light on mechanisms underpinning response. Clinical trials using this algorithm are needed, and if successful, will pave the way for personalised treatment plans in IBS.

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Distinct Abnormalities of Small Bowel and Regional Colonic Volumes in Subtypes of IBS Revealed by MRI

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2. Sir Peter Mansfield Imaging Centre, University of Nottingham, United Kingdom.

She graduated from the University of Belfast in 2002 and is a Consultant Gastroenterologist with an interest in nutrition and functional gastrointestinal disorders at Sheffield Teaching Hospitals NHS Foundation Trust (STHFT) since 2017. Ching completed her PhD at the University of Nottingham in 2015, and has published widely in the field of neurogastroenterology. Ching currently leads the nutrition service at STHFT with Professor Mark McAlindon.

Abstract

Irritable bowel syndrome (IBS) is a common condition and its pathophysiology remains to be elucidated. Diagnosis of IBS is purely symptom based owing to the lack of biomarkers available. Therefore, treatment for IBS remains unsatisfactory as this is based on patient's symptoms which can be unreliable. There is a need for objective measures, which should be non-invasive and patient acceptable, to assess the small and large bowel in this group of patients and allow more accurate targeting of treatments.

Recently, the magnetic resonance imaging (MRI) has been used as a non-invasive tool to measure the undisturbed gastrointestinal physiology and its function. There has been some insight into the small and large bowel volumes and motility in IBS patients. In this study, the aim was to use the MRI parameters to distinguish each IBS subtypes. As expected, the IBS patients in this study were predominantly female, significantly more anxious and had more non-gastrointestinal somatic symptoms. The fasting small bowel water content in non-constipation IBS group (IBS-nonC) were significantly less than healthy volunteers (HV). The fasting transverse colon volumes in the IBS constipation group (IBS-C) were significantly larger compared to the healthy control and the non-constipation IBS groups. Also, the average bloating score, based on a visual analogue scale, correlated with the transverse colon volume which was measure approximately 6.5 hours post prandially. The whole gut transit time for IBS-C was prolonged compared to HV and IBS-nonC. In conclusion, this observational study showed some novel insights into the gastrointestinal physiology of IBS. Thus, these findings of the constricted small bowel in IBS-nonC and the dilated transverse colon in IBS-C point toward significant differences in underlying pathophysiology of this disorder.

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Gut Microbiota: What is New

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Laurea summa cum laude in Medicine and Surgery at the University of Bologna, in 1988.

Postgraduate Schools of Internal Medicine and Gastroenterology. From 1990 to 1993 he was a Clinical and Research Fellow at the Gastroenterology and Liver Transplantation Departments of the University of Pittsburgh (USA).

He became Assistant Professor of Internal Medicine at the Catholic University of Rome in 1995 and from 2000 he is Associate Professor of Internal Medicine. He is a teacher at the Postgraduate Schools of Internal Medicine, Gastroenterology and Digestive Endoscopy, Allergology and Immunology at the Catholic University of Rome, Italy.

From 2006 to 2008 he was Secretary General of the Italian Association for the Study of the Liver (AISF) and currently he is the President of the Italian Foundation for Research in Hepatology (FIRE). He is member of several National (Italian Society of Internal Medicine-SIMI, Italian Society of Gastroenterology-SIGE, Italian Association Study of Liver Diseases-AISF) and International (American Association Study of Liver Diseases-AASLD; European Association Study of the Liver-EASL, European Helicobacter Study Group-EHSG) Scientific Societies.

In 2008-2009 he was National Coordinator of the Gut Microbiota Study Group of the Italian Society of Gastroenterology.

He is coordinator of the HCC program and of the Liver Transplant program at the Gemelli Hospital-Catholic University of Rome.

He is referee and in the editorial board of several National and International Scientific Journals and chief editor of the European Review of Medical and Pharmacological Science.

His fields of interests are: gut microbiota in physiological and pathological conditions, helicobacter pylori-associated diseases and diagnosis and treatment, pathophysiology, diagnosis and treatment of liver diseases and hepatocellular carcinoma, functional and organic gastrointestinal diseases (IBS, IBD, celiac diseases).

He has been invited for lectures to more than 240 national and international Universities and Institutions. Author of more than 800 papers: 460 of which as full papers on indexed International Scientific Journals. He was co-author of more than 1200 abstracts presented at National and International Meetings.

He has an impact factor for his publications over 1100 and an H-index over 55.

Abstract

New insights on human gut microbiota have recently made a breakthrough in many concepts of modern medicine. Most of these new data have been collected because of the advancement in our diagnostic tools: the development of next generation sequencing techniques allowed analyzing gut microbiota without the limitations of classic culture methods. Furthermore, introduction of functional techniques such as metabolomics and proteomics allowed for integrated analysis thus obtaining more robust data.

Among them, we know that the so-called dysbiosis, which means a loss of the balance and homeostasis of gut microbiota, is associated with an ever expanding list of diseases and conditions.

Moreover Increasing evidence suggests that response to immune checkpoint inhibitors, a novel treatment for advanced epithelial tumors (e.g. non-small cell lung cancer, melanoma, renal cell carcinoma), can be influenced by the composition of patients' gut microbiota.

Finally, the most interesting news on gut microbiota rely into its therapeutic modulation through selected antibiotics with eubiotic effects, probiotics and with fecal microbiota transplantation.



