



ABBOTT “EXPERT SOLUTIONS IN GASTROENTEROLOGY” – Summit - Beirut, Lebanon, 28th & 29th 2017

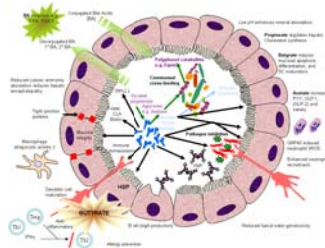
28TH APRIL 2017

Chair: G.Janssen-van Solingen,
Global Medical Director
Gastroenterology Portfolio, Abbott.

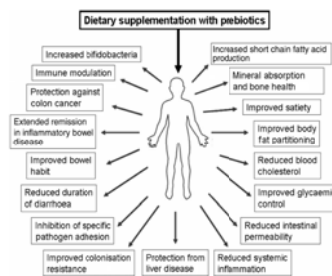
Dr. Kieran Tuohy From the Department of Food Science and Nutrition at Fondazione Edmund Mach, Trento, Italy/Visiting professor at University of Ulster), provided a lecture on the **‘Prebiotic Properties of Lactulose’**.

The intestinal microbiota and its metabolic output are emerging as important players in human health and disease risk. Indeed, **diet:microbe interactions in the gut have been shown to influence markers of many metabolic and immune related chronic diseases**, most notably metabolic syndrome and cardiovascular disease. Because both the composition of the gut microbiota and the profile and quantity of metabolites it produces appear to be modifiable by diet, much recent research interest has focused on developing **foods and ingredients which have the potential to influence host physiology** (e.g. immune function, inflammation, glucose/

Cholesterol homeostasis, cognitive function) through microbiota modulation.



Prebiotics are one such class of food ingredients. A prebiotic is defined as “a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health”¹, Gibson et al, 2010, ISAPP accepted definition <http://isappscience.org/publications/gibson-prebiotic-new-definition-isapp-10/>.



Lactulose, now called galactofructose, is one such prebiotic and has a long history with a positive safety profile in clinical

Gastroenterology SUMMIT



On April 28th & 29th 2017, a **Gastroenterology Summit** was organized for the MEAP region. It was attended by 150 physicians (**gastroenterologists, internal medicine, hepatologists**) from Egypt, Gulf, Levant, Kenya, Pakistan, and Saudi Arabia.

During the summit, on **Day 1**, there were 4 lectures: **Dr. Kieran Tuohy** from Italy provided a lecture on The **“Prebiotic properties of Lactulose”**. **Prof. Jyh-Ming Liou** from Taiwan provided a lecture on **“Recent updates on H.pylori Management”**; **Prof. Cem Kalayci**, from Turkey provided a lecture on **“Pancreatic Exocrine Insufficiency”**; and **Prof. Hani Tamin** from Lebanon provided a lecture on **“Statistics in Medicine”**.

On **Day 2**, there were also 4 lectures: **Prof. Tim Vanuytsel** from Belgium provided a lecture on **“Highlights on Rome IV Criteria”**; **Prof. Benoit Coffin** from France provided a lecture on **“Management of Acute Diarrhea”**; and **Prof. Karim Kammeruddin** provided a lecture on **“Management of Chronic Constipation”**, and Prof. Osama Abo El Fotoh Aly provided a lecture on **“The Role of Prokinetics In Motility Disorders and GERD”**.



practice for improving on bowel function. The presentation discussed the use of lactulose /galactofructose as a prebiotic and presented the **evidence for its ability to modulate both the composition and metabolic output of the gut microbiota**. It also discussed the recent health claim, approved by the European Food Safety Authority², that “lactulose contributes to a reduction in intestinal transit time”. Importantly, this health claim was judged to be applicable to the general population at a daily dose of 10g of lactulose per day. Lactulose also appears to improve mineral, especially calcium, absorption and has extra-European claims to this effect. This presentation will cover possible mechanisms by which lactulose mediates this effect in vivo.

1. Gibson, G. R., Scott, K. P., Rastall, R. A., Tuohy, K. M., Hotchkiss, A., Dubert-Ferrandon, A., et al. (2010). Dietary prebiotics: current status and new definition. *Food Sci. Technol. Bull. Funct. Foods* 7, 1–19. doi:10.1616/1476-2137.15880.
2. Scientific Opinion on the substantiation of health claims related to lactulose and decreasing potentially pathogenic gastro-gastro-intestinal microorganisms (ID 806) and reduction in intestinal transit time (ID 807) pursuant to Article 13(1) of Regulation (EC) No 1924/2006.

