MEDICAL GRAND ROUNDS

May 9, 1974

# HIATUS HERNIA
# REFLUX - ESOPHAGITIS

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## CASE REPORT

F.S. is a 43-year-old, slightly overweight, security guard. He presented with a 2-1/2 year history of burning epigastric and retrosternal pain. At times, the pain is accompanied by regurgitation of warm fluids in the throat. The pain, as well as regurgitation, are precipitated by bending forward and lying in bed, particularly on the right side. The symptoms are usually worse while sitting than while standing. The pain is initially relieved by eating food, but it usually reappears 30-45 min after eating. In addition, he also experienced several episodes of cramp-like, chest pain which came spontaneously. He had experienced two episodes of dysphagia. He denied any history of vomiting, hematemesis, anemia, or choking and coughing spells during sleep. Barium swallow and upper GI series 2 years ago revealed no evidence of hiatus hernia or gastroesophageal reflux, but a repeat study showed a small hiatus hernia but with no evidence of reflux. There was no evidence of peptic ulcer disease. Acid secretory studies were within normal range. Other laboratory studies were within normal range. EKGs before and after exercise were essentially normal. A recent x-ray 3 weeks ago, again showed a small hiatus hernia, but revealed no evidence of stricture or free reflux. Esophagoscopy revealed no evidence of esophagitis, but a small hernia was observed. Acid perfusion test was positive, and mucosal biopsy of the esophagus was reported as normal without any evidence of ulceration or infiltration. On closer examination, it did show mucosal changes consisting of basal cell hyperplasia and extension of papillae to the surface. Esophageal motility study showed many simultaneous, high amplitude contractions in the body of the esophagus, suggestive of diffuse esophageal spasm. The lower esophageal sphincter pressure was 20 mm Hg (normal: over 15 mm Hg.).

*Comments:* Captain Sanders hardly fulfills any criteria of being an interesting case. However, he presents a real bread-and-butter problem in clinical medicine. In recent years there have been several advances in our understanding of hiatus hernia and reflux esophagitis. There has been a clearer understanding of the clinical significance of small hiatal hernia and some appreciation of the pathology of reflux esophagitis. We have begun to understand the pathogenesis of lower esophageal sphincter incompetence, which causes gastroesophageal reflux. To be sure, no final answers as known, but a better understanding of the basic problem has prompted a rational approach in the diagnosis and treatment of these patients. This morning, I wish to review some of the newer concepts of hiatus hernia and reflux esophagitis.

## CLINICAL SIGNIFICANCE OF HIATUS HERNIA

Harrington, in 1948, suggested that hiatus hernia produced many symptoms which mimicked those of many abdominal organs, and called the hiatus hernia "the masquerader of the upper abdomen". This was followed by almost a witch hunt for hiatus hernias in a vast number of patients, in whom the clinician could not explain his patient's abdominal symptoms. It soon became apparent, however, that a large number of patients who had hiatal hernias had no symptoms, but the radiologists continued their

vigorous efforts to demonstrate a hernia

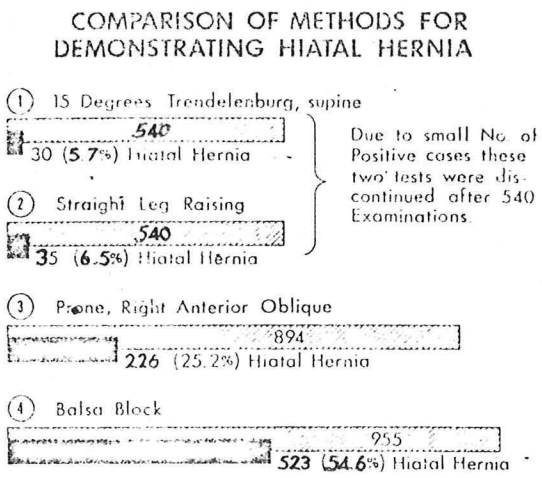
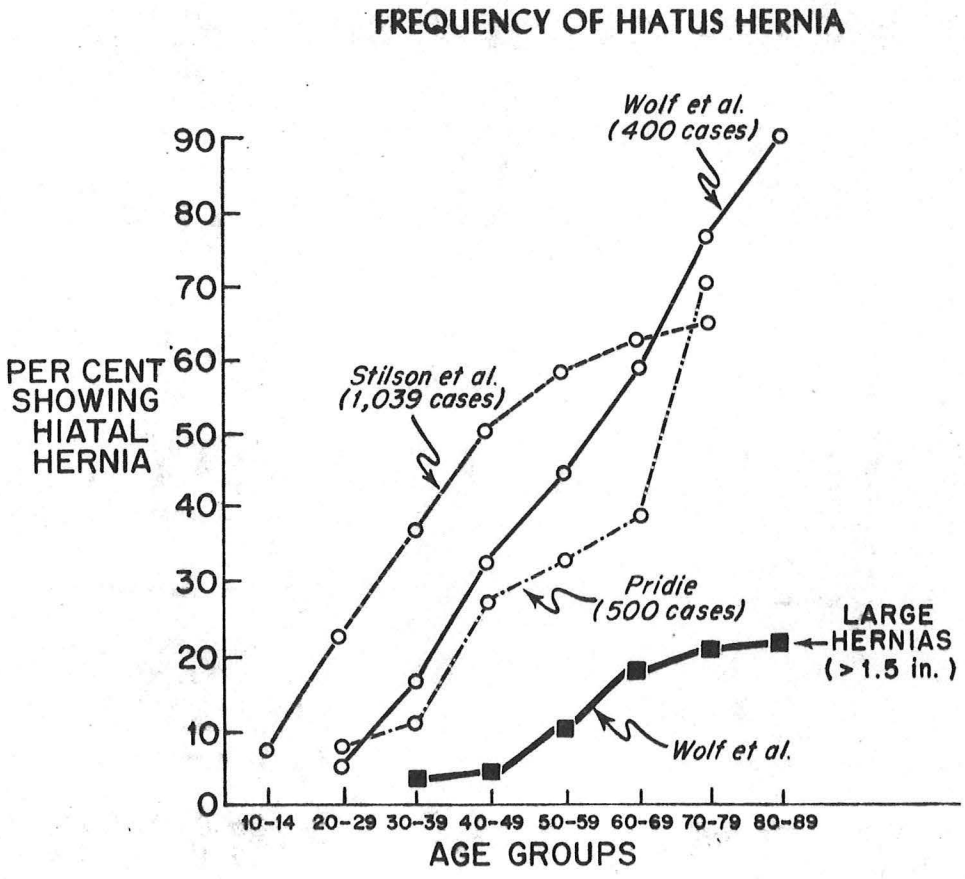



*Figure 1*

(Stilson et al., 1969)

These vigorous efforts, however, revealed hernias in an alarmingly large number of persons, who had demonstrated diseases of other organs or were completely asymptomatic.

*Figure 2*



Because of the high frequency of hiatus hernia, a wide variety of symptoms, which were initially attributed to hiatus hernia, were found to be unrelated to hiatus hernia, but the view that hiatus hernia causes gastroesophageal reflux and its esophageal and pulmonary complications has persisted. Fortunately, currently the hiatus hernia is being stripped of its last attribute. Recent studies have shown that: 1) a vast majority of patients with hiatus hernia do not have reflux, 2) frequency of hiatus hernia increases with age, but that of reflux does not increase, 3) a large number of patients (exact frequency varies from 5-50%) with reflux esophagitis do not have demonstrable hiatal hernia, and 4) recent studies have shown that symptoms of reflux correlated with the competence of the lower esophageal sphincter, and these symptoms occur irrespective of the presence of a small hiatus hernia.

*TABLE I*

*Lack of Correlation Between Symptoms of Reflux and Hiatus Hernia*

PERCENTAGE OF POSITIVE ANSWERS TO SYMPTOM QUESTIONNAIRE

| Examinations | Total 1039 | H. H. pos. 523 | H. H. neg. 431 | W. S. pos. 421 | H.H. pos. W. S. pos. 279 | H.H. neg. W. S. neg. 295 | All neg. 337 |
|---|---|---|---|---|---|---|---|
| Symptoms | Symptoms by Percentage | | | | | | |
| Dysphagia | 14.5 | 17.0 | 10.7 | 16.5 | 16.7 | 8.6 | 9.7 |
| Painful swallowing | 6.8 | 7.3 | 5.7 | 7.6 | 8.1 | 5.2 | 6.4 |
| Regurgitation | 34.1 | 34.2 | 33.2 | 34.8 | 35.3 | 34.2 | 34.0 |
| Pillow stain | 13.6 | 13.5 | 14.2 | 13.9 | 13.5 | 14.0 | 13.8 |
| Pain, chest or epigastric | 72.0 | 72.0 | 74.0 | 72.0 | 69.1 | 73.0 | 70.6 |
| Acid belch | 56.5 | 59.7 | 54.0 | 57.0 | 59.6 | 57.0 | 54.6 |
| Heart pain | 45.5 | 46.8 | 45.6 | 47.2 | 44.8 | 43.3 | 40.5 |
| Increase on bending | 20.6 | 19.1 | 23.0 | 20.4 | 18.7 | 21.8 | 21.4 |
| Increase with tight clothing | 35.7 | 35.6 | 36.3 | 34.3 | 34.4 | 40.0 | 36.3 |
| Increased pain with increased weight | 23.4 | 26.6 | 19.4 | 22.8 | 24.5 | 21.3 | 19.6 |

H.H. = Hiatus Hernia
W.S. = Water Siphon Test for Reflux

(Stilson et al., 1969)

On the basis of current evidence, it can be concluded that a small sliding hiatus hernia does not constitute a clinical entity.


