

Gastroesophageal Reflux: It Ain't Just a Little Heartburn

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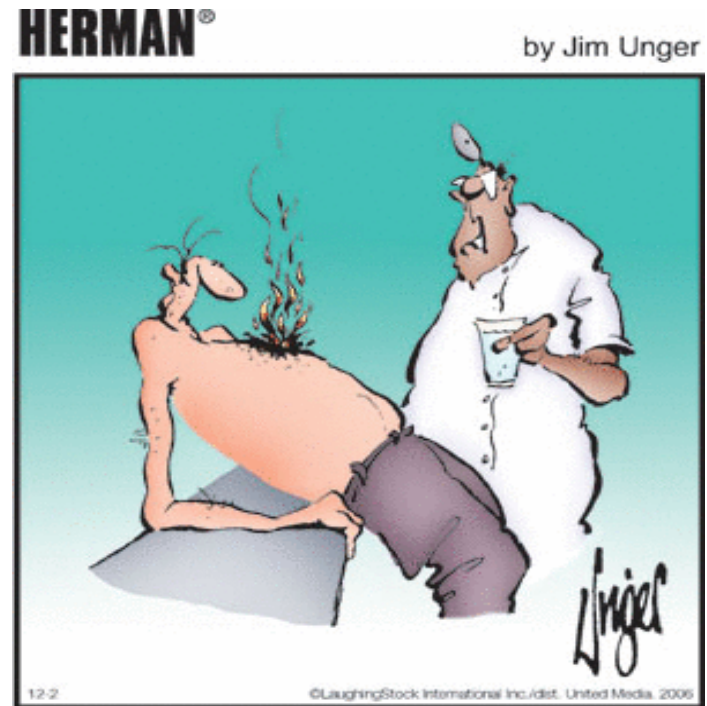
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Gastroesophageal Reflux Disease

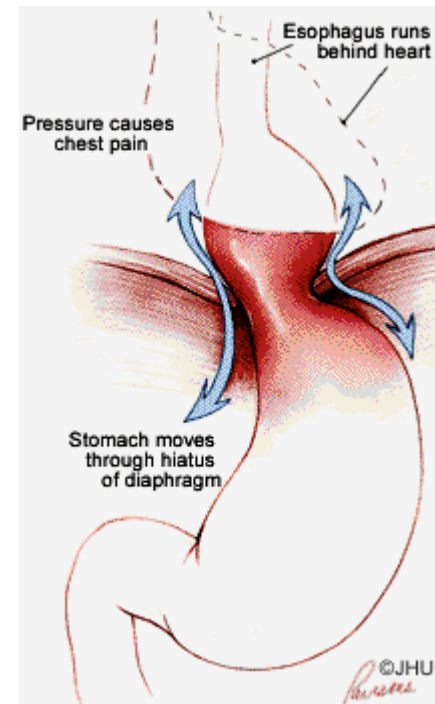
- Definition:
 - Symptoms and/or esophageal injury due to the abnormal reflux of gastric content into the esophagus



"It's just a touch of heartburn."

Symptoms of GERD

- **“Heartburn”**
- **Acid regurgitation**
 - Sour or bitter taste in throat or mouth
 - Esp. after large, late meals
- **Water brash**
 - Hot sensation in stomach
 - Excess salivation
- **Dysphagia and Odynophagia**
 - Difficulty swallowing or painful swallowing



Other Symptoms of GERD

Pulmonary

Asthma

Aspiration pneumonia

Chronic bronchitis

Other

Regurgitation

Chest pain

Dental erosion

ENT

Hoarseness

Laryngitis

Sore throat

Chronic cough

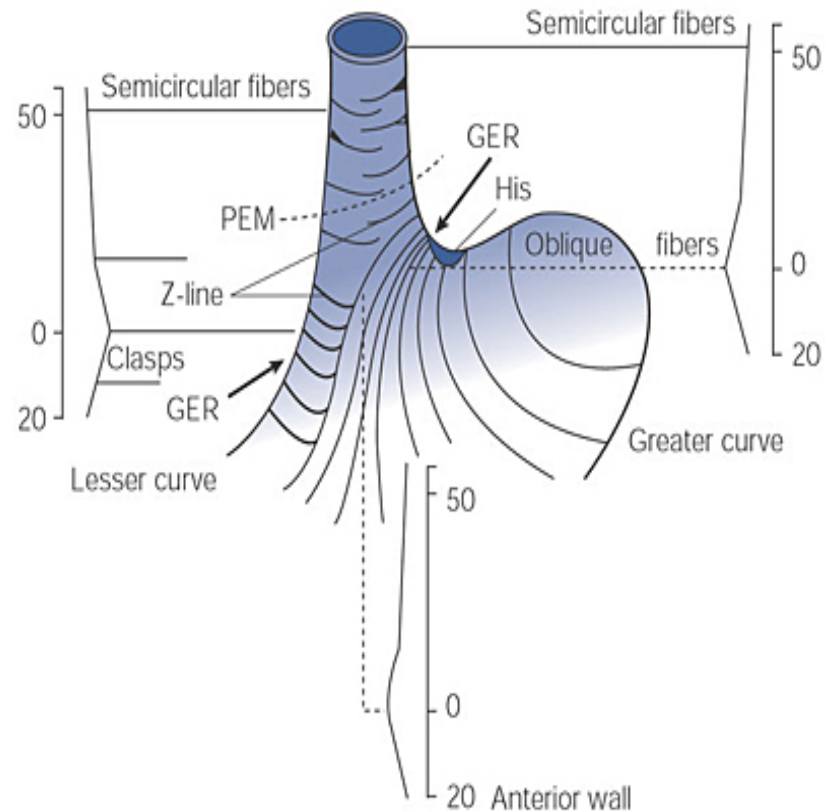
Frequent swallowing

Burning in the throat or
mouth



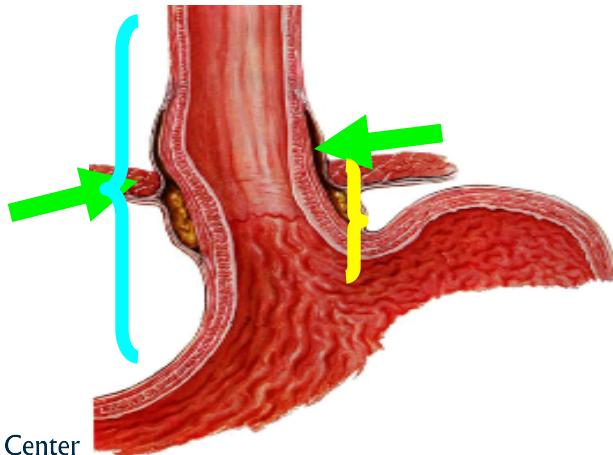
Physiology of the LES

- In humans, LES confines the gastric environment to the stomach
- Not an anatomical landmark, but LES is identified by a rise in pressure over the gastric baseline pressure (high pressure zone)