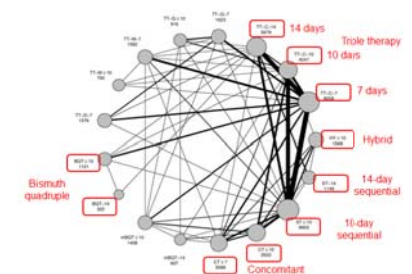
Prof. Jyh-Ming Liou

from the National Taiwan University, Taipei, Taiwan provided a lecture on ‘**Recent updates on *H. pylori* Management**’.

Gastric cancer remains the fifth most common malignancy and the third leading cause of cancer related mortality in the world. The numbers of gastric cancer related death in Asia were 353,100 among males and 174,000 among females, accounting for about two-third of gastric cancer deaths in the world in 2012. ***Helicobacter pylori* (*H. pylori*) has been shown to be the most important causal factor of gastric cancer.** Emerging evidence showed that early eradication of *H. pylori* before the development of gastric atrophy or intestinal metaplasia may reduce the risk of gastric adenocarcinoma. **Eradication of *H. pylori* may reduce the recurrence rate of peptic ulcer disease and may even reduce the incidence of peptic ulcer disease in the community.** Therefore, international experts recommended that *H. pylori* infected individuals should be offered eradication therapy, unless there are competing

considerations in the Kyoto Consensus.

The prevalence of *H. pylori* infection remains high in many Asian countries. Our recent systematic review and meta-analysis showed that the overall prevalence of primary *H. pylori* resistance were 17% (95% CI 15–18%) for clarithromycin, 44% (95% CI 39–48) for metronidazole, 18% (95% CI 15–22%) for fluoroquinolones, 3% (95% CI 2–5%) for amoxicillin, and 4% (95% CI 2–5%) for tetracycline in Asia. There are **several strategies to improve the efficacy in the first-line treatment of *H. pylori***, including **extending the treatment length to 14 days, the use of higher dosage of proton pump inhibitor or the p-cab vonoprazan, the use of four drug regimens, the addition of bismuth to triple therapy, and the use of susceptibility testing guided therapy.**



The use of effective rescue therapies in the second-line or third-line treatment may also



increase the cumulative eradication rates. It is hoped that *H. pylori* associated diseases may be eliminated through these efforts.

Prof. Cem Kalayci

from Private Practice/Gastroenterology Department of Florence Nightingale Hospital, Istanbul, provided a lecture on ‘Pancreatic Exocrine Insufficiency’.

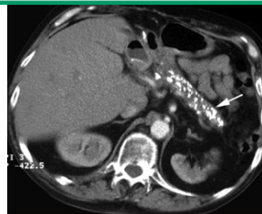
Etiology of pancreatic exocrine insufficiency (PEI) can be summarized in four categories: **loss of pancreatic parenchyma** (eg, chronic pancreatitis), **inadequate pancreatic stimulation** (eg, pancreatic surgical resection), **pancreatic duct obstruction** (eg, pancreas adenocarcinoma), or **pancreatic enzyme inactivation** (eg, Zollinger Ellison syndrome).

Symptoms due to PEI may vary from mild to severe. **Patients with mild PEI may be asymptomatic or have mild abdominal discomfort and bloating with normal bowel movements.** Clinically significant steatorrhea occurs when approximately 90% of pancreatic function has been lost. Severe PEI causes fat and protein maldigestion and weight loss. Malabsorption of the fat soluble vitamins (A, D, E, K) and vitamin B12 may also occur. Patients with PEI may

also complain of bloating, cramping, and flatulence.

Patients with severe chronic pancreatitis (CP) present with calcifications, ductal dilatation, enlargement of the pancreas, and peri pancreatic fluid collections on abdominal imaging (CT, MRI, US).

Chronic pancreatitis



Computed tomography (CT) scan of a patient with chronic pancreatitis demonstrates coarse calcifications (arrow) distributed throughout the body and tail of the pancreas.

Patients with advanced CP, cystic fibrosis, Shwachman-Diamond syndrome may have pancreatic atrophy on imaging. However, the most common cause of atrophy is the aging.

Direct and indirect tests are available for the diagnosis of PEI. Fecal elastase-1 is most commonly performed initial diagnostic test. If the diagnosis is in doubt direct tests can be performed (eg, endoscopic secretin test), if available.

