World Organization for Specialized Studies on Diseases of the Esophagus

OESO Newsletter – September 2022

Message to the members of OESO,
and to all those who have interest in Esophagology

The OESO-SEMPIRE

VIRTUAL EDUCATIONAL CHANNEL
21st meeting

From the Airway Reflux
OESO-SEMPIRE Pilot Center
Medical College of Wisconsin
Milwaukee, Wisconsin

Hosted by Nikki **Johnston**, Ph.D.
Professor of Otolaryngology and Communication Sciences
Director of Airway, Digestive and Voice Research
Education Coordinator

Friday, September 23, 2022

- **North America**,
  9 – 11 am Wisconsin / CDT

- **Europe CET:**
  Paris: 4 – 6 pm
- **North America:**
  West Coast: 7 – 9 am
  East Coast: 10 am – 12 noon
- **South America:**
  São Paulo, 11 am – 13 pm
- **Africa:** Bomet, Kenya, 5 – 7 pm
- **Asia:** Malaysia, Kuala Lumpur
  10 pm – 12 midnight
- **Australia:** Melbourne,
  Sat, 24 Sept, 12 midnight – 2 am

- Zoom technology applied

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Airway Reflux: Is it acid, non-acid, something else? Perspectives from Laryngology, Gastroenterology, Respiratory Medicine, Surgery, and Research.

- **Didactic presentation**
  Pepsin: molecular pathophysiology and diagnostic utility
  Tina **Samuels**, MS, Program Manager
  Gastroesophageal and extraesophageal reflux are prevalent and costly diseases. Recognition of the pathogenicity of nonacid reflux has stimulated interest in alternatives to acid-targeting diagnostics and therapeutics. Pepsin is the most deleterious enzyme in refluxate, eliciting inflammatory and carcinogenic effects irrespective of acid. Its presence in all refluxate and detection in saliva have situated pepsin as the most widely researched biomarker for reflux today. A summary of the emerging findings regarding pepsin-mediated damage during reflux and developments in pepsin-targeting diagnostics will be presented.

- **Didactic presentation**
  Fosamprenavir for the treatment of Laryngopharyngeal Reflux (LPR)
  Nikki **Johnston**, PhD
  Given the paucity of data supporting efficacy of acid-suppression therapy for laryngopharyngeal reflux (LPR), the America Gastroenterology Association recommends against its use in the absence of classic gastro-esophageal reflux disease (GERD) symptoms. With compelling evidence of nonacid proximal reflux of pepsin and its association with laryngeal and pharyngeal symptoms and endoscopic findings, a new treatment which specifically targets pepsin could be of great value. Fosamprenavir was found to bind to and inhibit pepsin, abrogating pepsin-mediated laryngeal inflammation and mucosal damage in an LPR mouse model. Fosamprenavir has a good safety profile, is well-tolerated, and targets a foreign virus, making it an ideal drug to repurpose/reformulate, allowing a more expeditious and limited safety assessment in a clinical trial compared to a new molecule. Furthermore, this new approach would be amenable to local treatment of readily accessible airways affected by LPR allowing lower dosing, limiting systemic side effects. FDA/IND approval has been obtained for a 12-week, randomized, placebo-controlled, double-blind, phase III clinical trial to assess the efficacy of oral fosamprenavir for the treatment of LPR. Safety, tolerability, and pharmacokinetic parameters of fosamprenavir administered by dry powder inhaler is also being assessed.

GIST OF THE 1ST CASE

Case 1:

Presenter: Prof. Jonathan **Bock**
Medical College of Wisconsin

46 year old male with many years of allergy and cough symptoms

- History of allergy shots, PFT's with variable inspiratory phase
- Longstanding spells of sudden SOB with exertion
- Cough, throat clearing, and globus specifically after meals
- No dysphonia, no dysphagia, no sig heartburn or reflux
- DeMeester score 9 but had 98 proximal reflux impedance events, 2 pH positive pharyngeal events, did well on Gaviscon
- Eventually referred for Linx procedure

GIST OF THE 2ND CASE

Case 2:

Presenter: Prof. Thomas L. **Carroll**
Director, BWH Voice Program
Brigham and Women's Hospital,
Harvard Medical School

Chronic cough with talking trigger in a patient with vocal fold paresis and voice change and classic GERD symptoms

38 year old female with 3 years of chronic cough and voice change. She underwent traditional empiric treatments for acidic reflux after negative allergy and asthma workup. Reflux testing off acid suppression confirmed distal acid after BID PPI failed. Vocal fold paresis and glottic insufficiency appreciated on laryngovideostroboscopy. Vocal fold augmentation relieved the cough.