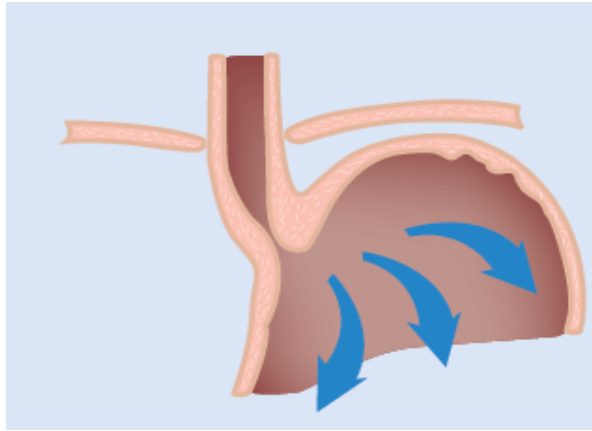


Components to a Competent LES

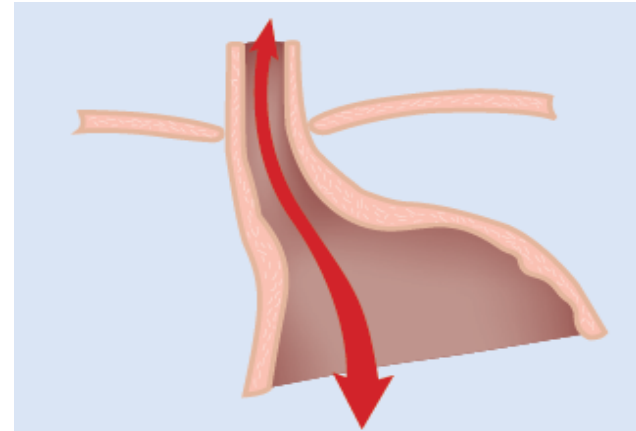
- Pressure
- Overall length
- Length exposed to the positive pressure environment of the abdomen



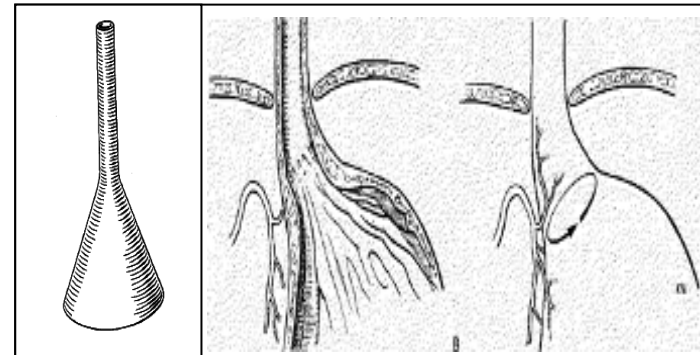
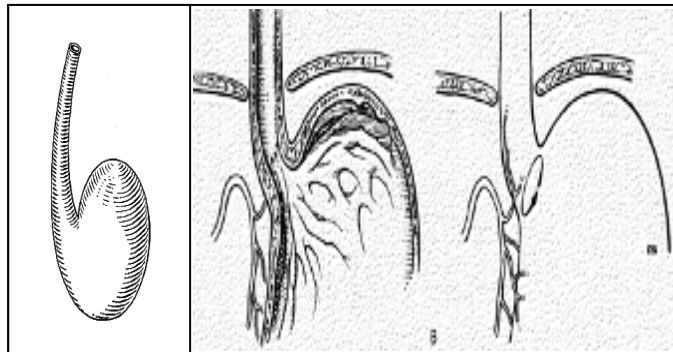
Anatomical change and loss of natural antireflux valve



Normal Anatomy
Fully Functional Valve Prevents Reflux



Abnormal Dysfunctional Valve
GERD



GERD is a common disease

- Heartburn in North American adults
 - 7% daily, 14% weekly, 36% monthly
 - 3% have severe disease (525,000 in US)
Camilleri et al. Clin Gastroenterol Hepatol. 2005 Jun;3(6):543-52.
- Incidence of GERD rises rapidly after 40 years of age
- Esophageal cancer is 8X more likely to occur in patients with weekly heartburn or regurgitation



Leading GI Symptoms Prompting an Outpatient Clinic Visit

Rank	Symptom	Estimated Visits
1	Abdominal pain	11,876,657
2	Diarrhea	3,766,261
3	Vomiting	2,653,944
4	Nausea	2,198,454
5	Constipation	1,830,406
6	Rectal bleeding	1,529,450
7	Heartburn	1,473,436
8	Dyspepsia, upper abdominal pain	918,935
9	Other GI symptoms, unspecified	897,052
10	Anorectal symptoms	873,119
11	Melena	811,019
12	Abdominal distention	786,901
13	Dysphagia	766,241
14	Lower abdominal pain*	751,521
15	Appetite decrease*	547,817

Source: NAMCS 2002.

*Estimates based on less than 30 encounters, which may be unreliable.

- Abdominal pain, diarrhea, vomiting, and nausea are the most common GI symptoms precipitating a visit to the physician.



Leading Physician Diagnosis for GI Disorders in Outpatient Clinic Visits

- GERD is the most common GI-related diagnosis given in office visits.

Rank	Diagnosis	Estimated Visits
1	GERD	5,512,159
2	Abdominal pain	4,169,406
3	Gastroenteritis	3,324,158
4	Constipation	2,562,166
5	Dyspepsia, gastritis	2,285,676
6	Irritable bowel syndrome	2,063,539
7	Hemorrhoids	1,537,746
8	Diverticular disease	1,493,865
9	Hepatitis C infection	1,237,708
10	Hernia, noninguinal	1,232,170
11	Colorectal cancer	1,208,752
12	Gallstone disease	1,109,408
13	Rectal bleeding	1,083,662
14	Hernia, inguinal	969,788
15	Colon, benign neoplasm	853,037
16	IBD *	834,856
17	GI bleed, melena*	753,680

Source: NAMCS 2002.

*Estimates based on less than 30 encounters, which may be unreliable.