The Microbiota Gut Brain Axis in the IBS

Stephen Collins
Canada

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Dr. Stephen M. Collins obtained his medical training at University College, London UK and his gastroenterology training at McMaster University, Canada before completing 3 years of research training in cell biology at the Digestive Diseases Branch at NIH. He has been a staff gastroenterologist at McMaster University since 1981 and Director of the Intestinal Diseases Research Unit from 1983-1993, and Head of the Division of Gastroenterology since 1993-2006. He is past president of the Canadian Association of Gastroenterology. His current research focuses on the roles of microbes in the initiation and maintenance of functional gastrointestinal disorders. He is currently Director of the Farncombe Research Institute and Associate Dean for Research at McMaster University.

Abstract

The microbiota-gut-brain (MGB) axis is now well established on the basis of murine and human studies. While compositional and functional changes in the microbiota have been described in subgroups of IBS patients, the significance of these findings is unclear. Thus, the extent to which the MGB axis is involved in the expression of intestinal and behavioral manifestations of IBS is the subject of ongoing research. Colonization of axenic mice with fecal microbiota from symptomatic IBS-D patients, but not healthy controls, alters gut and brain function in recipient mice. Specifically, mice colonized by IBS-D microbiota exhibit accelerated gut transit and alterations in epithelial function. Mice colonized with microbiota only from IBS-D patients with co-morbid anxiety displayed anxiety like behavior. These mice also exhibited evidence of innate immune activation. Our ongoing work investigates the nature of innate immune activation induced by the microbiota from IBS-D patients. Taken together, these findings suggest a role for the microbiota-gut-brain axis in at least a subgroup of IBS patients.

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IBS / Tropical Sprue Overlap

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MD (Internal Medicine PGIMER, Chandigarh, 1991)

DNB (National Board of Examination, New Delhi, 1992)

DM (Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sc. Lucknow, 1995)

FACG (American College of Gastroenterology, 2007)

Fellow, Rome Foundation

Fellow of National Academy of Medical Science, India

Personal profile

- Professor, Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India
- Medical Teacher with an experience of teaching post-graduate level (DM, PhD) students for more than 27 years
- Medical Researcher with 27 years of research experience with more than 264 publications
- Adjunct Professor, Centre for Biomedical Research, SGPGI Campus, Lucknow, India
- Administrator in the following administrative positions currently
 - Founder Member of the Indian Motility and Functional Diseases Association and the past Secretary General, Asian Neurogastroenterology & Motility Association (www.asianmotility.org)
 - Member of Rome Foundation (www.romecriteria.org)
 - Involved in several committees of the Rome Foundation such as international liaison committee (Chair), Research Committee (Chair), post-infectious FGID committee, Rome Asian working team, Executive Committee Member of Rome Global Epidemiological Study etc.
 - Involved in Medical Education through SPREAD (www.spreadhealth.in)

Editorial experience & capabilities

- Previously, Associate Editor (Luminal Gastroenterology); currently, Editor-in-Chief, Indian J Gastroenterol
- Associate Editor, J Neurogastroenterology Motility since 2010
- Senior Editor, J Digestive Endoscopy (Luminal Endoscopy section)
- Associate Editor, Digestive Diseases (Karger, Nutrition and Probiotics)
- Member of Advisory Board of Nature Review Gastroenterology and Hepatology
- Editorial Board Member, World J Gastroenterol, J Gastroenterol Hepatol

Achievements & Awards

- Chair of Epidemiology and Infection section of Asian IBS Consensus and Asian Dyspepsia Consensus Teams
- 34 awards
- Visiting Clinician, Mayo Clinic, Scottsdale, USA 2005 (November 2005)
- Visiting Consultant, Hamad Medical Corporation, Doha, Qatar
- Fellow of World Health Organization at Prince of Songkhla University, Hat Yai, Thailand (2009) for Biostatistics and Epidemiology training
- Delivered invited lectures more than 100 times in different countries such as USA, Japan, South Korea, China, Malaysia, Thailand, Philippines, Bangladesh, Vietnam, Italy, France, Singapore, Myanmar, Hong Kong, Qatar, Taiwan etc. Delivered at least 200 invited lectures in different parts of India
- Published more than 263 research papers, mostly in international journals (for details, log on to www.pubmed.gov and search "Ghoshal UC") with impact point of 908.5, RG Score 44.47 (research gate; https://www.researchgate.net/profile/Uday_Ghoshal2)

Abstract

Evidence is emerging that IBS, a hitherto enigmatic disorder thought to be predominantly related to psychological factors, has a microorganic basis in a subset of patients with the disease. Post-infectious IBS (PI IBS), commonly of the diarrhoea-predominant or mixed subtypes (defined as new development of IBS following acute infectious diarrhoea), is one such condition known to occur in up to 10–30% individuals after acute gastroenteritis. However, following acute infectious gastroenteritis, patients can also develop post-infectious malabsorption syndrome (PI MAS), popularly known as tropical sprue. As there is hardly any study on PI IBS that has rigorously excluded tropical sprue by appropriate investigations including small intestinal biopsy, the frequency of tropical sprue among patients with PI IBS is not much known. In a recent study from Bangladesh, PI-MAS, diagnosed by abnormal results in at least two of the three tests (D-xylose, fecal fat, duodenal biopsy), was present in 9% with PI-IBS. PI-IBS and PI-malabsorption have similar etiological agents and pathophysiological mechanisms. Small intestinal bacterial overgrowth (SIBO) has been suggested to be associated with IBS in general, and in particular diarrhoea-predominant IBS, including PI IBS. SIBO is also known to be associated with tropical sprue. As both IBS, particularly the subset probably associated with SIBO, and tropical sprue

improve with antibiotic treatment, these disorders might be linked. More studies are needed on this issue.

