GASTROESOPHAGEAL PH AND PRESSURE STUDIES

by

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A McGill University thesis submitted in partial fulfilment of the requirements for the degree of Master of Science in Surgery.

August, 1963.

To Colleen

PREFACE

The clinical and experimental investigations described in this thesis were carried out in the Experimental Surgical Laboratories of the Royal Victoria Hospital and McGill University. These studies were carried out from July 1, 1961, to July 1, 1962. The finding of both a long and short duration of esophageal acidity following gastroesophageal reflux was an original contribution and this was reported at the Forum on Fundamental Surgical Problems during the Forty-eighth Annual Clinical Congress of the American College of Surgeons in Atlantic City in October, 1962#.

A description of the multiphased esophageal pH test for the detection of gastroesophageal reflux and a comparison of the results of this test with other objective means of demonstrating reflux is currently being abstracted from this thesis for submission for publication in the surgical literature.

I wish to express my most sincere gratitude to Dr. James R. McCorriston. His interest in the hiatus hernia problem initiated this study. His constant availability, cooperation in providing clinical material, and willing and able support

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Piccone, V. A. and McCorriston, J. R.
Surgical Forum 13: 252, 1962.

in acquiring good equipment were an invaluable aid during the actual work. Beyond the project itself, I found his uncompromising search for technical excellence in surgery to be an inspiration to the aspiring young surgeon.

Dr. Donald Webster gave his permission and active support to the project. Dr. D. D. Munro provided subjects for the pre- and post-operative evaluation of the Allison type repair. Dr. John Gutelius provided critical appraisal of instrumentation and was helpful in developing the objectives of a multiphased esophageal pH test. My fellow research assistants, Dr. G. Gentile, Dr. H. Sangiovanni and Dr. H. Shibata, provided helpful, critical appraisal of the work.

Mr. J. Fraser was responsible for the photographs. I am indebted to Mrs. Jean Earley for her assistance in testing patients, the preparation of the Atlantic City abstract, and her assistance in the procurement of material and supplies. Graduate Nurses, Miss Beverly White, Miss Ann Read and Miss Felicity Noble and several of the student nurses are thanked for their help with the management of patients.

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A. FACTORS NORMALLY RESPONSIBLE FOR THE PREVENTION OF GASTROESOPHAGEAL REFLUX

Reflux of acid gastric secretions into the esophagus is an infrequent event in most people, but if this occurs frequently it will often result in esophagitis. Since pressure in the abdomen exceeds intrathoracic pressure, it would seem that, with a patient in the supine position, there should be a flow of gastric secretions into the lower esophagus. However, this does not normally happen and intra-abdominal pressures of up to 60 centimeters of water will be tolerated without the occurrence of gastroesophageal reflux.

Gastroesophageal reflux is often associated with hiatus hernia. It is generally assumed, then, that one or more factors normally maintain an effective barrier to reflux and that, with a sliding hiatus hernia, one or more of these factors is sufficiently impaired to allow reflux and the consequent development of esophagitis.

Considerable effort has been expended in an attempt to elucidate the factors responsible for the prevention of gastroesophageal reflux. Several main theories have been evolved, each of which seems conclusive against the background of its own experimental situation. Chevalier Jackson (78), in 1922, observed

the reflux-inhibiting action of the diaphragm through an endoscope, and Allison (65) made use of this "pinchcock" theory in his well-known repair of hiatus hernias. Von Gubaroff, in 1886, and later Marchand (62), Dick (63), Hurst (63), Dornhorst (61) and Barrett (59, 60) have all supported the concept of a flap-valve mechanism at the cardia. Schlegel, Code and Ellis (23) vigorously applied manometric techniques and showed evidence for an effective physiological sphincter in the lower esophagus. Creamer et al. (56) and Edwards (100) described a theoretical mechanism which depends on the behaviour of a flaccid tube passing from a compartment of higher pressure to a compartment of lower pressure. The evidence for each of these main theories of reflux prevention and the factors on which they depend will be discussed.

I Evidence for (1) the Existence of a Lower Esophageal Sphincter and (2) the Role of this Sphincter in the Prevention of Gastroesophageal Reflux

(a) Anatomic Studies:- Willis (1), in 1674, produced diagrams depicting thickened circular muscle in the esophagus just above the esophagogastric junction. Helvetius (2), in 1719, and Baillie (3), in 1807, described a sphincter in the lower esophagus. Laimer (4) and later Mosher (5) and Nauta (6) provided supportive data. Garlock (7) described a cardiac sphincter in the stomach, at the point of union with the esophagus, as being composed of thickened gastric mucosa and musculature but gave no further details. Lerche (8), in 1950, described a lower esophageal sphincter and a constrictor cardiae, situated at the upper and lower ends of the narrow vestibule separating stomach from esophagus. Lerche's studies were based on an extensive examination of considerable material. Lendrum (9), however, was unable to demonstrate a single sphincter after histological examination of 150 cardioesophageal junctions in individuals of all age groups. Hollinshead (10) states that there is no morphological gastroesophageal sphincter. Indeed, the concensus today is that the overall evidence from anatomic and histologic studies in human subjects does not support the concept of a gastroesophageal sphincter in terms of the usual criteria; i.e., there is no obvious

thickening of any muscular layer.

In some animals, such as, the bat, there is definite evidence of an anatomic sphincter. The bat, which hangs in an inverted position, has a gastroesophageal sphincter with musculature five times thicker than that in its stomach.

(b) Experimental and Clinical Surgery:- Merendino, Hoag and Kiriluk (12, 13, 14), in 1954, performed proximal subtotal gastrectomies in a series of dogs. The terminal esophagus and immediately adjacent cardia were preserved, but other factors generally considered responsible for the prevention of gastroesophageal reflux were all altered. In a second series the esophagogastric junction was also ablated. The two series were compared for the development of esophagitis. Proximal gastrectomy including resection of the junctional zone of esophagus resulted in a very high incidence of esophagitis. In the series with a preserved junction there was no esophagitis, even after histamine stimulation for 45 days. In both series the angle at which the esophagus entered the stomach was greatly altered by excision of the fundic area; any influence a fundic air bubble might contribute was removed, and the oblique muscle fibers, extending from the lesser curvature of the stomach around the esophagus and back, were ablated. Only the presence or absence of the terminal esophagus and immediately adjacent gastric area significantly determined the later development of esophagitis.

Ingram, Respess and Muller (15), and also Friesen and Miller (16), transected canine esophagi three centimeters above the diaphragm, closed the distal segment of the esophagus, withdrawing it into the abdomen, and then anastomosed the proximal segment to the stomach through the hiatal canal. Esophagitis developed above the anastomosis routinely. The pinchcock action of the diaphragm, higher intra-abdominal pressure on that portion of esophagus and other factors still remaining and usually considered important did not prevent reflux. After reconstruction of the original situation, the esophagitis disappeared.

Braasch and Ellis (17) repeated esophagogastrectomy (70% resection of stomach), placing the anastomosis above the diaphragm in some cases and below it in others. Resection of the junctional zone of esophagus resulted in esophagitis whether the anastomosis was above or below the diaphragm, again indicating the importance of the terminal esophagus in the reflux barrier mechanism.

While the studies of Merendino et al., Ingram and Muller, and Braasch and Ellis each implicate an indispensible factor inherent in the terminal esophagus, they do not define the specific properties of the junctional zone which are responsible. The relative roles of the intrinsic sphincter and mucosal folds are not apparent.

Further studies by Braasch and Ellis (17) involved use of

the Heller and Wendel procedures in dogs. Esophagocardiomyotomy or esophagocardioplasty resulted in barium reflux and esophagitis almost routinely. Similar results were recorded by Wangensteen, Brackney, Kelly and Campbell (18) in 1953 when comparing the results of Heller with those of Wendel procedures in dogs. A comparable situation exists in humans on whom Heller procedures were performed for achalasia. Hawthorne and Nemir (19) found 50% of their patients had radiologically demonstrated reflux and 16% had symptoms of reflux esophagitis. The evidence in this last group of studies specifically implicates the muscular layers of the terminal esophagus as being very important components of the reflux barrier.

(c) Manometry:- The use of direct pressure determinations in the esophagus has provided considerable information concerning the role of the lower esophageal sphincter. Pressure recording techniques were used in the esophagus as early as 1883 (Kronecker and Meltzer (20). In 1927, Payne and Poulton (21) suggested that the lower esophagus possesses a sphincteric mechanism. In 1937, Zeller, Werner and Burget (22) showed a cardiac sphincter in dogs, but were mainly concerned with its response to the act of deglutition rather than its serving as a barrier to gastroesophageal reflux. However, these various studies represented scattered events and manometric techniques were not used

intensively until the past decade.

Fyke, Code and Schlegel (23), in 1956, demonstrated a zone of high intraluminal pressure which they interpreted as confirmation of the existence of a physiological sphincter between the stomach and esophagus. Schlegel and Code also found this zone in dogs (24). The finding of a physiological sphincter in the terminal esophagus of human beings with manometric methods was confirmed by Botha, Astley and Carre (25), and by Atkinson, Edwards, Honour and Rowlands (26). Botha et al. (25) also showed, with radiopaque clips at the anterior border of the hiatus, that the point of maximal pressure was above the hiatus in four out of six subjects. Atkinson's group (26), in addition to confirming the findings of Fyke et al., also compared the pressures in this area with those of the pylorus, which has an anatomically recognizable sphincter, and were unable to find manometric evidence of sphincter function in the latter. Dornhorst and associates (27) added to the lack of unanimity concerning the interpretation of the high pressure zone in 1954. They found the high pressure zone to be localized to less than 5 millimeters of esophagus and felt that the cardia acted differently from known muscle sphincters.

However, much additional work on the high pressure zone was done. Fyke's group (23) had shown that the pressure in this "sphincter" is higher than in the stomach and considerably higher than in the rest of the esophagus. The resting pressure, recorded

with open-tipped catheters, is usually below 40 centimeters of water. Fyke, Code and Schlegel also regularly found a fall in pressure, 1.5 to 2.5 seconds after deglutition and, as the peristaltic wave swept through this level, that the pressure returned to its former elevated level, proceeding smoothly into a prolonged period of elevated pressure. Creamer, Olsen and Code (28), in 1957, using esophageal motility studies, demonstrated that the intraluminal pressure in the sphincteric region was normal in patients with achalasia. However, the decrease in pressure in this region that occurs normally with swallowing was absent and the increased pressure, normally the final component in the deglutitive reflex, occurred earlier than in normal subjects. Others (29) have also shown that the peristaltic wave is not transmitted to the sphincteric area in achalasia. Sanchez, Kramer and Ingelfinger (30), in 1953, concluded from esophageal motility studies that the differences between swallowing patterns in the vestibule (which corresponds to the high pressure zone) and the remainder of the esophagus suggests an independent motor function for the vestibule, even though it is integrated into the overall swallowing mechanism.