Trends in the Usage of Antacids and Gastroprotective Agents Over 5 Years

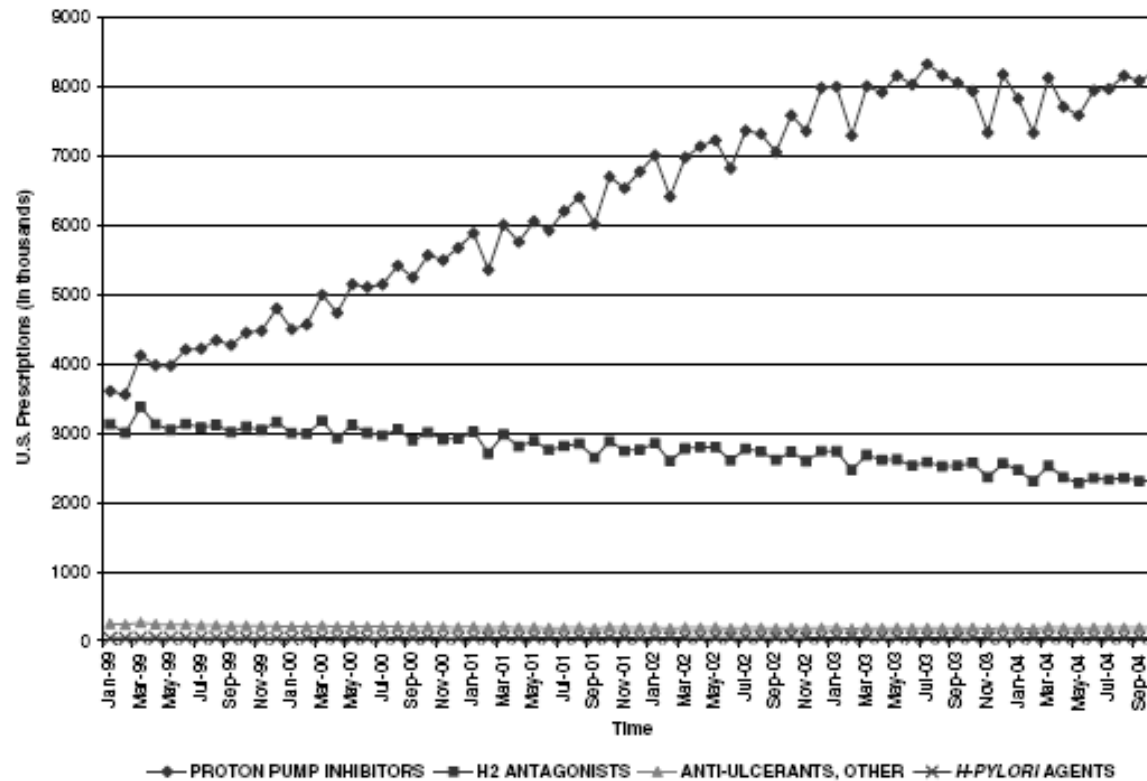


Figure 2. Trends in usage of antacid and gastroprotective agents over 5 yr, by total number of prescriptions.

Pharmacological Sales of Antacids in 2004

- Americans spend in excess of US dollars 10 billion/yr on proton pump inhibitors (PPIs)
- Two of the top five selling drugs in the United States are PPIs.

Table 10. Over-The-Counter (OTC) Gastrointestinal Drugs in the Top 200 OTC List (by Sales), 2004

Generic Name	Brand Name	2004 Top 200 Brand Name Rank	2004 Retail Sales	Percent Change from 2003
Omeprazole	Prilosec OTC®	6	\$242,820,500	+236.6%
Laxative tablet	Generic*	15	\$134,895,400	+0.7%
Antacid tablet	Generic*	16	\$126,193,000	-6.4%
Famotidine	Pepcid AC®	32	\$86,610,640	+8.4%
Ranitidine	Zantac 75®	43	\$67,506,940	-10.2%
Bismuth subsalicylate liquid	Pepto-Bismol®	49	\$59,535,700	-0.6%

Table 9. Generic Prescription Gastrointestinal Drugs in the Top 200 Generic Drug List (by Sales), 2004

Generic Name	2004 Top 200 Generic Drug Rank	2004 Retail Sales	Percent Change from 2003
Omeprazole	4	\$811,942,000	-43.0%
Ranitidine	31	\$222,809,000	-31.5%
Prednisone	55	\$158,169,000	-1.2%
Methotrexate	69	\$108,845,000	-7.8%
Promethazine	76	\$103,877,000	+6.6%
Methylprednisolone	87	\$ 91,601,000	-2.7%
Famotidine	98	\$ 85,774,000	-25.4%



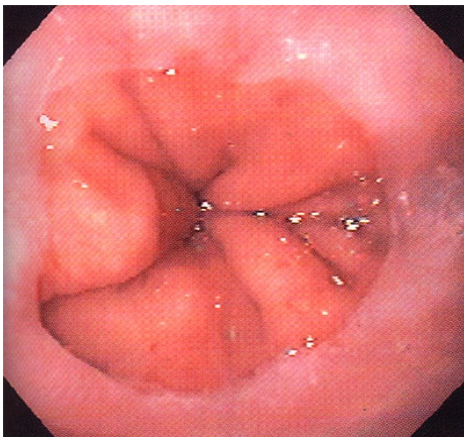
SO, WHAT'S UP DOC???



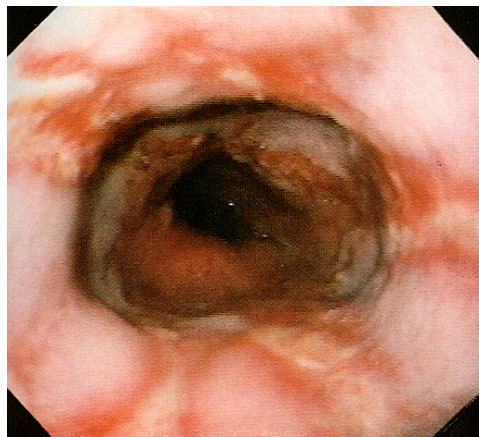
- ... if lots of people in the US have reflux?
- ... if we are increasing our utilization of PPIs?
- ...if this trend is rising?
 - Is it due to increased awareness of reflux
 - Or... has it truly increased in incidence?