Harrington, S.W.: *Surg. Gynecol. Obstet.* 86:735, 1948.
Palmer, E.D.: *Amer. J. Med.* 44:566, 1968.
Stilson,W.L, Sanders, I., Gardiner, G.A.: *Radiology* 93:1323, 1969
Wolf, B.S., Brahms, S.A. Khilnani, M.T. *Mt. Sinai J. Med. NY* 26:598 1959
Pridie, R.B.: *Gut* 7:188, 1966
Gahagan, T.: *Arch. Surg.* 95:595, 1967
Hiebert, C., Belsey, R.: *J. Thorac. Cardio. Surg.* 42:352, 1961
Cohen, S., Harris, L.D.: *NEJM* 284:1053, 1971
Winans, C.S. *Geriatrics* 27:69, 1972
Kramer, P.: *Gastroenterology* 57:442, 1969

*Comments:* The conclusion that hiatus hernia may not be a clinical entity may have come too late for several thousand men and women whose hernias have been fixed.

To be sure, it is not very clear if the presence of hernia may somehow contribute to the impairment of antireflux mechanisms.

## SPECTRUM OF THE PATHOLOGY OF REFLUX ESOPHAGITIS

Just a few years ago, it would have been concluded that Capt. Sanders had no evidence of esophagitis. Today, we know that esophageal damage produced by digestive diseases may take two forms. One form is obvious on x-ray examination, as well as endoscopic examination, and can be called: *gross esophagitis*. The other form reveals no gross evidence of esophagitis and can be called occult or *microscopic esophagitis*.

### (A) GROSS ESOPHAGITIS

Severe esophageal injury may produce 4 lesions: 1) erosive esophagitis, 2) esophageal strictures, 3) esophageal ulcers, and 4) columnar-lined esophagus. These lesions can exist singly, but most of the time they occur together.

i) *Erosive esophagitis:* Characterized by multiple, superficial erosions or ulcerations which are usually long and linear, lying in longitudinal folds. These changes are usually most marked in the distal-most part of the esophagus. These changes are easily recognized by endoscopic examination as friable red esophageal mucosa with erosions and bleeding.

ii) *Esophageal stricture:* Fibrous esophageal strictures are associated with marked fibrotic reaction in the lamina propria, which may extend into submucosal and periesophageal tissues. These are usually associated with erosive esophagitis.

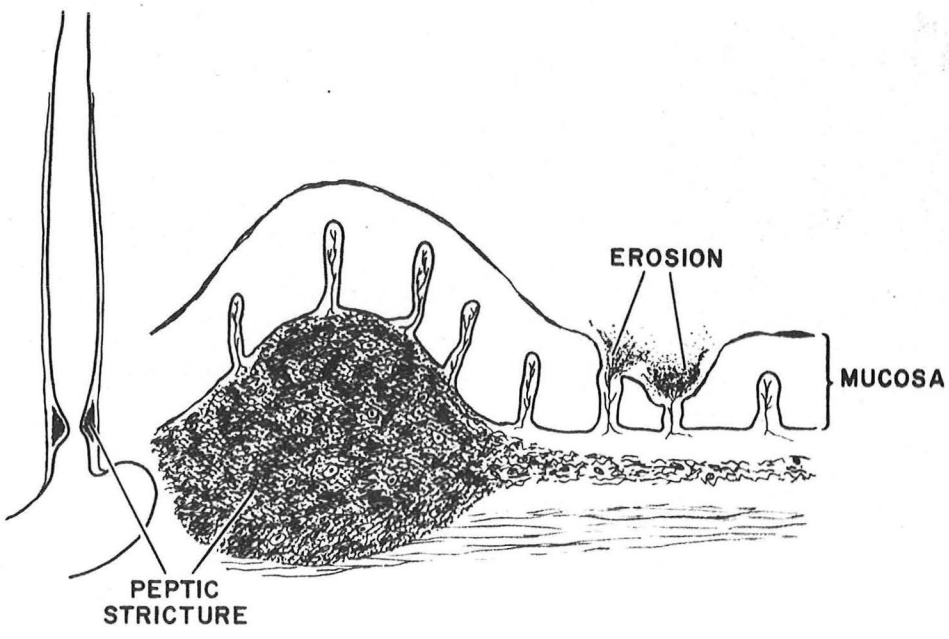



*Figure 3*

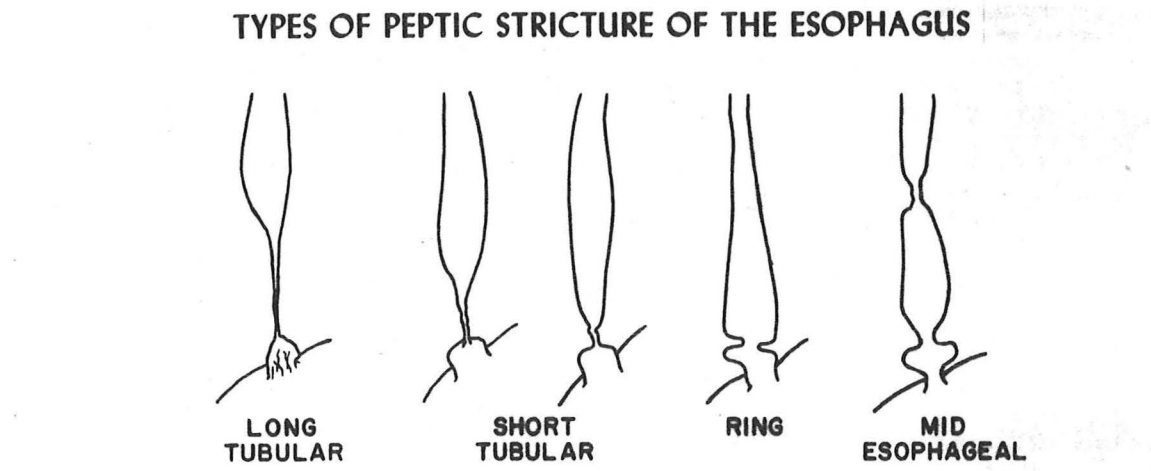



*Figure 4*

a) The long tubular strictures are rarely due to reflux esophagitis, except those associated with prolonged nasogastric intubation. Most of these strictures are non-peptic; they are usually due to ingestion of lye.

b) The short tubular strictures are the commonest type of esophageal strictures due to reflux esophagus.

c) The annular peptic strictures (washer ring strictures; ring-like peptic strictures) are very rare. Most of these are confused with the lower esophageal ring. The mucosal type of lower esophageal rings are sometimes considered as due to reflux esophagitis, but there is very little evidence that it is so.

d) Mid-esophageal strictures are usually associated with columnar-lined esophagus distal to the stricture (Barrett's esophagus).

iii) *Esophageal ulcer and columnar-lined esophagus:* Deep penetrating peptic ulcer of the esophagus is uncommon, but when present, it always occurs in the columnar-lined epithelium. Sandry studied 46 specimens of lower esophagus and stomach, which were resected for esophagitis; 29 out of 46 had esophageal ulcer. These were present alone in 3 specimens, but in 26 they were present in combination with chronic superficial esophagitis.