The fact that higher pressure in the sphincteric region is not caused by external compression of the esophagus by the diaphragm has been shown by the studies of Atkinson (31, 32, 33, 34). In 1957, this author demonstrated that the high pressure zone can still be detected in patients with hiatus hernia, but that in these

cases it is located at variable distances above the diaphragm depending on the extent of herniation (31). In 1959, Atkinson showed the zone still to be present in patients with diaphragmatic paralysis (32). In addition, it was absent following cardiomyotomy in cases where it had been present before the procedure (33, 34). Botha et al. (25), as noted above, had also shown that the zone of maximal pressure was actually above the diaphragm. These findings could not be expected if the high pressure zone was caused by extrinsic pressure on the esophagus from the diaphragm.

The high pressure zone is not always evident on passage of a single open-ended catheter through the lower esophagus but, on repeated passages with a single catheter or multiple determinations in a single passage by use of staged catheters, it may be evident (35). Because of increased tone in the area, a volume of fluid sufficient to displace the transducer may not be present. This explanation is supported by the fact that small balloons, which contain a readily displaceable volume of fluid, are more reliable for detecting the gastroesophageal junction. However, the higher pressures from balloons may be secondary to distension of the esophagus, triggering increased muscle tone or a secondary peristaltic wave (35).

The high pressure zone has also been studied in various conditions associated with gastroesophageal reflux. Besides hiatus

hernia, it has been the subject of investigation in progressive systemic sclerosis (scleroderma) in normal infants and in pregnancy. Creamer, Andersen and Code (36), in 1956, demonstrated with manometric techniques that the sphincter loses its tone in scleroderma. Carre and Astley (37), in 1958, found normal sphincteric pressures in patients with gastroesophageal reflux in infancy. Gastroesophageal reflux has been reported to occur in 50% of patients after a Heller procedure (19). Atkinson et al. (33, 34) found the pressure in the sphincteric zone to be greatly decreased after cardiomyotomy but Olsen, Schlegel, Creamer and Ellis (38) found the subhiatal portion of the sphincter to be preserved after cardiomyotomy. The latter authors believed this finding to be important in preventing reflux and recommended an effort to preserve the lower part of the sphincteric area.

Code, Schlegel, Kelly, Olsen and Ellis (39), in 1960, showed resting pressures exceeding 40 centimeters of water (open-tipped catheters) in 4% of 514 patients. They did not ascribe clinical significance to the "hypertensive sphincter". However, long esophagomyotomy for diffuse spasm of the esophagus was performed in 1959 (40).

The manometric studies demonstrating the nature of the lower esophageal sphincter are not free of enigmas. The time

between initiation of swallowing and relaxation of the high pressure zone is 3.7 seconds when measured by balloons and 2.8 seconds when open-tipped catheters are used (41).

However, there is little doubt about the actual presence of a zone of high intraluminal pressure in the lower esophagus and this, most probably, does represent a sphincter mechanism. Hill (42, 43) regards this as the single, most important factor in the maintenance of a physiological barrier to gastroesophageal reflux. Further, Hill states that the presence of acid gastric secretions in the terminal esophagus sets up reflex swallowing movements until the resultant peristaltic waves clear the area of acid.

Others (44), using combined manometric and cineradiographic studies, have redefined sliding hiatus hernia according to the location of the high pressure zone. The herniated loculus of stomach below the high pressure zone does not transmit peristaltic waves manometrically, and does not empty radiologically, as does an esophageal ampulla.

(d) Pharmacology:- In normal human beings, anticholinergic drugs lower the pressure at the gastroesophageal junction and cholinergic drugs cause increased pressure. Using directly determined esophageal pH changes as an indicator of acid reflux, Bettarello, Tuttle and Grossman also found reflux was more easily induced after anticholinergic drugs were administered (45). This

direct relationship between sphincter pressure and ease of reflux was felt to demonstrate the important role of the gastroesophageal sphincter in the reflux barrier mechanism.

Comparison of muscle strips from the lower esophagus and the junctional zone was made on the basis of the response to pharmacological and electrical stimuli. In immature cats, Schenk and Frederickson (46) found acetylcholine produced constriction of the longitudinal muscle and relaxation of the circular muscle from the gastroesophageal junction, whereas it produced contraction of both longitudinal and circular elements in segments from other parts of the esophagus. The acetylcholine action on the longitudinal muscle of the gastroesophageal junction was much less than its effect on the longitudinal muscle from above this zone. However, Ellis, Kauntze and Trounce (47) found that isolated circular human esophageal muscle from the gastroesophageal junction contracted in the presence of acetylcholine and that this response was blocked by atropine. However, nerve stimulation to the circular muscle strip caused a relaxation which was achieved through adrenergic receptors. They concluded that the circular muscle in the junctional zone had a distinct pattern of innervation.

The results from pharmacologic studies are far from uniform and are often at variance with nerve-section experiments. Ingelfinger (48) noted that pharmacologic tests on isolated muscle

may give no indication of tonic mechanisms that may exist in life.

(e) Nerve Section and Stimulation:- Neurologic control of the intrinsic sphincter of the lower esophagus has been investigated by both stimulation and section of nerves with study of the results by x-ray or manometric techniques. Kronecker and Meltzer (20), and Long, Nice, Thal and Truex (49) produced cardiospasm in dogs using a high cervical vagotomy. There was a narrowing in the esophagus at the gastroesophageal junction on x-ray examination. Hwang (50) et al. reported results which were entirely opposite, with complete paralysis of the lower esophagus after high cervical vagotomy in dogs. Ellis, Kauntze and Trounce (47) observed three patients with a high unilateral thoracic vagotomy, performed during pneumonectomy, which showed a picture radiologically indistinguishable from achalasia. Cannon (51), as early as 1911, concluded that the cardia is autonomous, being regulated by an intrinsic neuromuscular mechanism. Zeller and Burget (22), in 1937, studied the lower esophagus in unanesthetized dogs after bilateral cervical vagotomy. They found a failure of the cardia to relax in response to deglutition but this response returned to normal after the initial post-operative period.

Carveth, Schlegel, Code and Ellis (52), in 1962, studied esophageal motility in trained, unanesthetized dogs following

vagotomy of various types, phrenicotomy, myotomy and myomyectomy. After cervical vagotomy, the resting tone of the lower esophageal sphincter was markedly reduced and neither relaxation nor contraction of the gastroesophageal sphincter with deglutition was detected. Hilar vagotomy resulted in less impaired function. Neither resection of esophageal branches of the vagus nerve nor phrenicotomy changed the resting pressure or deglutitive responses of the gastroesophageal sphincter. Muscle-interrupting procedures similarly did not affect the gastroesophageal sphincter tone.

(f) Radiology:- The intrinsic sphincter is most readily seen radiologically in patients with a sliding hiatus hernia. The sphincter is herniated above the level of the diaphragmatic crura so that any narrowing noted on fluoroscopy is then clearly sphincteric and not to be confused with the pinchcock action of the diaphragm. The sphincter in the intrathoracic position is then seen to open well before the arrival of the peristaltic wave during deglutition. The sphincter closes again after the barium passes. It squeezes the barium out of its lumen, thus becoming radiolucent in contrast with the esophagus above and the herniated pouch of stomach below. The intrinsic esophageal sphincter has been demonstrated in this manner by Johnstone (53, 54) and also reported by Edwards (44) in 1961. Creamer and Pierce (55),

in 1957, correlated manometric and radiologic studies to investigate the radiological appearance of the manometrically determined sphincteric area. They found that the point of holdup of barium in the lower gullet coincides with the point at which respiratory pressure swings change from an abdominal to an intrathoracic type, rather than the upper end of the sphincteric area (which extends above the pressure pattern change area). They felt that the tonic contraction of the intrathoracic sphincteric area was easily overcome and formed no resistance to downward passage of barium. Creamer, Harrison and Pierce (56), in 1958, placed radio-opaque markers on the edges of the esophageal hiatus and found that the change in pressure patterns from abdominal to thoracic type occurred at the level of the hiatus. They further showed an abdominal segment of esophagus about 2 to 3 centimeters in length. Creamer postulated his anti-reflux mechanism on this finding of an intra-abdominal portion of esophagus.

(g) Endoscopy:- On endoscopy, in the normal individual, the intrathoracic esophagus shows a pale pinkish mucosa. The lumen dilates with inspiration and becomes smaller with expiration. However, at 38 to 40 centimeters from the upper incisor teeth there is a spastic area, and the rosette does not open on inspiration and is not influenced by respiratory movements. Slight stimulation of the terminal esophagus will cause the closed terminal esophagus

to open promptly. The pale pink mucosa continues for 1 or 2 more centimeters before gastric rugae are encountered, indicating that the zone of increased tone is in the esophagus.

In summary, on the basis of experimental surgical procedures as well as manometric, cineradiographic, pharmacologic and endoscopic studies, there is evidence of a lower esophageal sphincter which is an important factor in the prevention of gastroesophageal reflux.

Further consideration shows that the intraluminal pressure in the subdiaphragmatic portion of the sphincteric region is equal to the sum of the intra-abdominal (extrinsic) pressure plus the pressure exerted by the sphincter itself (intrinsic). If the intra-abdominal pressure is ⁄10 centimeters of water and the sphincter tone is ⁄10 centimeters of water, then the total intraluminal pressure in this portion of the sphincteric area is 20 centimeters of water. The intragastric pressure must reach this level before reflux can occur.

II The Flap Valve Mechanism in the Prevention of Gastroesophageal Reflux

Barrett (59, 60), Dornhorst (61) and Marchand (62) separately concluded that the main barrier to gastroesophageal reflux is a flap valve mechanism formed by the mucous membrane at the exact junction of stomach and esophagus. The flap is of two layers, consisting of the left side of the esophagus and the adjacent part of the fundus. Barrett (59, 60) stated that the efficacy of the valve "depends on the normality of the muscularis mucosa which moves the mucous membrane and causes it topout into the orifice." Dick and Hurst (63) contend that the obliquity of the cardia causes a valvular effect which contributes to the efficiency of the region in the prevention of reflux.

