

# La tasca acida nella MRGE: aspetti patogenetici e terapeutici

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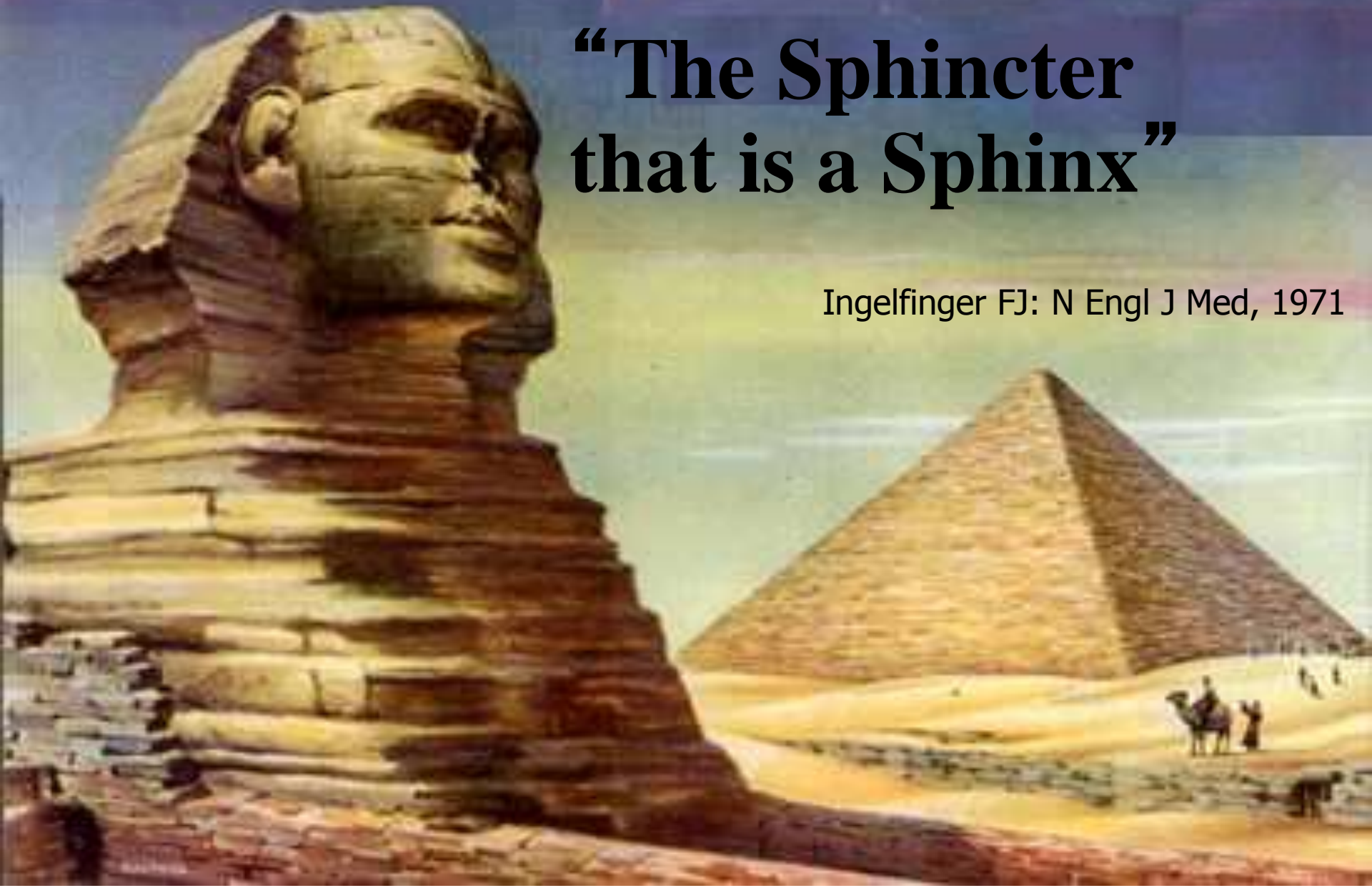
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Martino-IST, Genova

# Competence of the GE Junction

**“The Sphincter  
that is a Sphinx”**

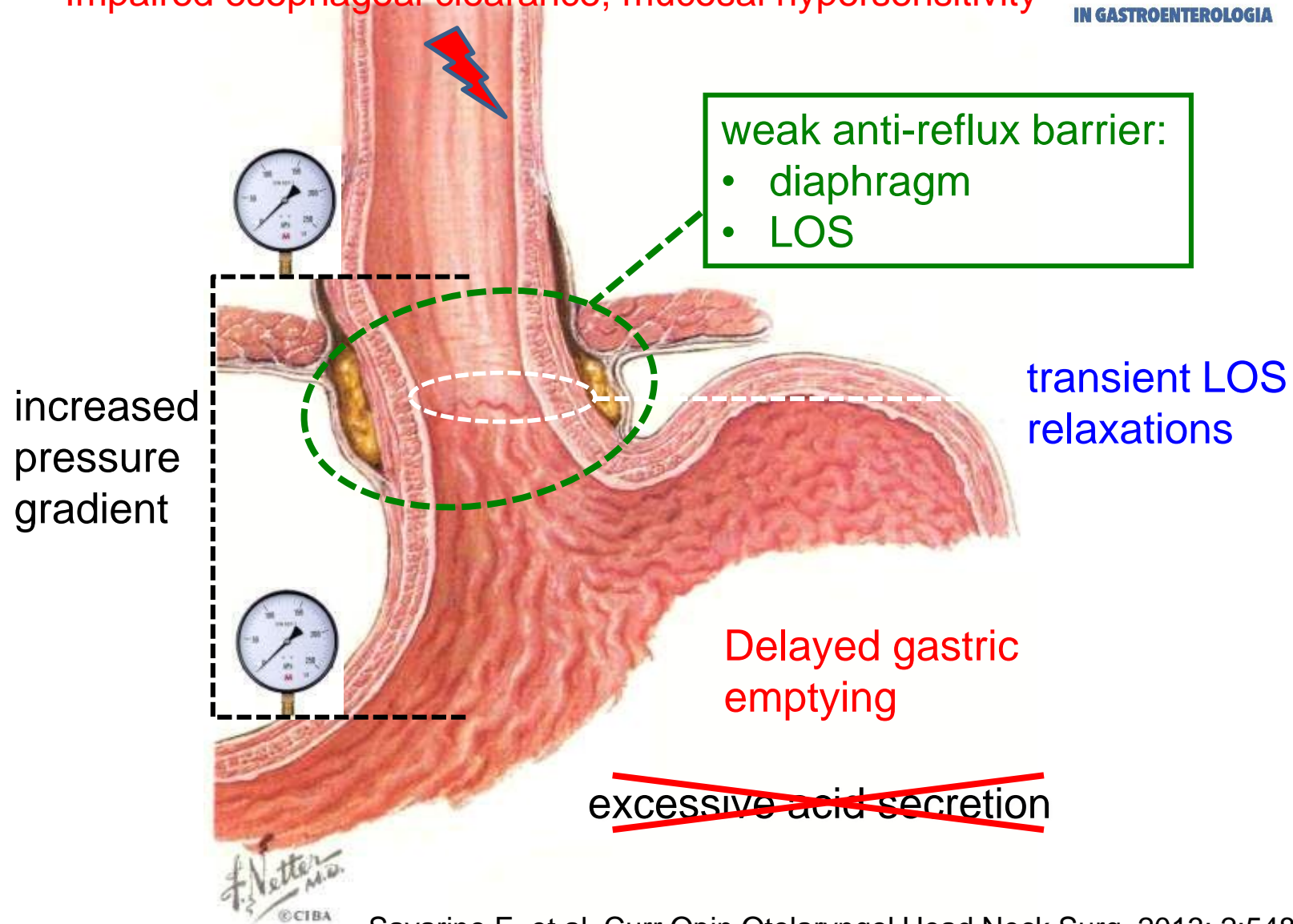
Ingelfinger FJ: N Engl J Med, 1971



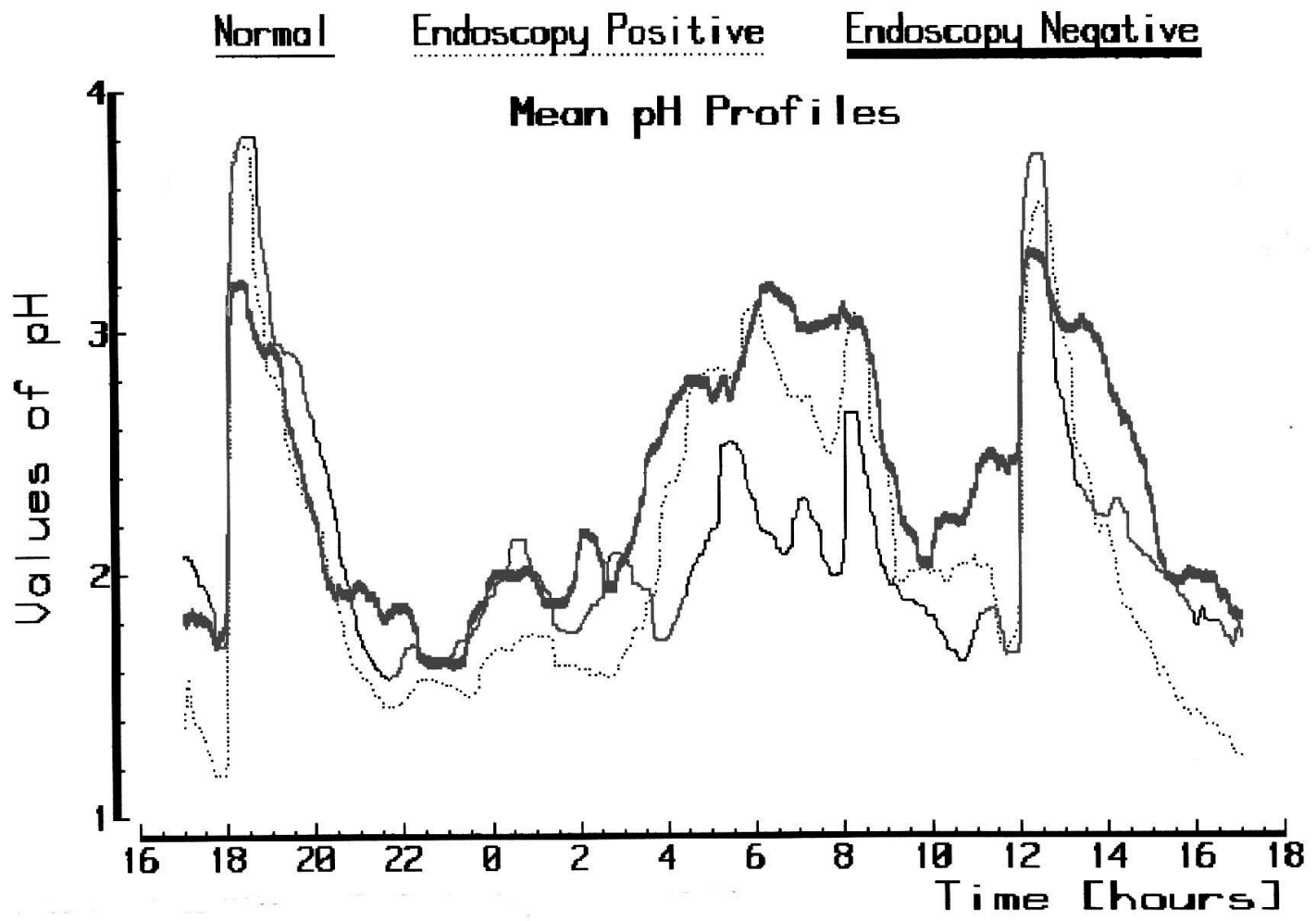
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# Pathophysiology of GERD

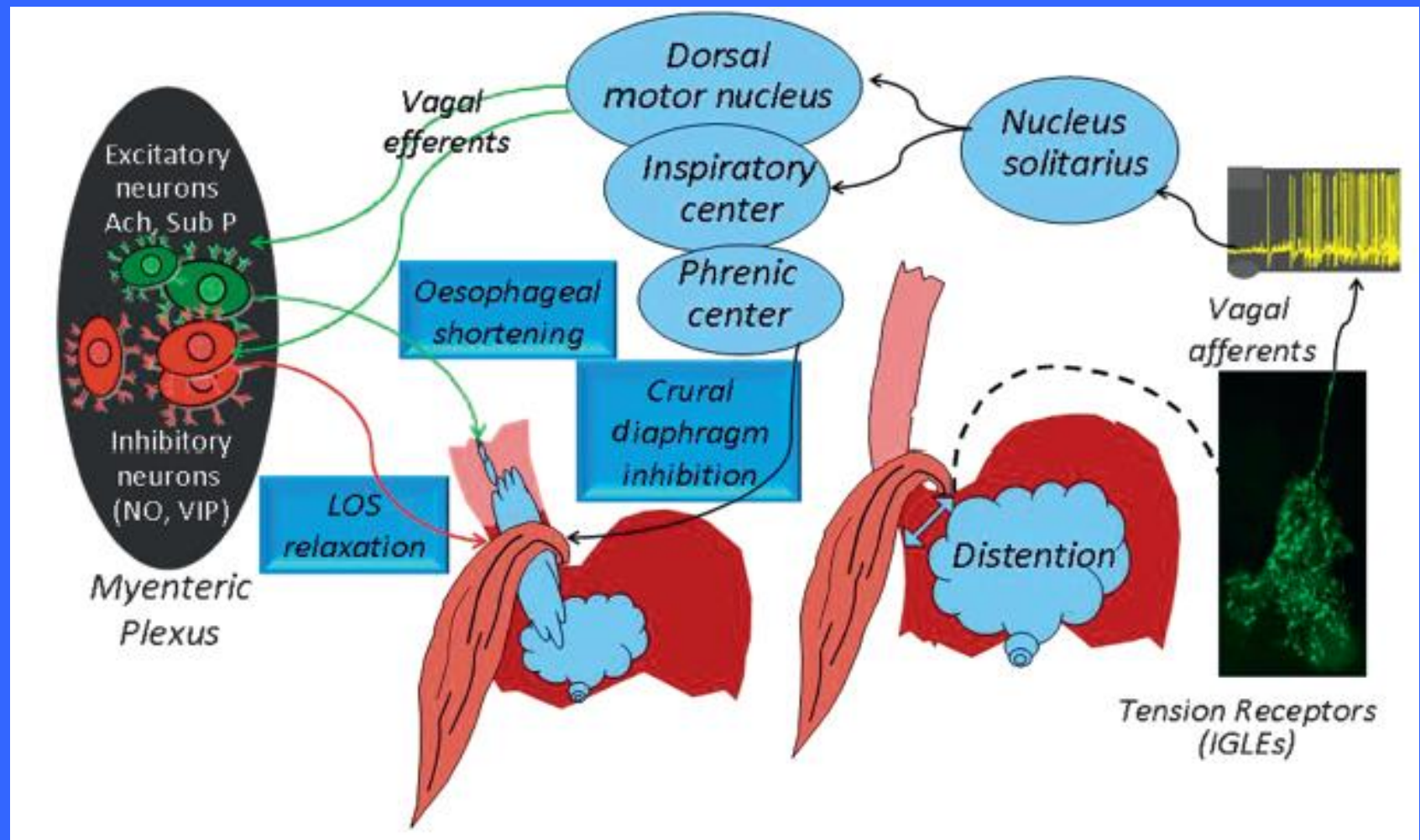
Impaired esophageal clearance; mucosal hypersensitivity