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Neuro-Immune Interactions: Clinical and Therapeutic Perspectives

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Prof. Boeckxstaens obtained his medical degree in 1987 and his PhD degree in 1991. In 1994, he completed his clinical training in Internal Medicine / Gastroenterology and accepted a staff position in the Department of Gastroenterology & Hepatology at the Academic Medical Center in Amsterdam, The Netherlands. In 2005, he became Professor of Neurogastroenterology at the Academic Medical Center and was appointed co-chair of the department of Gastroenterology and head of the gastrointestinal research. In 2007, he accepted a full professorship in Medicine at the University of Leuven (Belgium) in the department of Gastroenterology. He received several national and international prizes and received the prestigious European Research Council (ERC) Advanced Grant in 2014. He was Secretary and President of the Dutch Society of Neurogastroenterology. Currently, he is Associate Editor of Gut, member of the Editorial Board of Neurogastroenterology and Board Member of the Research Council of the University of Leuven, Belgium. He served as chair of the Rome IV committee on Fundamentals of Neurogastroenterology-Physiology Motility & Sensation. He has published over 300 peer-reviewed manuscripts and has an H-index of 50. The scientific expertise of the research group of Prof. Boeckxstaens relates to neurogastroenterology and neuro-immune interactions in the gastrointestinal tract. The mechanisms leading to diseases such as achalasia, gastroesophageal reflux disease, irritable bowel disease, chronic constipation, functional dyspepsia and postoperative ileus have been the main topics of interest over the past 20 years.

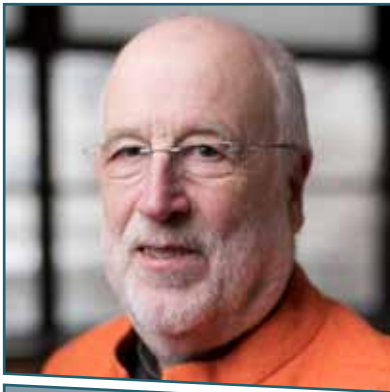
Abstract

The irritable bowel syndrome (IBS) is a complex functional disorder mainly if not solely diagnosed based on symptoms, as defined by the Rome IV criteria. As the vocabulary of the intestine to express discomfort or dysfunction is limited, IBS is a collection of disorders with a similar phenotype but with a variety of underlying pathophysiological mechanisms. One of the mechanisms that has gained a lot of interest lately is that of neuro-immune interaction. This hypothesis is mainly based on 1. histological studies showing increased inflammatory cells, including mainly T cells and mast cells, in colorectal and intestinal biopsies of IBS patients, and 2. on studies indicating upregulation of pro-inflammatory genes in biopsies or increased release of pro-inflammatory cytokines by IBS biopsies or peripheral blood. Although these data are somewhat inconsistent, a constant finding is that the supernatant of IBS biopsies contains biologically active mediators activating and sensitizing afferent nerves. These mediators are most likely released by enterocytes, T cells, macrophages and/or mast cells. The most intriguing question to be answered however is which triggers eventually lead to the activation of these cells. Stress, the microbiome and food components are proposed as main candidates. Of interest, evidence has been reported that food ingestion can trigger an immune reaction in the intestinal mucosa, while the microbiome (including fungi) can affect the intestinal immune system either direct or indirect via interaction with food or the luminal content. Identification of the triggers involved and mediators released clearly is of crucial importance to improve the clinical management of IBS patients. This should guide the clinician to either install dietary measures to eliminate certain food components or to select antagonists blocking the pro-nociceptive effect of the mediators released. Examples that already have reached the clinical arena are a diet low in FODMAPs and the use of histamine 1 receptor antagonists, but hopefully, many more will be identified soon.

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The Biopsychosocial Model of FGDs

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Abstract

While it generally accepted that gastrointestinal infections can cause functional disturbances in the upper and lower gastrointestinal tract – known as post-infectious irritable bowel syndrome (PI-IBS) and functional dyspepsia (PI-FD) – it has still not been widely recognized that such an infection can also initiate functional non-intestinal diseases, and that non-intestinal infections can provoke both intestinal and non-intestinal functional disturbances. A review of the respective literature and own data (1) allow to argue that medically unexplained functional symptoms and syndromes following an infection may have a biological (genetic, endocrine, microbiological) origin, and that psychological and social factors, which may contribute to the disease “phenotype” are secondary to this biological cause. If this holds true, then the search for psychological and social theories and factors to explain why one patient develops a chronic functional disorder while another does not is – at least for post-infectious states – misleading

and distracts from exploring and identifying the true origins of these essentially biological disorders. The biopsychosocial model may, as the term implies, always begin with biology, also for functional (somatoform) disorders.