Barrett (59, 60) used various forms of evidence to support the flap valve theory. He cited Allison's finding that the reflux barrier was intact in stomach-esophagus preparations removed from cadavers. Water, pumped into the pyloric end of the stomach, was held up at the cardia if the normal gastroesophageal angle was preserved but not if the parts were laid out like a bell with the esophagus as a handle. Marchand (62) showed that the pressure necessary to overcome the reflux barrier and drive fluid from the stomach into the esophagus was reduced from 28 centimeters of water to 3 centimeters

of water by decreasing the acuteness of the gastroesophageal angle. Further, removing the left leaf of the diaphragm and allowing the fundus to move upward into the thorax, thus increasing the acuteness of the angle, caused the escape pressure to reach 42 centimeters of water. Making the gastroesophageal angle temporarily obtuse in patients undergoing various abdominal operations showed the same effect on escape pressures as was demonstrated in the cadaver studies (66). Others (67), however, were unable to confirm the results of Marchand and found only 5 centimeters of water were needed to produce reflux in cadavers.

Marchand (62) also demonstrated that a clamp placed across the stomach from the left lip of the gastroesophageal junction to the greater curvature of the stomach greatly lowered the resistance to reflux in cadavers and interpreted this as supportive evidence for the importance of the angle in the prevention of reflux. Barrett (68) cites the discovery of Savage that the esophagogastric junction is incompetent after resection of the fundus.

Barrett (59, 60) further postulated that the oblique muscle fibers of the stomach, which run up the posterior surface of the stomach, over the cardiac incisura and back down over the anterior surface of the stomach, probably control the flap valve. These fibers form a sling around the cardia and contraction causes the flap valve to be approximated to the right side of the esophagus

thus covering the orifice and preventing reflux. It is difficult to understand how a mechanism dependent on a muscular action can continue to function in the cadaver as demonstrated in Marchand's work (62).

The importance of the acuteness of the gastroesophageal angle in the prevention of reflux is difficult to deny. The manner in which it achieves its protective role is less clear. Botha (69) placed a radio-opaque clip on the anterior edge of the hiatal opening and showed that there is a disproportionate descent of the diaphragm and the clip during inspiration. The gastroesophageal angle is made more obtuse and it is at this time that reflux may occur. The fact that the anatomical angle itself may mean little is shown by Marchand's (62) clamp across the fundus. In this experiment the anatomical angle is still present. That which has been changed is the functional separation of the fundic cavity from that of the remaining stomach. Gastric pressure dynamics are changed so that increased pressure is not transmitted to the fundic area. An explanation such as McCorriston's (70) therefore seems plausible. Further support for this concept may be interpreted from the results of O'Mullane, 1954, (74) who showed that the cardia is not made incompetent by total somatic paralysis under anaesthesia.

The important role of the gastroesophageal angle in the prevention of reflux cannot be discussed without mention of the

factors purported to be responsible for the maintenance of this angle. Allison (65) states that the Right crus of the diaphragm forms a loop about the terminal esophagus, pulling it downward and to the right and thus maintaining the acute gastroesophageal angle. He likens it to the puborectalis muscle looping around the rectum and creating a ninety-degree angle with the anal canal. Since the right crus takes origin from the bodies of the lumbar vertebrae, it is apparent that the gastroesophageal angle is maintained. by a well-anchored sling. Allison also credits the phrenoesophageal ligament with considerable importance in maintaining the gastroesophageal angle. The phrenoesophageal ligament consists of a reflection of the deep fascia on the undersurface of the diaphragm up through the hiatus to become continuous with the fascia propria of the esophagus. Allison states that the pull of the diaphragm on the esophagus in inspiration is more evenly distributed over that organ instead of being concentrated only at the cardia. The phrenoesophageal ligament then firmly holds the terminal esophagus down and the fundus is allowed to float freely upward under the concavity of the left hemi-diaphragm, thus maintaining an acute gastroesophageal angle. While Harrington's (72) opinion is similar to that of Allison, Barrett (59, 60) describes the phrenoesophageal ligaments as "strands of tissue which can be dissected out with the eye of faith" and feels that they can be

ignored in the repair of a sliding hiatus hernia.

A third factor credited with maintaining the acuteness of the gastroesophageal angle, or angle of Hiss, is the oblique sling of muscle fibers immediately beneath the muscularis mucosa of the stomach wall. These, as first described by Willis, form a sling running up along the lesser curvature of the stomach, over the incisura of the stomach and down the posterior side. Barrett (59, 60) believes these fibers contract and pout the mucous membrane of the flap valve over the cardiac orifice. The reported loss of the gastroesophageal angle after death and the ease of reflux in cadavers reported by Atkinson and Sumerling (73) both suggest a dynamic mechanism that maintains the acuteness of the gastroesophageal angle and is a responsible factor in the prevention of reflux.

Smiddy and Atkinson (74) found that careful division of the oblique gastric muscle near the gastroesophageal angle in dogs markedly reduced the resistance of the barrier mechanism to reflux and that cardiomyotomy and section of the crural fibers did not change the yield pressure.

Other factors in the maintenance of an acute angle are the dome of the left hemi-diaphragm and the liver tunnel. The concavity of the left hemi-diaphragm allows the fundus to rise into it. After phrenic nerve section, there is no reflux such

as would be expected if the diaphragm exerted an anti-reflux action; instead, the dome of the diaphragm is raised, the gastroesophageal angle is more acute, and reflux does not occur (89). The liver tunnel prevents the displacement of the stomach to the right and this, too, may prevent the fundus from dropping. However, if the esophagus is transposed to a more forward position so that it passes through the tendinous portion of the diaphragm, away from the liver tunnel, reflux is still prevented and the gastroesophageal angle is still maintained.

III The Role of the Flaccid Intra-Abdominal Esophagus in the Prevention of Gastroesophageal Reflux

Creamer, Harrison and Pierce (56), in 1959, demonstrated an intra-abdominal segment of esophagus using radio-opaque clips on the hiatal margin and barium to outline the esophagus. Cine-radiographic studies demonstrated that the markers were well above the opening of the esophagus into the stomach. Barium flowing downward was held up at the point in the esophagus where the pressure changed from intrathoracic to intra-abdominal levels (55, 56). When barium was held up in this way, the esophagus below this point (intra-abdominal esophagus) emptied, thus distinguishing this part of the esophagus from that in the thorax (56). The point at which barium passage was delayed and where manometric

studies showed a change from intrathoracic to intra-abdominal pressure swings was termed the "pressure barrier". The sphincteric zone extended both above and below this point and had no radiological counterpart (55, 56).

Having established the existence of an intra-abdominal segment of esophagus, Creamer then postulated an anti-reflux mechanism based on the behavior of a flaccid tube which passed sharply from a compartment of high pressure to one of low pressure (56).

The pressure difference creates a force which tends to evert and expel the tube into the low pressure compartment and to compress the sides of the tube together with the everting tendency. The greater the difference in pressure between the abdomen and thorax, the more firmly the tube is held closed. The intra-abdominal esophagus is prevented from being extruded into the chest by the phrenoesophageal ligament. Creamer et al. found the opening and closing of the intra-abdominal gullet was almost always associated with a change in the relative pressures of the stomach and esophagus. Opening occurred when intra-esophageal pressure increased to a level greater than that in the stomach or when the intragastric pressure exceeded the difference between the intra-abdominal and intrathoracic pressures. The pressure gradient for opening or closing the abdominal gullet was usually the same in all parts of any one experiment. Increased intra-abdominal pressure is also transmitted to the gastric lumen so that the net

effect of increased abdominal pressure is to increase the barrier to reflux. Only increased gastric pressure can decrease the resistance to reflux (56).

Creamer further postulated that the sphincteric zone is not detected radiologically above the diaphragmatic hiatus because the sphincter tone is overcome by negative intrathoracic pressure. Below the diaphragm the sphincter tone augments the effect of thoraco-abdominal pressure differences on the flaccid tube (56).

The function of the sphincteric zone was felt to be the conversion of the wide funnel-shaped intra-abdominal esophagus into a narrow tube which could act as the flaccid tube passing through compartments of varying pressure. In addition, the sphincter would produce mucosal folds which would plug the cardiac orifice and add to the resistance of the reflux barrier (56).

Critical review of this theory must include several considerations. First, it does not include any of the well-documented observations about the gastroesophageal angle. Also, it seems doubtful that rolling to one side should change intragastric pressure, yet it often produces reflux. Thirdly, the sphincter alone seems to explain many of the facts on which the flaccid tube theory is constructed. Very simply stated, the subhiatal sphincter intraluminal pressure is over 50 percent greater than in the area above the hiatus. Therefore, there is a holdup in barium at the

hiatus. In addition, the intragastric pressure must rise to at least that of the intra-abdominal portion of sphincter before reflux can occur. Only to explain reflux which occurs at pressures higher than this need the concept of a flaccid tube be considered.

IV The Pinchcock Action of the Diaphragm in the Prevention of Gastroesophageal Reflux

Chevalier Jackson (78), in 1922, described a pinchcock action of the diaphragm which he believed to be responsible for the prevention of gastroesophageal reflux. He stated that the diaphragm exerted a constricting pressure on the esophagus during inspiration, thus preventing reflux, and that during deglutition it relaxed to allow downward passage of food. Jackson's report was based on his observations during many esophagoscopic examinations. In the light of current knowledge, a critical appraisal of his work suggests that he may have been observing the combined action of the diaphragm and what is now believed to be a lower esophageal sphincter. The diaphragm does not relax with the deglutitive act but the lower esophageal sphincter does. Favoring the concept of a pinchcock theory is the fact that barium is held up at the diaphragm during inspiration, the time at which the diaphragm contracts.

A review of the anatomy of the diaphragm (10, 65, 79-85), with special emphasis on the esophageal hiatus, demonstrates the

structural basis for Jackson's concept of a "pinchcock".

The diaphragmatic crura take origin from the lumbar vertebrae and insert into the central tendon of the diaphragm. The right crus takes origin from the anterior surfaces of the upper three or four lumbar vertebrae and the intervening discs. These origins also blend with the anterior longitudinal ligament of the vertebral column. The crural fibers run upward on both sides of the aorta and at the level of the twelfth thoracic vertebra form the sides of the aortic opening behind the diaphragm. The two crura are then united anterior to the aorta by a tendinous arch, the median arcuate ligament. From here the right crus sends a definite bundle of muscle fibers toward the left side, anterior to the aorta and behind the esophagus, and then around the left side of the esophagus with the left crus. The main bundle of muscle fibers of the right crus lies on the right side of the esophagus. Both right and left limbs of the right crus again unite anterior to the esophagus, decussating with each other as they insert into the central tendon of the diaphragm at the level of the tenth thoracic vertebra, one inch to the left of the mid line. The esophagus thus passes from the thorax into the abdomen through a hiatus formed by the muscle fibers of the right crus. In addition, the right crus forms a sling which pulls the esophagus downward and to the right in a manner similar to that in which the puborectalis forms a sling around the anorectal junction.

The left crus in 30 percent of cases sends a small band to the right. These fibers are known as the muscle of Low and run to the region of the inferior vena cava hiatus.