# 24-hour gastric pH profiles of controls and GERD patients with and without esophagitis

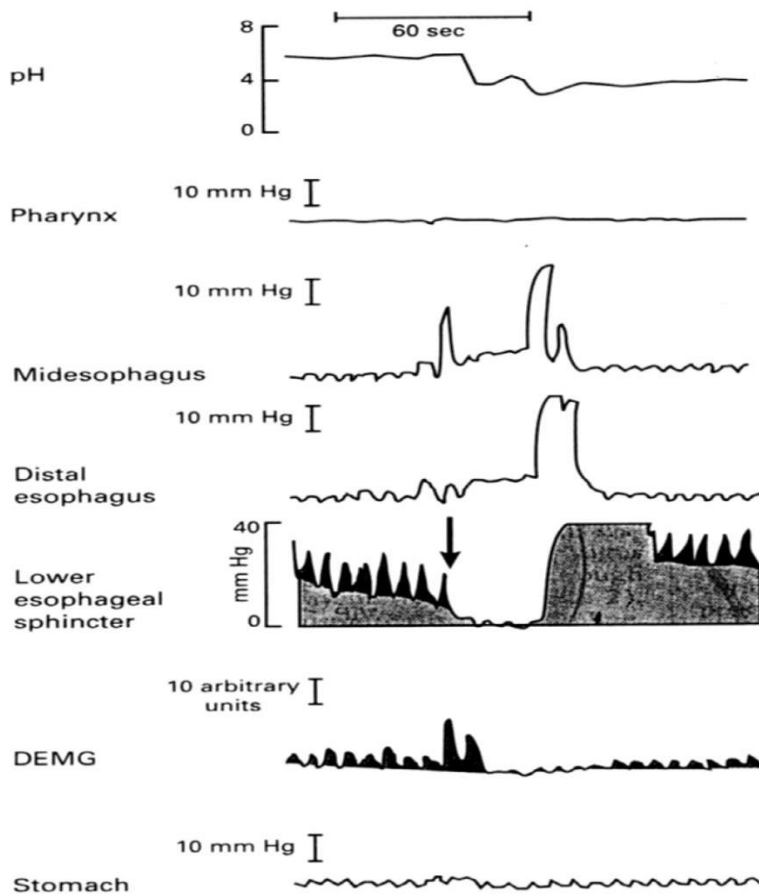


# Schematic diagram of the transient lower esophageal sphincter relaxation reflex

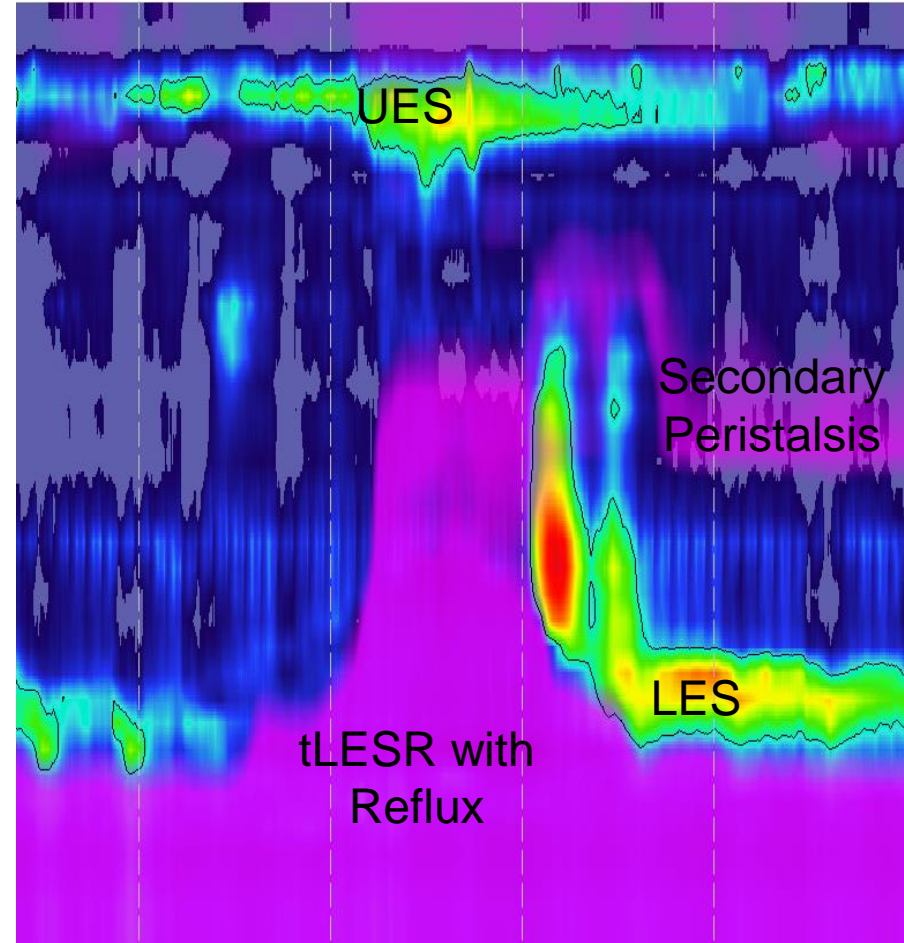


# Transient Lower Esophageal Sphincter Relaxation Reflex

## CONVENTIONAL MANOMETRY



## HIGH RESOLUTION MANOMETRY

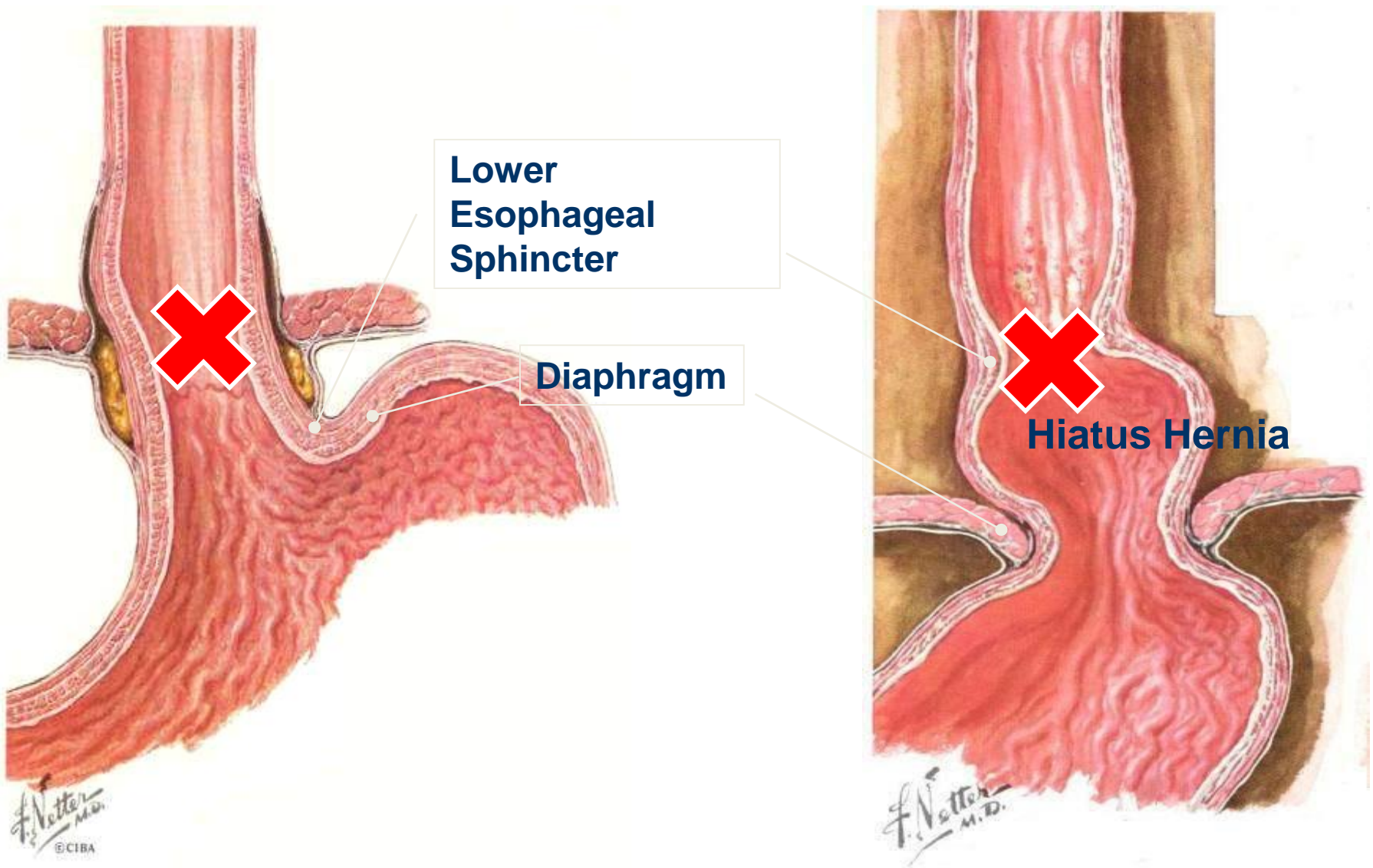


Mittal R et al, NEJM 1997

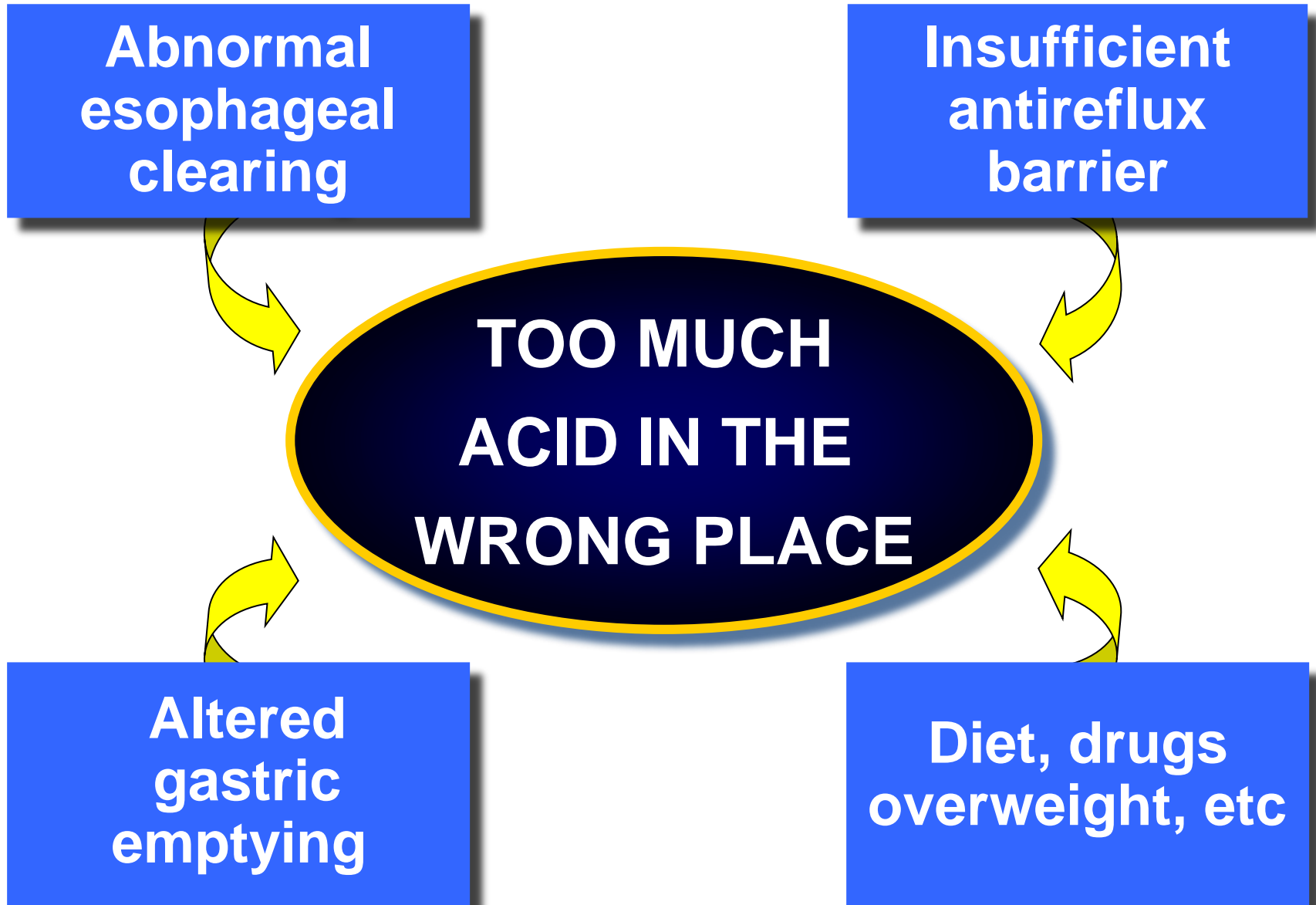
Savarino E, et al. Curr Opin Otolaryngol Head Neck Surg. 2013; 2:548-56



# The Anti-Reflux Barrier: Two Sphincters



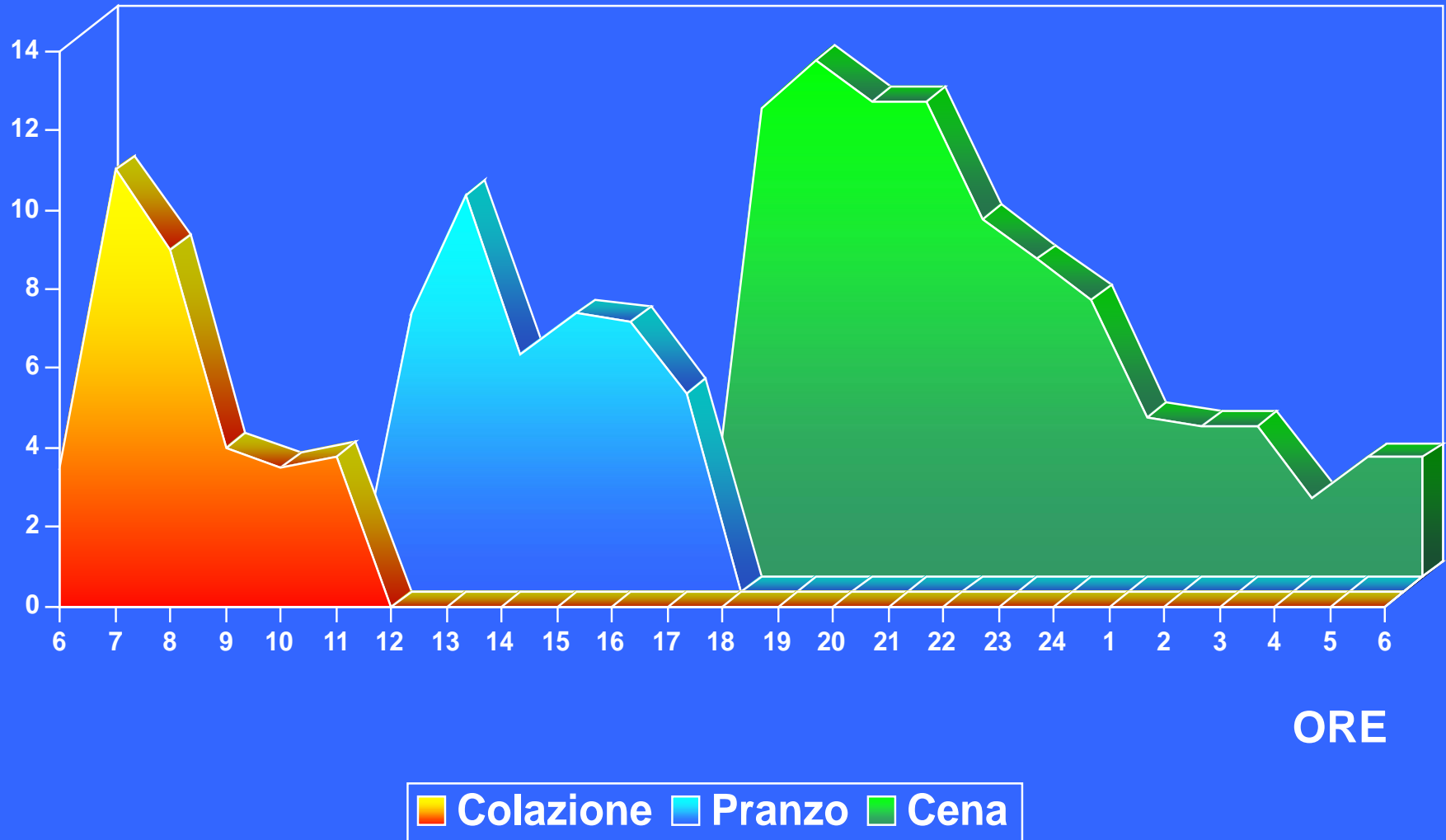
# Pathophysiology of GERD





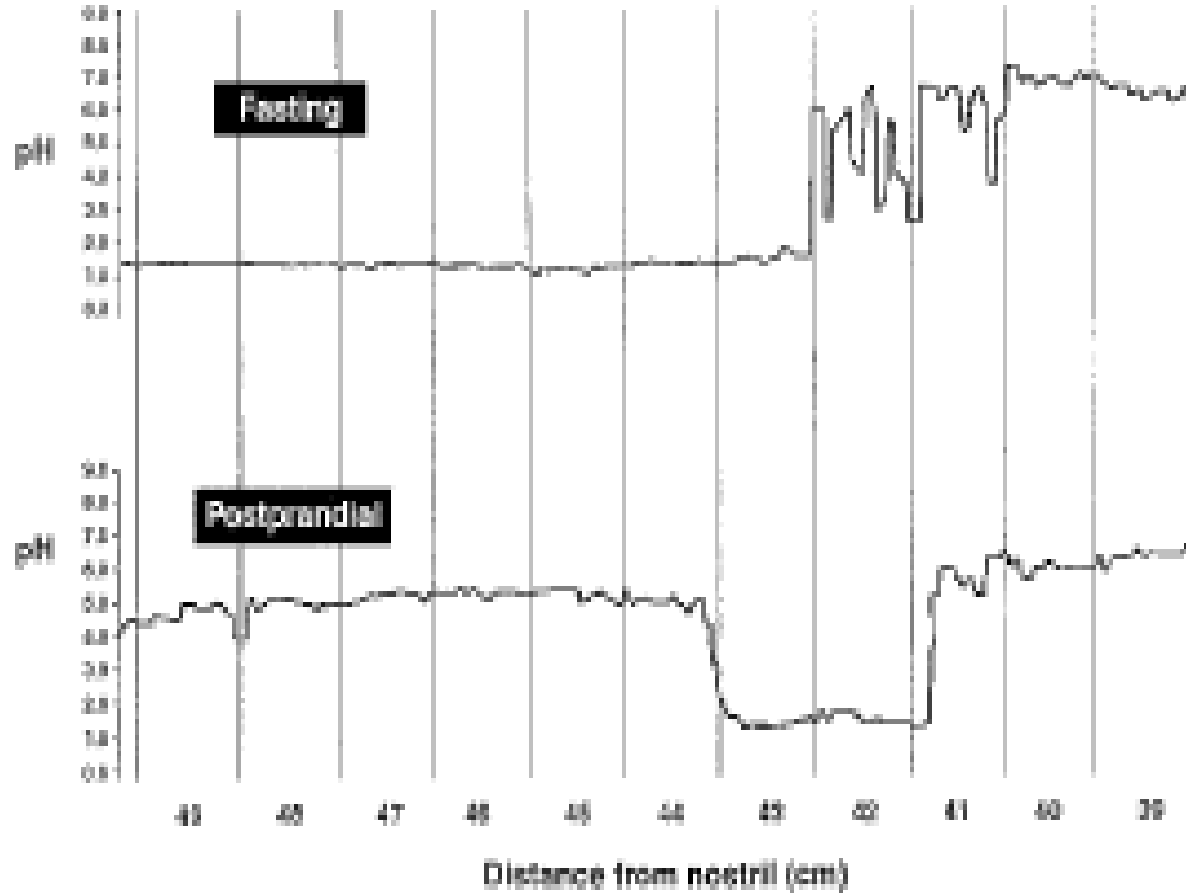
# L'esposizione esofagea diurna all'acido, particolarmente dopo i pasti predomina nella malattia da reflusso gastroesofageo

