British Society of Gastroenterology

Workshop

Neurogastroenterology & Motility Section
GI Physiology Associates Group

PROGRAMME & ABSTRACTS

22 JUNE, 2007

PERRIN LECTURE THEATRE
BLIZARD BUILDING
WHITECHAPEL, LONDON

Barts and The London
Queen Mary's School of Medicine and Dentistry

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FACULTY

British Society of Gastroenterology Workshop

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WELCOME NOTE

Assessment of gut biomechanical properties: relevance to gut function in health and disease

Dear Colleague

On behalf of the Neurogastroenterology and Motility Section and GI Physiology Associates Group of the BSG, we welcome you to East London for this Workshop. This is the first collaboration of its kind between these two groups, designed to encompass both practical and academic issues related to the topic of assessing gut biomechanical properties.

We are enormously grateful to our main sponsor, the SmartPill Corporation, and our other sponsors Oakfield Instruments Ltd, Medical Measurement Systems, Ardmore Healthcare Ltd, Unisensor AG, and Synectics Medical Ltd, for their generous support. I'm sure you will agree that we have assembled an outstanding group of speakers, who are renowned experts in their respective fields. Contemporary methodologies will be covered in-depth, with particular clinical emphasis on how assessing gut biomechanical properties has contributed to our understanding of the pathophysiology of functional disorders throughout the gastrointestinal tract. In addition, the afternoon session will involve a video demonstration of a rectal barostat study, and the Workshop will conclude with a panel discussion, where we would strongly encourage audience questions and participation.

Many people have helped with the organisation of this event, but I would like to pay particular tribute to Jackie Harbour, the Course Administrator, for her tireless hard work, and to Jan-Willem van der Wal, who spent many hours filming and editing the video presentation section of this Workshop.

We sincerely hope that you will enjoy the day, and I am pleased to confirm that the programme has been accredited by the Royal College of Physicians of London for 6 CPD points.

With best wishes

Mark Scott
Principal Organiser

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SCIENTIFIC PROGRAMME

MORNING SESSION

09:45 REGISTRATION AND COFFEE

10:25 Welcome note
Mark Scott

ASSESSMENT OF GUT BIOMECHANICS

Chairs: *Lesley Houghton, Satish Rao*

10:30 Biomechanical properties of the gastrointestinal tract: importance in relation to understanding normal gut physiology
Eamonn Quigley

11:00 Methods of study: what are we measuring?
Hans Gregersen

11:30 Organ tone, compliance, wall tension and visceral perception: use of the barostat
Michel Delvaux

12:00 Gastric accommodation: which test?
Guy Boeckxstaens

12:25 BREAK – TEA / COFFEE

PATHOPHYSIOLOGY OF FUNCTIONAL GI DISORDERS

Chairs: *Qasim Aziz, Bob Heading*

12:50 Oesophageal disorders
André Smout

13:20 Gastric and small bowel disorders
Ad Masclee

13:50 BREAK – LUNCH

AFTERNOON SESSION

Chairs: *Norman Williams, Peter Lunniss*

14:45 Colorectal disorders
Satish Rao

AFTERNOON SESSION (CONT.)

BAROSTAT STUDY

Chairs: *Mark Scott, André Smout*

15:15 Clinical applications and study protocol design for investigation of gut biomechanical function
Natalia Zarate

15:30 Equipment
Jan-Willem van der Wal

15:45 Video demonstration: barostat study of rectal function
Marc Gladman

16:15 Presentation of study results: interpretation of findings
Subash Vasudevan

16:20 BREAK – TEA / COFFEE

KEYNOTE LECTURE

Chairs: *Bob Heading, Eamonn Quigley*

16:50 Future directions and management of patients with functional GI disorders: can we address altered biomechanical function
Satish Rao

PANEL DISCUSSION – AUDIENCE QUESTIONS

Chairs: *Bob Heading, Eamonn Quigley*

17:20 Panel
Hans Gregersen, Michel Delvaux, Guy Boeckxstaens, André Smout
Ad Masclee, Satish Rao, Lesley Houghton, Marc Gladman

17:55 Closing remarks
Mark Scott

18:00 MEETING CLOSE

BIOGRAPHIES

Eamonn MM Quigley, MD FRCP FACP FACG FRCPI
Cork, Ireland

Eamonn Quigley is Professor of Medicine and Human Physiology and a Principal Investigator at the Alimentary Pharmabiotic Centre at the, National University of Ireland, Cork, Ireland. He serves as President of the World Gastroenterology Organisation (WGO-OMGE) and Vice-President of the American College of Gastroenterology.