The hiatus itself is elliptical. Behind are the diverging fibers of the right crus. On either side there are muscle bands of the right crus. Anteriorly one centimeter of muscle lies between the hiatus and the central tendon. The transverse ligament lies beneath the anterior decussating fibers and strengthens the posterior part of the central tendon.

Seen from the side, both crura pass upward along the lumbar vertebrae and then incline forward and upward at about the level of the twelfth thoracic vertebra. The fibers of the right crus form the hiatus at about a 45 degree angle to the vertical axis and make a tunnel that is about 3 centimeters long on the posterior wall and somewhat less anteriorly.

The esophagus is accompanied by several structures as it passes downward and to the left through the crural canal. Anteriorly and to the left is the left vagus nerve; posteriorly and to the right is the right vagus nerve. The esophageal branch of the left gastric artery also accompanies the esophagus and has been claimed by some to help prevent displacement of the stomach into the thorax (60). In addition, the hiatus contains the paracardiac lymph glands and some cellular tissue which forms a bursa-like cushion to the diaphragmatic hiatus (65). The accumulation of fat in the crural canal may

be the starting point of a weakness that predisposes to hernia according to Allison (65).

Collis, Satchwell and Abrams (84) have studied the innervation of the diaphragmatic crura and found that the portion of the right crus passing behind and to the left of the hiatus is supplied by the left phrenic nerve. The remainder of the right crus is supplied by the right phrenic nerve.

The concept of a diaphragmatic pinchcock as proposed by Jackson and supported by Allison thus seems justified by a review of the anatomic facts. In addition, the detailed anatomy of the hiatal canal has been presented.

Allison modified the pinchcock theory as it was originally proposed by Jackson. According to Allison, contraction of the right crus has two functions: (1) it compresses the walls of the esophagus from side to side, and (2), with a sling-like action, it pulls down and increases the angulation of the esophagus. During inspiration, when low intrathoracic pressure favours gastroesophageal reflux, diaphragmatic contraction thus acts to prevent the reflux. Allison feels that there is also an intrinsic mechanism which contributes to the reflux barrier and that this is related to the obliquity of the esophageal entry into the stomach. He suggests that, if the intrinsic mechanism is weak, the diaphragm alone may not be enough to ensure complete continence (65).

Surgical evidence to support the pinchcock theory is found in the work of Collis (86) and that of Giuseffi et al. (87). Collis used a narrow tube of stomach, passed this up through the hiatus and anastomosed it to the lower esophagus. Reflux into the esophagus did not occur and Milstein (82) felt that the diaphragmatic crura prevented reflux under these conditions. Giuseffi (87) divided the rim of the hiatus in dogs and reported subsequent development of esophagitis. In addition, transplantation of the esophagus to the central tendon usually failed to prevent reflux (82).

Wooler (88) pointed out several other facts to support Allison's concept. Radiologically barium is held up at the cardia during inspiration. With expiration, the diaphragm relaxes and barium flows through the cardia into the stomach. In addition, Wooler stated that two fingers held in the hiatus are squeezed if the phrenic nerve is stimulated.

Marchand (62) felt that pressure differences between the thorax and abdomen alone would sufficiently explain the holdup of barium. Smiddy and Atkinson (74) found section of the crura made no appreciable difference in the escape pressure of fluid pumped into the stomach of dogs.

Hoag, Kiriluk and Merendino (14) doubted that the diaphragmatic action would be important in the prevention of reflux because it could be effective only half of the time. They further

reasoned that, because of the extreme sensitivity of the esophagus to acid peptic secretions, partial protection would be inadequate.

Schlegel (52) found paralysis of the diaphragm by bilateral phrenicotomy did not change the pressure in the lower esophageal sphincter. Symptoms suggestive of gastroesophageal reflux did not occur after phrenic interruption in the treatment of tuberculosis (89). Atkinson and Summerling (34) found a high pressure zone but no respiratory pressure changes in this area following left phrenic nerve avulsion. As noted above, diaphragmatic paralysis during anaesthesia did not result in reflux (71). In addition, Braasch and Ellis (17) felt that the closure of the esophagus by the crura was not seen at esophagoscopy. Instead, the esophageal lumen at the level of the hiatus seemed to widen during inspiration and narrow during expiration. Lam and Kenney (90) reported that there was no contraction of the diaphragmatic crus of the dog when the phrenic nerve was stimulated. In addition to this, Creamer (91) found that reflux occurred only during inspiration, which would be hard to accept if the diaphragmatic pinchcock action were an effective anti-reflux mechanism. Smiddy and Atkinson (74) found section of the hiatal muscle did not significantly alter the gastroesophageal reflux barrier yield pressure.

V Additional Factors in the Prevention of Gastroesophageal Reflux

(a) The Role of the Mucosal Rosette:- Redundant folds of mucosa at the cardiac orifice and in the terminal esophagus have also been credited with a role in the prevention of reflux. Magendie (92) first described the folds and linked them with an anti-reflux mechanism. Botha (93), in 1958, extensively studied the folds. In autopsy dissections, mucosal folds were found at the cardiac orifice in some cadavers. During gastrectomy, Botha was able to identify routinely the folds occluding the junctional opening. Comparative studies in animals showed the mucosal folds to be present and cineradiographic methods were used by Botha to show that they played an important function in the gastroesophageal closing mechanism (94). He also did radiologic examinations in humans and found that the "empty segment" of esophagus above the cardia never could be filled from the stomach side in normal patients. Botha stated that nothing but mucosal apposition could produce such a smooth watertight seal. Thickened muscularis mucosa, Botha concluded, exerts an active muscle tone which draws the mucosal folds together and effects a watertight seal from below. According to him, the mucosal folds and the internal sphincter "act together in perfectly balanced harmony to form the closing mechanism between esophagus and stomach."

Esophagoscopy clearly shows that reflux occurs as the esophageal lumen is widened and the mucosal folds are smoothed out (57).

Radiologically these mucosal folds are sometimes evident on barium swallow and it has been stated that, if the folds are evident in the usual position, there is no hiatus hernia or reflux.

Creamer believes that the esophageal muscularis mucosa contracts and pushes the mucosa into folds, that is, the folds themselves are not important (96). Atkinson (97) suggests that, if the folds are important, reflux should occur with gastric mucosal atrophy. Allison (65) believes that to emphasize the rosette rather than the sphincter is to "place the cart before the horse".

(b) The Fundic Air Bubble:- Carver and Sealy (98) state that "a minor contribution to the competency of the cardiac valvular mechanism is the pressure effect produced by air in the cardia which tends to collapse the esophagus and increase the esophagogastric angle". The work of Marchand (62), involving a clamp across the fundus from the esophagogastric angle to the greater curvature and resulting in a failure of the reflux barrier, may be interpreted as favouring the concept of the fundic air bubble. The anatomical angle is not disturbed. However, the changing intragastric pressures cannot be transmitted to the fundic area, the flap valve cannot be shifted and esophagogastric incompetence results.

Unfortunately, the amount of experimental work done on the importance of the fundic air bubble is minimal and conclusions about its role in the prevention of reflux are unwarranted.

B. GASTROESOPHAGEAL REFLUX IN HIATUS HERNIA

There are several concepts of the pathophysiology of gastroesophageal reflux and these are based on the various mechanisms for the prevention of reflux. Hiatus hernia is an anatomical alteration. When a factor important in the prevention of reflux is disturbed, the reflux barrier mechanism loses its competency and gastroesophageal reflux may then occur under these conditions.

If the lower esophageal sphincter is considered to be the main barrier to reflux, the following sequence may explain reflux accompanying hiatus hernia. The intra-esophageal pressure in the sphincteric zone before herniation is the sum of the intra-abdominal and sphincteric pressures. With an intra-abdominal pressure of 40 centimeters of water and a sphincter pressure of 50 centimeters of water, the total pressure in the sphincteric area is 90 centimeters of water. However, with a hiatus hernia the lower esophagus is herniated into the thoracic cavity. The extrinsic pressure on the esophagus is then reduced from 40 centimeters of water to a negative pressure of about -10 centimeters of water. The total pressure in the sphincteric area is reduced from 90 centimeters of water to 40 centimeters of water. The barrier to reflux has been reduced to less than 50 percent of normal. The tone of the lower esophageal sphincter is known to vary from one person to another

and those with high sphincter tone may not experience reflux even with the sphincteric area in the thorax. Atkinson, Edwards, Honour and Rowlands demonstrated a definite correlation between the pressure in the sphincteric area and the presence of gastroesophageal reflux (31). However, in their study, some normal controls had sphincteric zone pressures as low as the patients with hiatus hernia and reflux. The changes in extrinsic pressure are much greater in the thorax than in the abdomen where the less rigid anterior abdominal wall has a dampening effect and it would seem that critical evaluation of the role of the sphincter should include the position of the sphincter in respect to the diaphragm as well as the mean pressure in the lumen.

Barrett (59, 60) believes that the acute angle between the esophagus and fundus of the stomach is made obtuse as herniation through the hiatus occurs. Because the flap valve mechanism is dependent upon the obliquity of the gastroesophageal angle, it is thus unable to function. The esophagogastric junction becomes a bell-shaped structure without a valve and acid gastric contents easily pass from the funnel up through the handle. Allison also felt that the same basic mechanism was involved but contended that the gastroesophageal angle was maintained by the phrenoesophageal ligament and the sling-like right crus rather than the oblique gastric muscle. Allison explained the fact that not all patients with hernias have reflux by ascribing a secondary anti-reflux role

to an intrinsic factor which, if strong enough, may prevent reflux even in the presence of a hernia.

In addition to maintaining the gastroesophageal angle, Allison (65) believed that the right crus exerted a squeezing action on the esophagus during inspiration, thus preventing reflux when pressure changes most favoured it. With hiatus hernia this action would, of course, still be present. Only when the hiatus is so enlarged that the crus does not squeeze the herniated stomach will reflux occur. Staged balloons of known diameter have been used to study the size of the hiatus. These experiments show it is not always enlarged with the presence of a hernia (99) and thus cast some doubt on the above theory.