Sandry, R.J.: Gut 3:189, 1962
Brunnen, P.L., Karmody, A.M., Needham, C.D.: Gut 10:831, 1969
Peters, P.M.: Thorax 10:269, 1955
Lodge, K.V.: J. Path. Bact. 69:17, 1955
Palmer, E.D.: Amer. J. Med. 44:566, 1968
Paulson, D.L.: Ann. Surg. 165:765, 1967
Barrett, N.R.: J. Thorac. Cardiovasc. Surg. 43:703, 1962
Goyal, R.K., Glancy, J.J., Spiro, H.M.: NEJM 282:1298-1305, 1355-1362, 1970
Allison, P.R.: Thorax 3:20, 1948
Burgess, J.N.: Mayo Clin. Proc. 46:728, 1971
Barrett, N.R.: Brit. J. Surg. 38:175, 1950
Barrett, N.R.: Surgery 41:881, 1957
Allison, P.R., Johnstone, A.S.: Thorax 8:87, 1953

## (B) *MICROSCOPIC ESOPHAGITIS*

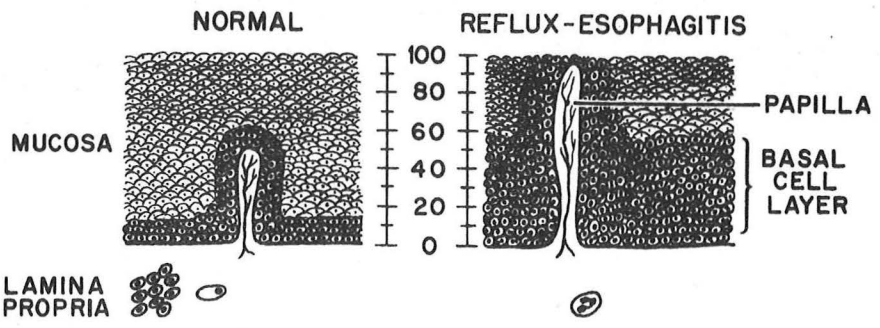
Palmer recognized that many patients with esophagitis may not have mucosal destruction and ulceration. In these patients, mucosal biopsy was interpreted by him as characterized by i) intact esophageal mucosa, ii) subepithelial fibrosis with accumulation of lymphocytes, plasma cells and occasionally neutrophils. Using these histologic criteria, several authors were disappointed by poor correlation between histologic and clinical esophagitis.

Recent studies with proper controls revealed that submucosal accumulation of lymphocytes and plasma cells were almost as frequently seen in patients with clinical esophagitis as healthy controls. However, polymorphonuclear infiltration was only seen in esophagitis, but this occurred only in a small number (18%) of patients.

Pope and his associates recognized mucosal abnormalities in patients with reflux esophagitis. They found that these patients showed mucosal changes of i) basal cell hyperplasia, so that basal cells formed over 15% of the thickness of the mucosa (normally 5 - 14%), and ii) extension of subepithelial papillae towards the surface so that they extended to over 66% of mucosal thickness (normal: less than 66%).

*Pathology of Microscopic Esophagitis*

*Figure 5*



Palmer, E.D.: Arch. Path. (Chic.) 59:51, 1955
Seigel, C.I., Hendrix, T.R.: J. Clin. Invest. 42:686, 1963
Cocco, A.E.: Bull. Gastroint. Endosc. 11:29, 1965
Ismail-Beigi, F., Horton, P.F., Pope, C.E.: Gastroenterology 58:163, 1970

## *PATHOGENESIS OF REFLUX ESOPHAGITIS*

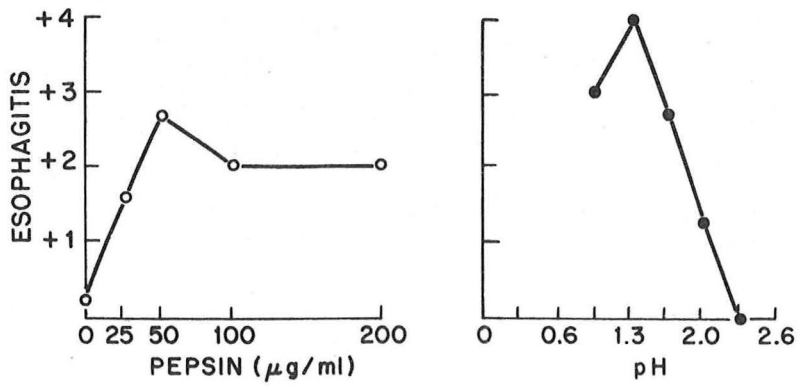
### *(A) THE CAUSATIVE AGENT*

In 1960, Palmer wrote: "During the past few years I have studied 238 original papers and monographs on the subject, dating from 1869 to the present, hoping to find proof of the statement so often quoted that refluxing stomach acid is responsible for esophagitis in human beings. None could be found." Palmer, of course, believes that the inflammatory process of what he calls "subacute erosive esophagitis" is not peptic, but is the result of vascular ischemia. He reported that subacute erosive esophagitis is frequently seen in patients with achlorhydria and following gastric surgery. Now we know, however, that reflux of bile and of small bowel juice may be as bad in causing reflux esophagitis as the acid reflux. Occurrence of esophagitis in patients with achlorhydria, therefore, does not indicate that reflux of acid-pepsin may not cause esophagitis. Although definitive evidence is scanty, a mass of indirect evidence suggests that reflux esophagitis is usually associated with the reflux of acid-pepsin.

Experimental studies have shown that the perfusion of acid and pepsin causes esophagitis in animals. However, these are acute experiments, employing infusions for brief periods of time, and they cannot be equated with the type of esophagitis produced in man. However, they do point out some interesting facts.

1. Acid alone is less damaging than acid-pepsin, and pepsin alone does not produce esophagitis above a certain pH.

**INFLUENCE OF pH AND PEPSIN CONCENTRATION IN ACUTE ESOPHAGITIS**




*(After Goldberg et al., 1970)*

*Figure 6*

2. Bile salts may produce esophagitis by themselves.
3. Bile salts accentuate the damaging effect of acid-pepsin on the esophageal mucosa.
4. Esophagitis may be produced in animals by pancreatic and small bowel juices.

Palmer, E.D.: NEJM 262:927, 1960
Goldberg, H.I., Dodds, W.J., Gee, S., et al.: Gastroenterolgy 56:223, 1969
Gillison, E.W., deCastro, V.A.M., Nyhus, L.M.: Surg. Gynec. Obstet. 134:419, 1972
Henderson, R.D., Mugashe, F.L., Jeegeebhoy, K.N., et al.: Canad. J. Surg. 16:1, 1973
Moffat, R.C., Berkas, E.M.: Arch. Surg. 91:963, 1965
Cross, F.S., Wangensteen, O.H.: Proc. Soc. Exp. Biol. Med. 77:862, 1951
Orlando, R.C., Bozymski, E.M.: NEJM 289:522, 1973

## *(B) PATHOGENESIS OF VARIOUS LESIONS OF ESOPHAGITIS:*

The wide spectrum of lesions that are produced due to acid-peptic reflux is very fascinating. The following concept of the pathogenesis of different lesions is a speculative way to explain many known facts. According to this concept, the different lesions of the reflux esophagitis are related to the equilibrium of the interaction between the esophageal defensive mechanisms and the aggressiveness of acid-pepsin.

*TABLE II*

| Aggressiveness of Acid-Pepsin | Mucosal Repair Process | | Esophageal |
|---|---|---|---|
| + | +++ | → | None |
| +++ | +++ | → | Histologic esophagitis (basal cell hyperplasia) |
| +++ | ++ | → | Erosive esophagitis and stricture |
| +++ | ± | → | Columnar cell invasion, Barrett's esophagus |

*Support for this concept:* 1) The histologic features of mucosal esophagitis indicates vigorous cell renewal. It can be interpreted to show that superficial layers of squamous epithelium are damaged by the gastric juice, and there is an attempt at replacement of these cells by the basal germinating cells. It is of interest that when superficial horny layers of epithelium are stripped experimentally, hyperplasia of basal cells is produced. When the damage by reflux is matched by the mucosal cell regeneration, no gross lesion results.

2) Erosive esophagitis usually arises *de novo*. It is sometimes implied that mild esophagitis of long duration may lead to stricture; however, there is little evidence to suggest that mild esophagitis leads to severe esophagitis: i) In almost 70% of patients with severe peptic esophagitis, the history of heartburn is less than 3 years. ii) It has been estimated that severe esophagitis occurs in about 5% of the cases with reflux. Since reflux esophagitis does not alter survival, one would expect a much larger pool of esophagitis, if mild esophagitis progressed to severe esophagitis. iii) Followup studies of patients with heartburn do not reveal any increase in incidence of complicated esophagitis. iv) Many patients with severe esophagitis present with bleeding with antecedent history of heartburn, and patients with strictures present with dysphagia and heartburn starting almost simultaneously. v) It is interesting to note that as a group, patients with severe esophagitis belong to the older age group, with their peak frequency in the 6th and 7th decade of life, suggesting that the repair process may be suboptimal. To be sure, however, there are no cell renewal studies of the esophageal mucosa in these patients.

3) Columnar lining of the esophagus follows reflux associated with esophageal mucosal destruction. Esophageal mucosa *in vitro* is columnar to start with, but it later gets replaced by squamous epithelium. No doubt, some cases of columnar-lined esophagus are congenital in origin. However, there is now good evidence to suggest that some cases of so-called Barrett's esophagus, or columnar-lined lower esophagus, are acquired: i) A progress of gastric type mucosa from the lower levels in the esophagus to higher levels has been demonstrated by serial biopsies in several individual patients. ii) Most of the patients with columnar-lined esophagus are over 60 years. iii) They usually have a short history of heartburn and/or dysphagia. iv) Reflux can usually be demonstrated in these patients. v) Experimental studies by Bremner show that when a strip of squamous epithelium is removed from the esophagus in the dog, replacement occurs by squamous epithelium if there is no reflux; however, in the presence of excessive reflux the raw area is replaced only by the gastric type epithelium.