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IBS, Dietary Factors and Gut Microbiome: The Non-Celiac Gluten Sensitivity Paradigm

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Advancing innovation in research, clinical care and education, Alessio Fasano, MD, has dedicated his life to improving the quality of life for people with celiac disease and other gluten-related disorders. He founded the Center for Celiac Research at the University of Maryland School of Medicine in 1996 and moved the Center to Massachusetts General Hospital (MGH) in Boston, Massachusetts, USA, in 2013, where he serves as chief of the Division of Pediatric Gastroenterology and Nutrition and professor of pediatrics at Harvard Medical School.

At MGH, Dr. Fasano oversees a clinical team that treats children and adults for celiac disease and issues related to gluten. As director of the Mucosal Immunology and Biology Research Center at MGH, he runs a research program with approximately 45 scientists and staff researching basic and translational science in cystic fibrosis, celiac disease, shigella vaccine, necrotizing enterocolitis, autism spectrum disorder and other topics.

In the 1990s, Dr. Fasano developed the anti-tissue transglutaminase (tTG) test, which is used extensively in initial blood screening for celiac disease. In 2000, he and his team discovered zonulin, a molecule which regulates the “tight junctions” between intestinal epithelial cells. Subsequent research by Dr. Fasano and others have linked the role of zonulin and intestinal permeability to a number of diseases including celiac disease and type 1 diabetes.

In keeping with his scientific and clinical accomplishments, Dr. Fasano is a highly prolific author in both peer-reviewed publications and general readership. As an international celiac expert, he appears regularly in diverse international and national media outlets such as the BBC, The New York Times, The Globe and Mail, RAIT, Good Housekeeping, Allergic Living and NPR. He is author of *Gluten Freedom*, which provides factual information along with lifestyle advice on matters related to gluten and health and disease, which is also published in Italian, French, German, Portuguese, Czech, and Polish with all proceeds going to celiac research.

Abstract

Improved hygiene leading to a reduced exposure to microorganisms have been implicated as one possible cause for the 'epidemic' of immune-mediated diseases, particularly non-infective chronic inflammatory diseases (CID), in industrialized countries during the past 3-4 decades now affecting millions of individuals. The social and financial burdens imposed by these chronic, debilitating diseases include poor quality of life, high health care costs, and substantial loss of productivity. That is the essence of the hygiene hypothesis that argues that rising incidence of these pathologies may be, at least in part, the result of lifestyle and environmental changes that have made us too "clean" for our own good. Interestingly, increase hygiene in some developing countries did not lead to an increase in CID as seen in industrializing countries, casting some doubts on the validity of the hygiene hypothesis.

Apart from genetic makeup and exposure to environmental triggers, three more elements have been recently identified being key players in the pathogenesis of CID. A third element is the inappropriate Increase in intestinal permeability, which may be influenced by the composition of the gut microbiota, has been proposed in the pathogenesis of these diseases. Intestinal permeability, together with antigen (Ag) sampling by enterocytes and luminal dendritic cells, regulates molecular trafficking between the intestinal lumen and the submucosa, leading to either tolerance or immunity to non-self Ag. This tolerance-immune response balance is influenced by the function of the immune system (both innate and adaptive immune response) as a forth element involved in the pathogenesis of CID. Finally, the composition of gut microbiome and its epigenetic influence on the host genomic expression has been identified as a fifth element in causing CID. The gut microbiome consists of more than 100 trillion microorganisms, most of which are bacteria. It has been just recently recognized that there is a close bidirectional interaction between gut microbiome and our immune system and this cross talk, particularly during infancy, is highly influential in shaping the host gut immune system function and, ultimately, the tolerance/immune response balance.

This observation led to a revisitation of the possible causes of CID epidemics. With the appreciation that the gut microbiome plays a decisive role in either generating (mucosal) tolerance or leading the way to the development of inflammatory conditions, alternative hypothesis have been formulated. There is growing evidence that many CID are characterized by a change in microbiome composition. While factors such as modality of deliver, neonatal feeding regimens, use of antibiotics, infections can influence microbiota composition, diet is by far the most important variable affecting gut ecosystem. Therefore, re-shaping gut microbiota through dietary manipulation is becoming an extremely active area of research for the prevention or treatment of a multitude of CID. Non-celiac gluten sensitivity will be discussed as a clinical example of this new paradigm.



IBS, Dietary Factors and Gut Microbiome: The Non-Celiac Gluten Sensitivity Paradigm

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Professor Spiller is Professor of Gastroenterology in the Nottingham Digestive Diseases Biomedical Research Unit at the University of Nottingham. Past Editor of Gut (2003-2009) and member of the Board of the Rome Foundation (2000-2015), he twice edited the British Society of Gastroenterology (BSG) Guidelines for the management of IBS. His main research interest is the pathophysiology of irritable bowel syndrome (IBS), particularly the role of infection, inflammation, diet and alterations in the microbiome as well as a long standing collaboration with the Sir Peter Mansfield Imaging Centre pioneering the use of MRI to image the underlying mechanisms in functional bowel diseases. Author/co-author of more than 362 scientific reviews and original publications. Current funding includes £2.2M EME grant for a multicentre trial of ondansetron in IBS with diarrhoea, £1.6M MRC grant studying colonic motility using MRI and High resolution manometry and £800K Newton grant examining the effect of fibre on intestinal physiology in IBS. Our group has also performed many investigator initiated research projects with industry including Norgine, Dr Falk, Ironwood and most recently Zespri.