His major research interests include motility, functional gastrointestinal disease, neurogastroenterology, gastro-oesophageal reflux disease and probiotics in health and disease. He has published over 450 original papers, reviews, editorials and book chapters, and has received numerous awards worldwide. He has been named an Honorary Professor by the Faculty of Medicine of the Universidad de la Republica Oriental del Uruguay, awarded Doctor 'Honoris Causa' by the University of Medicine and Pharmacy, Iuliu Hateiganu Cluj-Napoca, Romania, elected as a Distinguished Doctor to the Fellowship of the Royal College of Physicians, London and received the J Edward Berk Distinguished Lecturer award from the American College of Gastroenterology.

Professor Quigley graduated in medicine (MB BCh BAO) from the National University of Ireland, Cork in 1976 and completed his residency in internal medicine at the Western Infirmary and associated hospitals in Glasgow, Scotland. There followed a two-year research fellowship, leading to an MD degree by thesis, at the Mayo Clinic, Rochester, USA.

Hans Gregersen, DrMSci MPM MD
Aalborg, Denmark

Hans Gregersen got his MD degree from Aarhus University in Denmark in 1988. He started the scientific work in gastrointestinal motility as a medical student three years before graduation. He became interested in biomechanics early in his career and worked for two years as a guest professor at University of California San Diego. After returning to Denmark he became professor at the engineering school of Aalborg University in 1999 and at the Health Faculty of Aarhus University in 2001. He became director of research at Aalborg Hospital in 2001 where he led the process to become a university hospital in 2003. This was also the year where he officially established the Centre for Visceral Biomechanics and Pain with Professor Asbjørn Drewes. The centre is now an international centre with 40 employees and researchers affiliated and with several facilities Worldwide. Hans Gregersen has been a key player in the development of impedance planimetry, the multimodal probe, the in vivo length-tension curve, characterization of the zero-stress state, and the functional luminal imaging probe and he has published a number of basic science papers and clinical papers in the field of neurogastroenterology. He published several books on experimental surgical models (1996), gastrointestinal mechanics (2002) and experimental gastrointestinal ultrasonography (2006). Hans Gregersen was honoured with the Walton Award in 2006.

BIOGRAPHIES

Michel Delvaux, PhD MD
Nancy, France

Dr Michel Delvaux is Senior Attending Physician in the Dept of Internal Medicine and Digestive Pathology at the University Hospital of Nancy, France. After his medical school in Leuven, Belgium, he was certified as Gastroenterologist and obtained a PhD degree in Pharmacology at the University of Toulouse, France. His clinical activity is turned to functional digestive disorders, motility disorders and IBD. He is responsible for the Laboratory of Digestive Motility in the Department and takes an active part in the activities of the Endoscopy Unit, including for capsule endoscopy. Former member of the Executive Board of the Rome III Foundation, he is also a member of the Scientific Committee of UEGW and various scientific societies. He has published more than 200 original papers and scientific reviews in peer-reviewed journals.

Guy Boeckxstaens, PhD MD
Amsterdam, Netherlands

Guy Boeckxstaens was trained as gastroenterologist in Antwerp, Belgium. As part of his training, he fulfilled a 4 year period of basic research focussing on the nature of the non-adrenergic non-cholinergic neurotransmitter of the gut, resulting in a PhD in 1991. After finishing his clinical training in 1994, he moved to Amsterdam, The Netherlands, to join the Gastroenterology department then headed by Professor Guido Tytgat and to set-up a GI motility unit. To learn more about clinical motility, he visited the lab of John Dent and Michael Horowitz in Adelaide, Australia. Thereafter, he organized the GI motility unit in Amsterdam and initiated several research lines dealing with the pathophysiology of gastro-oesophageal reflux disease, functional bowel disease (dyspepsia, irritable bowel syndrome) and postoperative ileus. This has resulted in more than 100 peer reviewed international publications.