The fourth mechanism of gastroesophageal reflux, based on the flaccid tube theory of Creamer and Edwards (55, 56, 100) is again dependent on a change in anatomy. Normally the lower esophageal sphincter approximates the walls of the flaccid tube and then the difference in pressure between abdomen and thorax tends to compress and evert the intra-abdominal esophagus. The greater the pressure difference, the more firmly the tube will be held closed. Reflux can only take place if intragastric pressure exceeds the pressure difference between abdomen and thorax. With a hiatus hernia, the intra-abdominal esophagus is displaced upward and a loculation of stomach passes through the hiatus. The sphincter no longer approximates the intra-abdominal viscus and the

initiating phase of the anti-reflux mechanism is lost. Without the first phase, the second phase cannot take place and reflux is then possible. Edwards believes that, if the hiatal slit is narrow enough, the sides of the herniated stomach may be approximated and the intra-abdominal stomach then acts as the flaccid tube and still constitutes a potent anti-reflux mechanism. If the hiatus is slightly enlarged and only loosely approximates the viscus walls so that a leak may occur from the intra-abdominal to intrathoracic stomach, then pressure in the herniated stomach may overcome the resistance of a relaxed sphincter or a sphincter with a low resting tone producing reflux into the esophagus. A fully incompetent hiatus allows the full force of the intra-abdominal pressure to be transmitted to the herniated stomach and only the weak sphincter resistance remains to prevent reflux into the esophagus. In this way Edwards explains the variability of symptoms between patients. Criticism of this theory of reflux is based primarily on the proposed mechanism for the prevention of reflux and has been previously covered.

C. THE CONSEQUENCES OF GASTROESOPHAGEAL REFLUX

Moersh and Camp (101), of the Mayo Clinic, and, two days later, Winkelstein (102), of New York, first described the picture of peptic esophagitis in 1935. All of their patients were being investigated for heartburn and dysphagia. However, these investigators were basically unaware of the underlying cause of the lesion which they described so well.

Friedenwald et al. (103), in 1928, showed that traumatic ulcers of the esophagus healed poorly if bathed with hydrochloric acid. Selye (104), in 1938, produced peptic hemorrhagic esophagitis in rats by ligating the pylorus. Ligation of pylorus and cardia did not result in esophagitis. In 1948, Wangensteen et al. (105) found the esophagus was much more easily damaged by acid peptic secretions than by either gastric or duodenal mucosa. In 1950, Wangensteen and associates (106) used acid peptic perfusion of the feline esophagus and demonstrated a prompt and devastating result. The esophagitis was of a most severe nature and perforation often resulted. Hydrochloric acid in concentrations approaching those of the stomach had only a mild effect in comparison.

Concerning the cause of esophagitis in humans, Carver and Sealy (107) reported, in 1954, that there was an associated hiatus hernia in 76 percent of cases, surgical excision of the lower

esophageal sphincter in 13 percent, persistent vomiting in 11 percent and that 13 of the 130 patients reviewed also had a duodenal ulcer. Others have also reported the special liability of patients with hyperchlorhydria to develop peptic esophagitis associated with the high incidence of duodenal ulceration (108, 109).

Aylwin (110) collected refluxed gastric secretions from the esophagi of patients with hiatus hernia and correlated the degree of esophagitis to the enzyme activity of the juices bathing the esophagus at night. The severity of the esophagitis was also dependent on various physiological factors which modified the peptic activity of the gastric secretions and the defences of the esophagus. The daily secretion of 1500 cc. of alkaline saliva in particular was felt by Aylwin to be an important defensive factor.

Although the evidence for involvement of acid peptic secretions in the production of esophagitis is considerable, there are still tenacious advocates of other etiological theories. Palmer (111) biopsied 61 cases of esophagitis and concluded that the initial lesion occurs in the lamina propria and only secondarily involves the epithelial and muscularis layers. He reported 36 specimens with inflammatory involvement of the lamina propria and normal squamous epithelium. Palmer had 22 patients with esophagitis but no free gastric acid after stimulation with histamine. He felt that the esophagitis in these cases was the consequence of

vascular disorders. Ingelfinger (112) has pointed out that 16 of Palmer's cases with achlorhydria had had gastric surgery permitting ready access of intestinal juices to the distal esophagus.

In 1957, Barrett (113) submitted that gastric mucosa may be present above the esophagogastric junction. Others suggested that the relatively large volume of salivary secretions continuously passing over the area dilute the acid to inconsequential concentrations. In fact, peptic ulcers have been demonstrated in these heterotropic sheets of gastric mucosa (114, 115, 116).

Foci of infection, general debility and neurogenic disorders (117) have also been linked to the etiology of esophagitis and some patients, in fact, may have the basis of their disease in these primary conditions. However, the concensus today is that the presence of acid peptic secretions in the esophagus is the most common direct cause of esophagitis (118-123). While hiatus hernia is most often implicated with acid peptic reflux, it must be noted that the presence of a nasogastric tube may allow reflux and that there may a delay in esophageal emptying in recumbent patients (122).

Ingram, Keswani and Muller (124) did a correlative histopathologic study of experimental surgical reflux esophagitis and found that, in contrast to Palmer's concept, reflux esophagitis follows a definite sequential pattern starting with epithelial destruction. In their stage I there is necrosis of epithelium

which first involves only the superficial layers. Stage II shows desquamated areas of epithelium and scattered inflammatory infiltration of the submucosa. In stage III there is microscopic ulceration and marked inflammation in the lower esophagus. The deeper layers may be involved. Stage IV shows ulcers with rolled and irregular margins which tend to become confluent. Fibrous connective tissue is found to be replacing the cellular granulation tissue.

Moersh, Ellis and McDonald (125), in 1959, reviewed the pathologic changes occurring in severe reflux esophagitis using material taken at esophageal resection. They concluded that esophagitis was not a single entity but a group of conditions of related origin with correspondingly different pathology. Four different entities were described: (1) Marginal esophageal ulceration was seen in 64 percent of cases and in these inflammation was limited to a short segment of esophagus immediately above the junction. Ulceration was superficial and hiatus hernia was always present. The esophagus was considerably shorter than normal and somewhat fixed in position. Stenosis and stricture were common. (2) Extended linear esophagitis with superficial inflammatory changes occupying relatively long lengths of esophagus was seen in cases of hiatus hernia with duodenal ulcer and repeated vomiting. The presence of stenosis showed that superficial inflammation does not preclude this condition. (3) Solitary marginal ulcer was present

in two cases at the junction of the stomach and esophagus. There were marked interdigitations of squamous and columnar epithelium and it could not be determined in which area ulceration had occurred. Hiatus hernia was not present. (4) Deep ulceration in a columnar epithelium-lined esophagus (Barrett's ulcer) was present in one case. There was a stricture present with gastric mucosa extending 5 centimeters above and 2 centimeters below this lesion. The patient had hematemesis and dysphagia.

The complications of reflux esophagitis are stricture (126), anemia (127) and acute hemorrhage (128, 129). The bleeding may occur from the hiatus hernia which usually gives rise to the esophagitis.

D. THE OBJECTIVE DETERMINATION OF GASTROESOPHAGEAL REFLUX IN PATIENTS WITH HIATUS HERNIA

One of the problems with the objective evaluation of a patient with symptoms of reflux esophagitis is the insignificance of negative results from any one type of examination. Patients with symptoms of esophagitis may or may not have evidence of this condition on endoscopy, radiologic examination or acid perfusion of the esophagus (130-133). Further, confirmatory evidence from one diagnostic procedure may not be in agreement with the results of the other procedures (130, 132). In Bernstein's group of 20 patients with symptoms of esophagitis and a positive response to acid perfusion, esophagoscopic evidence of esophagitis was absent in 10 (131). Tuttle et al. (132) have suggested that, if Palmer (111) and Lodge (123) are correct in their claim that the intitial response of the esophagus to acid perfusion is inflammatory infiltration of the lamina propria, then patients with symptoms of esophagitis and a positive perfusion test but negative findings on endoscopy will show a histologically demonstrable esophagitis on biopsy. The consistency of one procedure, radiologic examination, is such that reflux may be evident on one examination but neither the hernia nor the reflux may show on any of several subsequent examinations (76a).

Flood (133) was able to demonstrate acid reflux in 50 percent of patients with hiatus hernia by using a nasogastric device at 30 centimeters beyond the incisors and then by testing separately the specimens for the presence of acid. However, he also found acid in the esophagi of 5 percent of normal individuals with this technique.

Tuttle and Grossman (134), in 1958, first described the direct intra-esophageal determination of acid with a glass pH electrode as a means of objectively demonstrating esophageal reflux. They used the principles outlined by Rovelstad (135, 136) for determining intragastric acidity with an intragastric glass pH electrode.

Rovelstad was not the first to use intragastric pH electrodes (137-139) but was one of the first to use the glass pH electrode for this purpose (140). He also demonstrated that the determination of pH in the upper portion of the alimentary tract is practical with a glass electrode in situ (136). He reviewed the disadvantages of aspiration and dye-determination techniques. First, there is the possibility of significant error in the interpretation of end points if Topfer's reagent or phenolphthalein is used. Secondly, serial aspirations of the stomach result in the formation of more gastric secretion and, therefore, possible changes in pH.

It is interesting to note the periodic potential changes

in the duodenum, stomach and esophagus when recorded continuously by the method of Rovelstad. These are probably action potentials generated by the smooth muscle of the gastrointestinal tract and may be correlated with peristaltic waves (141-143).

Tuttle et al. (134), as noted, used the in situ technique of pH determination, as developed by Rovelstad, to determine directly pH changes in the esophagus. Simultaneous recording of intraluminal pressure at the level of the glass electrode permitted precise localization of the sensing device at various levels above the diaphragmatic hiatus. After placing 300 milliliters of 0.1 N. HCl in the stomach, the sensing device is withdrawn 1 centimeter at a time and the pH is recorded in the proximal stomach and lower esophagus. Acid regurgitation was diagnosed only when a pH of 3 or less was encountered over an area of at least 2 centimeters above the esophageal hiatus and when these observations could be reproduced. The diaphragmatic hiatus was located by a change in pressure swings caused by respiratory movements from relatively high intra-abdominal values to negative intrathoracic values.

Using the direct determination of acid reflux by pH and acid perfusion tests, 81 subjects with clinical, endoscopic or radiographic evidence of esophagitis were studied. Sixty-four patients responded to acid perfusion and also had acid reflux on pH testing; 2 showed symptoms on acid drip but no regurgitation; 15 failed to respond to acid drip but showed reflux.

Hill (42, 43) used basically the same technique as Tuttle and associates but added acid reflux-inducing manoeuvres on the basis of the known fact that reflux may occur at one time but not at another. Tuttle et al. may have had some negative results in the acid reflux test based on the fact that they examined the esophagus while no reflux was occurring. One objection to both of these techniques is that the esophageal pH was measured as a naso-gastric device was being withdrawn through the junctional area. It is quite conceivable that some acid leaked through the junction zone behind the glass electrode and therefore gave false positive results. If the pH electrode had been stationed at 5 or 10 centi-meters above the junction, if time had been allowed for a normal esophageal pH environment to develop, and if then an attempt to induce reflux had been made, the results would be less open to criticism.