The invading columnar cells, which march in the esophagus under the umbrella of the persistent reflux, are by no means immune from damage by the continuing reflux. These cells do not as readily replace their dead, and acid-pepsin can ulcerate to the depths of the wall producing deep peptic ulcer.

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Rex, J.C., Andersen, H.A., Bartholomew, L.G., et al.: JAMA 178: 271, 1961

Brunnen, P.L., Karmody, A.M., Needham, C.D.: Gut 10:831, 1969

[Cont'd]

[Cont'd]

Bremner, C.G., Lynch, V.P., Ellis, F.H., Jr.: Surgery 68:209, 1970
Goldman, M.C., Beckman, R.C.: Gastroenterology 39:104, 1960
Mossberg, S.M.: Gastroenterology 50:671, 1966
Adler, R.H.: Geriatrics 20:109, 1965

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*Comments:* Reflux esophagitis is thus a resultant of interaction between reflux and esophageal mucosal defenses.

Thanks to our ignorance, I have nothing to say about mucosal defense. Let us now see why reflux occurs.

## *PATHOGENESIS OF GASTROESOPHAGEAL REFLUX*

Gastroesophageal reflux occurs whenever the pressure of the intragastric contents overwhelms the antireflux mechanisms. Various factors in the pathogenesis of gastroesophageal reflux are:

(A) Weakened antireflux mechanisms:

1) Impaired basal LES pressure and its adaptive response to stress

2) Loss of normal antireflux mechanical factors such as:

a) Intra-abdominal esophagus

b) Angulation at the gastroesophageal junction

(B) Over-aggressive gastric contents:

1) Gravity and posture

2) Increased intra-abdominal pressure

3) Distal obstruction

### *(A) WEAKENED ANTIREFLUX MECHANISMS*

#### *(1) Lower Esophageal Sphincter Incompetence*

*(a) Background:*

The lower esophageal sphincter is a specialized segment of muscle which is located at the junction of the esophagus with the stomach. It is identified as a zone of high pressure, interposed between the stomach and the esophagus. Sphincter pressures can be quantitated by perfused catheters. Patients with reflux have: i) lower basal sphincter pressures, as compared to

normal subjects. There is a significant overlap, however. The patients with severe esophagitis have much lower pressures than those with mild esophagitis.

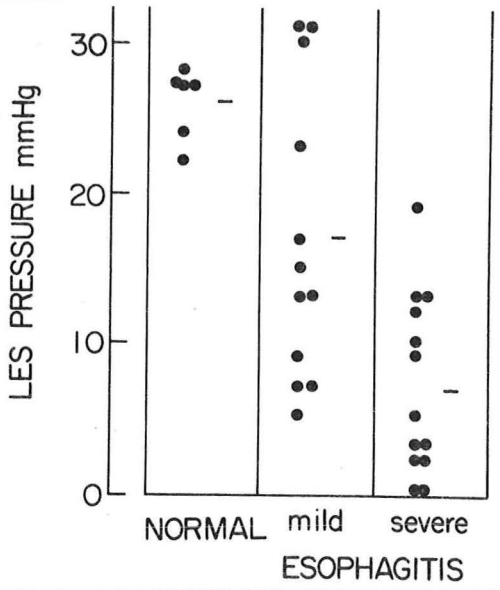



*Figure 7*

Pope, C.E.: Gastroenterology 52:779, 1967
Winans, C.S., Harris, L.D.: Gastroenterology 52:773, 1967
Haddad, J.K.: Gastroenterology 58:175, 1970

ii) The patients with reflux have impaired adaptive response to increase in abdominal pressure.

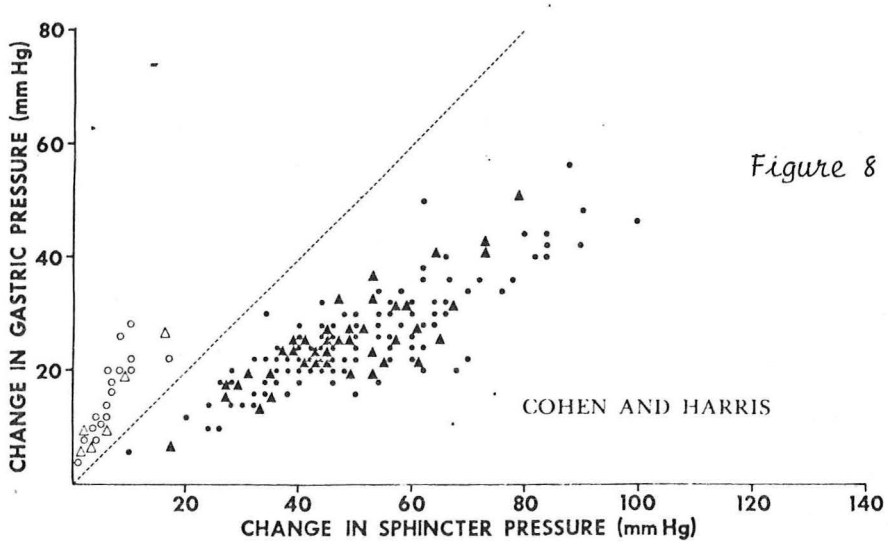



*Figure 8*

Figure 2. Increase in LES Pressure in Patients without Hernias That Accompanied the Increase in Intra-abdominal Pressure Caused by a Valsalva Maneuver (Δ and ▲) or by Either Inflation of an Abdominal Binder or Lifting of the Legs While the Patient Was Supine (o and ●).

Every value from every patient without a hiatus hernia is shown. The open symbols represent values obtained from symptomatic patients. The dotted line is the 1:1 response predicted for simple transmission of intra-abdominal pressure to the sphincter.

Lind, J.F., Warrian, W.G., Wankling, W.J.: Canad. J. Surg. 9: 32, 1966
Cohen, S., Harris, L.D.: NEJM 284:1053, 1971

*Comments:* Skeptics of only two decades ago will be glad to know that the lower esophageal sphincter is for real and, when healthy, provides a major, dynamic antireflux mechanism.

(b) *Pathogenesis of LES Incompetence:*

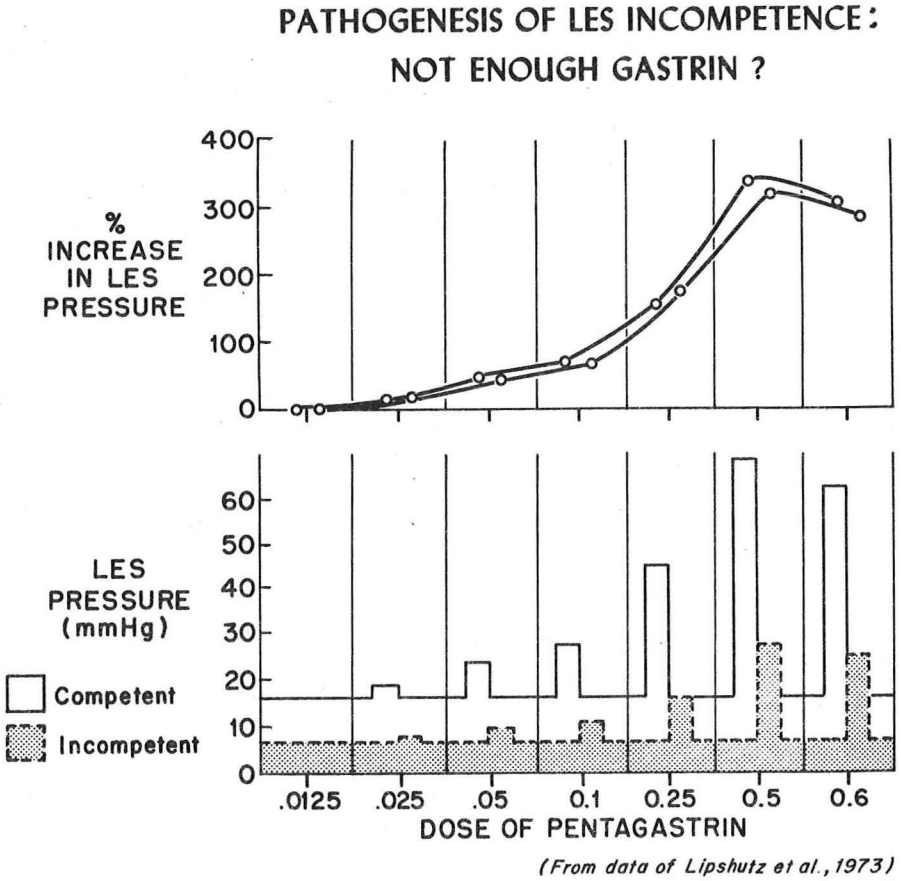
1) Neurohormonal factors:
   - i) Hypogastrinemia
   - ii) Cholinergic motor neurons dysfunction
   - iii) Vagal hypotonia

2) Myogenic factors:
   - iv) LES muscle disease

3) Mechanical factors:
   - v) Ineffective mucosal plug
   - vi) Abnormal insertion of the phrenoesophageal membrane
   - vii) Wide esophageal hiatus and hiatal herniation

i) HYPOGASTRINEMIA: On the basis of their results of a comparable per cent increase in LES pressure, Lipshutz and colleagues concluded that with gastrin stimulation incompetent sphincters could respond as well as the competent ones. However, there are several reservations in accepting these conclusions: a) if gastrin was all that the incompetent sphincters lacked, with enough gastrin they should have generated the same absolute pressure as the competent ones. This is not the case, as shown in the figure which is drawn from their data.