Currently, Dr Boeckxstaens is Head of the GI Motility Lab, scientific director of the GI department, president of the Dutch Society of Neurogastroenterology & Motility, and member of the Editorial Board of Gut and Neurogastroenterology & Motility.

BIOGRAPHIES

André JPM Smout, PhD MD
Utrecht, Netherlands

Professor André J.P.M. Smout was born in 1950 in Amsterdam, The Netherlands. He studied medicine at the University of Amsterdam and subsequently specialized in internal medicine and gastroenterology in Rotterdam and Utrecht, the Netherlands. After his registration as a gastroenterologist in 1984 he became staff member of the Department of Gastroenterology of the University Medical Centre in Utrecht. In 1994 he was appointed professor. In this position his daily activities are a mix of patient care, scientific research and teaching.

Since 1976 Professor Smout's research activities have incessantly been devoted to gastrointestinal motility and neurogastroenterology in health and disease. The subject of his doctoral thesis (1980) was the myoelectrical activity of the stomach, including electrogastrography. Over the years, he was involved in studies into the pathophysiology, diagnosis and treatment of functional bowel disorders and abnormal gastrointestinal motility, including gastro-oesophageal reflux disease. In 1989 and 1992 he worked for some months in the research laboratories of Professor Don Castell (Winston-Salem, NC, USA) and Professor Dr. Michael Horowitz (Adelaide, South-Australia), respectively.

Since 1994 Professor Smout is holder of the Chair of "Gastrointestinal motility disorders" at the University of Utrecht. He is author of almost 250 peer-reviewed scientific publications, several books and many book chapters on gastrointestinal motility and functional bowel disorders.

Satish Rao, PhD MD FRCP
Iowa, USA

Satish Rao, is director of neurogastroenterology and gastrointestinal motility at University of Iowa Hospitals and Clinics, and Professor of internal medicine, University of Iowa Roy J and Lucille A Carver College of Medicine. Last year, he received the 2006 American Gastroenterology Association (AGA) Masters Award in Gastroenterology.

He has developed a new system for studying ambulatory colonic motility in humans. He is pioneering several new techniques for studying and treating anorectal dysfunction, particularly for patients with constipation and incontinence, including computerized anorectal manometry, video fluoromanometry and biofeedback treatment. He is exploring the evaluation of combined techniques of motility with ultrasound or fluoroscopic imaging. He is also applying impedance planimetry to the study of the biomechanical properties of the intact human gut and evaluating visceral hyperalgesia and non-cardiac chest pain. His other interests are inflammatory bowel disease, in particular the role of enteral nutrition, noncardiac chest pain, IBS and atypical GERD.

BIOGRAPHIES

Jan-Willem van der Wal
Enschede, Netherlands

Jan-Willem van der Wal is the co-owner and co-founder of Medical Measurement Systems BV (www.mmsinternational.com). He has a degree in electronics and computer science, and is involved in R&D, development of new products and clinical evaluation of equipment and software. He initiated the Common Gastro File Format of the AMS/ESNM.

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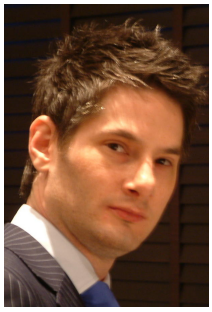
Natalia Zarate, MD
London, UK

Dr Natalia Zarate was born in Asturias, Spain. She graduated in medicine from the University of Oviedo and specialised in gastroenterology in Barcelona, Spain. After finishing her clinical training in 2000, she undertook a 2 year period of research in upper GI motility under the supervision of Dr F Mearin and Professor Malagelada in Hospital Vall d'Hebron, Barcelona. In 2002, she obtained a postdoctoral fellowship in the Intestinal Disease Research Programme at MacMaster University, Canada where she studied the role of interstitial cells of Cajal in human motor disorders under the supervision of Professor Jan Huizinga. She then moved to London, UK where she joined the GI Physiology Unit in the Centre for Academic Surgery at The Royal London Hospital. Dr Zarate's major research interests are the study of gastrointestinal motor function in health and disease and understanding of the mechanisms at a cellular level that control motility, especially the role of Interstitial Cells of Cajal.