Esposizione intraesofagea all'acido  
(% tempo a pH < 4)



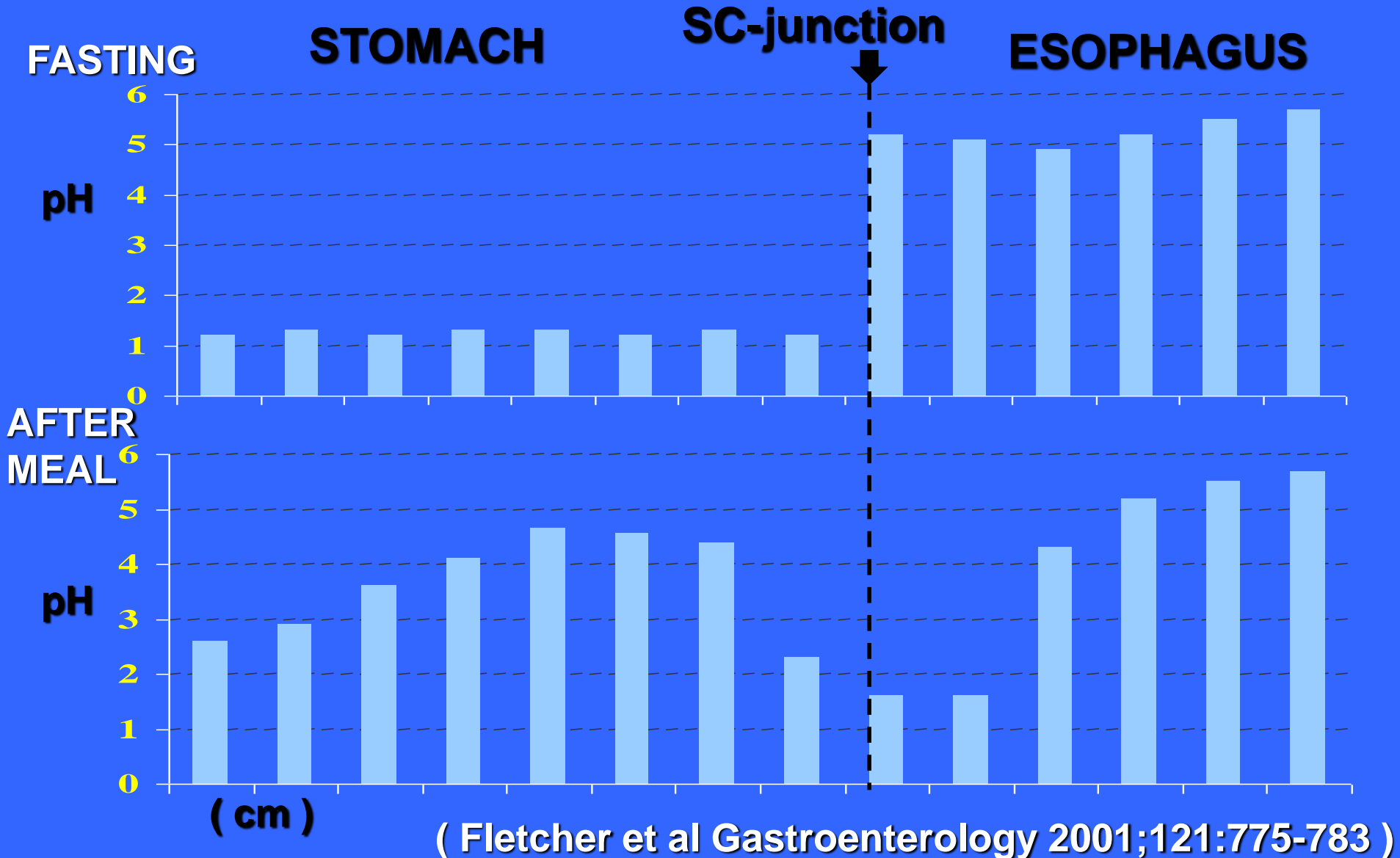
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## Example of a pH tracing during pull-through in 1 subject while fasting and again after a meal at the esophago-gastric junction



# Unbuffered acid pocket at Cardia & GE junction

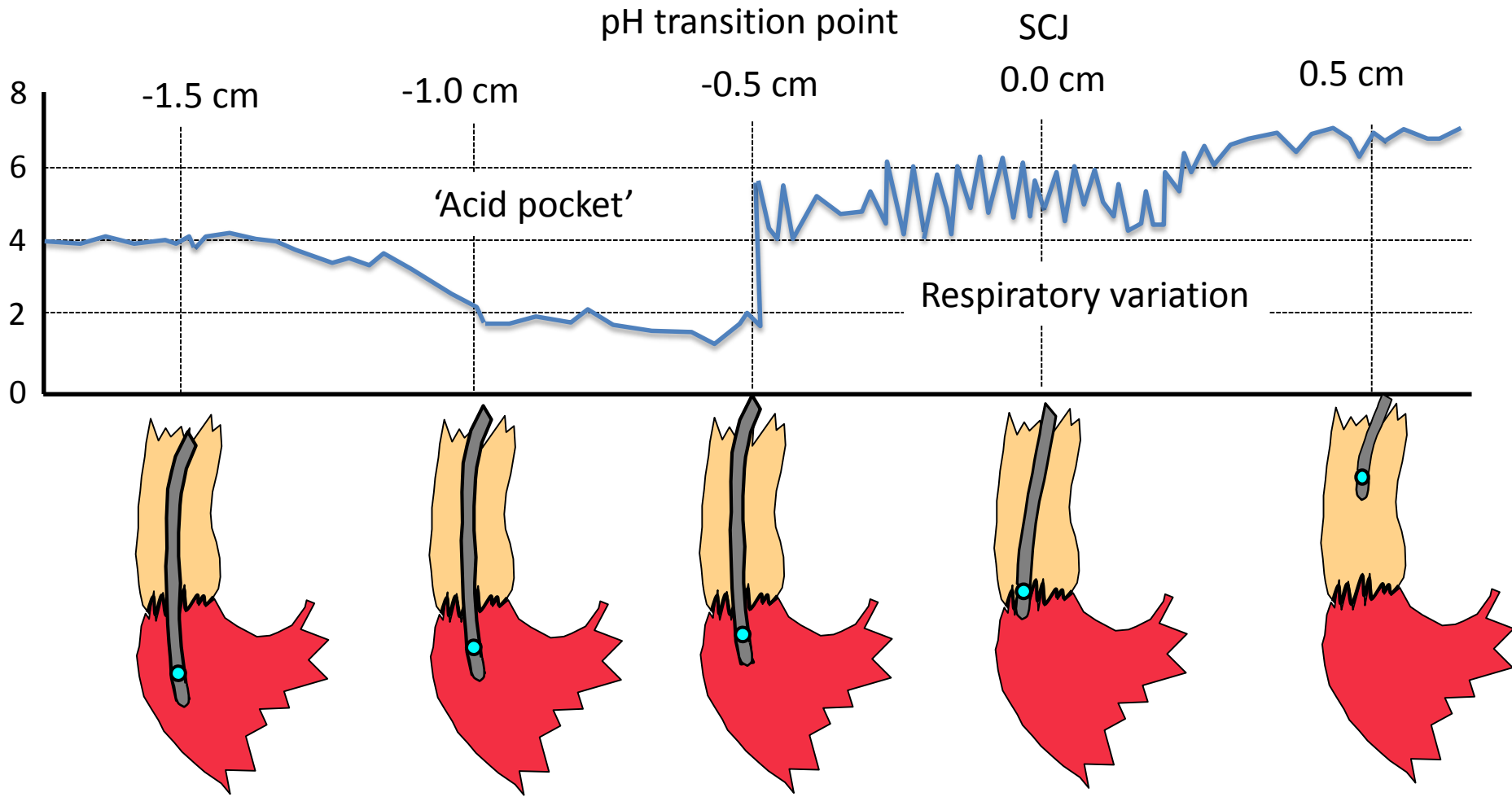
Mean of 10 subjects



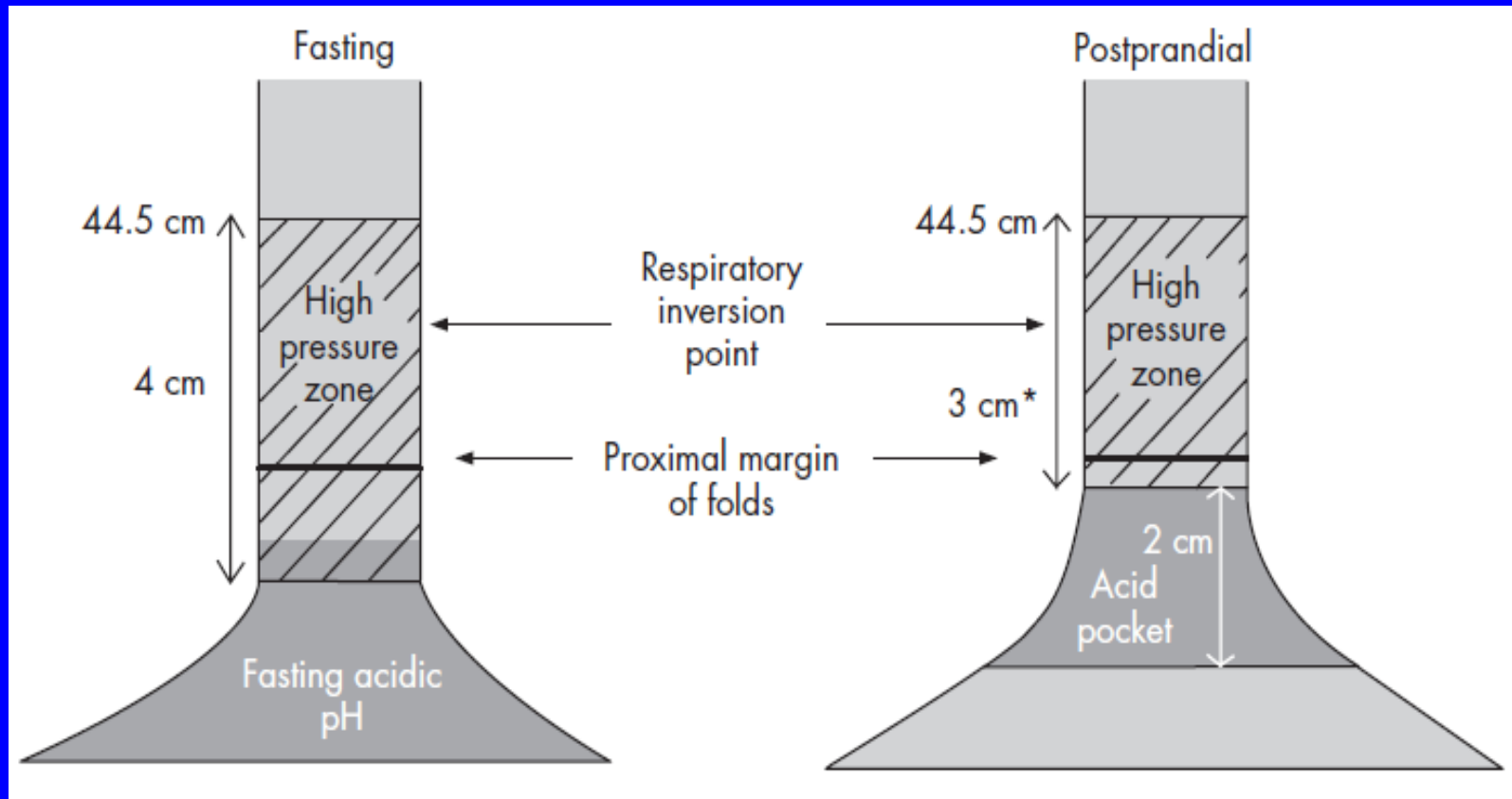
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# Relating the pH Transition to the SCJ & LES

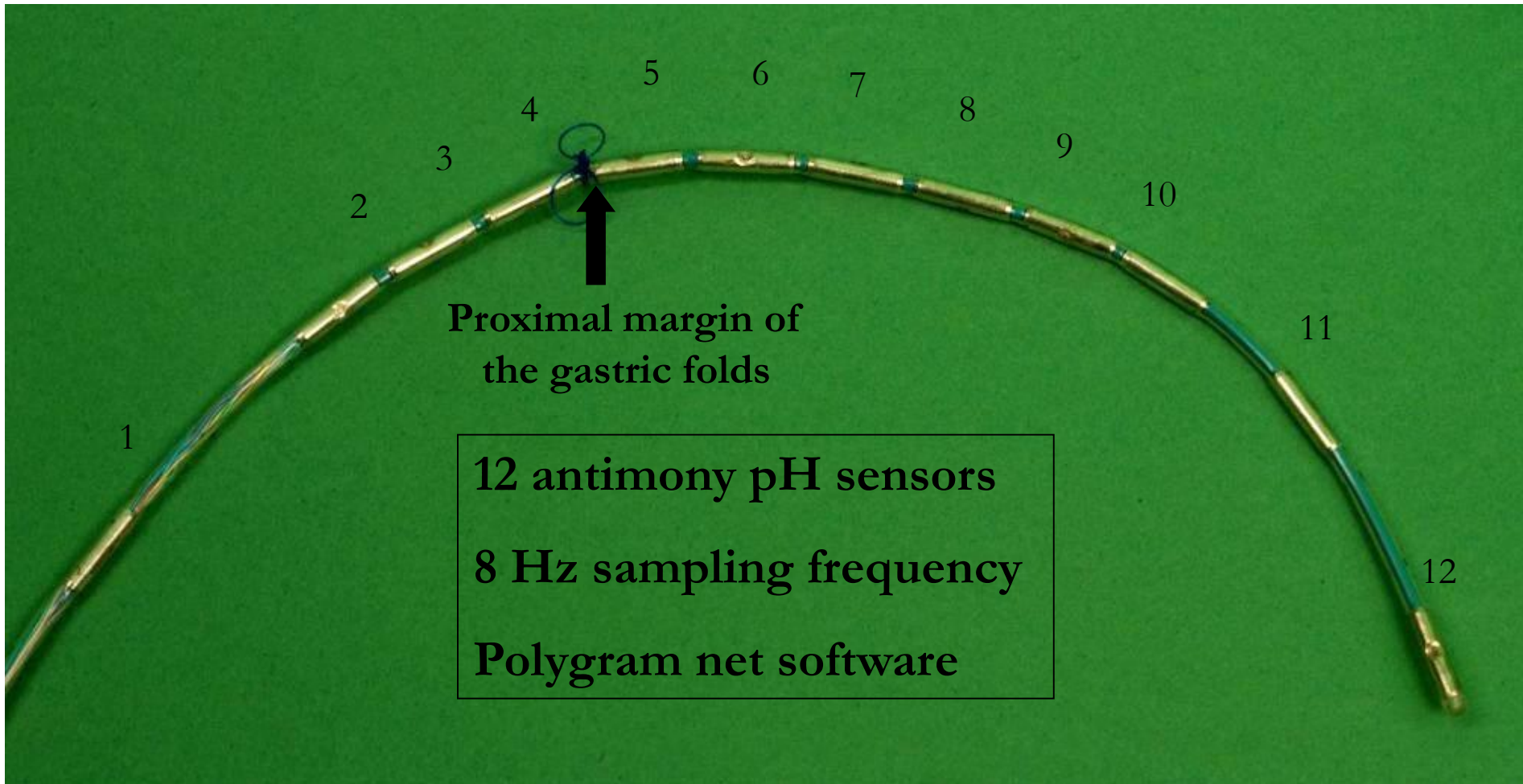
*Concurrent HRM, Fluoroscopy & pH-metry*



**Location of the acid pocket in fasting and post prandial conditions in healthy subjects. There is a significant shortening of the high pressure zone after meal ( $p < 0.05$ )**