*Figure 9*



b) Direct measurements have failed to reveal any difference in the basal serum gastrin levels in patients with reflux esophagus, as compared to normal subjects. c) The observation of reduced LES response to endogenous release of gastrin is not supported by observations of other workers.

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Lipshutz, W.H., Gaskins, R.D., Lukash, W.M., et al.: NEJM 289: 182, 1973
Cohen, S.: NEJM 289:215, 1973 (Editorial)
Farrell, R.L., Costell, D.O., McGuigan, J.E.: Clin. Res. 21: 512, 1973 (Abstr.)
Costell, D.O., Farrell, R.L., McGuigan, J.E.: NEJM 289:981, 1973 (Letter)
Lipshutz, W.H.: NEJM 289:981, 1973 (Letter)
Grossman, M.I.: NEJM 289:981, 1973 (Letter)

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d) The hypothesis that serum gastrin acting via the cholinergic motor neurons is responsible for LES closure is open to question. It has been reported that, in man, gastrin may act via cholinergic motor neurons to cause LES contraction, because the LES contraction with exogenous gastrin is antagonized by a small dose of atropine. However, if the endogenous gastrin also acted via the cholinergic neurons to keep sphincter closure, atropine should lead to abolition, or at least marked reduction in basal LES pressure; but this does not appear to be the case, as the basal LES pressure does not fall with small doses of atropine, although these small doses of atropine markedly antagonize the effects of endogenous gastrin and cholinomimetic agent.

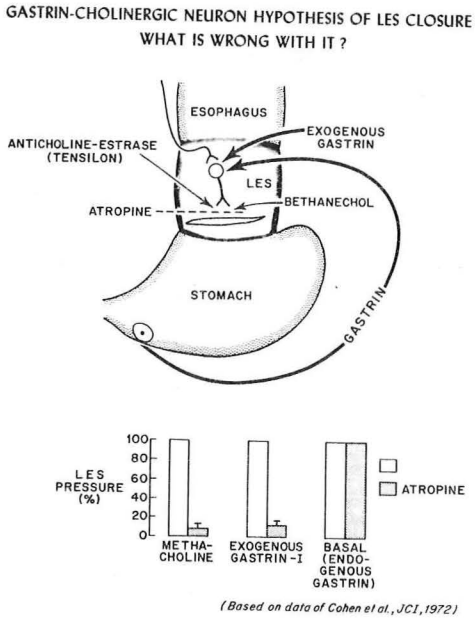



*Figure 10*

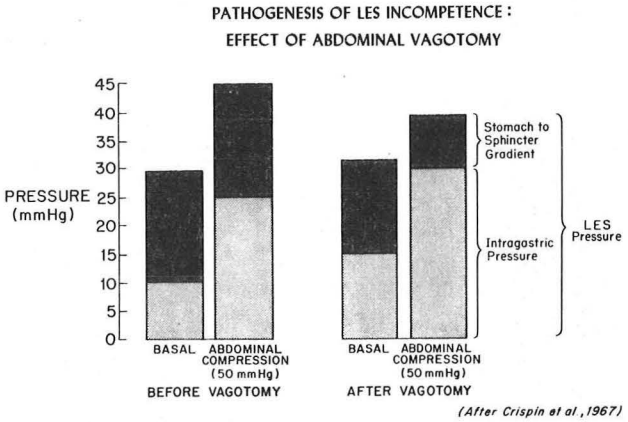
Lipshutz, W., Hughes, W., Cohen, S.: J. Clin. Invest. 51:522, 1972
Giles, G.R., Mason, M.C., Humphries, C., et al.: Gut 10:730, 1969
Castell, D.O., Harris, L.D.: NEJM 282:886, 1970
Cohen, S., Lipshutz, W.: J. Clin. Invest. 50:449, 1971
Cohen, S., Harris, L.D.: Gastroenterology 63:1066, 1972
Grossman, M.I.: Gastroenterology 65:994, 1973
Cohen, S.: Gastroenterology 66:479, 1974
Frank, S.A., Walker, C.O., Fordtran, J.S.: Gastroenterology 64:728, 1973 (Abstr.)
Cohen, S., Fisher, R., Lipshutz, W.: J. Clin. Invest. 51:2663, 1973

ii) CHOLINERGIC MOTOR NEURON DYSFUNCTION: It has been suggested that in patients with scleroderma, the LES incompetence may be due to diseased cholinergic neuron function. However, the available data are open to other interpretations.

Cohen, S., Fisher, R., Lipshutz, W.H.: J. Clin. Invest. 51:2663, 1972

iii) VAGAL HYPOTONIA: It has been observed that abdominal vagotomy may frequently lead to gastroesophageal reflux. Lind and colleagues have suggested that the vagus may carry cholinergic motor neurons to the LES, which may cause continuous closure of the LES. It has been suggested that vagal hypotonia may lead to sphincter incompetence and reflux esophagitis. However, direct studies on the vagus nerve have shown that the vagi do not carry cholinergic motor fibres to the LES. The sphincter incompetence after vagotomy may be due to the section of afferent neurons which are carried in the vagus and are responsible for reflex LES contraction. Abdominal vagotomy may cause section of afferent fibres in the vagi, which may be responsible for reflex LES contraction. This may be responsible for poor adaptive responses of the sphincter to abdominal compression in patients with abdominal vagotomy.

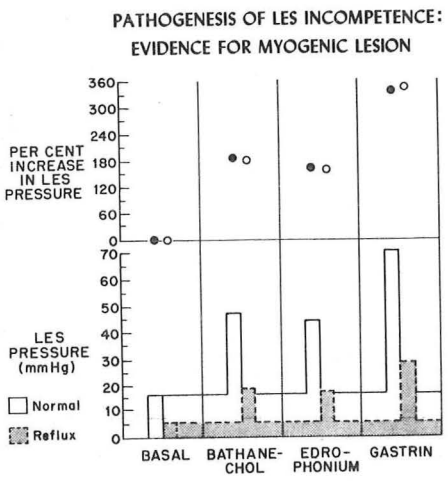
*Figure 11*



Crispin, J.S., McIver, D.K., Lind, J.F.: Canad. J. Surg. 10:299, 1967
Lind, J.F., Crispin, J.S., McIver, D.K.: Canad. J. yhysiol. Pharmacol. 46:233, 1968
Williams, J.A., Woodward, D.A.K.: Surg. Clin. No. Amer. 47:1341, 1967
Rattan, S., Goyal, R.K.: Clin. Res. 32:366, 1974 (Abstr.)

iv) DISEASED SPHINCTER MUSCLE: Many studies, which are cited previously, can be interpreted to show that the patients with reflux have sick sphincters (Grossman, 1973). In all studies, the absolute values of the basal sphincter pressure in patients with reflux are low. Moreover, in spite of a normal per cent increase in the sphincter pressure, the sphincter pressure cannot be brought to normal functional level. I consider these observations of tremendous significance in determining the rational therapeutic approach in these patients. Only if the LES muscle is incompetent because of lack of some stimulating agent, can the sphincter competence be restored by the use of appropriate stimulating agent. However, if the muscle itself is diseased and cannot respond on stimulation, then the role of drugs to improve sphincter competence would, obviously, be limited.

*Figure 12*




v) INEFFICIENT MUCOSAL PLUG AND NASOGASTRIC TUBE: The length-tension curves of all muscles indicate that they cease to develop any tension when they have shortened below a certain length. This length at which the tension ceases varies with different muscles. It would, therefore, appear that some luminal filling material or plug may be required to produce an effective luminal closure. Moreover, pressure diameter curves of the sphincter indicate that at some diameters of the lumen, the closure pressure may be inefficient. This may explain, in part, frequent occurrences of sphincter incompetence and reflux with an indwelling nasogastric tube.

Biancani, P., Goyal, R.K., Phillips, A.: J. Clin. Invest. 52:2973, 1973
Bingham, J.A.W.: Brit. Med. J. 2:817, 1958
Nagler, R., Wolfson, A.W., Lowman, R.M.: NEJM 262:1325, 1960
Nagler, R., Spiro, H.M.: NEJM 269:495, 1963

vi) ABNORMAL INSERTION OF THE PHRENOESOPHAGEAL MEMBRANE: Dillard believes that when phrenoesophageal membrane happens to be inserted into the sphincter, rather than above it, a stretch on this membrane may tend to mechanically open the LES and impair its competence.