Hill was interested in correlating the height of acid reflux with the severity of symptoms and checking this against the post-operative pH test after hiatus hernia repair. He also demon-strated the value of this sensitive technique in problems of diffe-rential diagnosis of chest pain.

The resistance and reflex function of the lower esopha-geal sphincter was studied by Fleshler, Hendrix, Kramer and Ingelfinger (144). The mechanism at the gastroesophageal sphincter was capable of withstanding a hydrostatic force obtained by

layering fluid in the esophagus. Creamer and Schlegel (145), however, pointed out that the true or yielding pressure of the sphincter cannot be measured by a column of fluid in the esophagus because the column of fluid distends the esophagus and this reflexly relaxes the sphincter. The resistance of the reflux barrier mechanism as an objective reflection of the conditions under which gastroesophageal reflux will occur cannot then be measured from above. Marchand (62), using a pressure regulating corset and radio-opaque media in the stomach, was able to define objectively the conditions under which reflux would occur at specific intra-abdominal pressures. The last point is mentioned because of the incorporation of the variable pressure corset in the method for detection of gastroesophageal reflux which is part of the subject matter in this thesis.

E. SUMMARY OF THE LITERATURE REVIEW

The mechanisms responsible for the prevention of gastroesophageal reflux have been reviewed. The reflux which may accompany hiatus hernia has been explained on the basis of a disturbance in any of several main anti-reflux mechanisms. The probable responsibility of acid peptic secretions for reflux esophagitis is seen to be based mainly on indirect evidence of overwhelming quantity. Finally, the possibilities for objectively determining the presence of reflux have been reviewed.

OBJECTIVES

A surgical consensus of the indications for hiatus hernia repair would probably range somewhere between repair of symptomatic hiatus hernias and hiatus hernias with objective evidence of gastroesophageal reflux or esophagitis. There would be less agreement on whether a transabdominal or transthoracic repair should be used and, if transabdominal, whether the crural fibers should be approximated anterior or posterior to the esophagus. Then, should the phrenoesophageal ligament be sutured to the undersurface of the diaphragm, and should the gastroesophageal angle be reconstructed with sutures between the fundus and esophagus and then the fundus and diaphragm?

Objectively determinable criteria are essential for evaluation of an operation. Radiology itself is not entirely dependable for the demonstration of hiatus hernia or the reflux which may accompany it. Demonstration of a hernia and reflux constitutes proof. However, if they are absent on a single x-ray examination, the possibility of their presence has not been excluded. Furthermore, it is not a functional concept to show a post-operative x-ray film demonstrating the stomach completely returned to the abdomen. The patient underwent surgery for direct or indirect evidence of reflux esophagitis and, postoperatively, it must be proven that gastroesophageal reflux is no longer present. To know dependably and with a considerable degree of certainty that gastroesophageal reflux is no longer present after an operation or how much its extent has been altered, would be to introduce a new level of objectivity in

the post-operative evaluation of surgical procedures for correction of hiatus hernia.

Dr. J. R. McCorriston and Dr. Donald R. Webster suggested the trial of direct intra-esophageal pH determinations for post-operative evaluation of hiatus hernia repairs in February, 1961. Studies by Dr. Philip Hill of Seattle indicated that the newly available, tiny intra-esophageal pH electrode was a sensitive indicator of changing pH conditions and that, coupled with a pressure monitor to demonstrate the location of the pH electrode, it could be used to measure how high acid would reflux into the esophagus. Dr. McCorriston was specifically interested in determining the acid reflux objectively preoperatively and how much the esophagogastric angle-restoring operation reduced the reflux.

The assigned objective of this study, then, was to:

(1) Evaluate the small glass pH electrode for use in intra-esophageal pH determinations.

(2) Study pH changes at the esophagogastric junction in normal persons.

(3) Determine the usefulness of esophageal pressure changes as a method of precisely locating the pH electrode.

(4) Develop a technique for detection of gastroesophageal reflux using the pH electrode, and to compare the accuracy and reliability of such a technique with other methods of objectively demonstrating reflux.

(5) Study the gastroesophageal reflux associated with hiatus hernia and various other conditions.

(6) Evaluate patients with hiatus hernia pre- and post-operatively in order to determine the effect of various operative procedures on gastroesophageal reflux.

APPARATUS, TECHNIQUES AND RECORDING OF DATA

I Measurement of pH with an In-Situ Small Glass Electrode

Hydrogen, quinhydrone and antimony electrodes were too complex, bulky and most impractical for use in in-situ pH determination in human beings. With the development of tiny glass electrodes, however, the in-situ determination of pH became a very practical procedure.

Haber and Klemensiewicz demonstrated that potential differences between glass and calomel electrodes varied with the pH of the conducting solution. MacInnes found that a special glass, now known as 015 glass which contains considerable water, could make the glass electrode a highly sensitive and accurate device. The glass electrode has since been so successful that it is used almost exclusively in the laboratory.

In spite of its success, the glass pH electrode is not yet theoretically well understood. Current supposedly crosses its surface by means of hydrated protons and this function is possible because 015 glass contains considerable water. Drying, therefore, destroys its function. When in use, the electrode must be calibrated with solutions of known pH. At least two solutions must be used to be certain of proper electrode function.

For the direct determination of gastric and esophageal pH, a tiny glass electrode of the type described (fig. 1) was stationed in the stomach or esophagus and a reference electrode (fig. 2) was

Reference Electrode

Glass Electrode

Shielded Lead Wire

Pressure Monitoring Catheter

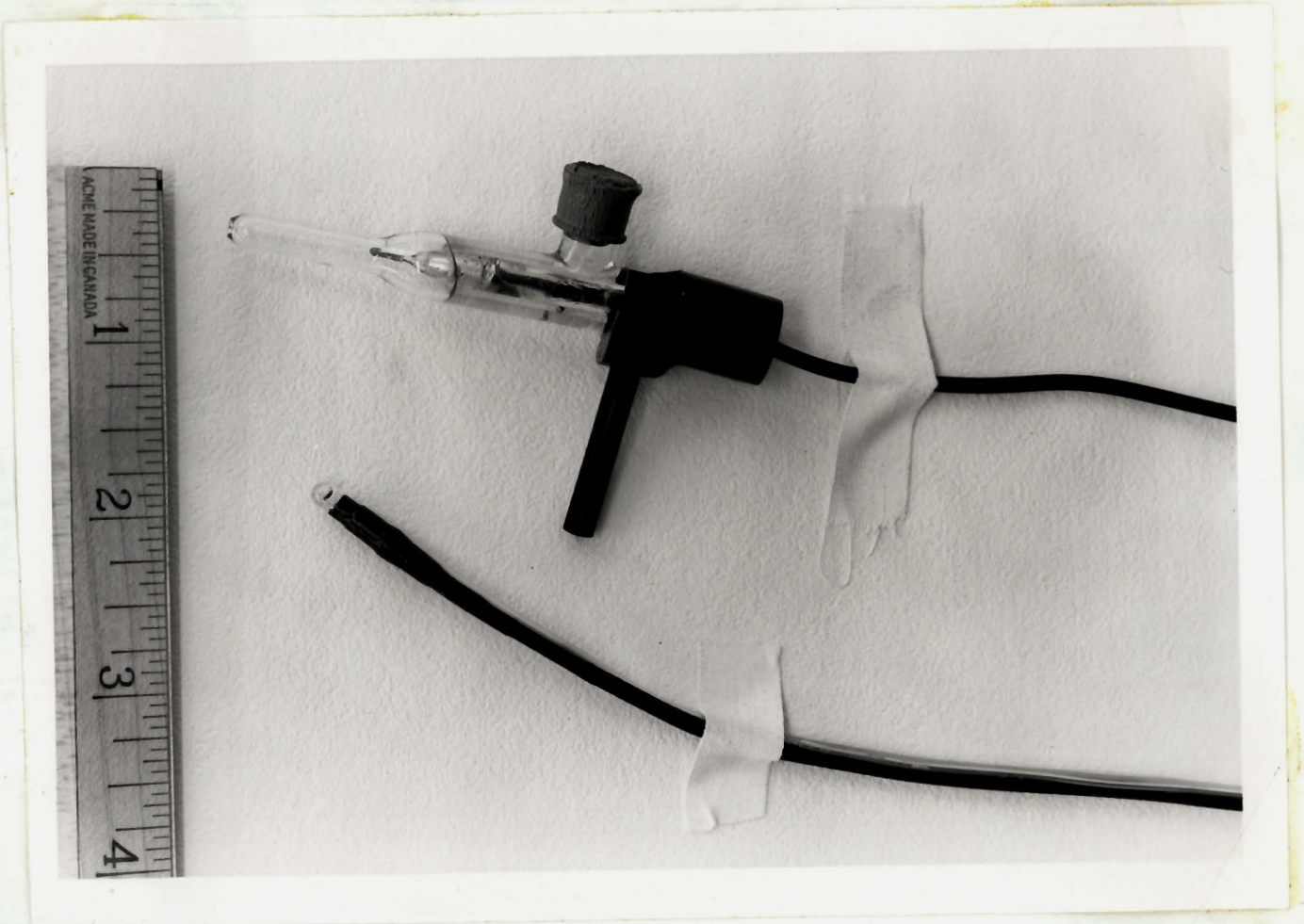

Fig. 1: (a) Below: The nasogastric data-gathering device consisting of the small glass pH electrode (Beckman) and the polyvinyl pressure monitor catheters.

(b) Above: The fiber junction reference electrode for pH measurements (shown with the pH electrode for comparison of size).