# High Resolution pH metry



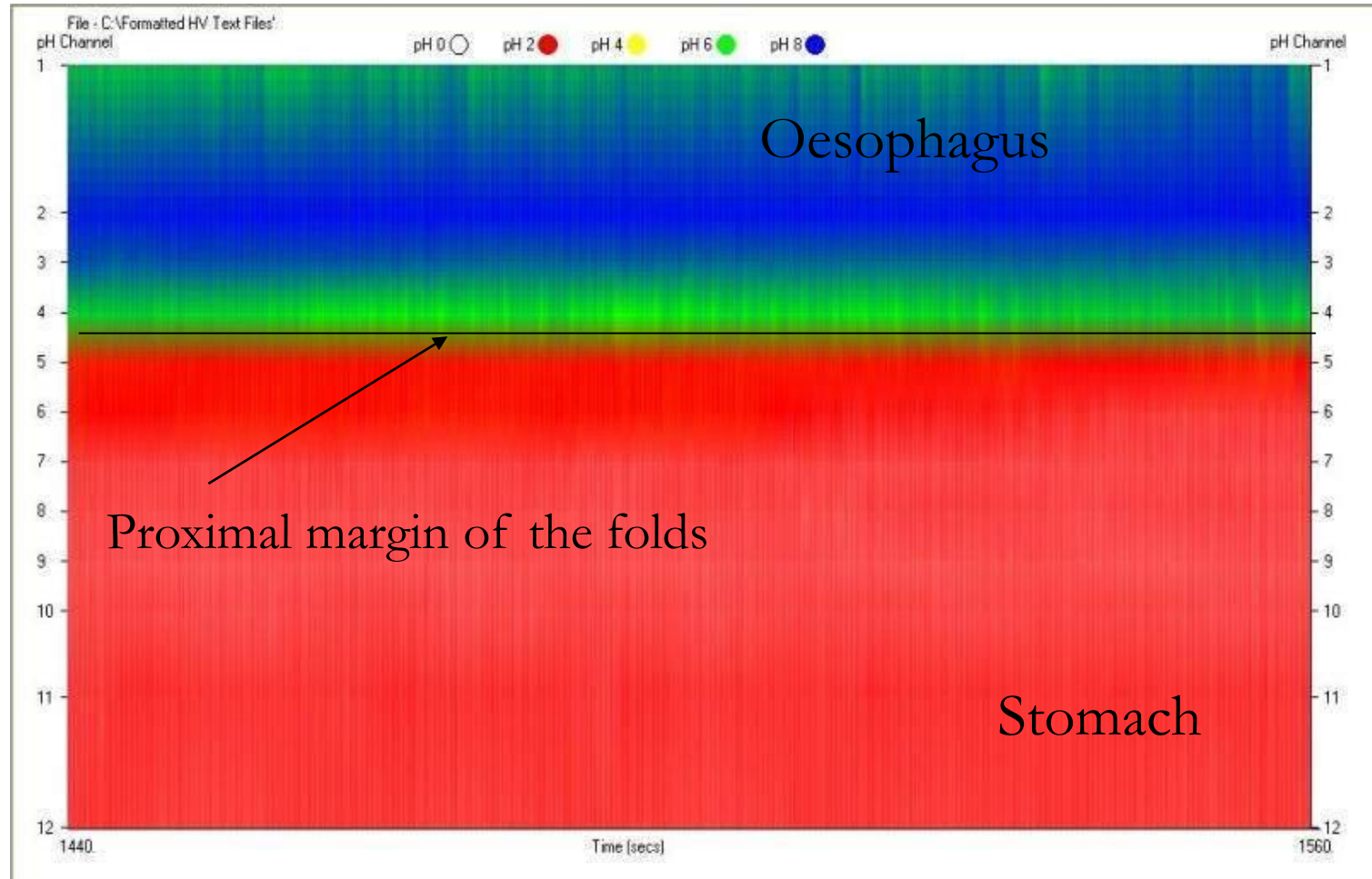
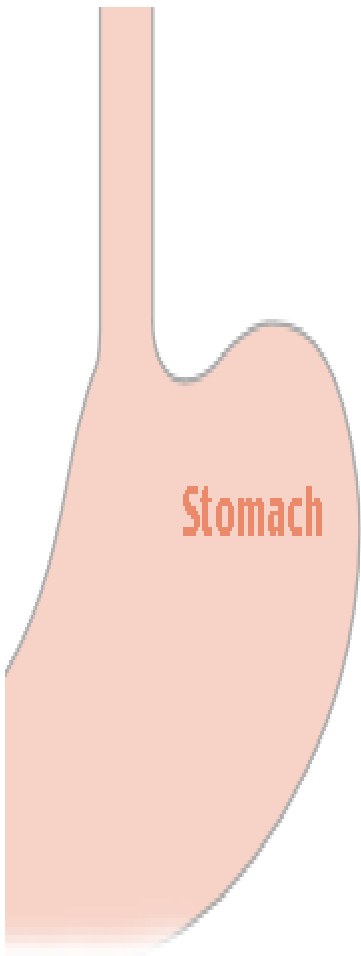
Custom made by Synectics

(Clarke et al Gut 2009;58:904-9 )

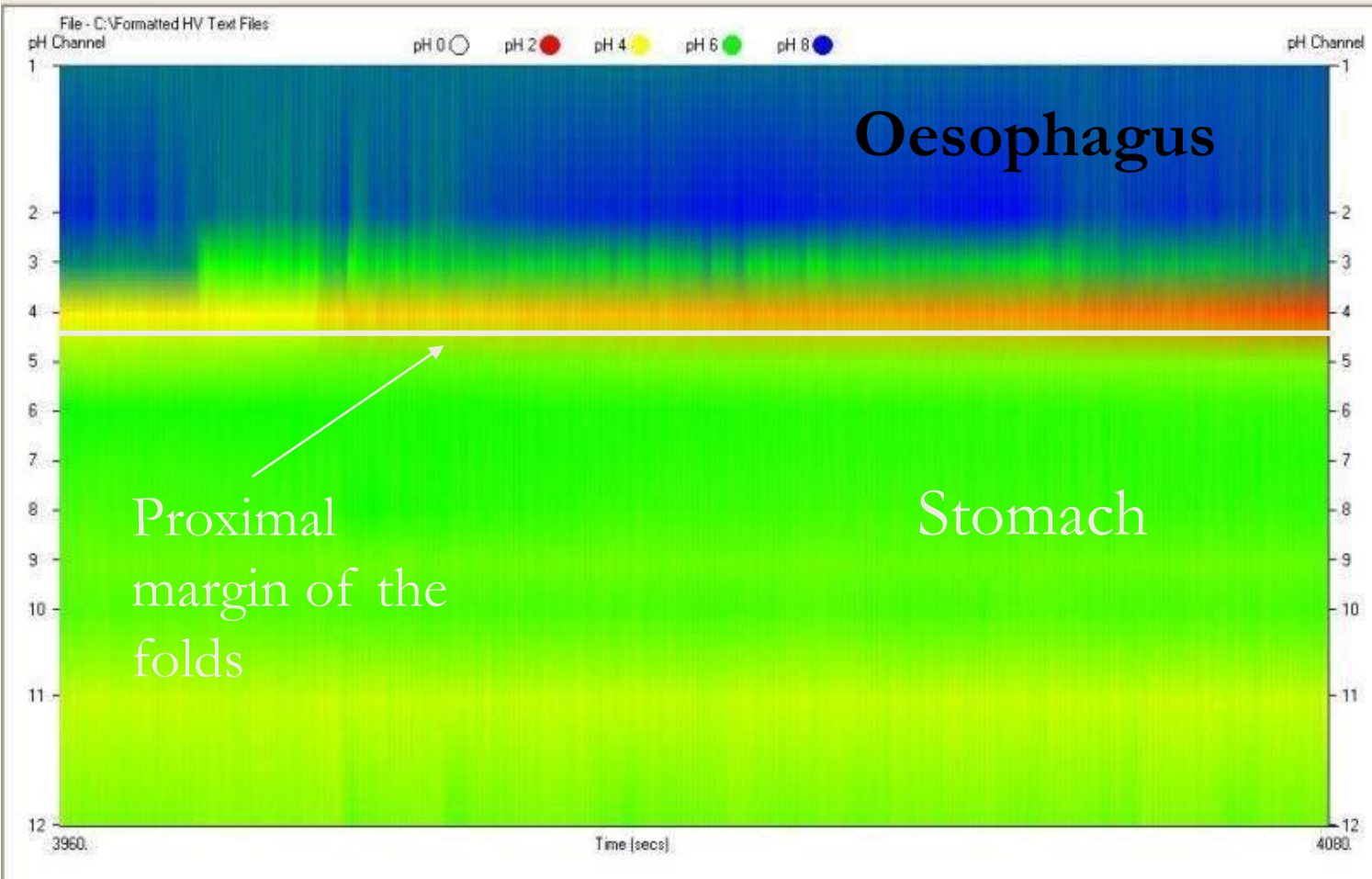
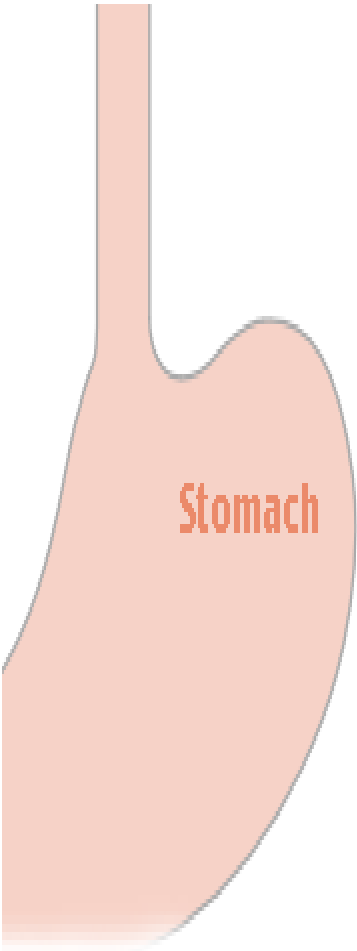
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# High Resolution pH - Fasting

## Colour Contour Display



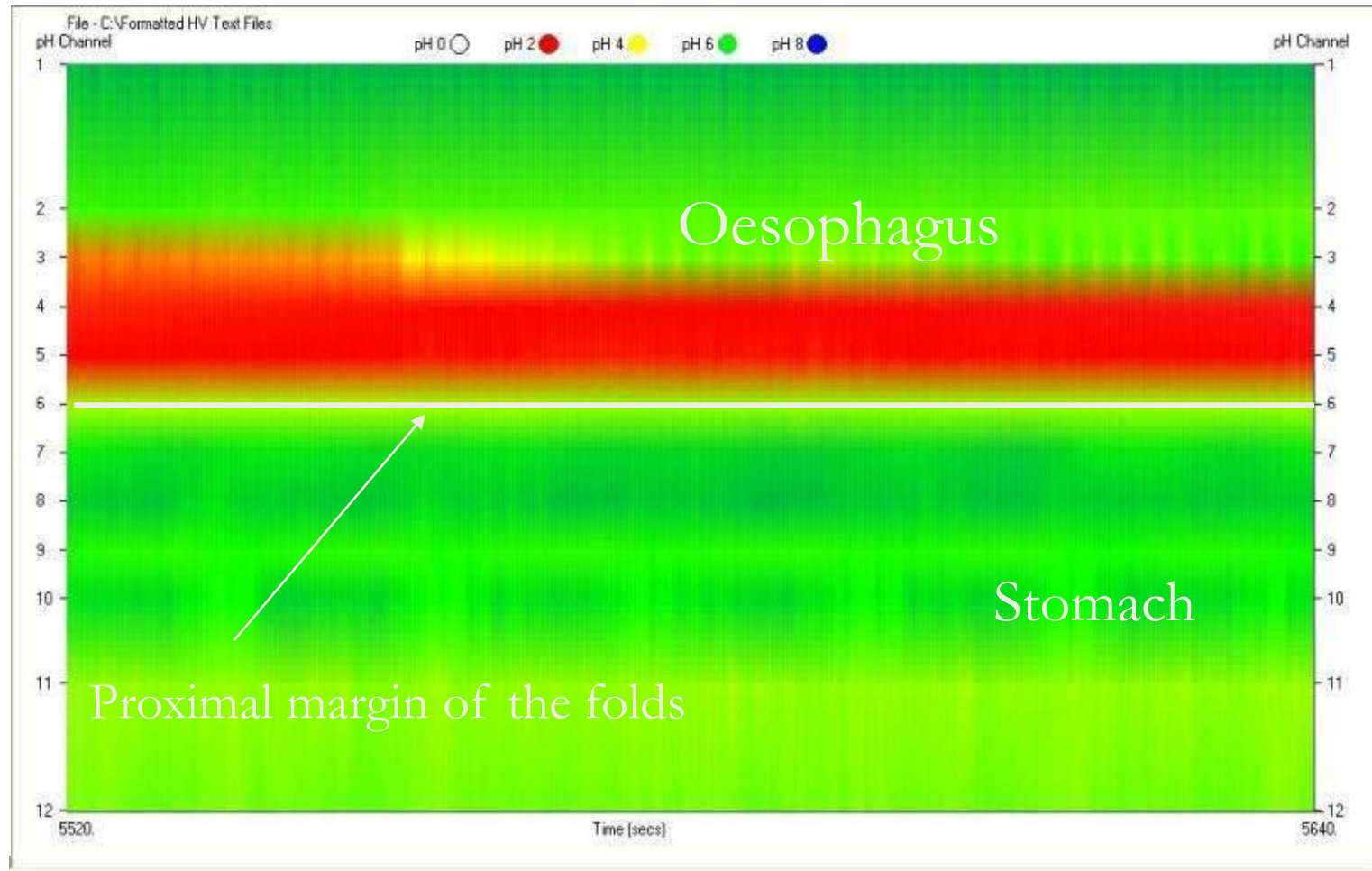
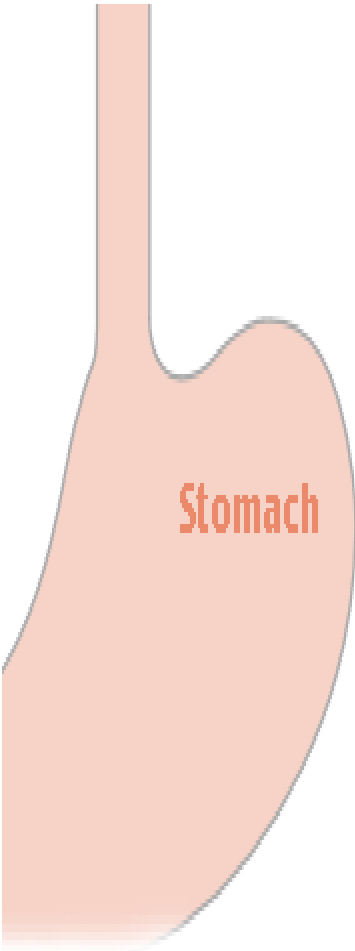
# High Resolution pH – 17 min after meal





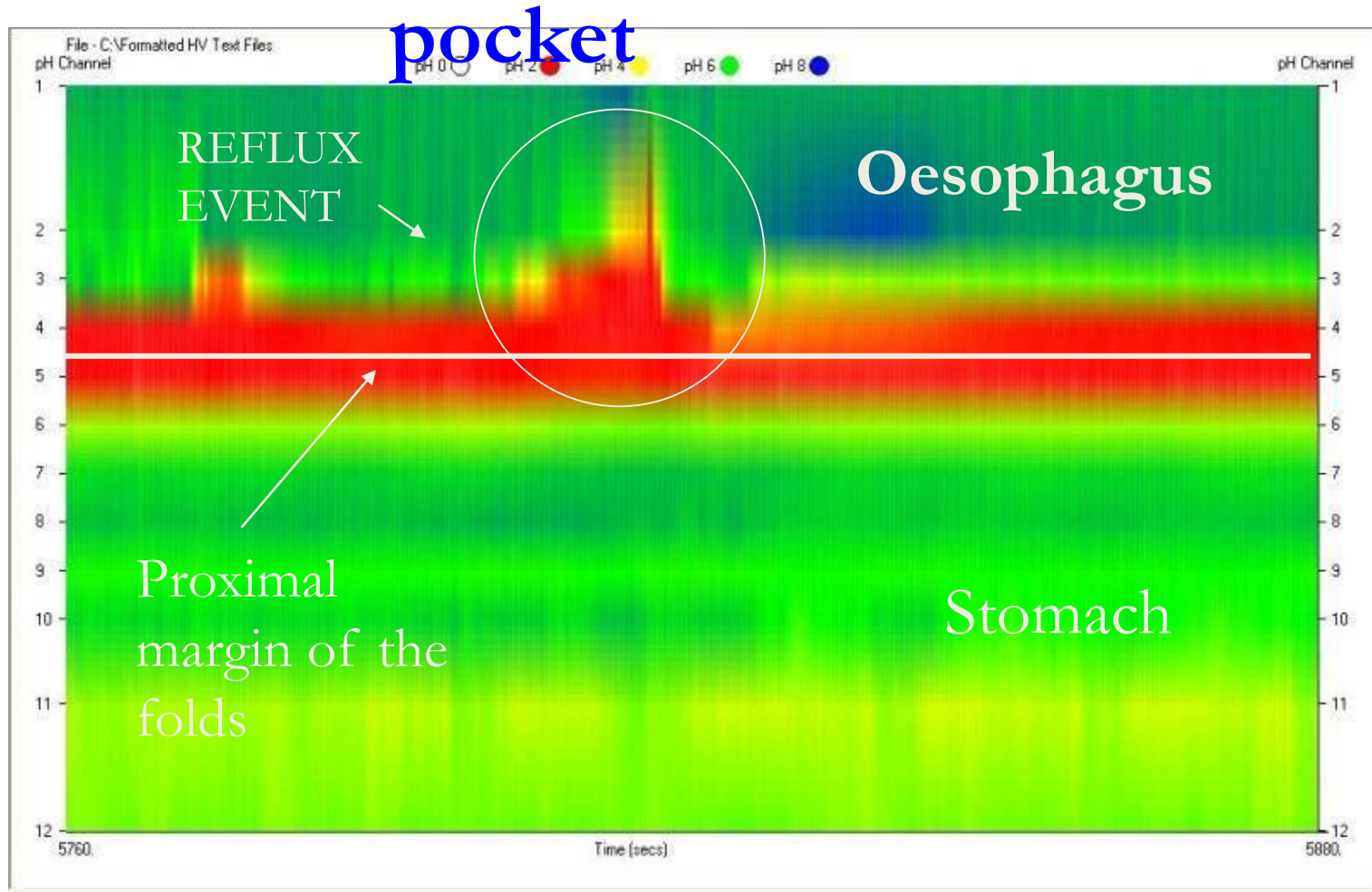
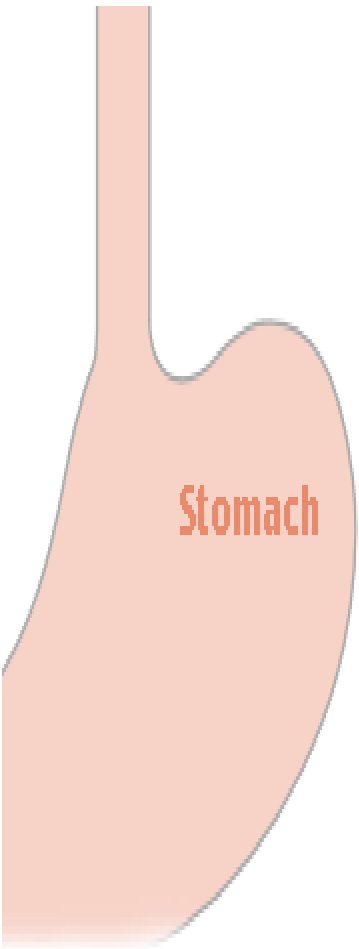
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# High Resolution pH – 45 min after meal