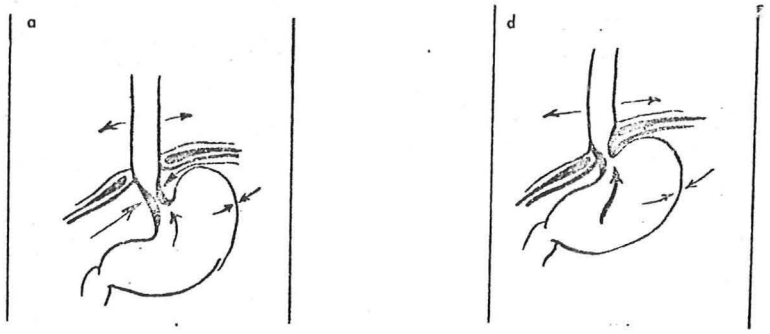
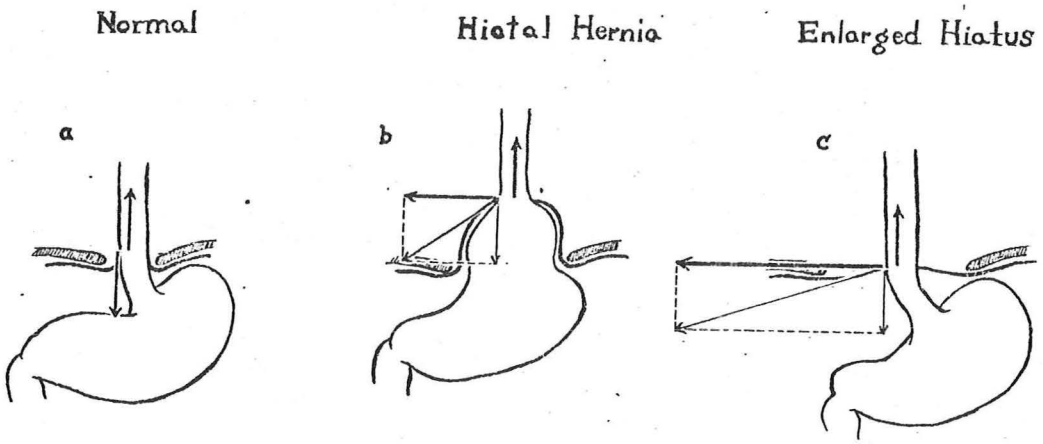



*Figure 13*

vii) HIATUS HERNIA AND PATULOUS HIATUS: It is argued that hiatus hernia may impair the competence of the lower esophageal sphincter because a) the sphincter now has to resist opening by negative intrathoracic pressure; b) the attached phrenoesophageal membrane may try to force it open.



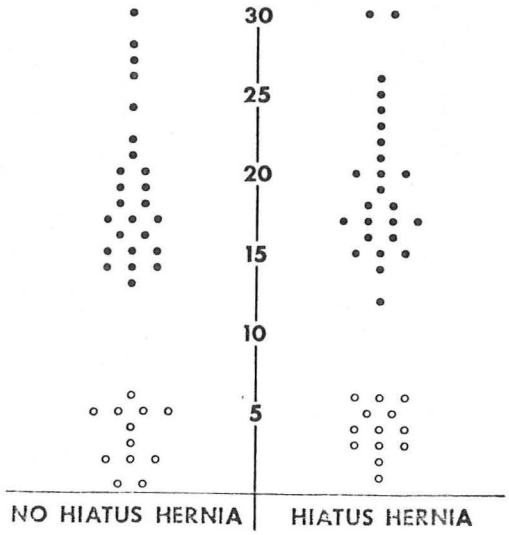

Vector analysis of the stresses involved in sliding esophageal hiatal hernia and in an enlarged muscular hiatus. The length of the arrow indicates the magnitude of the force. When the restraining structures pull in a direction which is at an angle to the force of intra-abdominal pressure (which tends to produce herniation) then this force can be broken down into its component parts, as diagrammed. It can be seen that the more divergent the ligament the greater is the force required to prevent hernia and consequently, the greater is the force tending to disrupt the sphincter.

*Figure 14*

However, direct manometric studies have shown that LES competence is not different in the subjects without reflux, with or without associated hernia. These studies show that normal sphincter function occurs even when

it is displaced in the chest.

*Figure 15*




Mean LES Pressures (in Millimeters of Mercury) of All Patients at Rest or Base Line.

The open circles represent values obtained from patients with symptomatic reflux. LES pressure did not correlate with presence or absence of hiatus hernia, but there was clear separation of symptomatic and asymptomatic patients.

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Wankling, W.F., Warrian, W.G., Lind, J.F.: Canad. J. Surg. 8:61, 1965
Cohen, S., Harris, L.D.: NEJM 284:1053, 1971
Lind, J.F., Cotton, D.J., Blanchard, R., et al.: Gastroenterology 56: 1078, 1969

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(2) *Impairment of Normal Antireflux Mechanical Factors*

a) Hiatal Hernia: It is considered that thoracic displacement of the gastroesophageal junction or herniation of part of the stomach may predispose to gastroesophageal reflux, even in the absence of LES incompetence because of the following reasons: i) loss of intra-abdominal esophagus, ii) loss of acute angulation (or the flap valve) at the gastroesophageal junction, and iii) pressure dynamics in the herniated sac

b) Loss of angulation, or the "flap valve", at the gastroesophageal junction in the absence of hiatal herniation.

c) Widened diaphragmatic hiatus with weakened pinchcock.

*Comments:* The precise role of the mechanical factors has been very hard to evaluate. The experimental work in animals on these factors is well summarized by Pope, who wrote: "The skeptical reader is impressed that dogs will do pretty much what you would like them to do. For instance, if you believe in the importance of the intra-abdominal esophageal segment, obliging canines with such a segment created surgically will lose their reflux. If you like flap valves, our canine friends will oblige with the loss of reflux. If you wish to wrap a pedicle of muscle around the lower end of the esophagus, gastric contents will be excluded from the canine gullet. If you are a friend of the fundoplication, the dogs will cease their regurgitation. If, on the other hand, you prefer to stick to the old standard method of approximating the leaves of the diaphragm, you can demonstrate in the dog that it is much more effective than fundoplication. If you are a true believer in the phrenicoesophageal ligament insert it in the wrong place and the sphincter will fail."

However, these appear to be very important as suggested by the efficacy of surgical treatment of reflux, which considers these factors in the reconstruction of the cardia, as discussed later.

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Pope, C.E.: Gastroenterology 59:460, 1970
Menguy, R.: Ann. Rev. Med. 23:313, 1972
Edwards, D.A.W.: Amer. J. Dig. Dis. 12:267, 1967
Longhi, E.H., Jordan, P.H.: Surg. Gynec. Obstet. 129:734, 1969
Braasch, J.W., Ellis, F.H., Jr.: Surgery 39:901, 1956
Jackson, C.: Laryngoscope 32:139, 1922
Code, C.F., Schlegel, J.F.: Edinburgh, Royal College of Surgeons, June 1962
Tocornal, J.A., Snow, H.D., Fonkalsrud, E.W.: Surgery 64:519, 1968
Bombeck, C.T., Aoki, T., Nyhus, L.M.: Ann. Surg. 165:752, 1967
Demos, N.J., Timmes, J.J., Di Bianco, J.: J. Thorac. Cardiovasc. Surg. 54:832, 1967
Earlam, R.J., Ellis, F.H., Jr.: Arch. Surg. (Chicago) 95:585, 1967
Sicular, A., Cohen, B., Zimmerman, A., et al.: Surgery 61:784, 1967
Anderson, H.N., May, K.J., Jr, Steinmetz, G.P., et al.: Ann. Surg. 166:102, 1967
Butterfield, W.C.: Surgery 69:910, 1971

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## (B) *OVER-AGGRESSIVE GASTRIC CONTENTS:*

For reflux to occur, there must be intragastric contents in the vicinity of the esophagogastric junction. However, there are very little objective data on the precise role and the mechanism of the contribution of the intragastric pressure in the genesis of gastroesophageal reflux.

Injection of air into the peritoneal cavity of dogs causes a corresponding increase in intra-abdominal pressure, but when dogs eat and fill their stomach with large amounts of food, no significant change in the intra-abdominal pressure takes place. This suggests that the muscle controlling the intra-abdominal pressure may refluxly relax in response to ingesion of food.

It has also been shown that when the stomach is empty, it can produce different pressures in different parts, but when filled with contents, any increase in pressure in any part is transmitted on all sides.

It is possible that in conditions which are associated with increased abdominal pressures, such as ascites, pregnancy, obesity, tight belts and binders, may predispose to reflux by not allowing the abdominal relaxation with gastric distention by eating. The role of gravity is not properly understood.