Complications from GERD

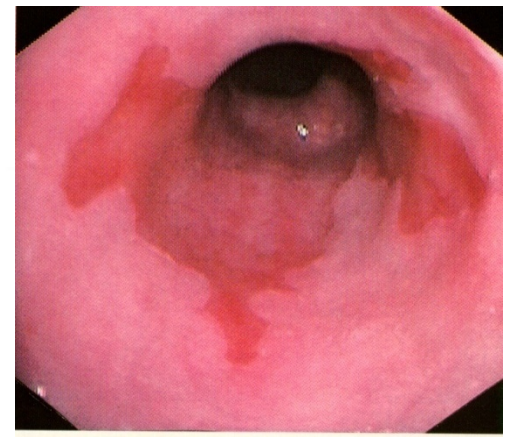
Normal Esophagus



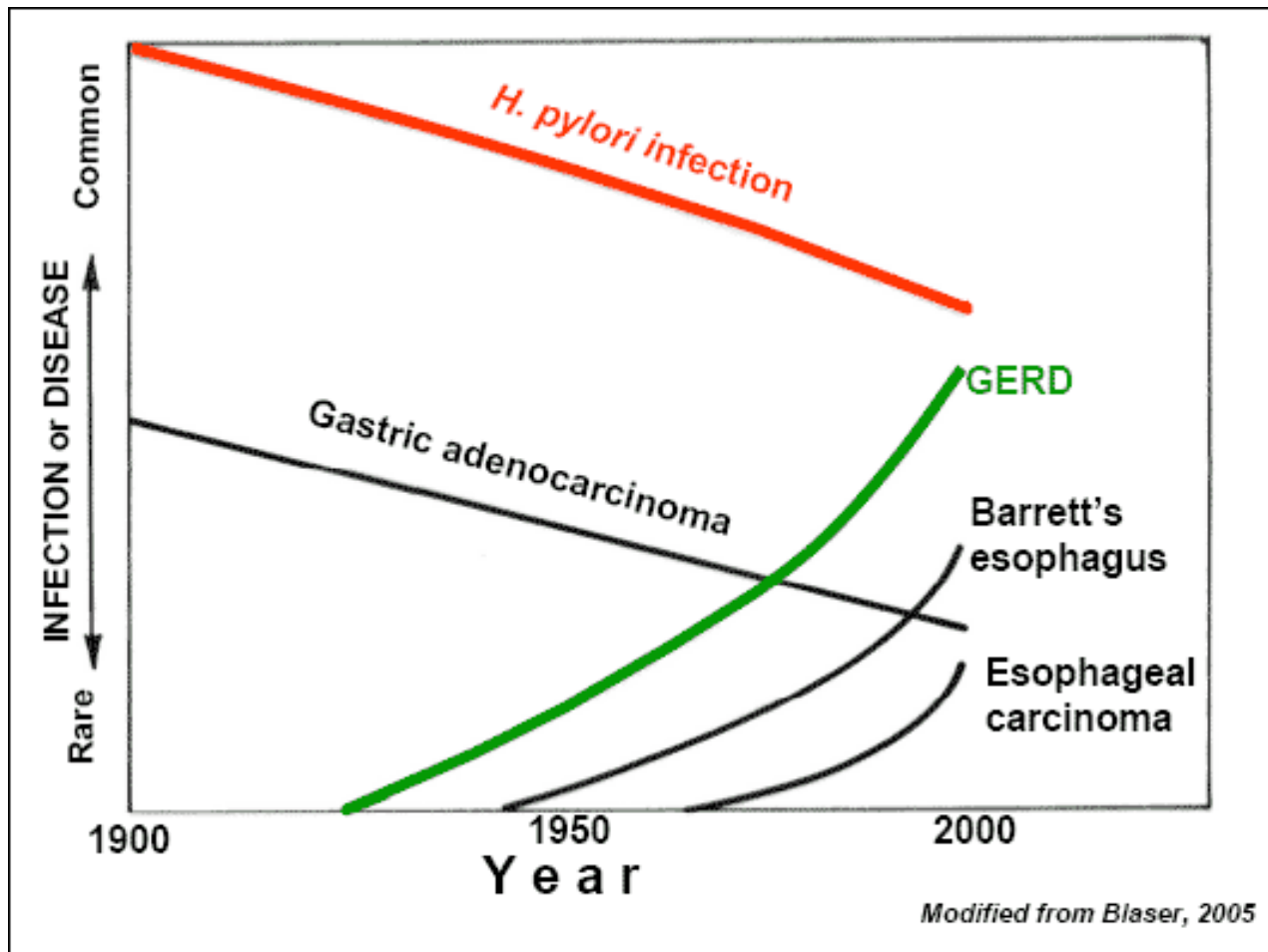
Erosive esophagus due to GERD



Barrett's esophagus = "pre-cancerous"