# High Resolution pH

## Short segment reflux from acid pocket



# Acid pocket is frequent source of postprandial reflux

## Studies with high resolution pH

Subject	Acidic oesophageal reflux (% time pH<4)	% reflux attributable only to the acid pocket
1	0.14	100
2	9.73	87.86
3	0.48	83.73
4	0.27	77.39
5	14.01	63.32
6	15	51.05
7	1.29	47.04
8	8.39	31
9	8.18	26.16
10	0.2	23.26
11	3.81	7.1
12	64.39	0.12
13	0	—
14	1.24	65.18
15	0	—
Median		51.05

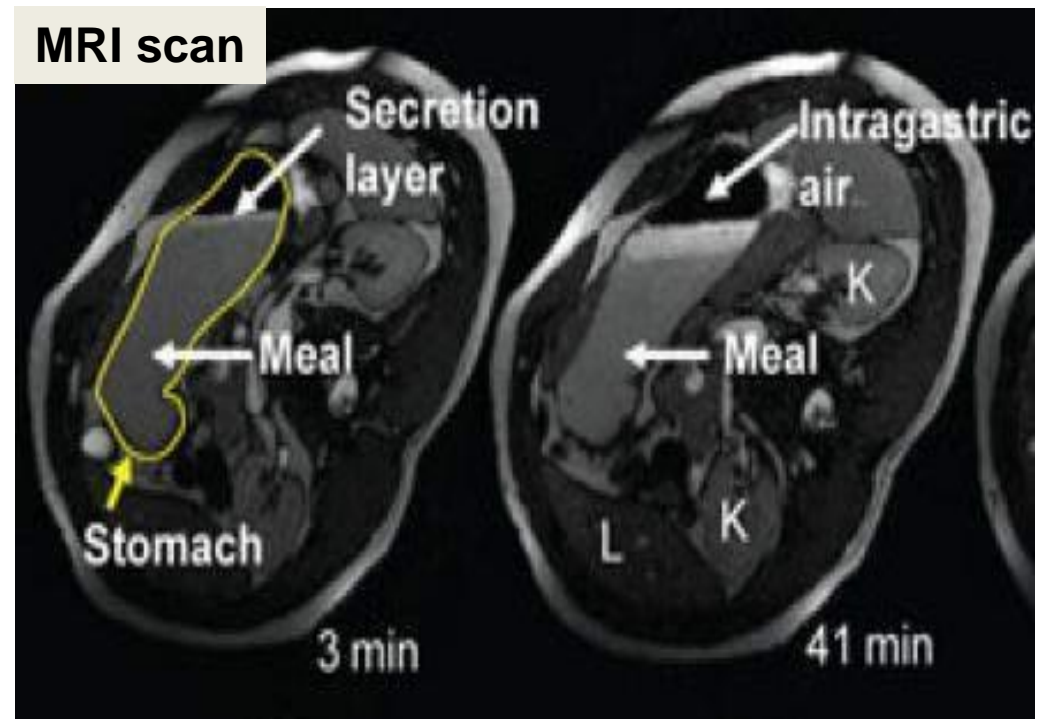
(Clarke et al Gut 2009;58:904-9 )

# Layering of unbuffered acid in proximal stomach

Following meal proximal stomach relatively immobile allowing layering of contents



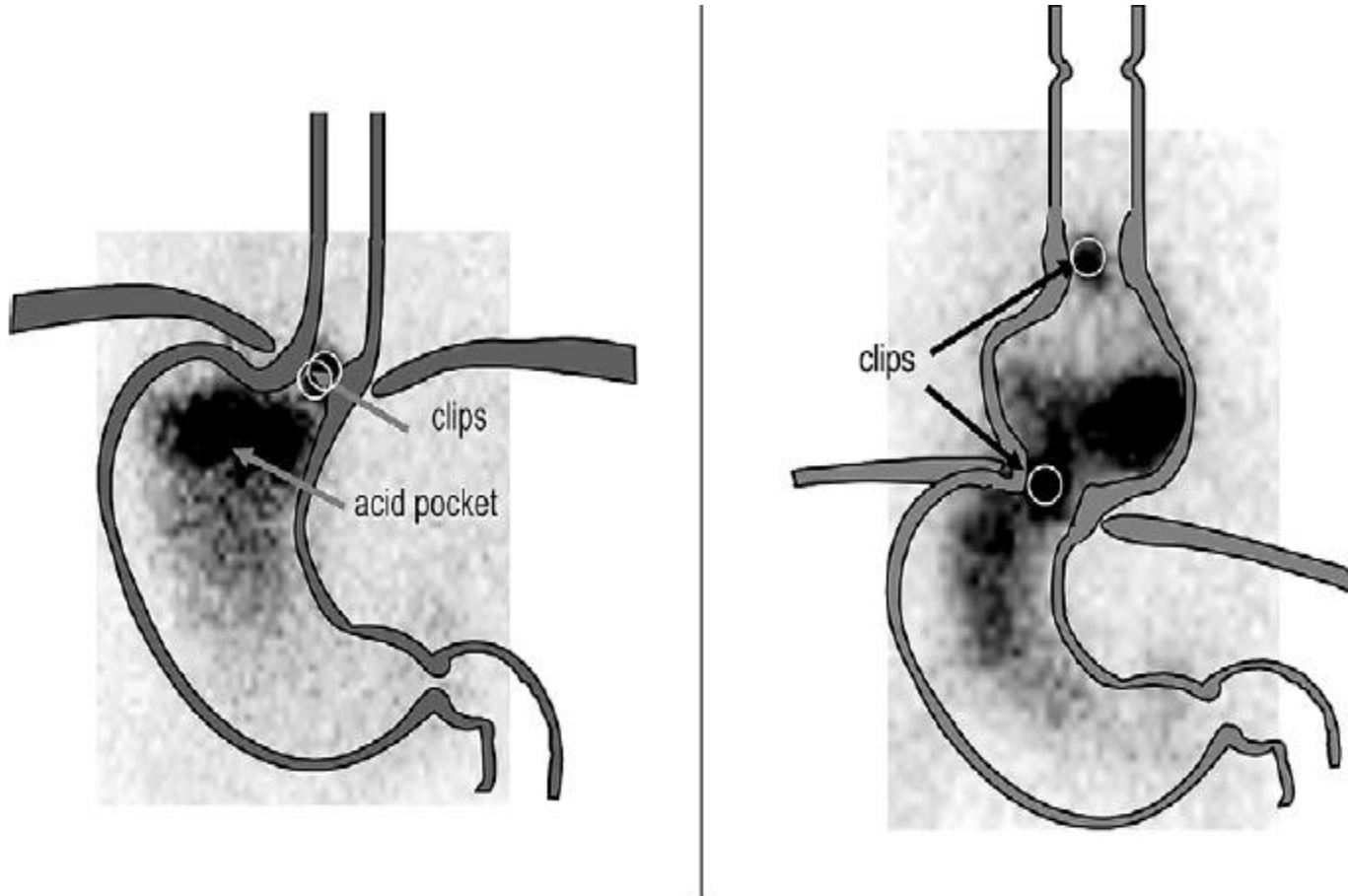
(From Marciani et al  
Brit J Nutrition 2006;95:331-9)



( From Sauter et al  
Neurogastroenterol Motil 2012;24:632-40 )

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# Scintigraphic images of the acid pocket in a normal subject and in a patient with hiatal hernia




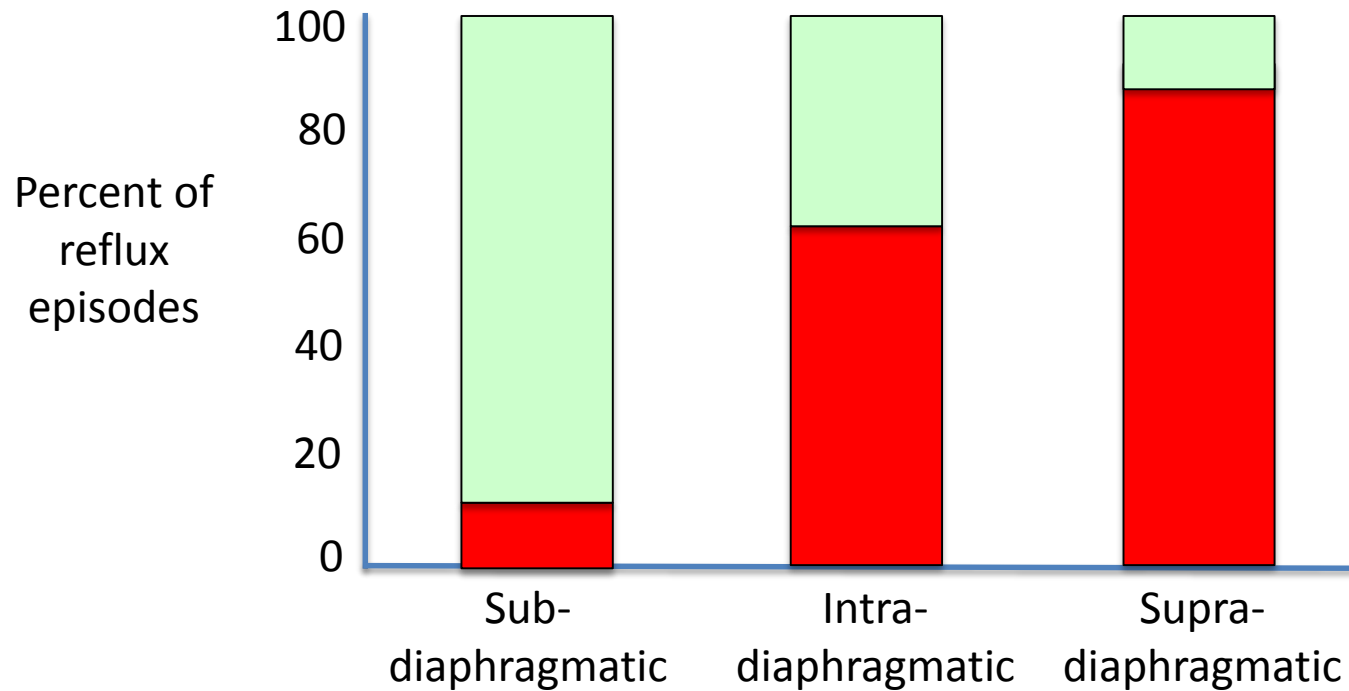
## Median pH and percentage of time at pH < 4.0 in the postprandial period

	Standardized meal		All meals together	
	0–60 min	61–120 min	0–60 min	61–120 min
<i>Median pH</i>				
Healthy subjects	3.0 (1.7–3.4)	2.2 (1.4–2.7)	2.9 (1.8–3.4)	2.2 (1.3–2.6)
GERD patients HH–	2.4 (1.8–3.0)	1.7 (1.4–2.2)	2.6 (2.1–2.8)	1.8 (1.7–2.3)
GERD patients HH+	3.2 (2.4–3.7)	2.0 (1.4–2.6)	2.4 (1.6–3.4)	1.7 (1.3–1.9)
<i>Percentage of time at pH &lt; 4</i>				
Healthy subjects	87 (72–98)	100 (99–100)	73 (63–83)	90 (78–100)
GERD patients HH–	96 (90–99)	100 (100–100)	84 (76–91)	98 (95–100)
GERD patients HH+	88 (43–96)	100 (99–100)	81 (61–89)	99 (92–100)
GERD, gastroesophageal reflux disease; HH, hiatal hernia.				

Grigolon A et al, Am J Gastroenterol 2009

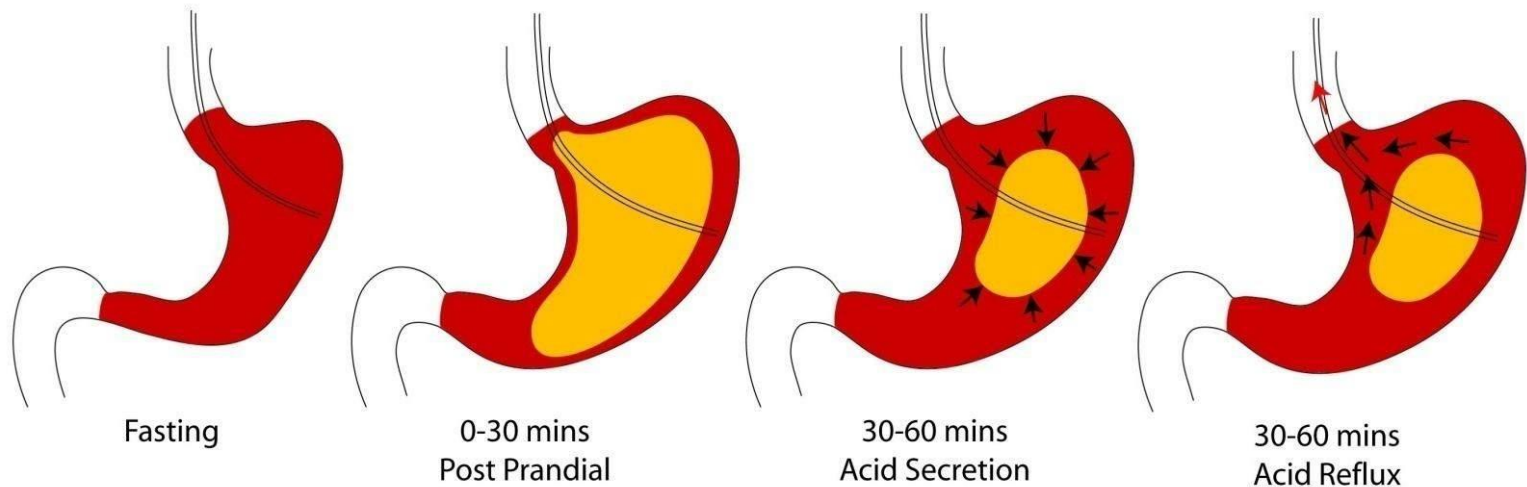
# Position of acid pocket vs acidity of reflux

 *Acidic*       *Weakly acidic*



# ACID COAT

**Fundus relaxes after meal so mixing limited, consequently**



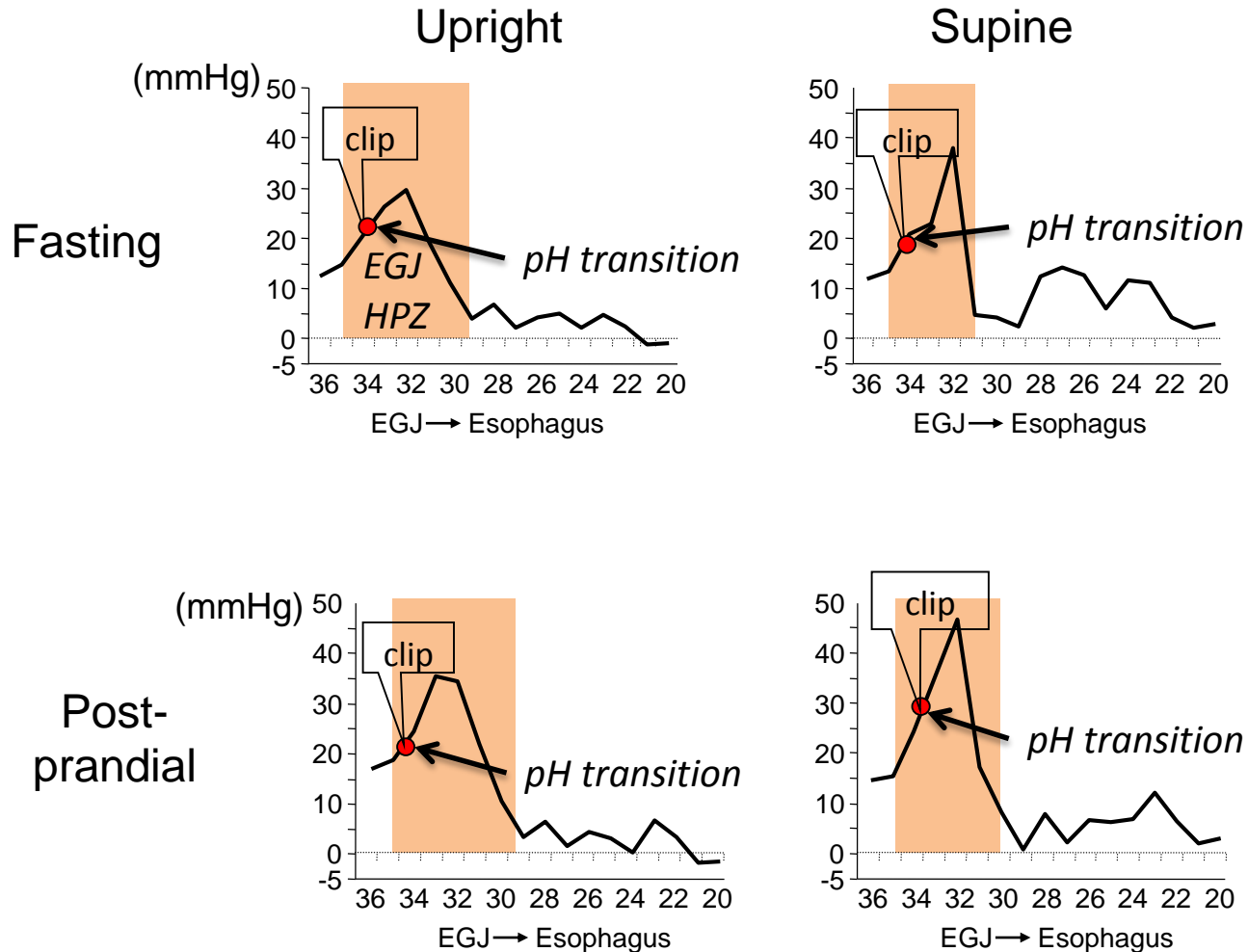
**- Acidity will be greatest nearest mucosa – i.e. closest to acid source and furthest away from bulk of food buffer**