*Comments:* There is a pitiful paucity of data on intra-abdominal pressures, which are of obvious importance in the pathogenesis of reflux.

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Ingelfinger, F.J.: Gastroenterology 41:264, 1961
Wolf, B.S.: J. Mt. Sinai Hosp. NY 27:404, 1960
Simpson, J.A., Conn, H.O.: Gastroenterology 55:17, 1968
Lind, J.F., Smith, A.M., Melver, D.K., et al.: Canad.Med.Assn. J. 98:571, 1968
Nagler, R., Spiro, H.M.: Amer. J. Dig. Dis. 7:648, 1962
Nagler, R., Spiro, H.M.: J. Clin. Invest. 40:959, 1961

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## THERAPY OF REFLUX ESOPHAGITIS

This is considered under three headings: a) medical treatment, b) surgical treatment, and c) treatment of complications.

### (A) MEDICAL TREATMENT

This includes:

1) Use of physical and mechanical principles to prevent reflux.
2) Dietary instructions.
3) Neutralizing the refluxant, e.g., gastric acid.
4) Drugs to increase sphincter pressure: Avoid drugs which impair sphincter pressure.
5) Mechanical foam barrier.

#### 1) *Use of physical and mechanical factors:*

These include measures to: i) have gravity work against reflux and not for it; ii) avoid excessive increases in the intra-abdominal pressure; and iii) avoid postures which impair LES competence and make the cardia most dependent.

The patients should be instructed to:

1. Elevate the head end of the bed with blocks (at least 8", or higher).
2. Not to sleep on their right side. It is a common experience that refluxers experience most symptoms when they lie on their right side. Enhancement of reflux in right lateral posture has been demonstrated by pH recordings. Moreover, it has been shown that lying on the side and sitting up lowers the sphincter pressure as compared to supine posture.
3. Weight reduction, if obese.

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Pattrick, F.G.: Gut 11:659, 1970
Babka, J.C., Hager, G.W., Castell, D.O.: Amer. J. Dig. Dis. 18: 441, 1973

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*Comments:* In my experience and opinion, these maneuvers are of the greatest value in medical therapy of reflux esophagitis. Unfortunately, very little objective data on the usefulness of these measures are available in the literature.

#### 2) *Dietary and other instructions:*

i) No. of Meals: Usually these patients are instructed to eat frequent

small feeds. However, the usefulness of such a maneuver is questionable because reflux frequently occurs after a meal in these patients. It has been observed that a meal causes an increase in the LES pressure. Even so, we observed that all the patients showed evidence of reflux in the post-cibal hour, as determined by continuous pH recording. These patients should be advised to have three regular meals and keep the acidity under check with antacids administered at appropriate times. The evening meal should be taken 2 hours before retiring.

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Bejar, J.,Goyal, R.K.: Gastroenterology 62:721, 1972

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ii) Type of food is also important. Greasy foods have been shown to reduce LES pressure. They should be avoided. Chocolate lovers may not like it, but chocolate lowers the LES pressure and aggravates symptoms of reflux. Spicy food and acidic juices are usually avoided by the patient himself. They may also impair LES pressure, as well as irritate the inflamed esophageal mucosa.

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Babka, J.C., Castell, D.O.: Amer. J. Dig. Dis. 18:391, 1973
Nebel, O.T., Castell, D.O.: Gastroenterology 63:778, 1972

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iii) Smoking: Smoking causes a marked reduction in LES pressure and predisposes to gastroesophageal, as well as duodenogastric reflux of bile. Smoking should be avoided altogether.

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Dennish, G.W., Castell, D.O.: NEJM 289:1136, 1971
Stancin, C., Bennett, J.R.: Brit. J. Med. 3:793, 1972

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iv) Alcohol: Ethanol ingestion may irritate the esophageal mucosa and may cause heartburn. In higher doses, it may impair the lower esophageal sphincter competence and predispose to reflux.

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Hogan, W.J., de Andrade, S.R.V., Winship, D.H.: J. Appl. Physiol. 32:755, 1972

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3) *Drugs to neutralize or reduce acid secretion:*

If the acid can be adequately neutralized, there will be no problem of peptic esophagitis. Neutralization of acid is done with the use of antacids, which form the cornerstone of therapy of esophagitis.

There have been recent advances in the control of gastric acidity, and these will be reviewed next week.

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Richardson, C.T.: PMH Grand Rounds (In preparation)

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*4a) Drugs to improve LES competence:*

i) Antacids: Antacids help to neutralize the gastric acid. At high pH, the pepsin is inactivated and acid-pepsin reflux in the esophagus may not produce heartburn. Costell and Levine have reported that antacids may also act to increase LES pressure and may, therefore, help to prevent reflux by this mechanism.

Castell, D.O., Levine, S.M.: Ann. Int. Med. 74:223, 1971

ii) Cholinergic agents: It has been shown that oral bethanechol (urecholine) causes an increase in the LES pressure which lasts over 120 minutes after a single dose of 25 mg. These authors used bethanechol to treat heartburn in a randomized double-blind crossover study. Bethanechol was used in the dose of 25 mg q.i.d. Antacid was used ad lib. They reported that bethanechol treatment produced symptomatic improvement in a larger percentage of the patients, and also reduced the antacid intake, as compared to placebo treatment. No objective evaluation of reflux was done. These authors, however, concluded: "Bethanechol may be a welcome addition in the therapy of refractory heartburn."

Farrell, R.L., Roling, G.T., Castell, D.O.: Amer. J. Dig. Dis 18:646, 1973
Farrell, R.L., Roling, G.T., Castell, D.O.: Gastroenterology 64:726, 1973 (Abstr.)

iii) Metoclopramide (Maxolon, Beecham Laboratories): This agent has received considerable attention outside of the United States, as an enhancer of gastrointestinal motility. It has been shown to cause an increase in the LES pressure when given intravenously, as well as when administered orally. It has been touted as an agent of great promise in the treatment of reflux esophagitis, but results of the clinical trial are not yet available. The mechanism of action of metoclopramide is not fully understood, but it is supposed to act by sensitizing the human gastrointestinal muscle to acetyl choline.

Heitmann, P., Mollu, N.: Scand. J. Gastro. 5:621, 1970
Dilawari, J.B., Misiewicz, J.J.: Gut 14:380, 1973
Stancin, C., Bennett, J.R.: Gut 14:275, 1973

iv) Prostaglandin $F_{2\alpha}$: It was shown that $PGF_{2\alpha}$ causes dose-dependent contraction of the LES in the opossum. Dilawari and colleagues have shown that this agent causes sustained contraction of the LES in man and have proposed its usefulness in patients with reflux esophagitis.

Rattan, S., Goyal, R.K.: Proc. Soc. Exp. Med. Biol. 141:573, 1972
Dilawari, J.B., Newaman, A., Poleo, J., Misiewicz, J.J.: Gut 14:822, 1973, (Abstr.)

*Comments:* Reviewers evaluation of the role of drugs which cause LES contraction in the therapy of reflux esophagitis:

All drugs which may cause LES contraction will be proposed as possible cures for reflux esophagitis, but only a few will survive the test of time.

Assuming that we have a suitable drug that may increase LES pressure, the limiting factor in the therapy will be the state of the muscle of the sphincter. Incompetent sphincters with muscle that is incapable of contracting cannot benefit by these agents. The problem is how do we sort out these patients? One way is the estimation of the basal sphincter pressure. There is evidence to suggest that contractile capability of a particular sphincter is related to the resting sphincter pressure. Therefore, I believe that these agents may have a very valuable role in selected patients with reflux esophagitis, who have relatively good LES pressure which is capable of responding to these agents.

*4b) Drugs that may impair LES competence:*

These drugs should be avoided if possible. These are β-adrenergic agonists, α-adrenergic blocking agents, muscle relaxants such as nitroglycerine, papavarine, nitrites, anticholinergic agents in large doses.

*5) Mechanical foam barrier:*

The floating antacid: It is thought that alginic acid and sodium bicarbonate react with each other in the presence of saliva in the oral cavity to form highly viscous solution of sodium alginate (pH 5-6), which may float on the surface of gastric contents as a thick layer or "raft". The alginic acid and sodium bicarbonate mixture is marketed as Gaviscon. The scientific data on the usefulness of this agent have been scanty. One report has recently appeared, however. Stancin and Bennet treated 3 randomized groups of 20 patients with gastroesophageal reflux with alginate plus antacid compound (Gaviscon), antacid alone or a placebo tablet. There was significant improvement in the per cent duration of low esophageal pH after Gaviscon, but not with placebo or antacid alone, but the duration of symptoms during the second test was improved by both Gaviscon, as well as the antacid. There was no significant improvement in the symptoms during the 2-week period of therapy.

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Stancin, C., Bennet, J.R.: Lancet 1:109, 1974
Amdrup, E., Jakobsen, B.M.: Acta Chir Scand. 396:16, 1969

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*Comments:* Such agents may, in fact, be very valuable, but further studies are required to demonstrate their usefulness.