Trend of the Relationship of GERD to Barrett's and Esophageal Cancer



Rising Incidence of Esophageal Cancer

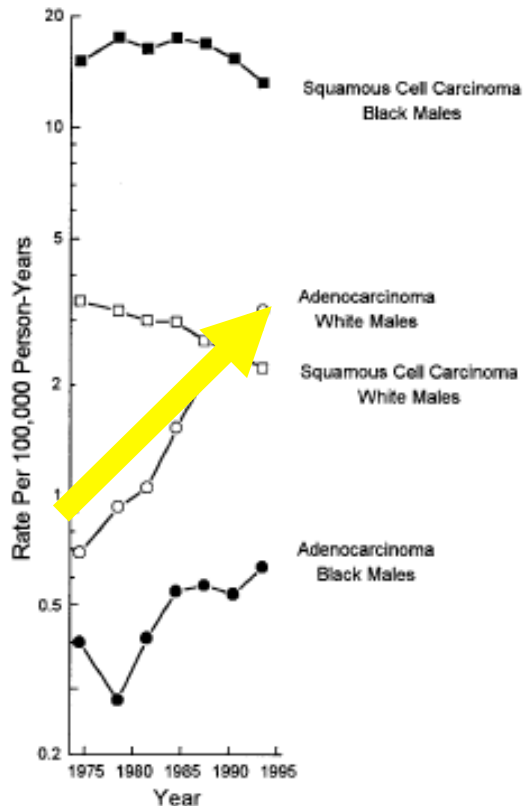
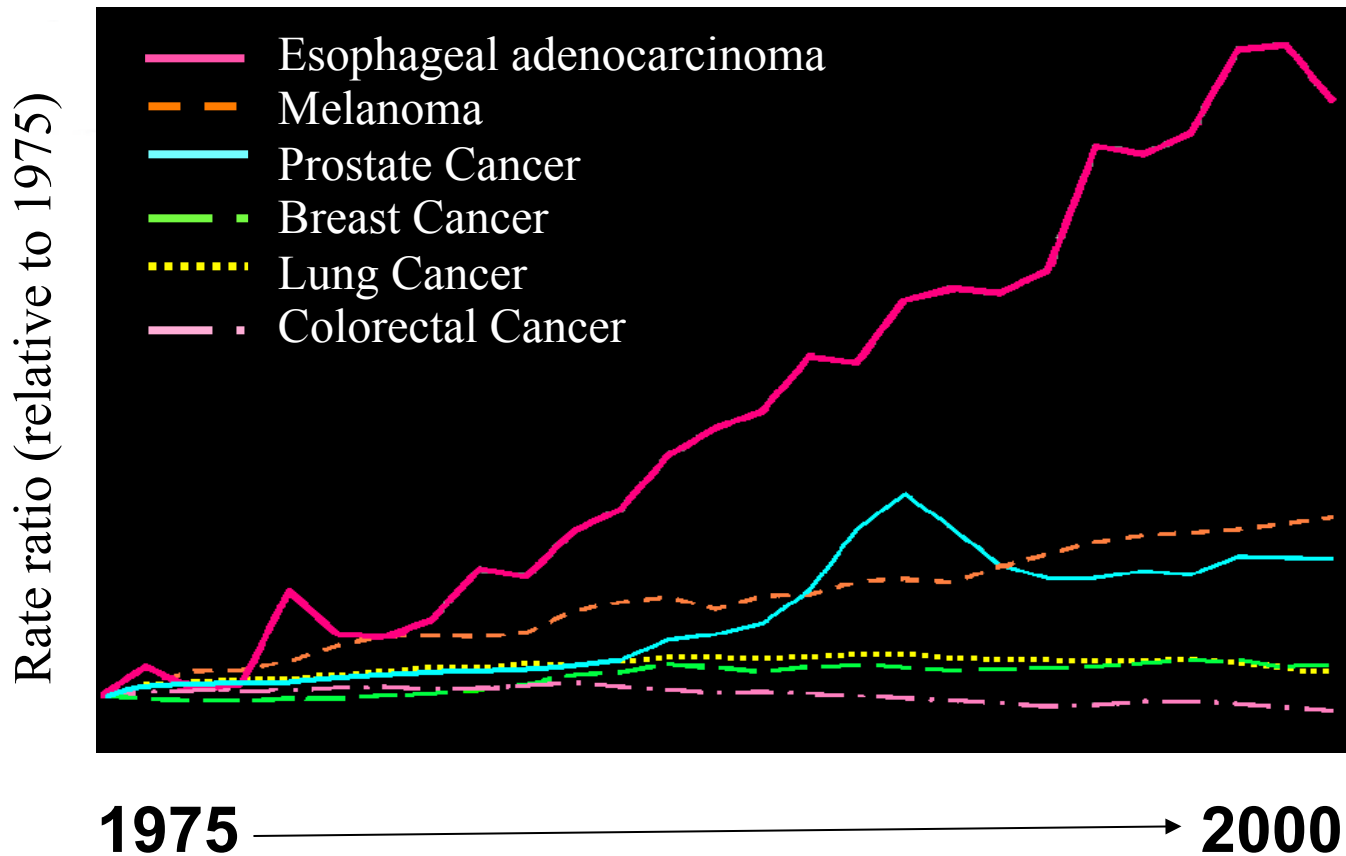


FIGURE 1. Trends in age-adjusted incidence rates for esophageal carcinoma among U.S. males by race and cell type, 1974–1976 to 1992–1994.

Devesa et al. *Cancer* Nov 1998

- Esophageal adenocarcinoma is now the fastest growing form of cancer in the U.S., and its incidence is rising faster than breast cancer, prostate cancer or melanoma.
- If esophageal adenocarcinoma continues at its current rate, it is estimated to exceed colon cancer by 2015

Esophageal Cancer Epidemic



Pohl H and Welch HG. *J Natl Cancer Inst* 2005;95:142-146

Summary

- The incidence of GERD is increasing throughout the years.
- The complications of GERD are increasing in incidence as well
- The incidence of esophageal cancer is increasing.
- More and more patients are being prescribed PPIs/antacids/H2 blockers.



But WAIT!!! Is giving PPIs the
answer?



Predictive Factors of Barrett Esophagus: Multivariate Analysis of 502 Patients With Gastroesophageal Reflux Disease

[Guilherme M. R. Campos, MD; Steven R. DeMeester, MD;
Jeffrey H. Peters, MD; Stefan Öberg, MD; Peter F. Crookes,
MD; Jeffrey A. Hagen, MD; Cedric G. Bremner, MD; Lelan
F. Sillin III, MD; Rodney J. Mason, MD; Tom R. DeMeester,
MD](#)

Arch Surg. 2001;136:1267-1273.

Methods

- Five hundred two consecutive patients with GERD identified
 - Documented by 24-hour esophageal pH monitoring
 - Complete demographic, endoscopic, and physiological evaluation
 - Divided in groups according to the presence and extent of BE
 - 328 patients without BE and 174 with BE
 - 67 short-segment BE and 107 long-segment BE



Demographic Data and *Helicobacter pylori* Infection in Patients Without BE, and Those With SSBE and LSBE

Table 1. Demographic Data and *Helicobacter pylori* Infection in Patients Without BE, and Those With SSBE and LSBE*

Variable	No BE (n = 328)	SSBE (n = 67)	LSBE (n = 107)	P Value
Median age (range), y	52 (15-86)	53 (20-86)	51 (22-83)	...
% Male	62.8	73.1	82.2] <.001
Male-female ratio	1.7:1	2.7:1	4.6:1	
Median body mass index (range)	26.9 (15.0-48.7)	27.6 (19.8-37.9)	27.0 (20.6-44.9)	...
Median duration of symptoms, y	5	10	12	≤.02
<i>Helicobacter pylori</i> infection, %	(n = 266) 13.5	(n = 45) 8.9	(n = 71) 14.1	...

*P value for % male and male/female ratio are by χ^2 linear trend analysis. All other P values were for individual comparisons between the groups. BE indicates Barrett esophagus; SSBE, short-segment BE; and LSBE, long-segment BE.