The mainstay of treatment in severe maldigestion and steatorrhea due to PEI is a low fat diet and PERT (Pancreas Enzyme Replacement Therapy). PERT may also be indicated in patients with celiac disease, HIV, IBS and diabetes.

According to **HaPanEU**, enteric-coated microspheres or minimicrospheres of less than

2 mm in size are the preparations of choice for PEI. Enzyme preparations should be taken with meals. If more than one capsule/tablet per meal must be taken, it may be beneficial to take one part of the dose at the beginning with the rest being distributed during the meal.



A dose of 40,000–50,000 PhU is recommended to be taken with the main meals, and half of that dose with snacks. If symptoms persist, adding H2 receptor antagonists or proton pump inhibitors is often effective.

References

World J Surg. 1998;22:254.
 Dig Liver Dis. 2015; 47:1013-20.
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 Pancreas. 2008;37(4):418
 UEGJournal (supplement) 2017;1-47

Prof. Hani Tamim

from the American University of Beirut/Biostatistics unit at the Clinical Research Institute, provided a lecture on ‘Statistics in Medicine’.



An introduction to the fundamental concepts in statistics and their use in clinical research was provided.

The objective of the session was to introduce **the core concepts in statistics**. The theoretical concepts in descriptive statistics, including: **measures of central tendency** (mean, median, and mode), **measures of dispersion** (standard deviation, range, and interquartile range), and **graphical representations** were presented.

Descriptive analyses: continuous variable

◊ Central tendency

- > Mean
- > Median
- > Mode

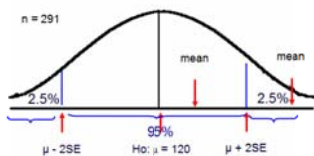
$$\bar{X} = \frac{\sum_{i=1}^n X_i}{n}$$

◊ Dispersion

- > Variance
- > Standard deviation
- > Range

$$SD = \sqrt{\frac{\sum_{i=1}^n (X_i - \bar{X})^2}{n-1}}$$

Moreover, the session introduced the **concept of statistical inference** as applied in clinical research, such as: **probability distributions, confidence intervals, hypothesis testing, and p-values**.



In addition, **different statistical tests frequently used** for inferential statistics were presented, such as chi-square, t-test, ANOVA, and correlation.

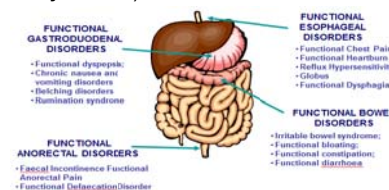
20TH APRIL 2017

Chair: Prof. Cecilio Azar,
 Department of Internal Medicine,
 Division of Gastroenterology,
 American University of Beirut Medical Center (AUBMC) /Head of GI Division Middle East Institute of Health (M.E.I.H)/ Consultant Gastroenterologist at Clemenceau Medical Center (CMC).

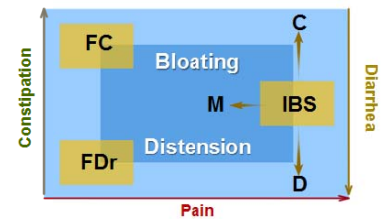
Prof. Tim Vanuytsel

from the Translational Research Center for Gastrointestinal Disorders (TARGID)/ Division of Gastroenterology & Hepatology, University Hospital Leuven, Belgium provided a lecture on **“Highlights on Rome IV Criteria”**.

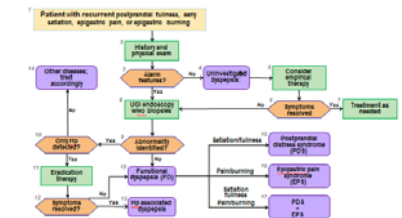
In 2016, the **updated Rome IV criteria for Functional Gastrointestinal Disorders** were published. Through a collaboration between the Gastroenterology journal and the Rome Foundation, Rome IV was launched with a series of reviews on FGIDs (published in May 2016).



Since the publication of Rome III already, there has been a marked and **exciting expansion in scientific understanding of these disorders**, which has led to an **improvement in diagnosis and treatment options**.



In this lecture, the **operational definition and classification system for FGIDs** was further elucidated, as well as pathophysiology with specific focus on **Irritable Bowel Syndrome (IBS) and Functional Dyspepsia (FD)**.