BIOGRAPHIES



Marc Gladman, MBBS DFFP DRCOG PhD MRCOG MRCS (Eng)
London, UK

Mr Marc Gladman graduated from King's College Hospital School of Medicine in 1996. Having completed postgraduate training in General Surgery and Obstetrics and Gynaecology, he completed a PhD thesis on the clinical and physiological implications of rectal hyposensitivity. He remains committed to the pursuit of an academic career in the field of neurogastroenterology and has just been appointed as a UKCRC Clinical Lecturer in Surgery at Barts and The London, Queen Mary's School of Medicine.

Subash Vasudevan, MRCS
London, UK

Mr Subash Vasudevan was born in Chennai, India. He graduated from the Dr MGR Medical University, Chennai in 1999. After undertaking postgraduate surgical training in India, he moved to the UK. He completed a basic surgical training rotation and obtained the membership of the Royal College of Surgeons. Following this he joined the Centre for Academic Surgery and the GI Physiology Unit at the Royal London Hospital as a Clinical Research and Teaching Fellow. His current PhD project involves studying the role of blunted rectal sensation (rectal *hypo*sensitivity) in functional hindgut disorders.

ABSTRACTS

BIOMECHANICAL PROPERTIES OF THE GASTROINTESTINAL TRACT:
IMPORTANCE IN RELATION TO UNDERSTANDING NORMAL GUT PHYSIOLOGY

Eamonn Quigley

In its most basic form, the gastrointestinal tract can be described as consisting of two tubes, one short, one long, separated by two cylindrical reservoirs, each demarcated from the other and the external environment by a valve which controls entry and prevents back-flow. The complexities of form and function that enable this apparently simple plumbing system to process complex and ever-varying inputs into simple molecules, cope with luminal contents that vary in chemical nature and physical characteristics along its length, provide the organisms first line of defence and one of its primary excretory routes, and respond on a minute-by-minute basis to its internal environment, as well as distant directives, continue to beguile physiologists and challenge clinicians. The neuromuscular apparatus that subserves these functions and is capable of developing and integrating complex responses in health and disease comprises two basic components: smooth muscle and nerve. Throughout the gastrointestinal tract, the fundamental physiology of smooth muscle is adapted to the contractile properties of a particular region, be it the generation of tone, sustained in sphincters or fluctuating in the “reservoirs”, or propagating contractions which can turn the tubes into pumps. Gut muscle cannot be seen isolation; its integration and, especially, its ability to respond to environmental change, are dependent on the “wiring” provided by the enteric nervous system and the networks of interstitial cells of Cajal. The fundamental biomechanical properties of the gastrointestinal tract, such as compliance and elasticity, may be related to some degree to other, passive, anatomical components but it is the active components that render this series of organs capable of generating, at a single site, fluctuations in tone, shortening and lengthening, peristalsis and a whole repertoire of complex motor responses. An examination of the myogenic and neural factors that lead, for example, to oesophageal peristalsis, the accommodation response of the proximal stomach, or power propagating contractions in the colon, illustrates the ability of integrated myo-neural responses to supplement basic biomechanical properties and provide the motor phenomena which promote organ function and homeostasis. Herein lies the challenge for the physiologist: studies of isolated components, while revealing fundamental information on individual components of this system will always be incomplete as they will fail to simulate the integrated responses that characterize the behaviour of the living organism.

Notes

ABSTRACTS

METHODS OF STUDY: WHAT ARE WE MEASURING?