Characteristics of the Gastroesophageal Reflux Barrier and Motility of the Distal Esophagus in Patients Without BE and Those With SSBE and LSBE

Table 2. Characteristics of the Gastroesophageal Reflux Barrier and Motility of the Distal Esophagus in Patients Without BE and Those With SSBE and LSBE*

Variable	No BE (n = 328)	SSBE (n = 67)	LSBE (n = 107)	P Value
Prevalence of hiatal hernia, %	55.8	73.1	94.4	≤.01†
Hiatal hernia length, cm	2 (0-3)	3 (0-3)	4 (3-5)	≤.03†
Prevalence of defective LES, %	69.2	80.6	99.1	[≤.001‡ .06§
LES total length, cm	2.0 (1.4-3.0)	1.8 (1.4-2.8)	1.6 (1.0-2.4)	[≤.05‡ .21§
LES abdominal length, cm	0.8 (0.4-1.4)	0.8 (0.2-1.0)	0.2 (0.0-0.8)	[≤.001‡ .24§
LES pressure, mm Hg	7.0 (4.0-11.6)	5.0 (3.6-8.4)	3.0 (1.6-5.0)	≤.01†
Prevalence of abnormal distal esophageal amplitude, %	20.7	37.3	43.9	[≤.001 .39¶
Distal esophageal amplitude, mm Hg	64 (42-96)	45 (30-67)	46 (32-61)	[≤.001 .73¶

*Data are given as median (interquartile range) unless otherwise noted. BE indicates Barrett esophagus; SSBE, short-segment BE; LSBE, long-segment BE; and LES, lower esophageal sphincter.

†For all individual comparisons between the groups.

‡For the comparisons no BE vs LSBE and SSBE vs LSBE.

§For the comparison no BE vs SSBE.

||For the comparisons no BE vs SSBE and no BE vs LSBE.

¶For the comparison SSBE vs LSBE.

Esophageal Acid and Bilirubin Exposure in Patients Without BE and Those With SSBE and LSBE

Table 3. Esophageal Acid and Bilirubin Exposure in Patients Without BE and Those With SSBE and LSBE*

Variable	No BE (n = 328)	SSBE (n = 67)	LSBE (n = 107)	P Value
% Total time pH<4	7.6 (5.6-11.3)	9.3 (6.8-14.7)	16.5 (11.2-34.1)	≤.001†
No. of reflux episodes	77 (51-119)	95 (57-178)	184 (105-268)	≤.04†
No. of reflux episodes >5 min	4 (2-6)	5 (2-7)	7 (4-15)	≤.02†
Longest reflux episode, min	17.8 (10.2-29.0)	18.0 (13.3-26.0)	28.0 (19.2-50.0)	[≤.001† .52§
PEAE, %				
Postprandial	17.4	6.0	0.9	[≤.001†
Upright	23.2	13.4	8.4	
Supine	32.0	38.8	26.2	
Bipositional	27.4	41.8	64.5	
	(n = 132)	(n = 32)	(n = 42)	
Prevalence of abnormal bilirubin exposure, %	53.0	84.4	88.1	[≤.001 .64‡
Bilirubin absorption >0.2, % time over 24-h period	3.0 (0.1-10.7)	13.3 (2.8-26.5)	17.3 (6.9-34.3)	[≤.002 .19‡

*Data are given as median (interquartile range) unless otherwise noted. BE indicates Barrett esophagus; SSBE, short-segment BE; LSBE, long-segment BE; and PEAE, pattern of esophageal acid exposure.

†For all individual comparisons between the groups.

‡For the comparison SSBE vs LSBE.

§For the comparison no BE vs SSBE.

||For the comparisons no BE vs SSBE and no BE vs LSBE.

Multivariate Analysis:

Table 4. Multivariate Analysis: Factors Predictive for the Presence of Any Length of Barrett Esophagus*

Variable	Odds Ratio (95% CI)	P Value
Abnormal bilirubin exposure	4.2 (1.9-9.7)	.001
Hiatal hernia		
>4 cm	4.1 (2.1-8.0)	<.001
2-4 cm	2.4 (1.4-4.6)	.002
Defective LES	2.7 (1.4-5.4)	.004
Male sex	2.6 (1.6-4.3)	<.001
Defective distal contraction amplitude	2.2 (1.4-3.5)	.001
No. of reflux episodes >5 min		
>7 min	2.2 (1.1-4.6)	.03
4-7 min	2.1 (1.2-3.7)	.006
Duration of GERD symptoms >5 y	2.1 (1.4-3.2)	.001

*CI indicates confidence interval; LES, lower esophageal sphincter; and GERD, gastroesophageal reflux disease.

Table 5. Multivariate Analysis: Factors Predictive for the Presence of Long-Segment Barrett Esophagus*

Variable	Odds Ratio (95% CI)	P Value
Hiatal hernia		
>4 cm	17.8 (4.1-76.6)	<.001
2-4 cm	8.5 (2.3-31.7)	.002
Defective LES	16.9 (1.6-181.4)	.02
Longest reflux episode		
>31.7 min	8.1 (2.8-24.0)	<.001
19.9-31.7 min	6.8 (2.3-20.1)	.001

*Baseline values are for short-segment Barrett esophagus. CI indicates confidence interval; LES, lower esophageal sphincter.



Conclusion

- The independent predictors for the presence of BE are:
 - increased esophageal bile exposure
 - alteration of the geometry of the gastroesophageal junction by a hiatal hernia
 - a defective LES
 - male sex
 - duration of reflux symptoms
 - poor esophageal clearance
- **Increased esophageal exposure to bile** is the most important independent predictive factor and was the only independent predictive factor for the presence of BE.
- Identification of these factors in patients without BE and prompt intervention with antireflux surgery may prevent the development of BE.



Therefore...

- Medical treatment (PPI, H2 antagonists, antacids) may relieve the symptoms from gastric reflux
 - Decreases acidity
 - Does not protect against bile/mixed reflux
- Does not address the true pathophysiology of GERD → mechanical dysfunction of LES
 - The combined refluxate of gastric and duodenal juices causes severe esophageal damage
- Antireflux surgery re-establishes the barrier between the stomach and the esophagus → thereby avoiding the damage induced by mixed gastroduodenal reflux



Problems with PPIs

- **Long-term complications with chronic drug therapy**
 - At risk for osteoporosis
 - Barrett's and esophageal cancer risk increase
 - Drug-drug interaction issues
 - i.e. Plavix



Risks Associated with Long-Term PPIs

↑ 4x the risk of gastric polyps ⁴

↓ Gallbladder motility ¹
↑ Bacterial gastroenteritis ²
↓ Innate immunity ³

↑ Risk of hip fracture ⁵

↑ Osteoporosis-associated fractures ⁵

↑ Renal failure ← acute interstitial nephritis ⁶



References

¹ Cahan et al. *Surg Endosc* 2006; 20:1364-7.

² Garcia Rodriguez et al. *Clin Gastroenterol Hepatol* 2007; 5:1418-23.

³ Alkim et al. *Dig Dis Sci* 2008; 53:347-51.