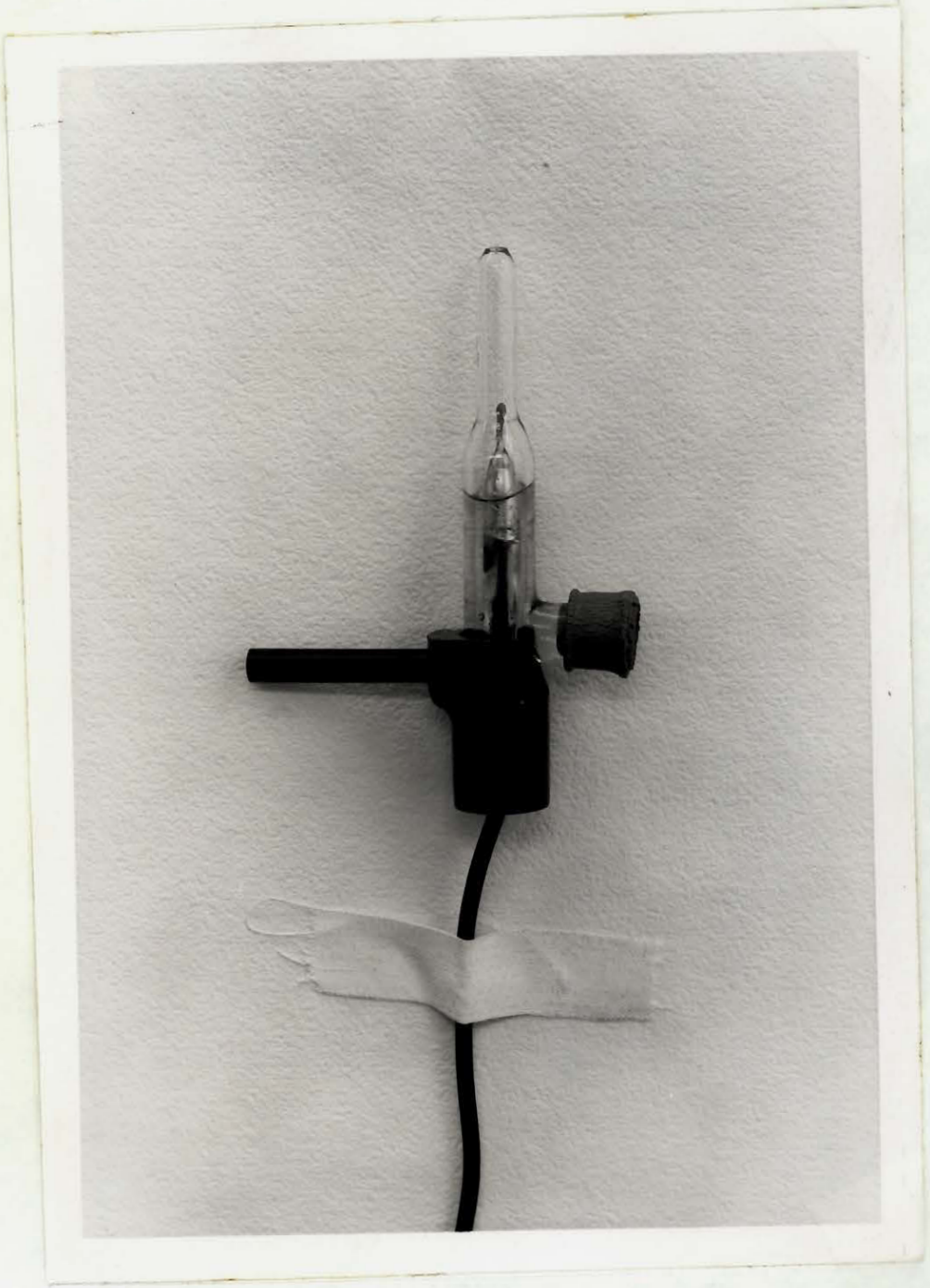

Fig. 2: Close-up view of fiber junction reference electrode. The change in electrical potential between the glass pH electrode and the reference electrode in a solution is directly related to the pH of the solution.

placed in the mouth. The body fluids between the two electrodes constituted a salt bridge across which the electrical potential difference was measured. The composition of the solution forming the salt bridge remained constant except for the material bathing the stomach or esophageal mucosa. Since the composition of the salt bridge, excluding gastric or esophageal contents, was constant, any change in potential across the bridge must be a reflection of changing pH in the stomach or esophagus.

The pH electrode used in this study was a Beckman 39042 gastro-intestinal glass electrode. It was sealed to the end of a long, shielded lead wire and therefore could easily be passed into any part of the upper gastro-intestinal tract.

The reference electrode was a Beckman 1085 fiber junction type (fig. 2). This utilized an internal element of silver-silver chloride type. The internal element was surrounded by an outer chamber containing 4.0 M. potassium chloride solution saturated with silver chloride. Imbedded in the immersion tip of the outer chamber is an asbestos fiber which allows a flow of electrolyte solution from the electrode to establish contact with the test solution. The sole purpose of the reference electrode is to permit measurement of the potential developed by different solutions at the surface of the glass electrode.

A Beckman Zeromatic pH meter (fig. 3) was used to actually measure acidity changes. This unit had an accuracy of 0.1 pH units

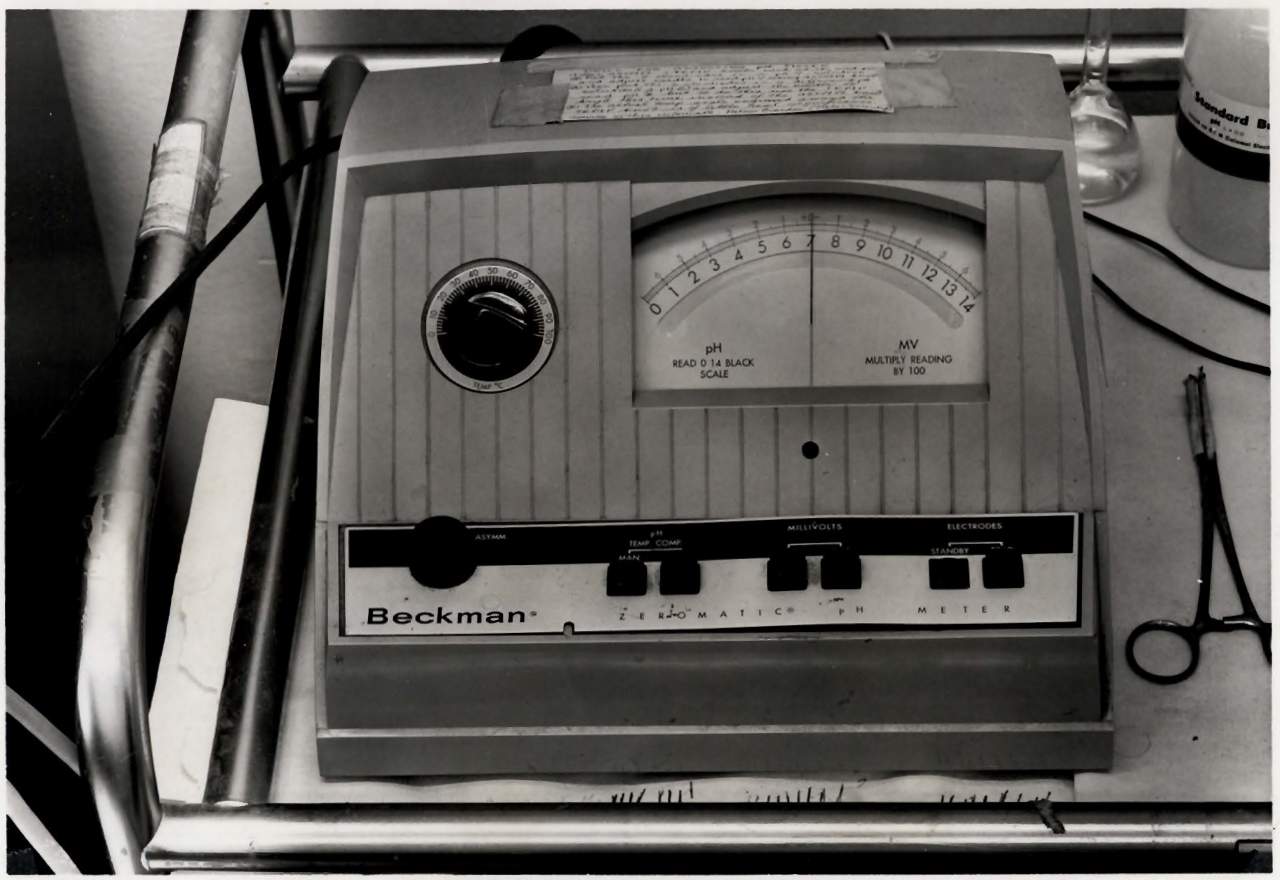

Fig. 3: The Beckman Zeromatic pH meter used for pH determinations. The unit is accurate to 0.1 pH units and has a reproducibility of 0.02 pH units. It was coupled to a Sanborn multichannel recorder for simultaneous recording of pH and esophageal pressures.

and a reproducibility of 0.02 pH units. It could be read visually or coupled to a potentiometer-type recording device. The output was over a 1400-millivolt range and additional resistance (1000 ohms) had to be added across the output jack to accomodate this instrument to a Sanborn recording instrument.

II Location of the Glass Electrode by Simultaneous Manometry

The accurate location of the pH electrode is essential to interpretation of the pH values obtained. An acid pH reading is expected in the stomach and, if obtained from the esophagus, is an indication that acid peptic gastric secretions are being refluxed into the esophagus. Therefore, to understand the significance of a pH value, it is first necessary to know where the reading has been obtained. Determination of the distance above the esophagogastric junction that is affected by acid reflux is also dependent upon accurate location of the pH electrode in relation to the junction.

Two ways of locating the electrode are possible. Fluoroscopy provides easy visualization of the wire lead of the glass electrode but the esophagogastric junction and the esophageal hiatus are not readily determined by x-ray examination. Measurement of esophageal intraluminal pressures immediately adjacent to the electrode and relating these to the known change from positive to negative

pressures at the esophageal hiatus seemed to provide an excellent technique for locating the electrode relative to a readily determinable and dependable reference point (fig. 4). An open-ended, pressure-monitoring catheter in the stomach shows a slightly positive pressure of about 50 centimeters of water. This pressure varies slightly with respiratory movements due to the compression of abdominal contents with each downward movement of the diaphragm. As the pressure-monitoring catheter is withdrawn, centimeter by centimeter, past the diaphragm and into the intrathoracic portion of esophagus, the mean pressure suddenly becomes negative because of: (1) elastic contraction of the lungs and, (2) transmission of this negative intrapleural pressure to the mediastinal structures. Combined cineradiographic and manometric studies have demonstrated that the sudden pressure change is at the diaphragmatic hiatus and that the esophagus usually extends about 2.0 centimeters below this point. According to Hill, the pressure change is a definite and constant finding which serves as a most useful landmark. Just below this pressure inversion point (Hill), or the biphasic wave, there is a 2-centimeter portion of esophagus which is characterized by higher mean pressure than is found in the stomach. This corresponds radiologically to the intra-abdominal esophagus and is not always obvious on manometric recordings. The lower margin of the high pressure zone represents the esophagogastric junction and it is at this point