Abstract

Exclusion diets have identified a range of foods which precipitate symptoms in IBS patients including particularly wheat, onions and dairy products 1. The FODMAP concept attempts to link symptoms to colonic fermentation of poorly absorbed mono-di and oligo-saccharides. The small osmotically active components have been shown to cause considerable inflows of water into the small bowel and subsequently the ascending colon. Longer polymers, such as inulin cause little osmotic disturbance in the small bowel but are delivered intact into the colon where they are fermented often producing large volumes of gas. The normal colon can accommodate this without symptoms while IBS patients experience bloating and distension despite similar amounts of gas 2. Work with lactose in subjects with adult acquired hypolactasia show that lactose ingestion increases visceral sensitivity possibly by distending the gut 3. Impact of low FODMAP diet includes substantial fall in total microbiota and gas production 4 but the precise mode of action remains unclear. Predicting who will respond is difficult but in children there is a suggestion that responders have a microbiota which is enriched with species with greater saccharolytic capacity and higher faecal levels of enzymes which break down wheat starch 5.

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Probiotics

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Cesare Cremon graduated Summa cum Laude in Medicine at the University of Bologna, Italy. He subsequently qualified in Internal Medicine at the same University. Currently he is involved in clinical gastroenterology diagnostic and therapeutic endoscopy, teaching and research at the Bologna University Hospital Authority St. Orsola-Malpighi Polyclinic.

Cesare Cremon's main research interest related to basic and clinical aspects of functional gastrointestinal disorders, neurogastroenterology, gut microbiota, and diverticular disease. He has authored more than 60 indexed peer-reviewed articles and reviews on these topics (with a global Impact Factor of about 430 points; h-index Scopus = 30), published in various biomedical journals, including Gastroenterology, Gut, American Journal of Gastroenterology, and Alimentary Pharmacology and Therapeutics. He is, or has been, referee for several biomedical journals, including Gut, Nature Review Gastroenterology and Hepatology, Alimentary Pharmacology and Therapeutics, Inflammatory Bowel Diseases, Neurogastroenterology and Motility, and Digestive and Liver Disease. He is a member of the following society: Società Medico-Chirurgica di Bologna, Italian Society of Gastroenterology (SIGE), and Italian Group for the Study of Gastrointestinal Motility (GISMAD). Cesare Cremon has received national and international awards including the best communication of 10th and 13th Italian Congress GISMAD (2002 - 2008), and the poster of distinction at DDW 2013.

Abstract

Probiotics are defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host". Probiotics may prevent the overgrowth of pathogenic bacteria, increase the resistance of the gut to invasion by pathogens, strengthen epithelial barrier function, or ameliorate disease processes by inducing the secretion of soluble factors.

However, the exact mechanism of action by which probiotics exert their beneficial actions in humans is only partially known, because these aspects have been evaluated mainly in preclinical studies or in small sample size trials.

Systematic reviews of the literature and meta-analyses indicate that probiotics, as a class, have a small but significant therapeutic effect on IBS symptoms. However, the quality of probiotic trials in IBS and their sample sizes remain suboptimal. The great variety of species, strains, and doses of probiotics tested in clinical trials make it difficult to provide generalizable advice about the optimal probiotic strategy in IBS. Interestingly, a recent systematic review based on Delphi consensus indicates that specific probiotics help to reduce overall symptoms and abdominal pain in some patients with IBS. Similarly, the World Gastroenterology Organisation Global Guidelines on probiotics and prebiotics suggest that some probiotic strains may ameliorate pain and provide global relief with a consistent reduction in abdominal bloating and flatulence in patients with IBS.

Recently, we have evaluated the in vitro effect of the probiotic *Escherichia coli* Nissle 1917 on permeability alterations induced by mediators released by IBS mucosal biopsies. This strain reinforces the integrity of epithelial monolayer and reverts the increase of permeability induced by IBS mucosal biopsy mediators, suggesting a potential role of this probiotic in the treatment of IBS. In addition, we have performed a randomized, double-blind, placebo-controlled, cross-over pilot study to assess the efficacy and mechanism of action of *Lactobacillus paracasei* CNCM I-1572 in patients with IBS. This probiotic improves IBS symptoms, although not in a statistically significant manner, through modulation of the gut microbiota, its metabolic pathways, and proinflammatory cytokines. Additional good-quality randomised clinical trials are required to assess the role of probiotics in the management of patients with IBS.



Kiwifruit for IBS-C: Effect on Symptoms and Microbiota

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Juliet joined Zespri in July 2014 as an Innovation Leader, Health & Nutrition overseeing the scientific research that supports health communications in the global markets. Prior to this, Juliet was an academic research scientist for 20 years (including her PhD thesis research) and has a BSc from Kings College London and a doctorate from Oxford University, both in human parasitology. Juliet has lived and worked in the UK, Africa, Australia and New Zealand studying parasites and latterly human health and nutrition. During her 9 years at Plant & Food Research NZ, she led major research programmes with government and industry support involving in vitro, in vivo and human clinical trial work. The research focussed on interactions between micro- and macronutrients, their digestion, absorption, and fermentation through the gut and the downstream effects of foods and their metabolites on human health throughout the body.