Hans Gregersen

The gastrointestinal tract serves a mechanical function, therefore it is important to define and measure smooth muscle contractile parameters such as peristaltic force, tone, and active length-tension relations. Furthermore, it is important to quantitate tissue elasticity (elastic moduli) and how a mechanical stimulus affects the mechanosensitive receptors in the wall. The talk focuses on a number of techniques and their limitations. One of the simplest ways to stimulate the gastrointestinal tract is to blow up a balloon in the lumen and to measure the balloon pressure, balloon volume or both. Simple volume stimulations suffers, however, from a number of limitations, especially from the fact that the shape of the distending balloon is now known and that phasic contractions often cannot be distinguished from muscle tone. This is important because a distending balloon tends to elongate rather that to stretch the wall due to the stiffness of the wall. Examples of these limitations will be given in the talk. Other techniques that do not have these limitations and that are based on fewer assumptions have been developed. Impedance planimetry measures the bag cross-sectional area in a saline-filled bag using a simple electrical principle. Hence, the tissue properties at the mid-bag location can be determined, and the change in bag length (elongation) can be derived. Impedance planimetry has recently been further developed into three new techniques, the multimodal probe, the axial force probe and the functional luminal imaging probe (FLIP). The multimodal probe has in addition to the mechanical stimulation also added features for thermal, chemical and electrical stimulation, in order to further characterize the receptors in the gastrointestinal wall. It has been used to demonstrate differences between patients with oesophageal symptoms. The axial force probe uses an impedance principle to measure the axial force in the oesophagus rather than the luminal pressure. From the initial studies it is evident that there are differences between pressure and force measurements, demonstrating that pressure only in part reflects the propulsive force developed by oesophageal muscles. FLIP utilizes impedance planimetry with multiple electrodes and CSA measurements. Hereby it is possible to obtain a 3D-profile of the organ surrounding the bag. Until now FLIP has been validated and used to characterize the lower oesophageal sphincter. 3D geometry of organs can also be obtained using medical imaging such as MRI and 3D ultrasound. Ultrasonography also provides capabilities for mechanical strain and elastic measurements using strain rate imaging and elastography.

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ABSTRACTS

ORGAN TONE, COMPLIANCE, WALL TENSION AND VISCERAL PERCEPTION:
USE OF THE BAROSTAT

Michel Delvaux

The knowledge about the biomechanical properties of the gut wall have dramatically increased since the introduction of the barostat, which measure changes in tone of the gut wall and hence, is able to detect not only contractions but also relaxations of the studied organ. The barostat is built to maintain a constant pressure in a flaccid bag that is inserted in the lumen of the organ. To maintain the intra-bag pressure constant, the device insufflates air into the bag when the organ relaxes, decreasing the pressure and conversely withdraws air when the organ contracts, increasing the pressure. Consequently, the barostat allows mainly to measure changes in tone rather than absolute values.

Few pathological situations have been linked to changes in tone of digestive organs. In patients with dyspepsia, some studies an impairment of gastric accommodation to a meal. In patients chronic constipation, the rectal tone may be decreased in those with a megarectum but it is not known whether these changes results from the megarectum or reflect the pathophysiological mechanisms responsible for it. On the other hand, in patients with ulcerative colitis, chronic diarrhoea or faecal incontinence, the rectal tone is often increased.

The barostat is also used to evaluate sensitivity in patients with functional bowel disorders. In these patients, visceral sensitivity to distension of the digestive organs is enhanced, these patients feeling pain at lower distending pressures than controls. Using a barostat for distension studies allows the simultaneous measurement of volume and pressure in the distending bag and thus the calculation of the compliance of the gut wall. Compliance reflects the capability of the organ to adapt to the distension imposed by the bag. It is a complex measurement that results from various forces, including the contractions occurring through the studied segment, the tone of the organ and the pressure of the surrounding structures on the wall. The compliance is defined by the relationship between the pressure and the volume. Its is expressed as the slope of the pressure-volume curve and should never been expressed as the P/V ratio at one given point. Indeed, its measurement is influenced by the anatomy of the subject and the level of distension that the bag imposes to the gut. Some studies have also indicated that the tension induced by the bag, which can be roughly defined as the pressure/surface induced by the distending bag could be a determinant of gut sensations induced by luminal distension and explain differences between healthy subjects and patients with functional bowel disorders.

Notes

ABSTRACTS

GASTRIC ACCOMMODATION: WHICH TEST?