GIST OF THE 3RD CASE

Case 3:

Presenter: Prof. Alyn **Morice**
Head, Cardiorespiratory Studies
Castle Hill Hospital
Hull York Medical School, UK

34 year old female with chronic cough

- 1967 born
- 1988 chronic dry cough
- 2009 gastro-oesophageal reflux (heartburn and cough)
- 2011 Manometry (St Elsewheres) Hypotonic LO(E)S. “Motility within normal limits”
- 2012 (March) Nissen fundoplication (St Elswheres) peptic symptoms improved. Still coughing
- 2012 (October) seen in the Hull Cough Clinic, HARQ score 45 out of 70

Hull Airway Reflux Questionnaire

Cough hypersensitivity syndrome: a distinct clinical entity.
Morice AH, Faruqi S, Wright CE, Thompson R, Bland JM
Lung. 2011 Feb;189(1):73-9.

Within the last MONTH, how did the following problems affect you? 0 = no problem and 5 = severe/frequent problem						
Hoarseness or a problem with your voice	0	1	2	3	4	5
Clearing your throat	0	1	2	3	4	5
Excess mucus in the throat, or drip down the back of your nose	0	1	2	3	4	5
Retching or vomiting when you cough	0	1	2	3	4	5
Cough on first lying down or bending over	0	1	2	3	4	5
Chest tightness or wheeze when coughing	0	1	2	3	4	5
Heartburn, indigestion, stomach acid coming up (or do you take medications for this, if yes score 5)	0	1	2	3	4	5
A tickle in your throat, or a lump in your throat	0	1	2	3	4	5
Cough with eating (during or straight after meals)	0	1	2	3	4	5
Cough with certain foods	0	1	2	3	4	5
Cough when you get out of bed in the morning	0	1	2	3	4	5
Cough brought on by singing or speaking (for example, on the telephone)	0	1	2	3	4	5
Coughing during the day rather than night	0	1	2	3	4	5
A strange taste in your mouth	0	1	2	3	4	5

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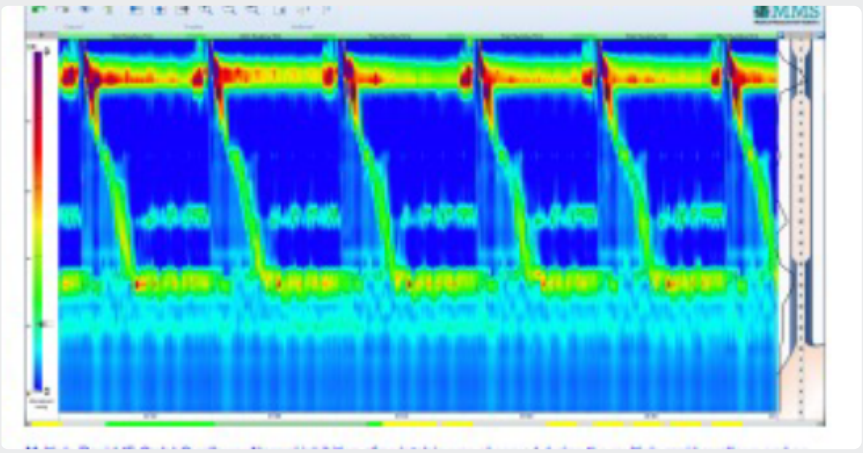
TOTAL SCORE_____/70

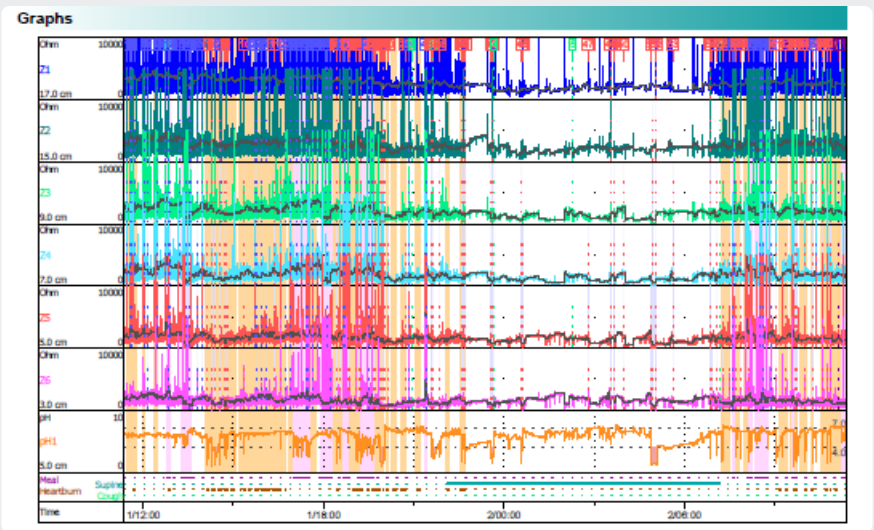
- Trials of promotility agents, azithromycin, metoclopramide,

domperidone, baclofen unsuccessful initially a good response to slow release morphine and chlorpheniramine.