## (B) SURGICAL TREATMENT

The surgical treatment of reflux has followed three paths:

1) Measures to correct anatomic hernia

2) Measures to reduce acid secretion

3) Reconstruction of the cardia to make an antireflux barrier

1) Anatomic correction of hernia: In the past, the surgical repair for "symptomatic hiatus hernia" consisted in anatomic reduction of herniated gastric pouch, approximation of diaphragmatic crus with or without plication of the herniated sac. Allison's technique is an example of this approach. Such operations are associated with a recurrence of symptoms of reflux in 17-42% of patients after surgery. Such procedures have no place in current surgical therapy of reflux.

*TABLE III*

*Results of Allison Procedure for Esophageal Hiatal Hernia*

| Author | Recurrence | |
|---|---|---|
| | Clinical | Radiological |
| Allison | — | 6% |
| Brintnall et al | 42% | 48% |
| Borgeskov et al | 40% | 34% |
| Edwards et al | 20% | 62% |
| Raphael et al | 14% | 25% |
| Pearson et al | 17% | 60% |

Allison, P.R.: Surg. Gynec. Obstet. 92:419, 1961
Brintnall, E.S., Blome, R.A., Tidrick, T. R.: Am. J. Surg. 101:159, 1961
Borgeskov, S., Pedersen, O.T., Frederiksen, T.: Thorax 19: 327, 1964
Edwards, D.A.W., Phillips, S.F., Rowlands, E.N.: Brit. Med. J. 2:714, 1964
Raphael, H.A., Ellis, F.H., Jr., Carlson, H.C., et al.: Arch. Surg. 91:228, 1965
Pearson, J.B., Gray, J.G.: Brit. J. Surg. 54:530, 1967
Berman, E.J., Berman, J.K.: Arch. Surg. 89:179

2) Anatomic reduction of hernia plus a "duodenal ulcer operation": In the late fifties and sixties, several surgeons combined vagotomy and pyloroplasty or a partial gastrectomy with a Billroth I or II anastomosis - an operation designed to reduce gastric acidity - with the anatomic repair of hernia in order to reduce the incidence of "failures". This approach was based on the assumption that severity of esophagitis correlates with the degree of gastric acidity. However, it has been shown that 1) severity of esophagitis does not correlate with the patient's level of gastric acidity, 2) incidence of reflux is not increased in patients with duodenal ulcer, 3) vagotomy, as well as anterectomy, may impair the competence of the LES, and 4) destruction of pyloric sphincter mechanisms may lead to alkaline reflux, which may lead to severe esophagitis. Because of these considerations and also those of adding complications of "ulcer-type surgery", it is unwise to combine "duodenal ulcer-type operation" in the treatment of reflux esophagitis.

Herrington, J.L.: Arch. Surg. 84:1962
Tanner, N.C.: Am. J. Surg. 115:449, 1968
Pearson, F.G., Stone, R.M., Parrish, R.M., et al.: Am. J. Surg. 117:130, 1969
Abernethy, R.J.: Brit. J. Surg. 54:859, 1967
Silber, W.: Gut 10:614, 1969
Squire, B.H., Glick, S., Benn, A.: Thorax 23:683, 1968
Gillison, E.W., Capper, W.M., Airth, G.R.: Gut 10:609 1969
Southam, J.A.: Brit. J. Surg. 56:671, 1969

3) Reconstructive surgery of cardia. These operations aim at: a) creation of esophagogastric flap valve mechanism, b) exaggerated abdominal esophagus, and c) approximation of the diaphragmatic crus. The main operations of this type are:

i) Nisson fundoplication

ii) Hill repair

iii) Belsey Mark IV

i) Nisson's fundoplication: Consists of wrapping the fundus of the stomach around the distal end of the esophagus, so that the esophagus is completely surrounded by a tunnel of gastric fundus. Generally, transabdominal route is used; however, if indicated, thoracic route may be used.

Nissen, R., Rossetti, M.: Coll. Surg. 43:663, 1965
Ellis, F.H., Jr.: Surg. Clin. N. Am. 51:575, 1971
Bombeck, C.T., Aoki, T., Nyhus, L.: Ann. Surg. 165:1967
Moran, J.M., Pihl, C.O., Norton, R.A., et al.: Am. J. Surg. 121:403, 1971
Polk, H.C., Jr., Zeppa, R.: Ann. Thorac. Surg. 7:202, 1969
Menguy, R.: Surg. Clin. N. Am. 50:45, 1970

ii) The Hill repair: This consists in suturing the phrenoesophageal membrane to median arcuate ligament of aortic hiatus. This posterior gastropexy helps to plicate the lesser curve of the stomach around the distal esophagus so as to create a valve-like mechanism.

Hill, L.D.: Arch. Surg. 102:296, 1971
Hill, L.D.: Ann. Surg. 166:681, 1967
Hill, L.D., Chapman, K.W., Morgan, E.H.: J. Thorac. Cardiovas. Surg. 41:60, 1974

iii) The Belsey Mark IV: Through a left thoracotomy incision, the fundus of the stomach is brought up through the esophageal hiatus, and the fundus is wrapped around the antero-left lateral two-thirds of the distal esophagus.

Baue, A.E., and Belsey, R.H.R.: Surgery 62:396, 1967
Hiebert, C., Belsey, R.: J. Thorac. Cardio. Surg. 42: 352, 1961

Effectiveness of these repairs:

"A defect common to many reports dealing with surgical correction of hiatal hernia is an inadequate or lack of objective preoperative and postoperative evaluation of reflux and severity of esophagitis causing the patient's symptoms." Subjective patient satisfaction suggests that these procedures all achieve over 90% patient satisfaction. Hill reports recurrence of symptoms and reflux in only 3.3% of the patients treated by him.

Studies which objectively evaluate the efficacy of operative repair in a prospective fashion have started to appear. Bejar and colleagues reported a prospective study in 22 patients with advanced esophagitis. They found that at the end of one year, 11/12 medically treated patients had reflux, whereas only 2/10 patients treated by fundoplication had evidence of reflux. The patient showing improvement,showed about 100% increase in pressure after surgery, but the response of the sphincter pressure was not increased by abdominal compression. Pope studied 40 patients with reflux esophagus who were treated with 3 different techniques of repair. Their findings, after a followup of 3-6 months, are summarized in the following table:

*TABLE IV*

| Technique | No. Cases | LES Pressure | | Reflux | Improvement in Histology |
|---|---|---|---|---|---|
| | | Preop | Postop (3-6 Months) | | |
| Allison | (6) | 10.2 ± 3 | 12.2 ± 3.9 | 3/6 | 2/5 |
| Hill | (9) | 6.7 ± 1.5 | 13.2 ± 2 | 4/9 | 5/7 |
| Fundoplication | (25) | 7.3 ± 1.2 | 14.8 ± 1.8 | 7/25 | 11/13 |

[After Pope et al.]

*Comments:* On surgical treatment of reflux esophagitis: At the present time, there is no good evidence to suggest that these operations prevent complications of esophagitis. I think a rational approach should include consideration of construction surgery on cardia in patients who i) have totally incompetent sphincters, ii) the sphincters fail to respond adequately to stimulants, iii) reflux cannot be controlled by conservative treatment, iv) patient has gross esophagitis (endoscopic) or has incompetent upper sphincter and has unequivocal symptoms of pulmonary aspiration.

Bejar, J., Biancani, P., Spiro, H.M., et al.: Gastroenterology 64:695, 1973 (Abstr.)
Pope, C.E., Eastwood, C.F., Eastwood, I.R.: Clin. Res. 31:208, 1973

## (C) TREATMENT OF COMPLICATED ESOPHAGITIS

1) Stricture: These patients usually have a very incompetent LES, either primarily or due to the stricture. These strictures should be dilated by bougies, and these may require repeated dilations to keep them open (Benedict, 1966). The reflux should be treated with antacids initially. However, if they do not readily respond, they should have reconstruction surgery of the cardia and dilation of the stricture at the time of surgery. In some cases, Thal's procedure may be useful.

2) Barrett's ulcer and midesophageal strictures: As these lesions probably result because of a marked impairment of the mucosal defense, it would be rational to do all one can to completely neutralize the refluxing agents. These should be treated by reconstruction of the cardia to prevent any reflux, and if there are parietal cells lining the mucosa, additional antacid therapy should be continued. Irradiation to the esophagus to inhibit parietal cells may be useful in selected cases. The stricture is treated by dilation with bougies.

Benedict, E.B.: Surg. Gynec. Obstet. 122:613, 1966; Amer. J. Dig. Dis. 11:761, 1966
Thal, A.P.: Ann. Surg. 168:542, 1968
Polk, H.C., Jr., Zeppa, R.: Ann. Thorac. Surg. 7:202, 1969
Hill, L.D., Gelfand, M., Bauermeister, D.: Ann. Surg. 172:638, 1970