⁴ Jalving et al. *Aliment Pharmacol Ther* 2006; 24:1341-8.

⁵ Targownik et al. *CMAJ* 2008;179:319-26.

⁶ Geevasinga et al. *Clin Gastroenterol Hepatol* 2006; 4:597-4..

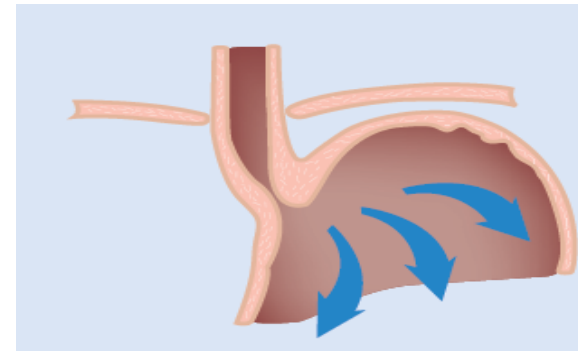


PPIs are not the solution for severe or chronic reflux

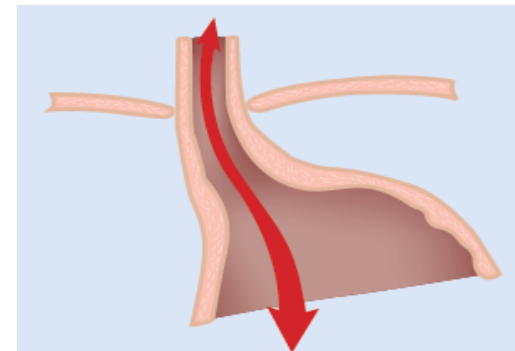
Does not stop

- Reflux
- Non Erosive Reflux Disease (NERD)
- Regurgitation

**ANATOMICAL
PROBLEMS NEED
ANATOMICAL
SOLUTIONS!!!**



Normal

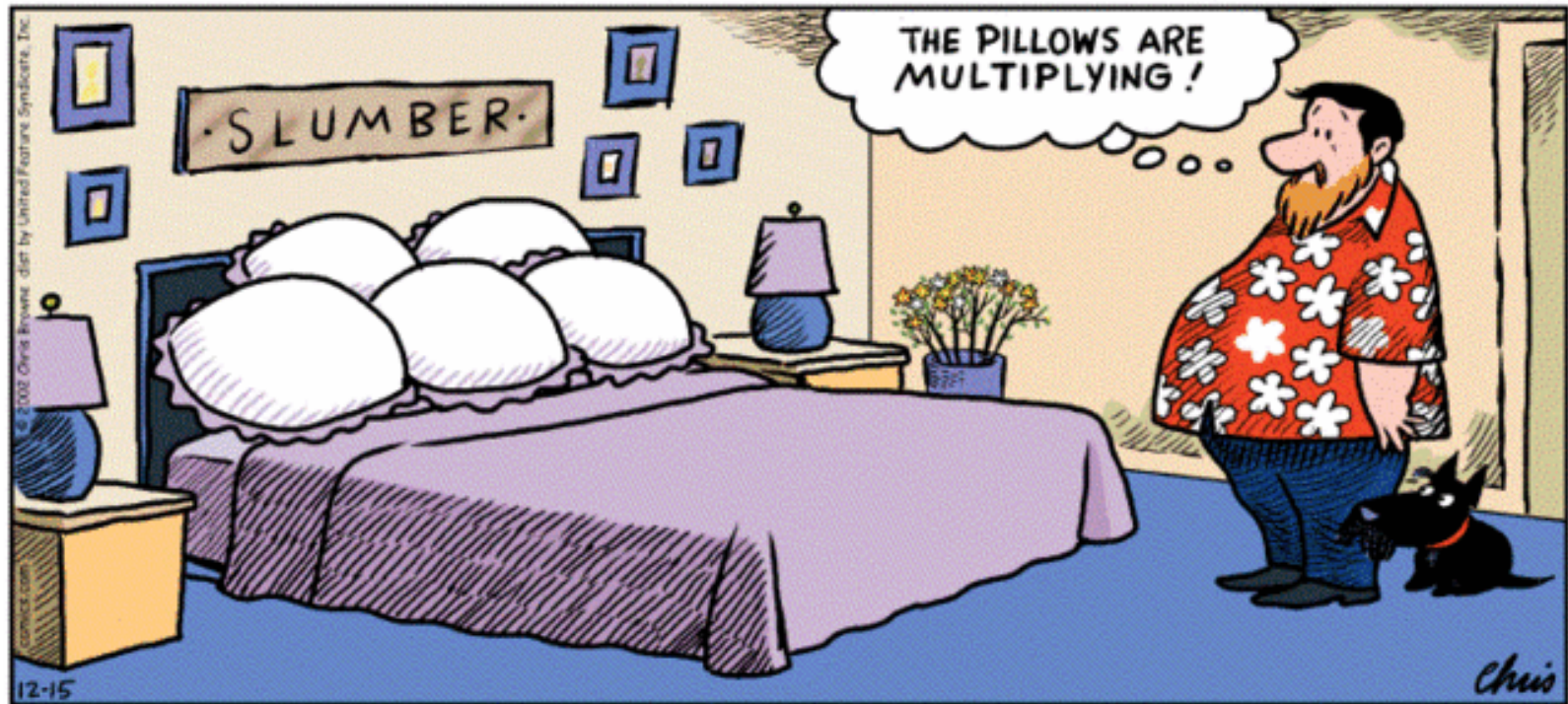


Abnormal

Tighten the Squeaky Screw... Don't Oil It.