**Would be consistent with prokinetic agents minimizing acid pocket**



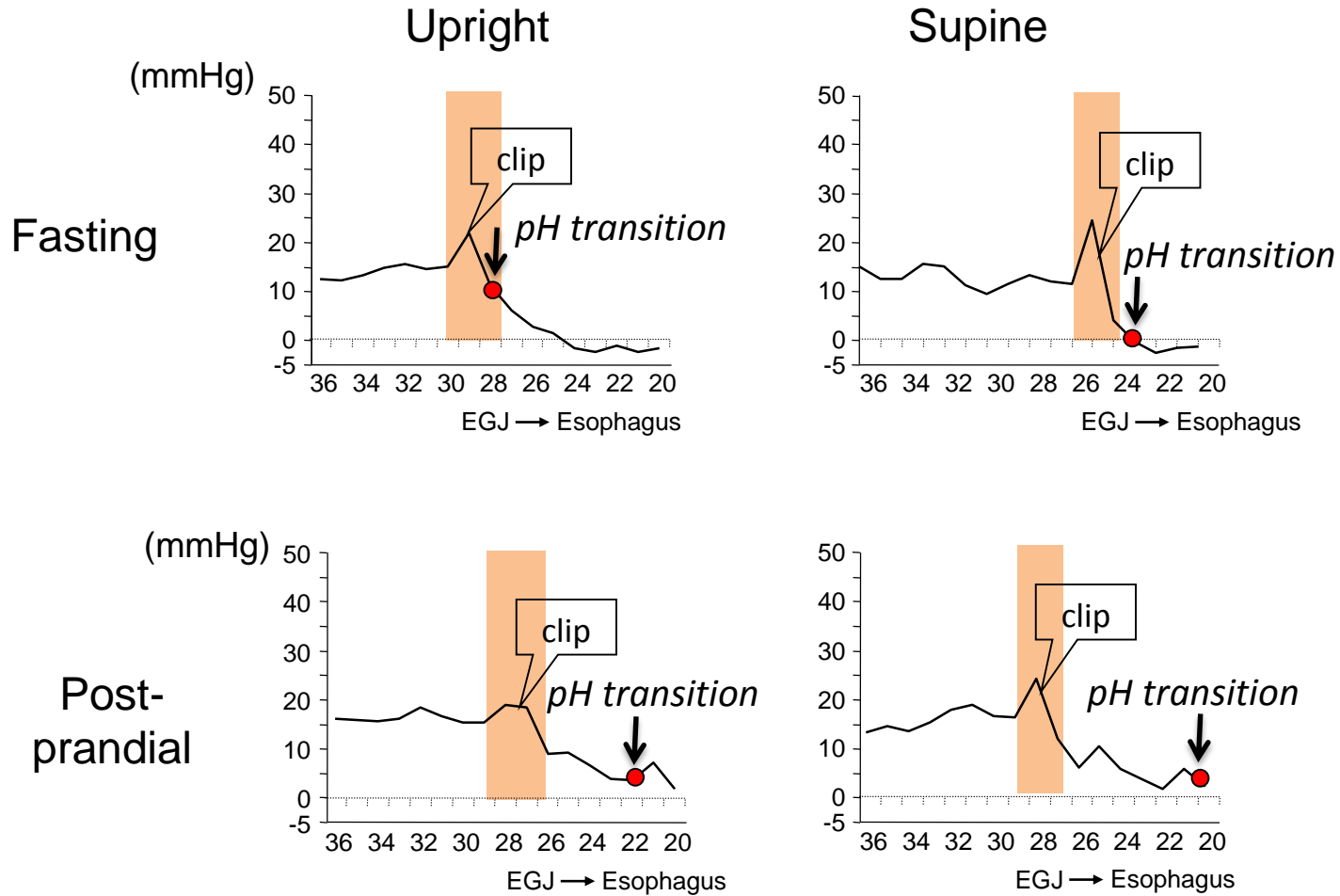
# Relating the pH Transition to the SCJ & LES

## *Normal Control*



# Relating the pH Transition to the SCJ & LES

## *Reflux Patient*

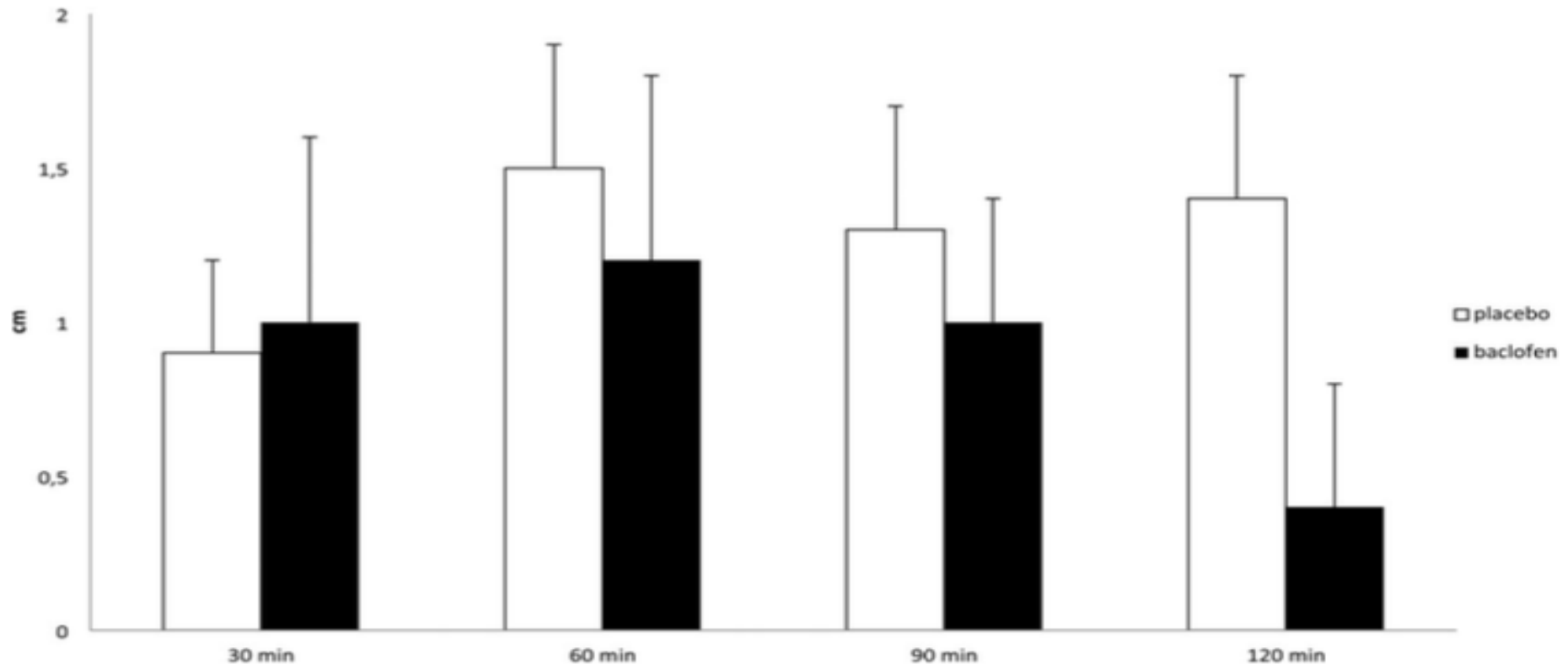


## **Salient features of the acid pocket pertinent to heartburn/GERD**

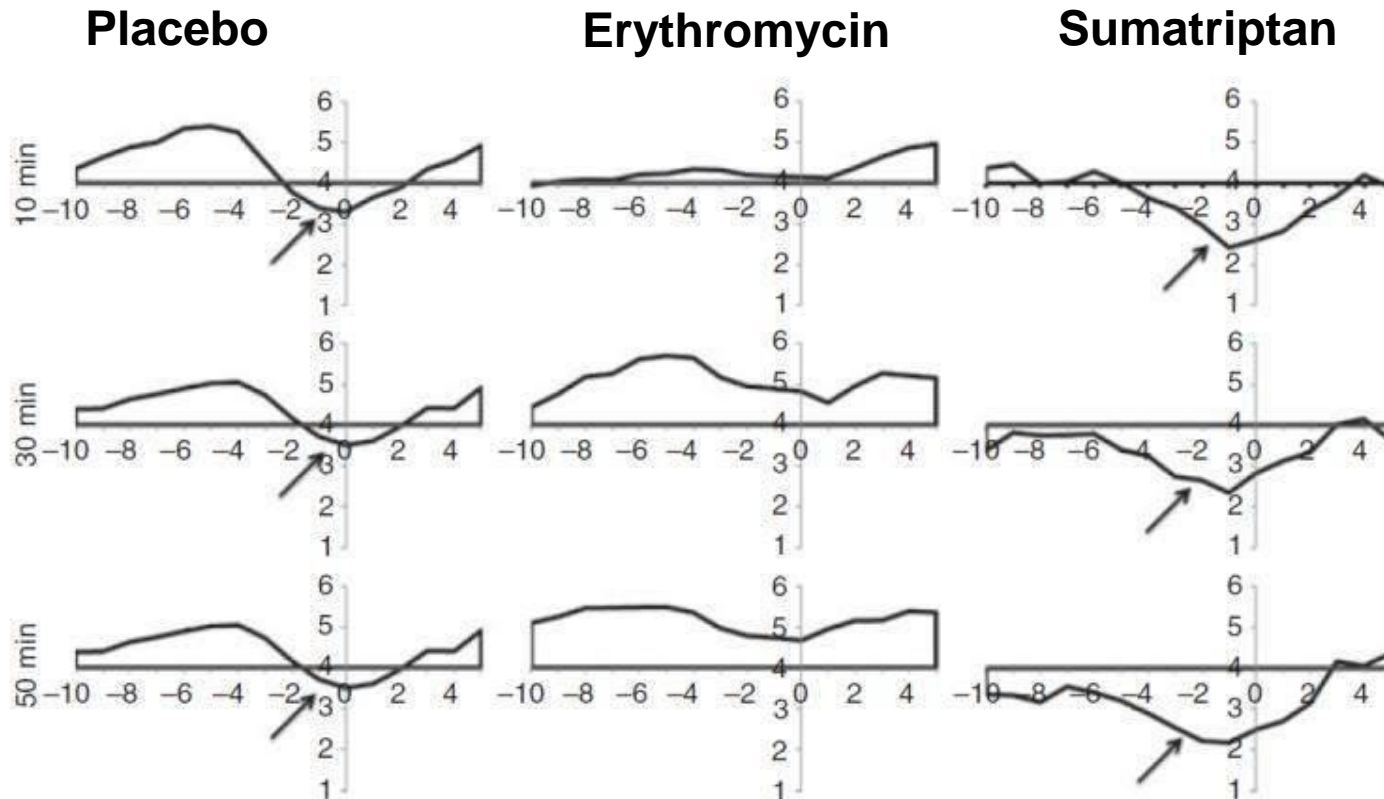
- **Following a meal the proximal stomach, very close to EGJ, largely escapes the buffering effect of the food and remains highly acidic – acid pocket**
- **Reservoir for acid reflux beginning within 15 minutes of a meal**
- **Can cause ‘proximal migration’ of the acid interface across the SCJ**
- **Exacerbated by hiatus hernia and low LES pressure**

*The Acid Pocket as a  
Therapeutic Target*

# Nor placebo nor baclofen significantly affected the proximal extent of acid pockets detected after the meal in GERD patients



# Pharmacological modification of gastric motility alters acid pocket



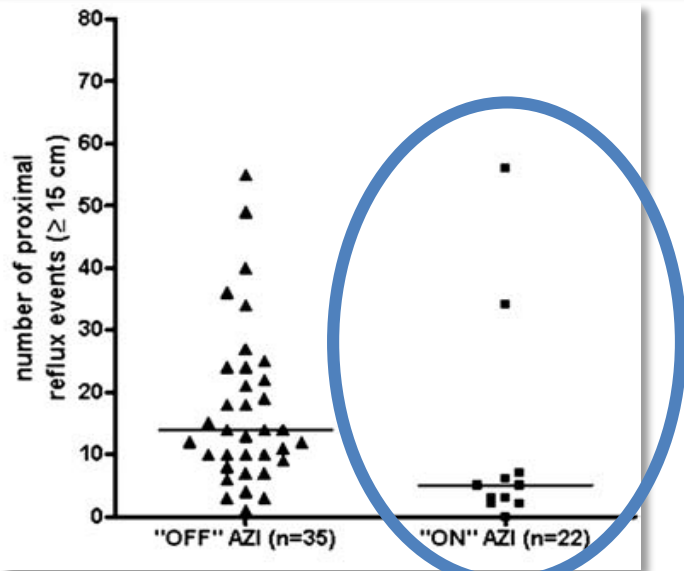
( Boeckstaens et al APT 2011;33:1370-7 )

**Lack of mixing of acid and food in proximal stomach may contribute to acid pocket**

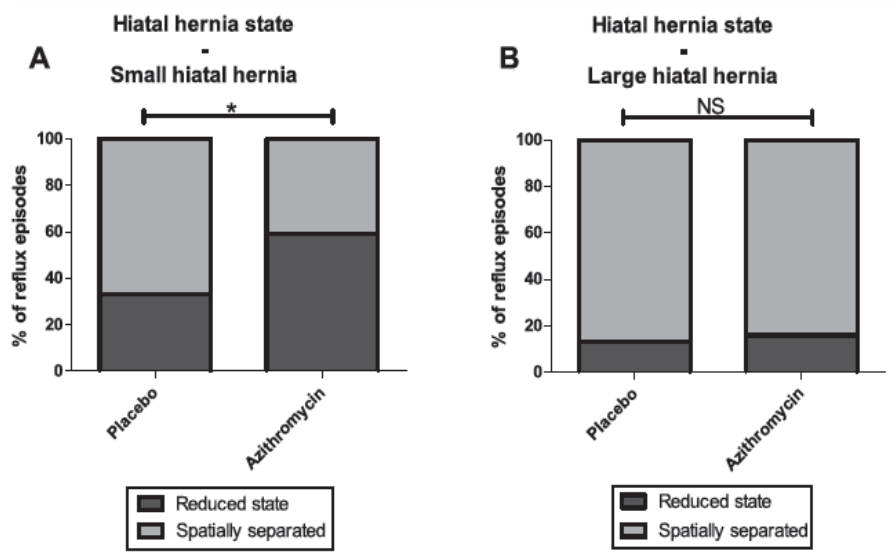
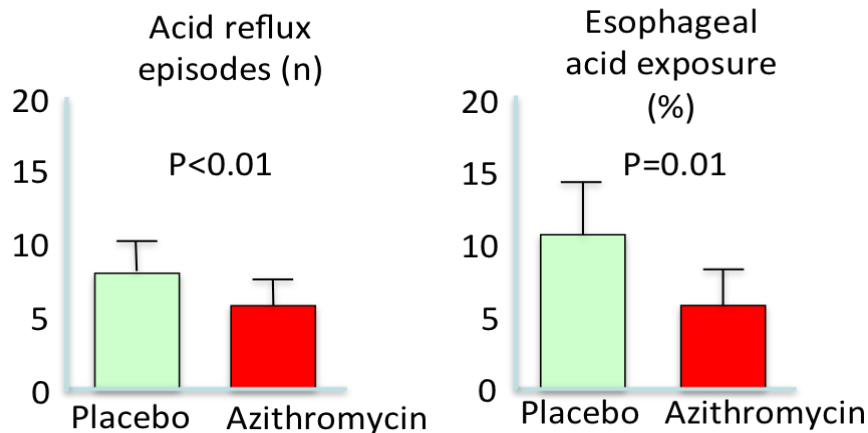
# Effect of Azithromycin on Gastroesophageal Reflux