A summary of **differences between Rome III and Rome IV** was provided as well as a general approach as to care of patients with FGIDs.

Prof. Benoit Coffin

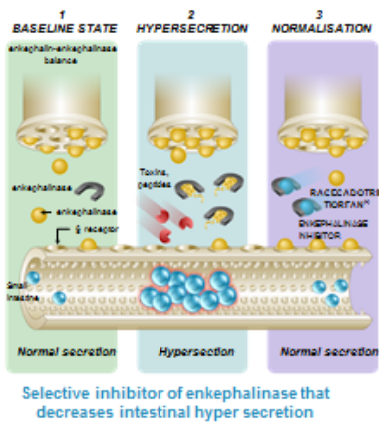
from the Gastroenterology Unit Hôpital Louis Mourier, Assistance Publique-Hôpitaux/ Gastroenterology, Denis



Diderot-Paris 7 University, Paris, France provided a lecture on the topic of **“Management of acute diarrhea”**.

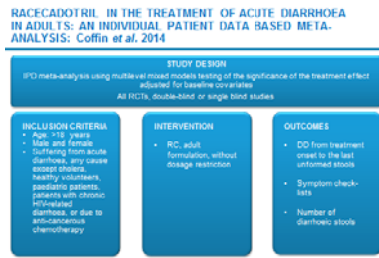
Worldwide, acute diarrhoea (AD) constitutes a **major cause of morbidity and mortality**, especially among the very young or very old patients. Most AD cases are caused by enteric infections but resolve spontaneously within a few days **without needing antibiotic therapy**.

Racecadotril is an anti-diarrhoeal drug with a **pure intestinal antisecretory mechanism of action** without an antimotility effect and with a positive safety profile.



The efficacy of racecadotril for the symptomatic treatment of adult AD was analyzed in a **meta-analysis** based on literature (MAL) findings that collected results summaries from articles through an adequate literature review and aggregated the differences. Four randomized clinical trials

were identified following this analysis with raw data (n=669). An **Individual Patient Data meta-analysis** was conducted to assess racecadotril efficacy, whatever its dose, versus placebo in adult acute diarrhoea. Individual Patient Data meta-analysis following multi-level mixed models testing of the significance of the treatment effect adjusted for baseline covariates.



Diarrhoea duration was the common main criteria. The clinical global impression evaluated at baseline by the physician was found to be the essential predictor influencing the outcome. **As compared to placebo, the 100 mg dose, the minimum effective dose, induced a 80% increase of the recovered patient proportion at anytime** (Hazard Ratio = 1.8 [1.3, 2.5], $p < 0.001$), a 60% increase of the responder proportion i.e. recovery within 3 days ($p < 0.001$), a 47% reduction of abdominal pain and nausea and an overall 33% decrease of sick days ($p < 0.001$). In conclusion, as compared to placebo, racecadotril induced several significant effects, such as **reducing the diarrhoea duration, the number of stools and associated**

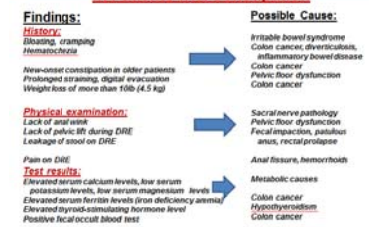
symptoms, leading to less lost productivity.

The lecture focused on the **burden of acute diarrhea, definitions, guidelines and management** with particular focus on racecadotril as novel anti-diarrhoeal medication.

Prof. Karim Kammeruddin, from Baqai Med University, Nazimabad, Karachi provided a lecture on the topic of **“Management of chronic constipation”**.

It was outlined that **constipation itself is not a disease but a symptom**. It may be associated with some diseases, such as hypothyroidism etc.

Clinical Findings and Possible Associated Causes in Patients with Constipation



Diagnosis is therefore an important aspect in constipated patients.

Constipation is **one of the most common gastrointestinal complaints** among women and the elderly, although all age groups can be affected.

Constipation is very common amongst pregnant women and children, which makes the **safety profile of any treatment of paramount importance.**

Two **definitions of constipation** exist; the **patient definition** and



the clinical definition. The patient definition of constipation is a perceived change in bowel habit or defecatory behavior by patients, who generally describe their symptoms as straining (52%, hard, pellet-like stools (44%), inability to defecate when desired (34%) and infrequent defecation. (33%).

Other reviews include pain or difficulty during defecation, or a sensation of incomplete rectal evacuation.