Guy Boeckxstaens

Functional dyspepsia is a common disorder of the upper gastrointestinal tract characterised by a wide spectrum of symptoms, including epigastric pain, bloating, postprandial fullness, early satiation, nausea and vomiting. In the last decade, especially with the introduction of the barostat, our understanding of normal gastric function and the relationship between abnormal proximal stomach function such as visceral hypersensitivity and impaired accommodation has increased enormously. It became clear that the proximal stomach, through a vago-vagal mechanism, relaxes on meal intake. The accommodation of the proximal stomach to meal provides a reservoir for the ingested food thereby reducing the increase in intragastric pressure and associated gastric sensations. Most importantly, these studies have revealed that this accommodation response to a meal was impaired in a certain subset of patients especially those presenting with early satiation and weight loss. Improvement of gastric accommodation with agents that relax the stomach were reported to increase meal intake and to decrease symptoms in this subset of patients. As such, impaired accommodation was identified as an important therapeutic target for patients with functional dyspepsia and drugs relaxing the stomach were developed to correct this motor abnormality. Ideally, patients with an impaired accommodation response to a meal should be selected to be treated with such drugs. Although the gastric barostat is still considered the gold standard, it is an invasive and time consuming technique not really suited for routine clinical use. This has been the drive to develop new non-invasive techniques to measure gastric accommodation. These techniques include drink tests, SPECT scanning, 3D-ultrasound and dynamic MRI. Briefly, drink tests, either with water or a caloric liquid, were initially proposed as interesting tools that could potentially replace the barostat. Comparative studies however demonstrate that there is a poor correlation between barostat and drink test data. The other 3 imaging tests may represent an interesting alternative, although it should be emphasised that, in contrast to the barostat, no distending force is applied on the gastric wall. Therefore, these techniques largely measure changes in gastric volume, that is the volume of the ingested meal, gastric secretion and air, but fail to detect small changes in gastric tone. It remains questionable therefore whether these tools will be useful to detect patients with impaired accommodation. In this presentation, the pros and cons of these techniques and their potential for clinical use will be discussed.

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ABSTRACTS

OESOPHAGEAL DISORDERS

André Smout

In today's clinical practice the gold standard for the diagnosis of oesophageal motor disorders is oesophageal manometry. It is becoming increasingly clear, however, that intraluminal manometry provides a limited and somewhat distorted view on phasic contractions of the oesophageal wall and no information whatsoever on oesophageal tone, wall tension and compliance. For the diagnosis of functional oesophageal disorders (functional heartburn, functional chest pain, functional dysphagia and globus) manometry is only useful because it helps to exclude the presence of recognised motor disorders.

Application of techniques that help to assess oesophageal wall thickness (such as endoscopic ultrasound) and to assess pressure-volume relationships in the oesophagus (balloon distension, barostat) and that allow measurement of the cross-sectional area (such as impedance planimetry) has made it possible to study aspects of oesophageal function that had remained terra incognita using manometry.

The number of publications on biomechanical properties of the oesophagus in disease states is still limited. Endoscopic ultrasound studies have shown that sustained oesophageal contractions, mainly taking place in the longitudinal muscle layer, can be the cause of chest pain and heartburn. These contractions can not be detected by means of intraluminal manometry. Using impedance planimetry, it was discovered that patients with non-erosive reflux disease (NERD) are hyposensitive to oesophageal distension as assessed by cross-sectional area and balloon volume, but no differences between NERD patients and controls were seen for pressure and tension. Using barostat techniques it was found that the compliance of the oesophageal body was significantly higher in patients with achalasia than in controls, whereas the LOS compliance in these patients was normal. Patients with GORD have been shown to have a highly compliant LOS in comparison to controls. Non-achalasic patients with total oesophageal aperistalsis also have a significantly increased compliance of the oesophageal body.

The above-mentioned new techniques for assessment of oesophageal biomechanical properties have increased our understanding of the pathophysiology of various oesophageal disorders. Thus far, they have not yet become clinically useful tests.

Notes

ABSTRACTS

COLORECTAL DISORDERS

Satish Rao

The defecation unit comprises of the sigmoid colon, the rectum, pelvic floor muscles and the anal sphincter apparatus. The anorectum is an important end organ that actively participates in the perception, storage and orderly elimination of digestive residues. To accomplish these complex functions these organs are well equipped with unique muscular properties, autonomic, somatic and enteric innervation, neurohumoral regulation and an intricate afferent and efferent brain-gut interaction.