Abstract

Three separate randomized, controlled, single-blind clinical trials were performed in New Zealand, Italy, and Japan to assess the effect of green kiwifruit on digestive comfort. Each study was powered individually but used the same protocol comprising three cohorts: 20 healthy controls, 20 with functional constipation (FC) and 20 with irritable bowel syndrome with constipation (IBS-C), according to Rome III criteria. The study duration was 16 weeks; 2-week lead in, 4-week first intervention, 4-week washout, 4-week second intervention, and final 2-week follow-up. The cross-over design was completed using kiwifruit intervention (2 green kiwifruit per day [Actinidia deliciosa var. Hayward]), compared to a positive control intervention of psyllium (7.5g of psyllium per day). The primary outcome measure was quantification of

complete spontaneous bowel movements (CSBM). Secondary outcome measures included the Gastrointestinal Symptom Rating Scale (GSRS, not presented), the IBS-QoL questionnaire, stool consistency (Bristol Stool Scale), together with objective measures of gastrointestinal transit times. Faecal samples were also collected for DNA extraction and microbiota ecology analysis was evaluated using 16S RNA technology.

Results

A total of (178) participants were analysed under ITT protocol (n= 61 healthy, n= 57 FC and n = 60 IBS-C). Consumption of green kiwifruit significantly increased the primary outcome measure of CSBM by 2.1/ week for the combined constipated groups compared to an increase of 0.92 / week with psyllium. Repeated measures analysis showed that kiwifruit treatment was significant ($p < 0.001$) after 1 week of daily consumption and remained significant for the duration of treatment. The green kiwifruit intervention also resulted in significant improvements in digestive comfort, and quality of life scores. Both primary and secondary outcome measures returned to baseline once treatment with kiwifruit ceased. Microbiota analysis from Italian and New Zealand cohorts have been analysed and demonstrated some beneficial changes to phylogenetic abundance following the kiwifruit intervention.

Conclusions

Results suggest non-inferiority of kiwifruit compared with psyllium and therefore support first line empiric treatment with fibre should consider the use of kiwifruit as an appealing and efficacious alternative.



Clinical Effect of a Probiotic Mixture on Gut-Specific Anxiety and HR QoL

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Dr. Jordi Serra, born in Barcelona, Spain, 1959, completed the Medical school at the Autonomous University of Barcelona 1984. Specialist in Gastroenterology and Hepatology 1993 by the Swedish medicine board after training at the Uppsala University Hospital. Doctoral Thesis (Ph. D.) 1998 at the Autonomous University of Barcelona, Spain. Associate investigator at University Hospital Vall d'Hebron, Barcelona, until 2008. From January 2009 Head of the Motility and Functional Gut Disorders Unit at University Hospital Germans Trias I Pujol, Badalona, Spain. Dr. Serra is also a Researcher of the Spanish Center of research CIBERehd and Member of the Steering Committee of the European Society of Neurogastroenterology and Motility. Main areas of research are the functional gut disorders, with special focus on the role of sensory/motor disorders and intestinal gas in the development of abdominal symptoms.

Abstract

The effect of a new probiotic combination I.31 (*Lactobacillus plantarum* CECT7484 and CECT7485 and *Pediococcus acidilactici* (CECT7483) on IBSQOL and Visceral Sensitivity Index (VSI) was assessed in a multicenter, randomized, double-blind, placebo-controlled intervention clinical trial with three parallel arms. 84 patients (53 female, 31 male; age range 20-70 years) with IBS and diarrhoea according to Rome-III criteria were randomly allocated to receive one capsule a day for 6 weeks containing: a) I.31 high dose (n=28); b) I.31 low dose (n=27); c) placebo (n=29).

During treatment, IBSQoL increased in all groups, but this increment was significantly larger in patients treated with I.31 than in those receiving placebo ($p=0.008$). After 6 weeks of treatment, IBSQoL increased by 18 ± 3 and 22 ± 4 points in the high and the low dose groups, respectively ($p=0.041$ and $p=0.023$ vs placebo), but only 9 ± 3 in the placebo group. Gut-specific anxiety, as measured with VSI, also showed a significantly greater improvement after 6 weeks of treatment

in patients treated with probiotics (by 10 ± 2 and 14 ± 2 points, high and low dose respectively, $p < 0.05$ for both vs 7 ± 1 score increment in placebo). No adverse drug reactions were reported following the consumption of probiotic or placebo capsules.

In conclusion, the probiotic combination I.31 is superior to placebo in improving IBS-related quality of life and gut-specific anxiety in patients with IBS and diarrhea.

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Diagnosis and Management of Bile Acid Diarrhea

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Professor Julian Walters MA, MB, DSc, FRCP is based at Imperial College London, where he is Professor of Gastroenterology. An active clinician, researcher and teacher, he has focussed on the role of bile acids in diarrhoea. He has published papers on increasing recognition of bile acid malabsorption, overproduction and diarrhoea, diagnostic rates and effective treatment. Regulation of bile acid production by the ileal hormone FGF19, and response to FXR agonists are key aspects of current research.

Abstract

Bile acid diarrhoea (BAD) occurs when increased amounts of bile acids are present in the colon. Bile acids stimulate electrolyte and water secretion and increase motility. The increase in bile acids can be secondary to bile acid malabsorption, such as that following ileal resection in Crohn's disease. Recognition in these patients of the disorder and appropriate treatment can give great symptomatic improvement. Bile acid diarrhoea is also found after cholecystectomy.

The primary, idiopathic form of BAD occurs when there is no apparent structural cause. This is very common in patients diagnosed with diarrhoea-predominant IBS or functional diarrhoea, and is linked to overproduction of bile acids and reduced feedback inhibition. There is a lack of recognition of the disorder and patients report considerable delay before being diagnosed.