Prospective Cohort Study  
N = 47 LTx pts On and Off Azithromycin

	Lung transplant recipients		P-value
	"OFF" AZI n = 35	"ON" AZI n = 12	
Esophageal acid exposure (%)	2.9 (0.7-7.3)	0.2 (0.1-2.0)	*0.0081
Esophageal volume exposure (%)	0.73 (0.5-1.4)	0.21 (0.12-0.92)	*0.016
Total number of reflux events (24 h)	41 (30-61)	22.5 (7-37.5)	*0.012
Number of acid reflux events	24 (16-41)	8 (4-18)	*0.0037
Number of non-acid reflux events	14 (8-21)	13 (4.5-16.5)	0.52
Ratio acid/non-acid reflux events	1.8 (1.28-2.94)	0.61 (0.35-1.92)	*0.0076
Proximal extent of reflux (# of reflux events >15 cm)	14 (9-24)	5 (2-7)	*0.0086
% of proximal reflux events	40 (28-53)	28.6 (21-59)	0.42
Total number of nocturnal reflux events	5 (2-9)	0 (0-5)	*0.014



Crossover, placebo-controlled Trial (Azi 250mg/day)  
N = 16 pts with GERD and Hiatal Hernia



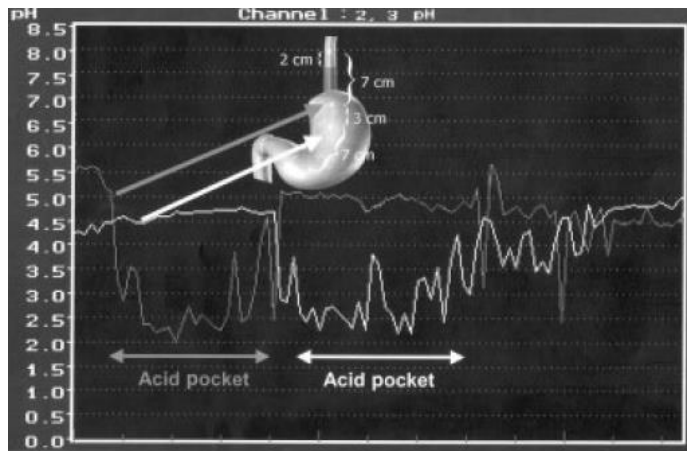
# 7

# Preventing formation of the acid pocket

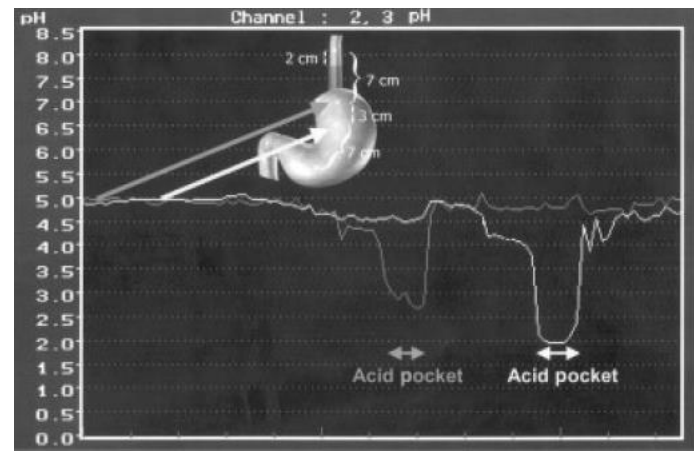
*Inhibit postprandial acid secretion with PPI*

- Rabeprazole 20 mg vs placebo: day 1 of treatment  
 50% reduction in detectable acid pocket during pH pull through after standardized meals  
 Reduced length and increased nadir pH of acid pocket

Placebo

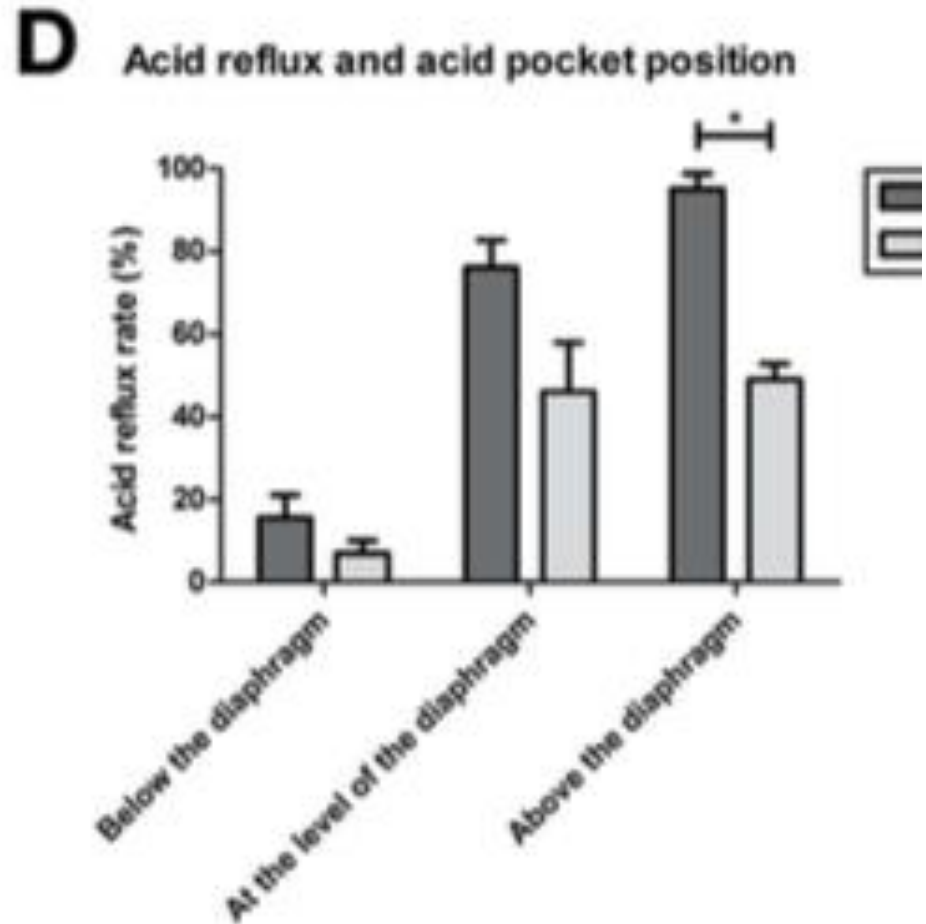
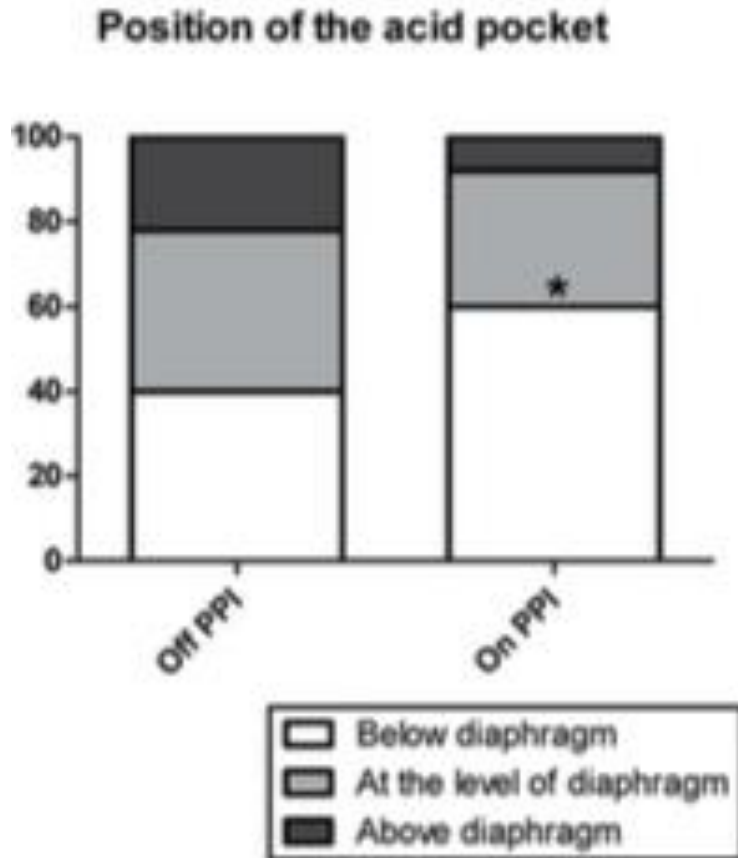


Rabeprazole



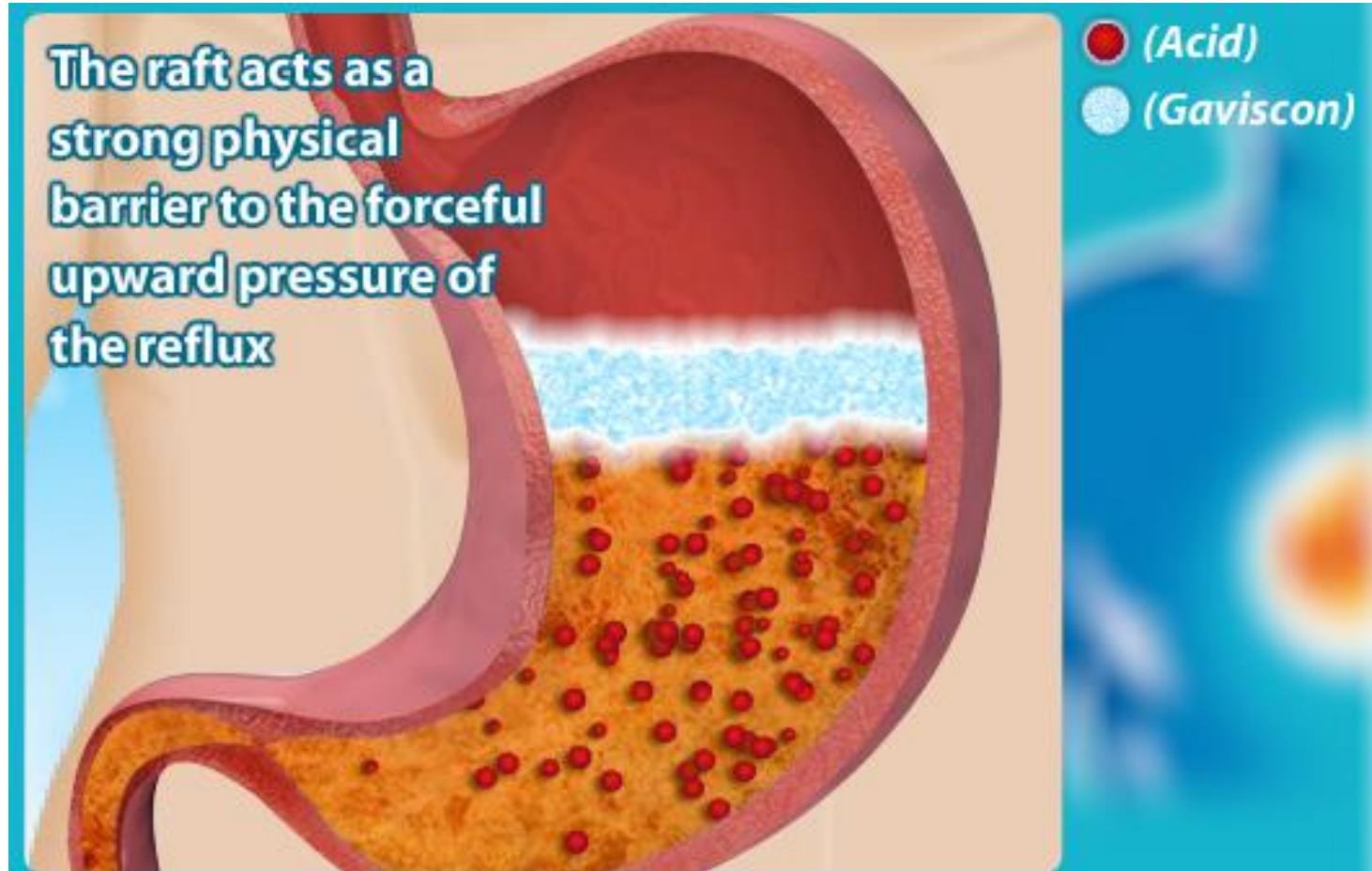


On PPI, the acid pocket was significantly more often located below the diaphragm compared with off PPI ( $p < 0.05$ )

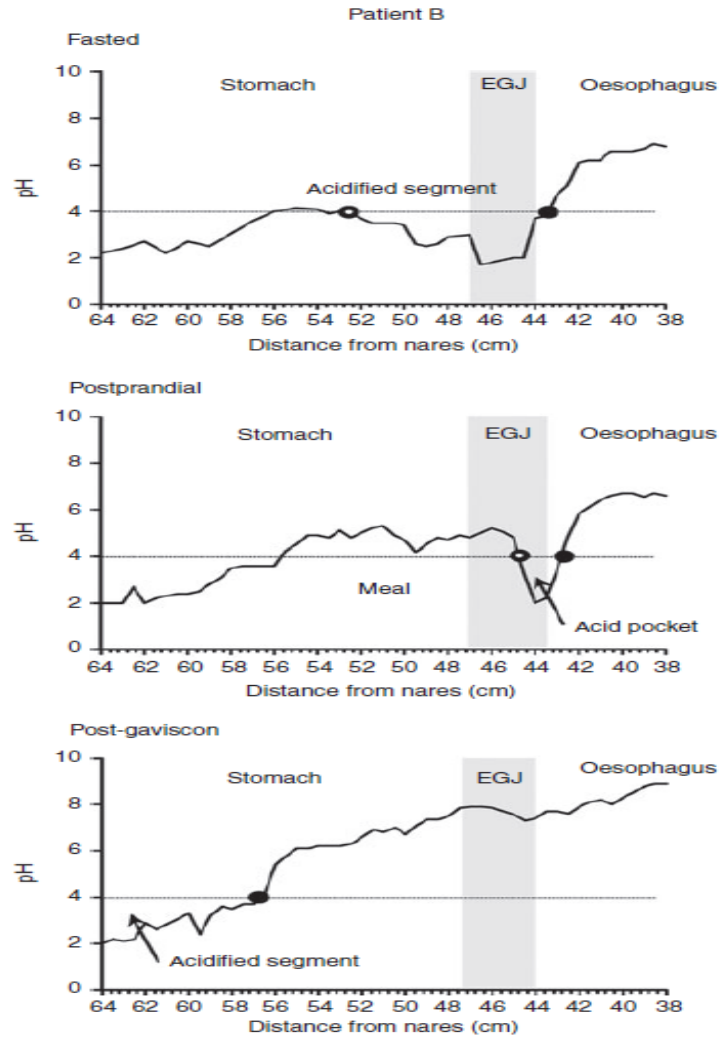
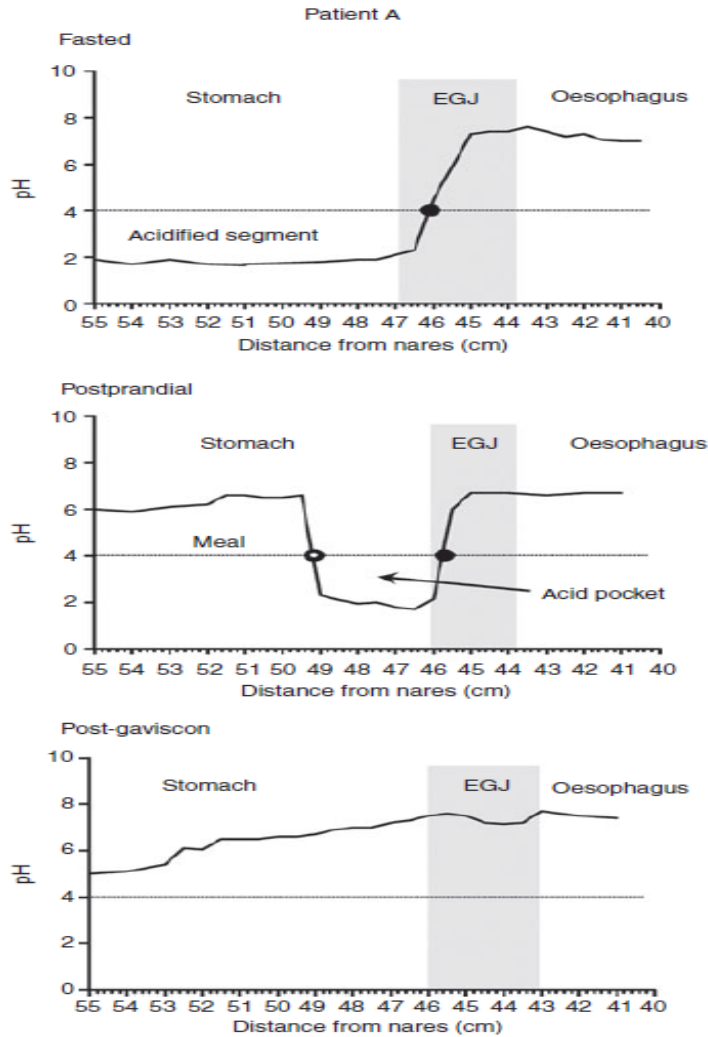