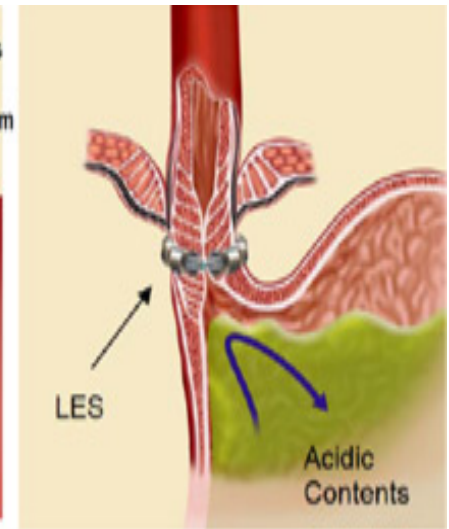
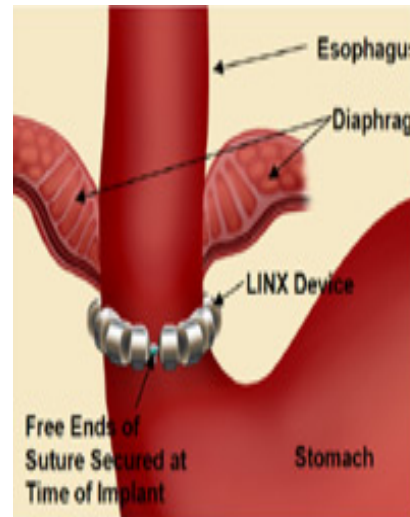
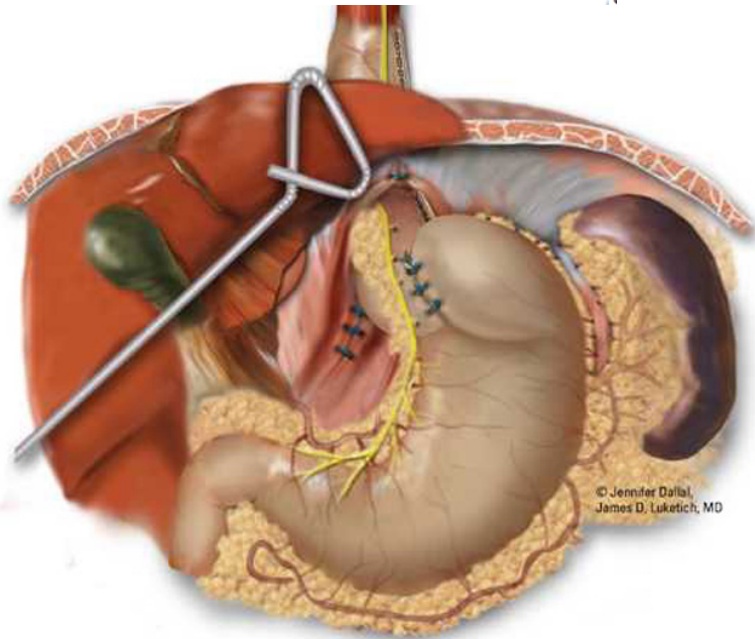
RAISING DUNCAN

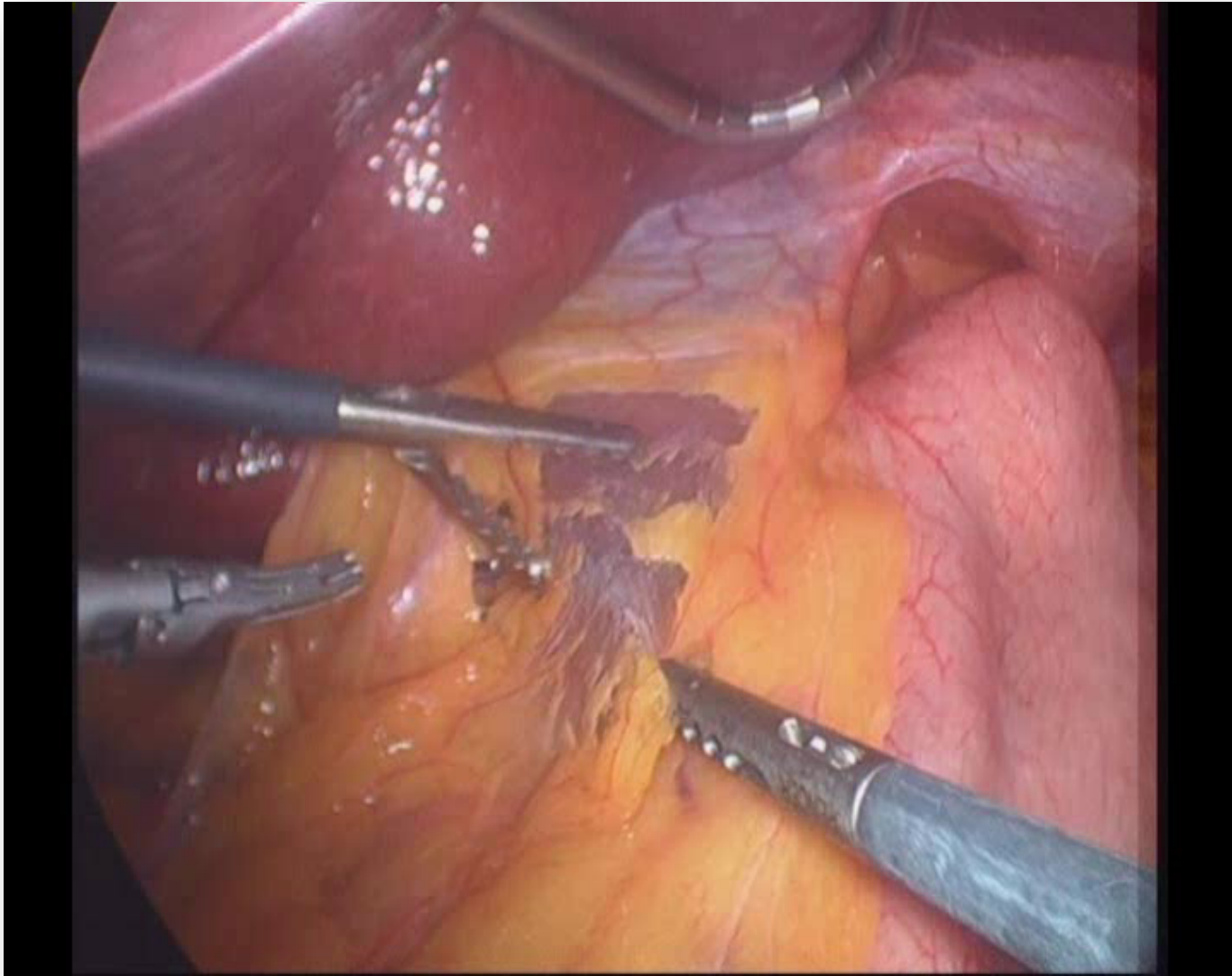
BY CHRIS BROWNE



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Current Surgical Options





Summary

- GERD is an disease of anatomy
 - Surgical intervention should always be considered
- Long term proton pump inhibitor use can lead to complications
 - Osteoporosis
 - Potential risk for increasing malignancy
 - Drug-drug interaction
 - Medical costs
- Surgical Intervention has several modalities
 - Open/Laparoscopic Fundoplication
 - Linx magnetic ring



For more information
or to make an appointment
please visit:

www.heartburncenterofcalifornia.com

Or call: (925) 932-6330