- 2014 hiatus hernia on endoscopy
- 2019 referred back to Hull cough clinic. Prominent features voice change, metallic taste, cough on phonation, and the post-prandial cough at 10 minutes.
- Drug trials of P2X3 antagonists and NK1 antagonist without success



100% ineffectual. Normal LO(E)S, but HH.



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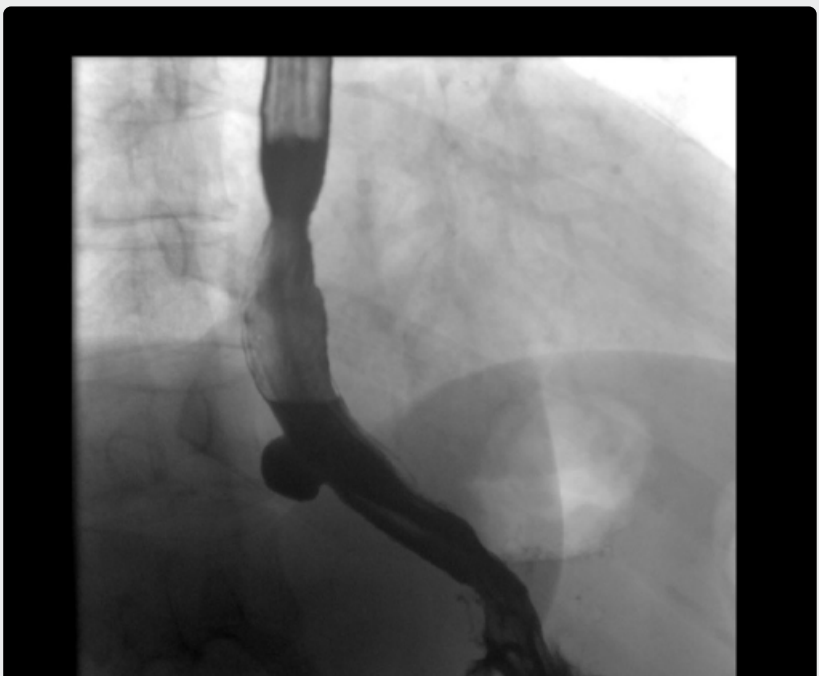


- Esophageal diverticulum plus HH and dysmotility.
- MTD - proceed to surgery
- 2019 redo Nissen fundoplication, recurrent for large paraoesophageal hiatus hernia, no diverticulum. Scarring ++. Repaired using Bio-A reinforcement

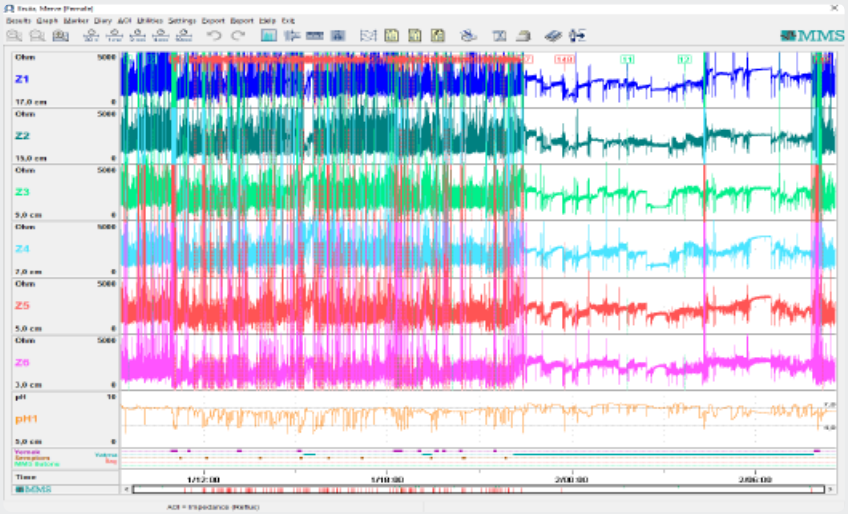
GIST OF THE 4TH CASE

Case 4:

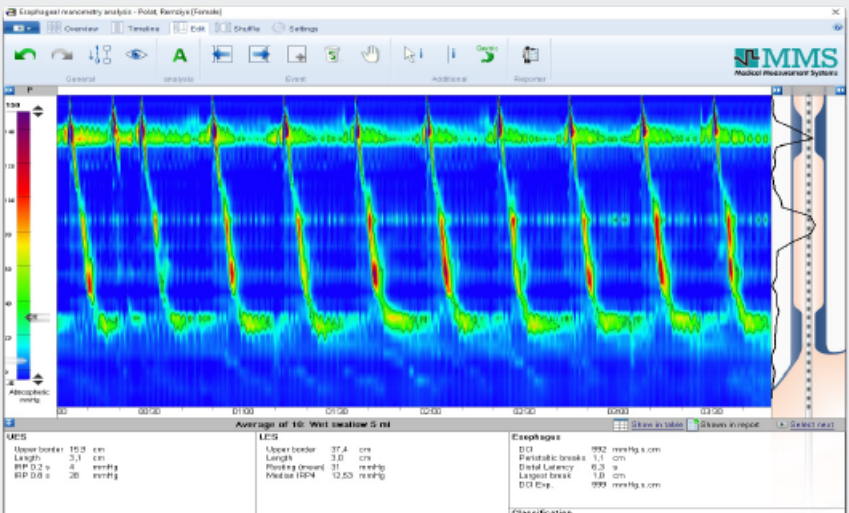
Presenter: Prof. Serhat **Bor**
Chair, Department of Gastroenterology
Ege University, School of Medicine
Izmir, Turkey

27 year old female referred for the evaluation of anti-reflux surgery

She has been suffering because of heartburn, acid regurgitation and especially hoarseness daily for three years. She wakes up with heartburn and cough.
PPI response is less than 50% for all symptoms.
There is no alarm symptom. Upper gastrointestinal Endoscopy shows LA-A esophagitis.



24 h MII-pH monitoring shows “weak acid reflux”. SAP and SI are negative.
High resolution esophageal manometry is normal



The patient is also consulted by Psychiatry. She diagnosed with somatisation disorder.
Her strong desire for antireflux surgery was discusssed during the reflux team meeting and refused. She was put on alginate. She refused the neuromodulators at the beginning but convinced. Amitryptillin 10 mg was started and increased to 20 mg. She is in a much better situation now.

Panel for discussion

- Serhat **Bor**, Izmir,Turkey
- Joel **Blumin**, Milwaukee, USA
- Jonathan **Bock**, Milwaukee, USA
- Thomas **Carroll**, Boston, USA
- Alyn **Morice**, Hull, UK
- Edgar **Figueredo**, Seattle, USA

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Registration is free, but mandatory:

Free registration

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*Twenty Pilot Centers worldwide are currently listed in the network of the OESO-SEMPIRE Platform of Excellence in Esophagology to take part in the program of the **OESO Virtual Educational Channel** in Esophagology.*
*Such a program is in line with true multi-disciplinarity, the essence of OESO since its creation, and the mission defined by UNESCO in the **Chair of Digital Education** attributed in 2018, at the University of Geneva, to the OESO Foundation.*

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The previous "Staff meeting discussions" were organized in

- **2020:** May 28 (Pilot Center of Milan), July 22 (Pilot Center of Stanford), October 3 (Pilot Center of Bomet, Kenya), October 29 (Pilot Center of Beijing), December 10 (Pilot Center of Geneva),
- **2021:** January 29 (Pilot Center of Melbourne), February 25 (Pilot Center of Bordeaux), March 19 (Pilot Center of Stanford), April 15 (Pilot Center of Paris), May 26 (Pilot Center of Milan), June 23 (Pilot Center of Sao Paulo), August 21 (Asian Pacific Digestive Week), October 19 (Pilot Center of Mainz), November 22 (Pilot Center of Bordeaux), December 9 (Pilot Center of Geneva),
- **2022:** January 20 (Pilot Center of Kota Bharu), February 22 (Pilot Centers of Beijing, Shanghai and Guangzhou), March 24 (Pilot Center of Boston), May 4 (Pilot Centers of Melbourne and Kenya) and July 19 (Pilot Center of Kota Bharu).

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- ***Wherever you are in the world,***
- ***Whatever your specialty,***
- ***Whatever your level,***

the 21st clinical case of the OESO-SEMPIRE Platform will afford you the opportunity to participate in a global multidisciplinary staff meeting dedicated to 4 challenging cases of esophagology.
It will involve specialists in various disciplines, and participants from any country can connect to the discussions.

Looking forward to seeing you soon!

Robert Giuli, MD, FACS
Professor of Surgery
Founder & Deputy Executive Director of OESO

The next clinical case coming up for discussion will be proposed on October 7 by Prof Italo Braghetto, Santiago Chile.

Date and details on time will be announced on the OESO website and in next Newsletters.

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