# Gaviscon: Mechanism of Action

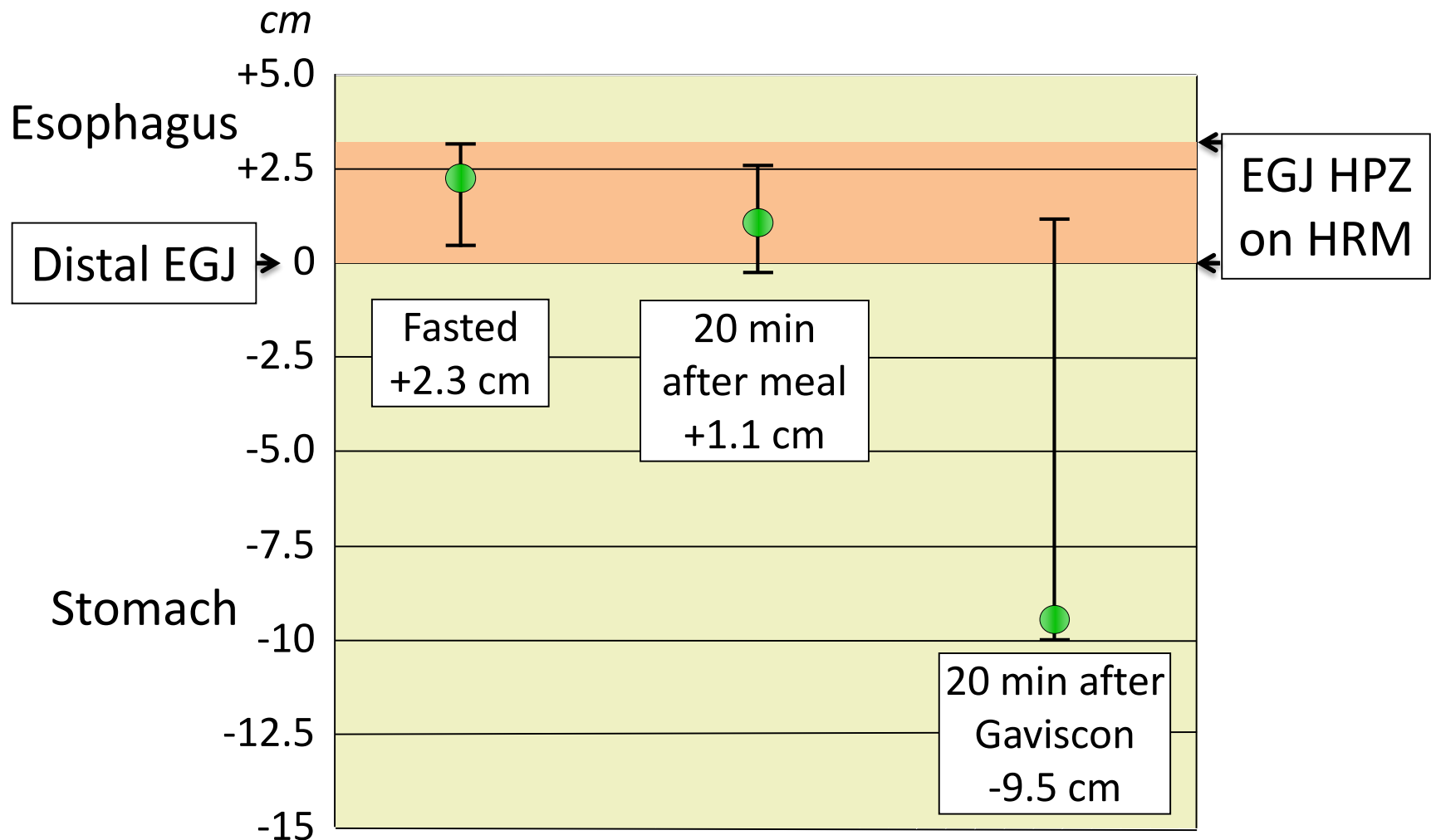
## *Containing the acid pocket?*

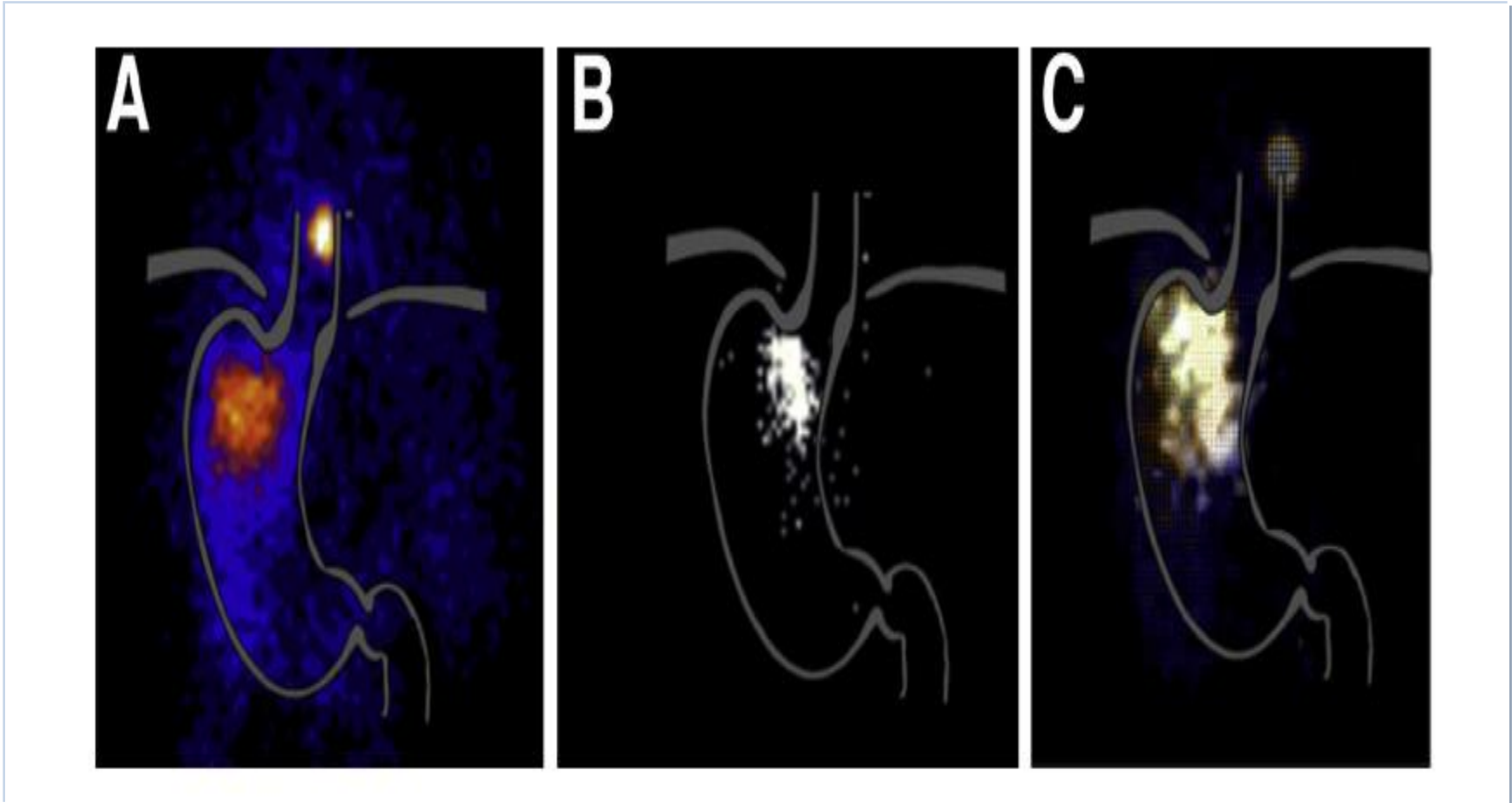


# Examples of pH pull-throughs in two GERD patients

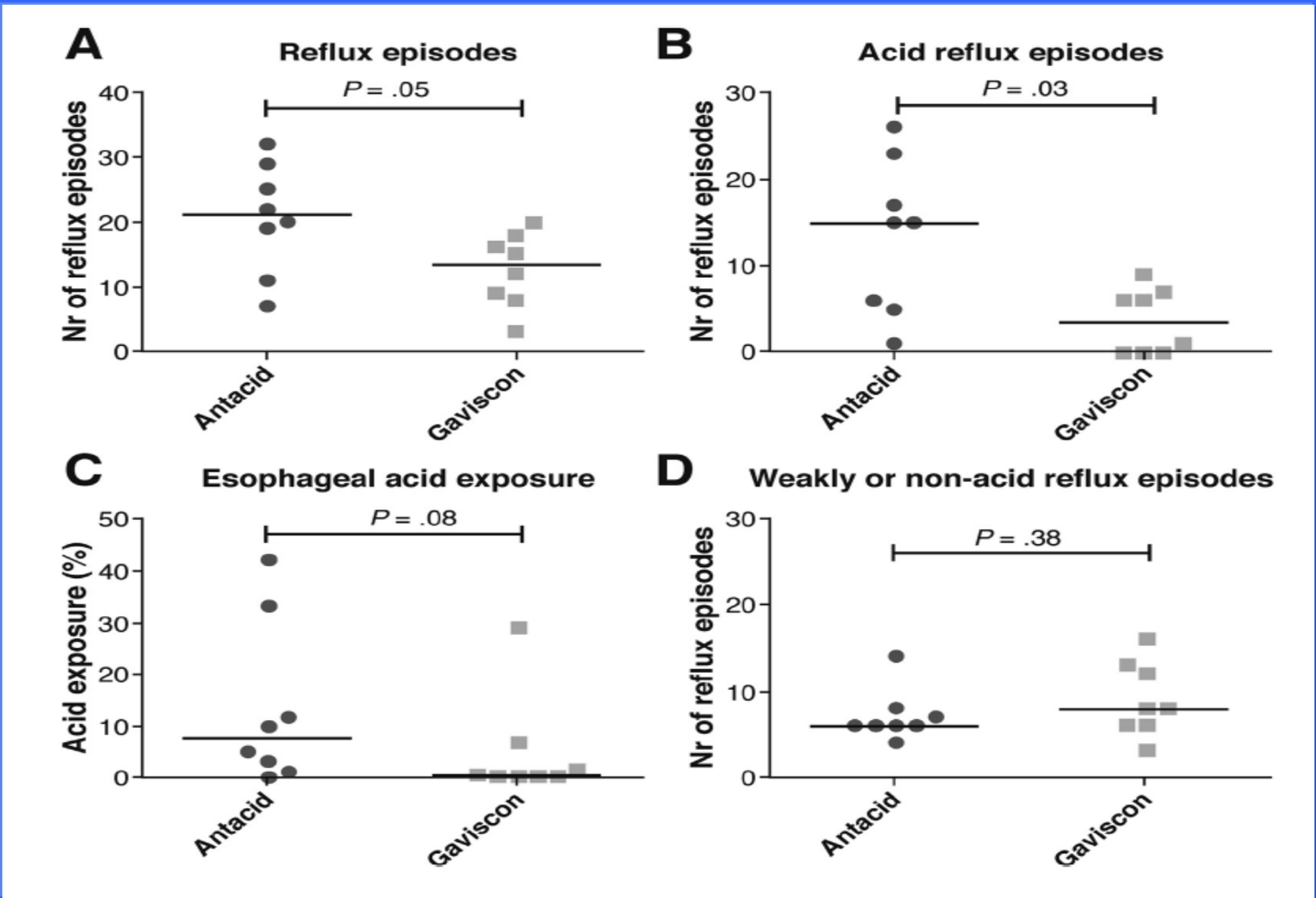


# Gaviscon effect on location of transition (pH<4) to “acid pocket” (n= 10 GERD patients)

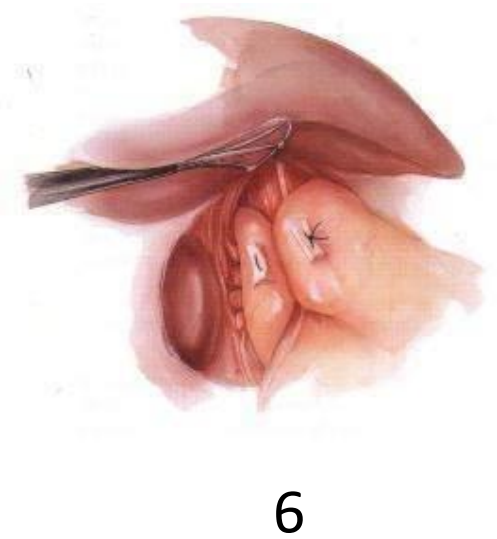
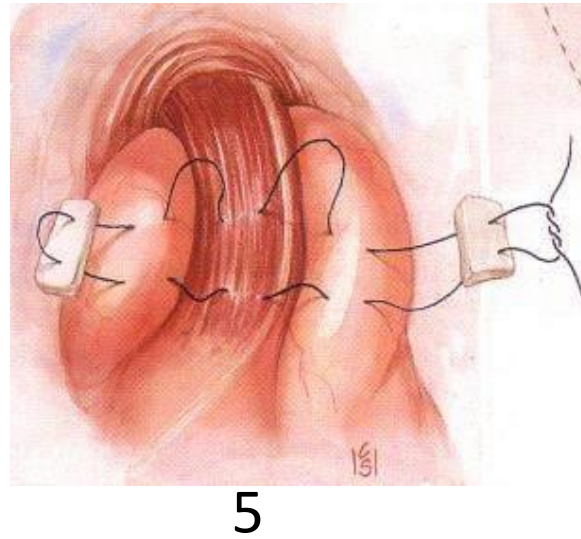
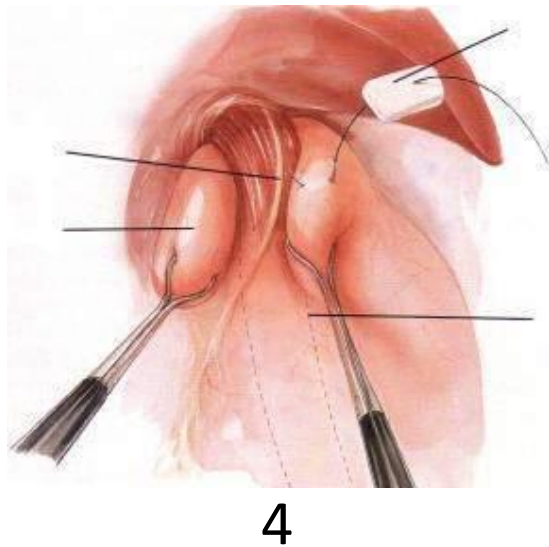
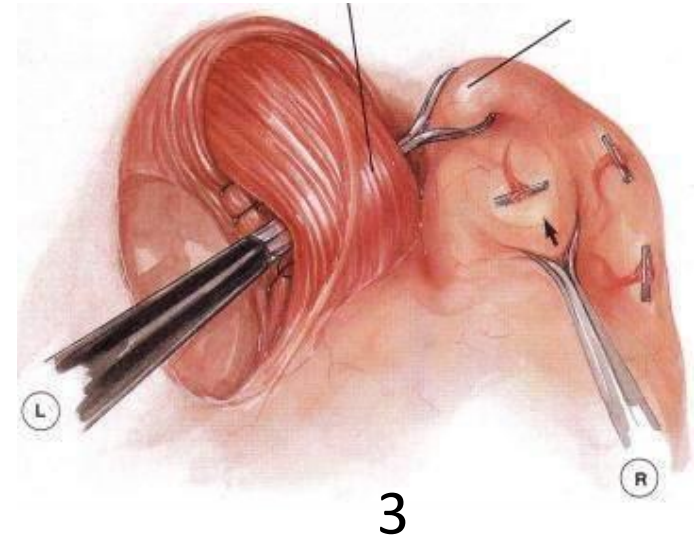
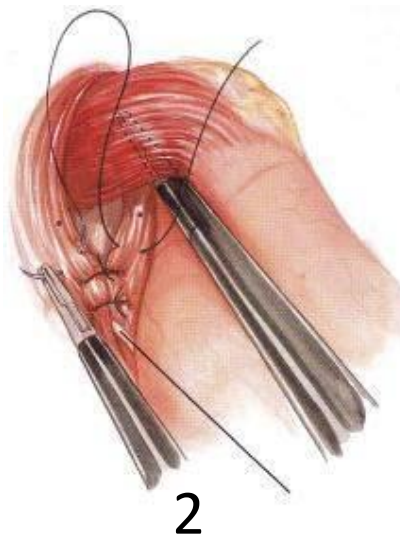
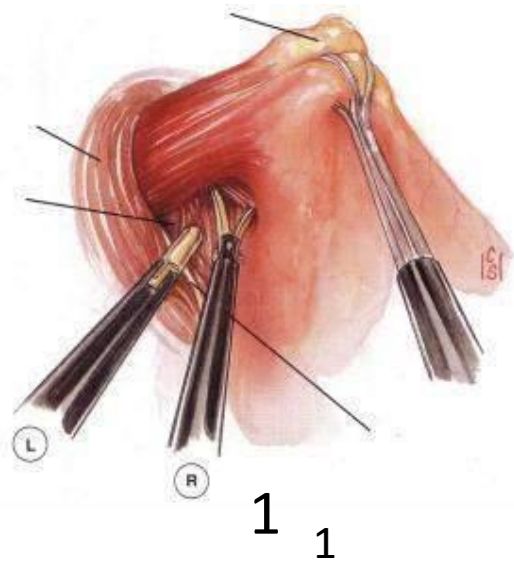




The mean number of reflux events (A), acid reflux episodes (B) and esophageal acid exposure (C) were reduced by alginate-antacid compared with antacid, but the mean number of weakly acidic reflux episodes was higher than alginate-antacid (D).



# Laparoscopic Nissen Fundoplication



# Conclusions

- The acid pocket is a region of high acidity at the gastro-esophageal junction after a meal
- It appears due to the proximal cardia region of stomach escaping the buffering effect of meal and is visible 15 min after it
- The acid pocket measures 3.0-6.5 cm in length in GERD patients
- Its presence is exacerbated by hiatus hernia and low LES pressure
- There is evidence that it is the source of postprandial reflux
- At present, alginate ± antacid seems to be the only drug favoring its complete displacement below the diaphragm





**GRAZIE PER  
L'ATTENZIONE**