Several diagnostic approaches have been tried. Measurement of faecal total bile acids is not easy for the patient or the laboratory, requiring a defined diet and collection over at least 48h. Biomarkers measured in blood include 7 α -hydroxy-4-cholestenone (a bile acid precursor) and FGF19 (which regulates new bile acid synthesis). These are not widely available and values can vary during the day and with food intake.

The SeHCAT test uses a radiolabelled bile acid (75Se-tauroselcholic acid) to measure whole body bile acid retention (and hence faecal loss) by gamma-camera scanning 7 days apart. This measures bile acid loss over multiple cycles of secretion and reabsorption. Seven day retention >20% is normal, 5-10% representing moderate disease and <5% severe disease. Response to specific treatment is more likely with lower values. Systematic reviews show that over 25% of patients with diarrhoea who have these tests are positive, giving a population prevalence in excess of 1%.

Management of BAD is currently based on treatment with various bile acid sequestrants such as colestyramine or colesevelam. These bind bile acids in the intestine and help stool frequency and form. They are not always well-tolerated and can cause abdominal discomfort and bloating. Limiting fat intake may help by reducing bile acid secretion. FXR agonists, such as obeticholic acid, can stimulate FGF19 to reduce bile acid production but they need to be shown to be cost-effective.

As the response to treatment can be variable, it is important to have made a definitive diagnosis of BAD. Currently, the SeHCAT test enables a clear diagnosis to be made, which provides reassurance, as well as indicating the likelihood of therapeutic success. The large proportion of IBS patients who in fact have BAD need to be diagnosed and offered appropriate treatment.

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Microbiota-directed Therapies in the Management of IBS

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Professor Scarpignato's main research interests focus on digestive clinical pharmacology, gastrointestinal motility, and upper GI pathophysiology. He has authored 580 publications (of which 350 are full papers or book chapters) on these topics and has also edited 28 books on clinical evaluation of GI function and on Pharmacology & Therapeutics of Digestive Diseases. He is or has been on the editorial boards of Pharmacology, Gut, Digestion, Digestive Diseases, Current Gastroenterology Reports, Alimentary Pharmacology & Therapeutics, BMC Gastroenterology, BMC Medicine, World Journal of Gastroenterology, American Journal of Pharmacology & Therapeutics, Therapeutic Advances in Drug Safety and Current Clinical Pharmacology, amongst others. He is also a Section Editor (GI and Liver Pharmacology) of Fundamental and Clinical Pharmacology and of Gastroenterology International, and has been co-Editor of two prestigious book series, Frontiers of Gastrointestinal Research and Progress in Basic and Clinical Pharmacology.

Professor Scarpignato is a Fellow of the Royal College of Physicians (London), The American College of Physicians, the American College of Clinical Pharmacology, the American College of Gastroenterology and of the American Gastroenterological Association. In addition, he is a member of several national and international scientific societies, including the British Pharmacological Society and the American Society for Pharmacology and Experimental

Therapeutics (ASFET). He is presently the Secretary General of the World Organization for Specialized Studies on Diseases of the Esophagus (OESO) and Governor for Italy of the American College of Gastroenterology (ACG). His biography has been included into the 2009-2010 Edition of Who's Who in Medicine and Healthcare.

Abstract

The advent of omics techniques has allowed to gain new insights into the microbiota role in health and human disease. As a consequence, much efforts have been directed to the prevention and treatment of gastrointestinal (GI) and extra-GI diseases through its modulation. Strong evidence now supports the role of bacterial, viral and parasitic infections in triggering IBS, and - despite data are limited and not always consistent - it is evident that IBS patients have an altered fecal and colonic microbiota compared to healthy individuals [1]. Small intestinal bacteria might also play a role, with SIBO (small intestinal bacterial overgrowth) being variably associated with IBS [2].

Given the importance of microbiota in the pathophysiology of IBS [3] and in symptom generation of some patients [3, 4], manipulation of intestinal microecology through the use of antibiotics and probiotics has been attempted over the last decade. The best-studied antibiotic in IBS is rifaximin, a poorly absorbed, gut-specific agent, which does not share with systemic antimicrobials the detrimental effects on gut microbiota [5] but actually displays eubiotic [6, 7] and anti-inflammatory [7] properties. Its efficacy in SIBO eradication is well documented [8] and its benefits on symptom relief over placebo in patients with IBS well studied in both short- (TARGET 1 and TARGET 2) and long-term (TARGET 3) trials [9]. However, to prevent antibiotic misuse, a specific predictor of the response to rifaximin treatment is needed. Breath testing for SIBO could represent a mean to enrich rifaximin responders amongst IBS patients [10]. By using SIBO as a biomarker of IBS, the therapeutic gain of rifaximin over placebo, reported by the TARGET trials, may well be extended to reach a clinically significant figure. And indeed, in a recent meta-analysis [8], improvement or resolution of symptoms with rifaximin in patients with eradicated SIBO was found to be 67.7% (95% CIs: 44.7-86.9).

Given their generally safe profile, probiotics appear to be attractive as potential manipulators of the gut flora in IBS. Despite difficulties in the interpretation of clinical trials with probiotic formulations, a 2014 meta-analysis by the American College of Gastroenterology Task Force on the Management of Functional Bowel Disorders [11] found a benefit with probiotics when considered as a whole, a finding confirmed by a recent systematic review [12]. However, evidence does not support the use of an individual probiotic species [11, 12]. Studies with specific strains indicate that although some probiotics may ameliorate individual IBS symptoms, few have a global benefit. Therefore, the idea of universal probiotics for IBS is not evidence-based.