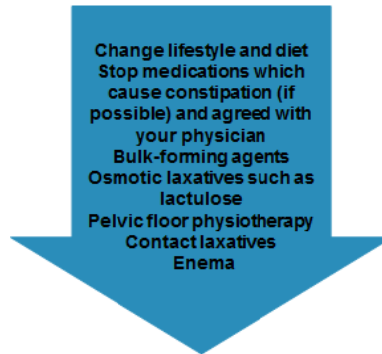
Various treatments are recommended for the management of constipation. Baseline treatment includes:

- A change in lifestyle and diet
- An increase in dietary fiber (20 – 30 g per day)
- An increase in fluid intake (~ 8 x 200 ml glasses per day)
- Additional exercise

What is the overall approach to managing constipation?

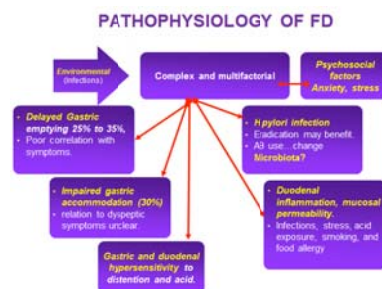
- > Understand etiologies that may contribute to symptoms.
- > Align treatment with underlying mechanism.
- > Discontinue medications that cause constipation and can be safely stopped.
- > Suggest a bowel habit diary and diet history to correlate dietary factors with stool consistency and timing.
- > Determine if there is coexisting defecatory disorder.
- > Outline the expected goals.
- > Provide patient education about treatment rationale.

Considering the major difficulties involved in achieving a lasting lifestyle change, the success of such measures is often unsatisfactory and temporary. Consequently, laxatives are frequently used.

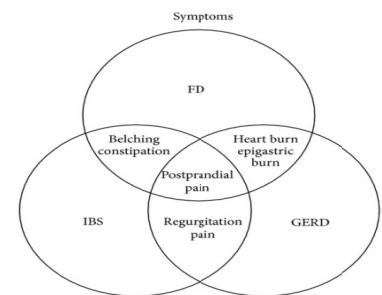


Prof. Osama Abo El Fotoh Aly from the Department of Internal Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt, provided a lecture on the topic of “The role of prokinetics in motility disorders and GERD”.

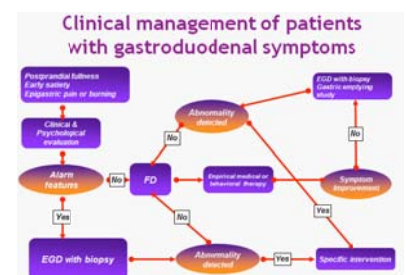
The updated Rome criteria, culminating in the Rome IV criteria published in 2016, provide valuable insights into the classification, diagnosis and management of functional gastrointestinal disorders (FGDs).



Rome IV places further emphasis on the different subtypes of Functional Dyspepsia (FD), being postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), rather than focussing on the syndrome as a whole and acknowledge that gastroesophageal reflux disease (GERD) and irritable bowel syndrome (IBS) can be part of the functional dyspepsia spectrum.



This lecture addressed the changes regarding the definition and diagnostic criteria concerning Functional Dyspepsia in particular (FD) in Rome IV, and also focussed on gastroparesis and gastroesophageal reflux disease (GERD).



Current and future treatment options were shared with the



audience, with **specific focus** on the efficacy of prokinetics in the management of these disorders.

- Prokinetics exert a significant beneficial effect in FD and gastroparesis and may positively impact symptomatic refractory GERD as an add-on to PPI.
- Different groups/types of prokinetic drugs are available for treatment.
- Non-selective serotonergic agonists and dopamine antagonists carry the risk of serious adverse effects due to their cardiac toxicity due to prolonged Q-T interval and serious arrhythmia.
- Itopride, prucalopride and velusetrag (Phase 2) have a positive safety profile.
- Future selective agents which have high affinity to the gut receptors, but low affinity to cardiac receptors are stepping out of the shadow.
- Prokinetic means simply to **promote gut movement** and transit.
- in gastroparesis:
 - Accelerate gastric emptying.
 - Increase antral contractility.
 - Central antiemetic effects
 - Proximal gastric relaxation.
 - Suppression of visceral sensation.
 - Improvement in gastric dysrhythmias.

up the potential for new and different treatment options.



Recent advances have provided new insights and opened