Colorectal disorders are very common and account for at least 30% of referrals to a gastroenterologist. Altered biomechanical properties of the defecation unit can lead to significant neuromuscular dysfunction and can result in symptoms that are commonly encountered in patients with ulcerative colitis, faecal incontinence, seepage, irritable bowel syndrome, dyssynergic defecation, solitary rectal ulcer syndrome (SRUS) and rectal hyposensitivity.

Diarrhoea in ulcerative colitis is not due to rapid colonic transit or transport of large volume stool but due to hind gut dysfunction. These patients demonstrate rapid transit of small volume stools through the distal colon and the urgency and tenesmus are due to a hypersensitive, poorly compliant rectum that generates strong contractions which overwhelms the anal barrier.

The pathophysiology of faecal incontinence is often multifactorial. This includes weakness or significant loss of structural integrity of the external and internal anal sphincters, loss of endovascular cushions preventing a tight seal, impaired rectal reservoir function, rectal hyposensitivity, central neurogenic mechanisms and pudendal neuropathy. Although these mechanisms explain most patients with incontinence, those with faecal seepage usually have adequate sphincter function and intact pudendal nerves. Here, the chief problem appears to be dyssynergia, hyposensitivity to small volumes of stool and impaired rectal evacuation; mechanisms akin to those seen in nursing home residents and children with functional faecal retention.

Rectal hypersensitivity is regarded as a biological hallmark of patients with irritable bowel syndrome and may account for pain in these patients. This may be due to altered sensorimotor function peripherally or altered perception and regulation of visceral sensation centrally or both. In some, meal induced alterations in either rectal tone or distal colonic transport suggests a gut-mediated neuroenteric dysregulation. In contrast rectal hyposensitivity (RH)- lack of awareness for stooling has only recently been systematically investigated. Its underlying mechanisms are not fully unknown. RH was seen in 44-58% of constipated patients and 23% with other anorectal dysfunctions and in IBS patients with abuse. This may be due to altered sensory perception or altered rectal wall compliance or both.

Dyssynergic defecation accounts for 30-40% of patients with chronic constipation. These patients demonstrate paradoxical anal contraction, impaired push effort or inadequate anal relaxation or a combination. Nearly 50% of patients have RH and over 60% have coexisting slow colonic transit. Recent studies of cortical evoked potentials from the anus and rectum have provided invaluable insights regarding the gut-brain axis in dyssynergia. The

pathophysiological mechanisms involved in SRUS include dyssynergia, and rectal hypersensitivity and likewise radical hysterectomy is associated with profound dysfunction of the anorectal unit.

An improved understanding of the pathophysiological and neurobiologic mechanisms that are involved in the genesis of these clinical syndromes may lead to the development of better treatments for these problems.

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Notes

ABSTRACTS

CLINICAL APPLICATIONS AND STUDY PROTOCOL DESIGN FOR INVESTIGATION OF GUT BIOMECHANICAL FUNCTION

Natalia Zarate

The development of the barostat has contributed significantly to the understanding of gastrointestinal sensorimotor function, particularly in relation to the study of functional gastrointestinal disorders.

Pressure and / or volume controlled mechanical distensions of a particular region of the gut allows assessment of its biomechanical properties, as well as the study of gut reflexes elicited under physiological and experimental conditions. In addition, visceral sensitivity to distension can be determined.

Careful design of the study protocol is of the utmost importance to obtain meaningful information with this technique. Both the patient population under study and the somewhat invasive nature of the procedure demand for control of psychological factors likely to influence the outcome of the study. Various distension protocols are available: the ascending method of limits (AML) is frequently used, and is characterised by a progressive increase in the intensity of distension, which can be achieved through continuous (ramp distension), stepwise or phasic distension. In order to control for the influence of anticipation on sensory scores, random (or semi-random) distension protocols are also possible. Understanding of these different distension paradigms, and their advantages and limitations is desirable. In addition, the rate (slow vs. fast) and mode (fixed pressure vs. fixed-volume) of distension, need to be considered, as these will influence results and interpretation of the study.

Evaluation of visceral sensitivity with the barostat is achieved through determination of different thresholds of sensation as well as rating the intensity of the perceived sensation with the aid of visual analogue scales. Reproducibility in both health and functional GI conditions has been demonstrated.