In conclusion, recent pharmacological approaches targeting enteric bacteria (with poorly absorbed antibiotics, like rifaximin, or probiotics) and/or intestinal inflammation (with rifaximin) have shown to be capable of controlling IBS symptoms. Well-designed RCTs, enrolling adequately selected, homogeneous populations of patients, are however needed. The future of management of many functional GI disorders, including IBS, will likely rely on the so-called “microbiota-directed therapies”.

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Management of Abdominal Pain

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Professor Tack's scientific interest focuses on neurogastroenterology and motility, and includes diverse topics such as the pathophysiology and management of gastrointestinal functional and motor disorders, the physiology and pharmacology of the enteric nervous system, gastrointestinal hormones and the control of satiation and food intake. He has published more than 580 articles and 40 book chapters on various aspects of scientific and clinical gastroenterology.

Abstract

Functional abdominal pain in the context of irritable bowel syndrome (IBS) is a challenging problem for primary care physicians, gastroenterologists and pain specialists. The evidence for the current and future non-pharmacological and pharmacological treatment options targeting the central nervous system and the gastrointestinal tract to manage pain in IBS will be reviewed. The evidence for fiber is limited and only isphagula may be somewhat beneficial. A diet low in fermentable carbohydrates and polyols (FODMAP) seems effective in subgroups of patients to reduce abdominal pain, bloating and improve the stool pattern. The efficacy

of probiotics is difficult to interpret since several strains in different quantities have been used across studies. Antispasmodics, including peppermint oil, are still considered the first-line treatment for abdominal pain in IBS. Second-line therapies for diarrhea-predominant IBS include the non-absorbable antibiotic rifaximin and the 5HT3 antagonists alosetron and ramosetron, although the use of the former is restricted because of the rare risk of ischemic colitis. In laxative-resistant, constipation-predominant IBS, the chloride-secretion stimulating drugs lubiprostone and especially the guanylate cyclase C agonists plecanatide and linaclotide which may exert direct analgesic effects, reduce abdominal pain and improve the stool pattern. In patients refractory to gut directed therapy, tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitors (SSRI) are both effective to obtain symptomatic relief, but only TCA's have been shown to improve abdominal pain in meta-analyses. Cognitive interventions such as cognitive behavioral therapy and hypnotherapy have demonstrated excellent results in IBS patients, but the limited availability and labor-intensive nature limit their routine use in daily practice. Based on data in chronic somatic pain, serotonin noradrenaline reuptake inhibitors (SNRIs), tetracyclic antidepressants, azapirones, atypical antipsychotics and delta ligand agents may also be effective. Many of these agents, as well as psychological therapies, can be used in "augmentation" therapy, to further increase the efficacy of first line modulators like TCAs and SSRIs.

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New Therapeutic Perspectives

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Dr. Camilleri's research interests include clinical enteric neurosciences, gut neurohormonal control, obesity, irritable bowel syndrome, and pharmacology and pharmacogenomics. He is principal investigator and co-investigator on research funded by the National Institute of Diabetes and Digestive and Kidney Diseases. He has published extensively in high-impact scientific journals such as New England Journal of Medicine, Gastroenterology, American Journal of Physiology, Neurogastroenterology and Motility, Gut, and American Journal of Gastroenterology.

Throughout his training and career, Dr. Camilleri has received numerous awards and honors, including the 2012 Ismar Boas Medal from the German Society of Digestive and Metabolic Disease, the 2012 American Gastroenterological Association Distinguished Mentor Award, the Janssen Research Award, the Joseph B. Kirsner Award from the American Gastroenterological Association, and is listed in "Best Doctors in America" for GI and GI motility.

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Dr. Camilleri is currently President of the American Gastroenterological Association Institute. He has served as Chair of the Food and Drug Administration's Gastrointestinal Drugs Advisory Committee and as a member of study sections of National Institutes of Health.

Abstract

The objectives of this presentation are to review new therapeutics in lower functional GI disorders:

- a. Diet (gluten withdrawal, low FODMAP diet and the role of fecal microbial transplantation)
- b. New drugs for constipation (including the guanylate cyclase C agonists, ileal bile acid transporter inhibitor, and FGF19 analog)
- c. New drugs for diarrhea (including brief comments on combination opioid agent, non-absorbable antibiotic, bile acid sequestrants – all covered by other speakers in this session)
- d. Central neuromodulators (specifically antidepressants)
- e. A look to the future with novel peripherally active analgesics that avoid central opioid effects such as addiction and respiratory depression. Two examples on this novel concept will be detailed: increased analgesia and reduced adverse events with a G protein-biased (B-astressin excluding) μ -opioid receptor ligand and targeting μ -opioid receptors under acidic conditions (such as inflammation or anoxia) with fluorinated formulation of fentanyl

In conclusion, although there is still considerable unmet clinical need, especially for the pain component of IBS, promising therapy is on the way, and we need collaboration among basic and applied pharmacologists, partnering between pharmaceutical, academia and clinical trialists to impact these common diseases.

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IBS DAYS

New insights for a better management of irritable bowel syndrome