Notes

ABSTRACTS

EQUIPMENT

Jan-Willem van der Wal

The presentation about the barostat equipment will focus on the technical aspects of the barostat and the catheters. Different barostat distension methods like rigid reservoir, dual stage and bellow type will be discussed. The setup of the system, calibration and checking before the patient study. The production of the catheter, selection of the tubing (single, dual or multi lumen), catheter length and diameter are important selection criteria. Single or dual bag inflations in two different organs must be chosen before a study is performed. Interfacing the barostat signals (pressure and volume in the bag) with other signals like oesophageal, LES or pyloric pressures, swallow, respiration and pH signals can be useful. With this combined setup a better understanding of the function of the organs can be found.

Notes

ABSTRACTS

FUTURE DIRECTIONS AND MANAGEMENT OF PATIENTS WITH FUNCTIONAL GI DISORDERS: CAN WE ADDRESS ALTERED BIOMECHANICAL FUNCTION

Satish Rao

At present, the management of functional gastrointestinal disorders remains a challenge because of limited therapeutic options, often based on small clinical trials or poorly controlled studies. Regrettably, our ability to treat these patients has not kept pace with our current understanding of the mechanisms that are involved in the pathogenesis of these conditions.

Systematic studies have confirmed that patients with functional (noncardiac) chest pain exhibit a hypersensitive, hyperreactive and a poorly compliant oesophagus and that visceral hypersensitivity is the chief pathophysiological mechanism. In an experimental study Ketamine, a central NMDA blocker was shown to reverse oesophageal hypersensitivity suggesting a therapeutic role for such compounds. Recently, it was shown that infusion of adenosine led to alterations in oesophageal sensorimotor function that were similar to those seen in patients with FCP. This finding suggests a pathogenic role for adenosine. This explains why, Theophylline an adenosine receptor blocker was effective in improving oesophageal hypersensitivity and chest pain in FCP subjects. Likewise a study of oesophageal sensorimotor function revealed why some patients with GERD continue to experience symptoms of chest pain despite successful Nissen fundoplication; these patients have underlying visceral hyperalgesia.

Although mechanistic perturbations have been shown in patients with functional dyspepsia, and some that were felt to be related to serotonin dysfunction, serotonin modulators such as Tegaserod have not been shown to definitively improve symptoms in large RCTs. On the other hand, patients with symptoms of upper gut dysmotility and those with unexplained gas and bloating may obtain relief with Tegaserod. This could be due to Tegaserod-induced enhancement of upper gut motility, particularly in the jejunum and ileum.

A clear understanding of the pathophysiology of dyssynergic defecation has led to the development of behavioural approaches that aim to remedy the underlying dysfunction(s). Recent RCTs have shown that biofeedback therapy is superior to sham or laxatives and that this improvement is due to alterations in dyssynergia, sensory function and colonic transit. Also, preliminary studies have revealed that dyssynergics have impaired ano-cortical and recto-cortical evoked potentials suggesting impaired gut-brain axial function. Whether biofeedback therapy improves brain-gut dysfunction merits further appraisal.

The treatment of rectal hyposensitivity is unsatisfactory and there is no approved therapy. One study suggested that biofeedback (BT) improved rectal sensation. However, sensory conditioning is time consuming, labour intensive, is ineffective in many with rectal hypo-sensitivity and has not been tested in a controlled trial. Recently, it was suggested that sacral nerve stimulation may relieve constipation by improving rectal sensation. In a randomized study of 12 patients, rectal electrical stimulation improved rectal sensation; whereas in 10 patients, BT without sensory conditioning did not affect rectal sensation, emphasizing the need to combine sensory conditioning with BT. In our pilot study, patients who failed the traditional approach of syringe-assisted sensory training showed significant improvement in sensation and bowel function with barostat-assisted sensory conditioning. Finally, vertical reduction rectoplasty has been advocated for the treatment of patients with megarectum.

Finally, use of novel therapeutic compounds such as Linactolide, a guanylate cyclase agonist that accelerates colonic transit or drugs that alter rectal sensation and compliance may be useful in the management of many of these patients

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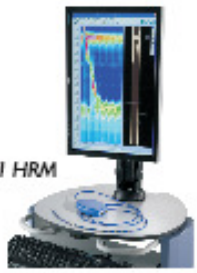
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