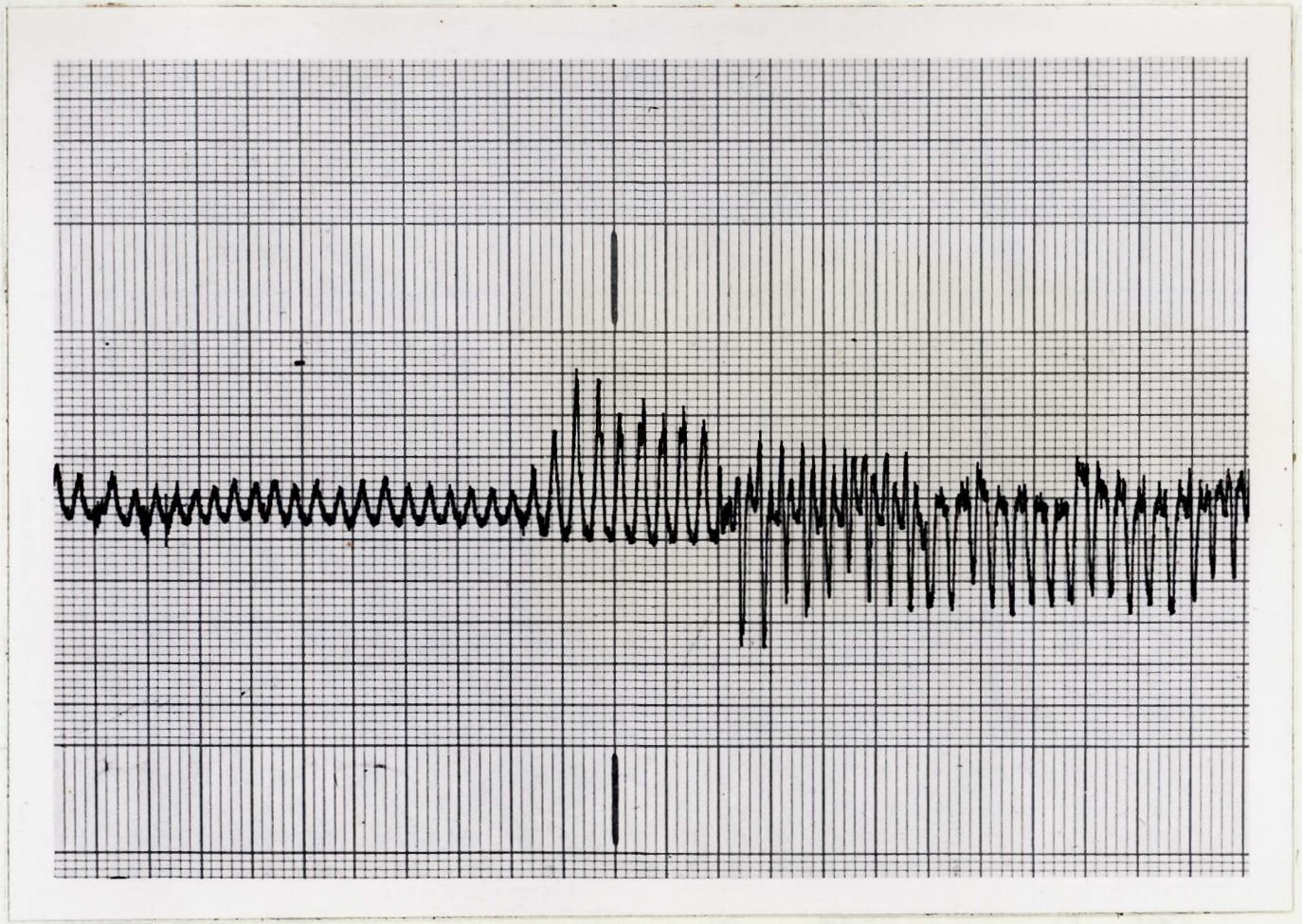

Fig. 4: This pressure tracing was taken as an open-ended, water-filled catheter was withdrawn across the gastroesophageal junction. The gastric-type tracing with a low amplitude wave, the high pressure zone and the low pressure, high amplitude tracing of the intrathoracic esophagus are seen. The sequence of events is not always so well demonstrated.

that the pH should be expected to change from low gastric to higher esophageal values. However, it is apparent, by placing the pH electrode adjacent to the open end of a pressure-monitoring tube, that a pressure curve is obtained which will, from its characteristics, reveal the presence of the electrode in the stomach, intra-abdominal esophagus and intrathoracic esophagus.

The precise location of the pH electrode within any of these areas was indirectly determined. The pressure catheter and pH electrode lead wire were bonded with tetrahydrofuran and the data-gathering device was marked in centimeters from the electrode. This apparatus was passed via the nasogastric route. The exact distance between the external nares and the diaphragmatic hiatus (the pressure inversion point) was noted. The electrode location at any subsequent time was then easily determined by subtracting the distance between the nares and the electrode from the previously measured distance between the nares and the hiatus.

The pressure-monitoring catheters consisted of plastic tubing with a 0.044-inch internal diameter. Polyvinyl tubing was used because the pH cable covering was also polyvinyl and the two could easily be fused with tetrahydrofuran. The open tip of the pressure-monitoring catheter was then permanently and immediately adjacent to the pH electrode.

The head of the data-gathering device with its two sensitive

elements thus provided simultaneous, immediate and continuous monitoring of pH and pressure changes at various locations in the stomach and esophagus. By relating the known distance of the device from the nares to the known distance from the nares to a constant point on the pressure curve, the exact location of any pH measurement could then be determined.

III Pressure Measurement and Recording

Pressures were measured and recorded using Sanborn low displacement, type 267-A transducers, a carrier amplifier, D'arsonval-type galvanometer, and direct-writing stylus (fig. 5).

Dependability of the hydraulic system was improved by using distilled water which has been heated to reduce the content of dissolved air.

The sensitivity of the system was set and calibrated either electronically or hydraulically. Electronic calibration utilizes a signal equivalent in millivolts to 200 millimeters of mercury pressure to produce a stylus deflection of 2 centimeters at an alternator setting of X100. Therefore, at an alternator setting of X10, a stylus deflection of 1.0 centimeters is equivalent to 13.7 centimeters of water pressure.

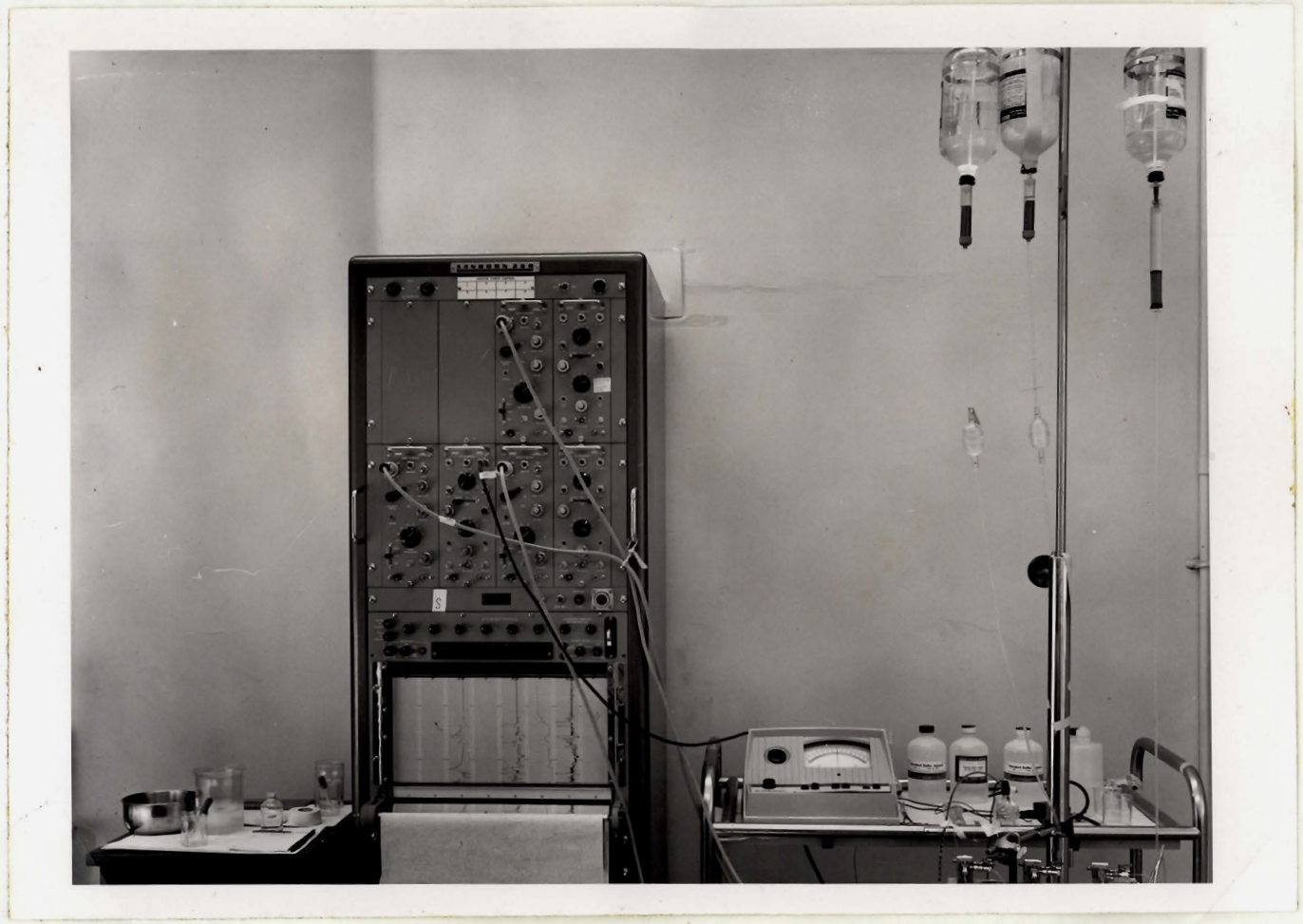

Fig. 5: Complete instrumentation for the described gastroesophageal pH and pressure studies. The multichannel (Sanborn 350) recorder, pH meter, three transducers, buffers and electrodes are all visible.

IV Recording of pH Values

The recording of pH values from the Beckman pH meter was performed using a d.c. amplifier, a D'arsonval-type galvanometer and a direct-writing stylus (fig. 6).

The pH electrode is standardized against two buffer solutions of known pH; usually buffer solutions of 1.0 and 7.0 pH units are employed. With the pH system thus standardized, the potentiometric signal is fed across a 1000 ohm resistor and into a Sanborn d.c. amplifier. With the attenuator of the d.c. amplifier set at X1, the sensitivity control is set so that a 1.0 m.v. calibration signal produces a stylus deflection of 1.4 cm. A change of one pH unit then deflects the stylus 0.5 cm. With the position control set at the lower edge of the channel, there will be a spread of 0 - 10 pH units across the recording paper.

V Modifications in Apparatus and Recording of Data

(1) Improved Accuracy in the Detection of the High Pressure Zone:

Open-ended, water-filled catheters were originally chosen for monitoring esophageal pressures because this technique had been so extensively employed previously with excellent results and because of the many technical difficulties encountered in using balloons. Code and Schlegel had used open-ended systems in their originalwork

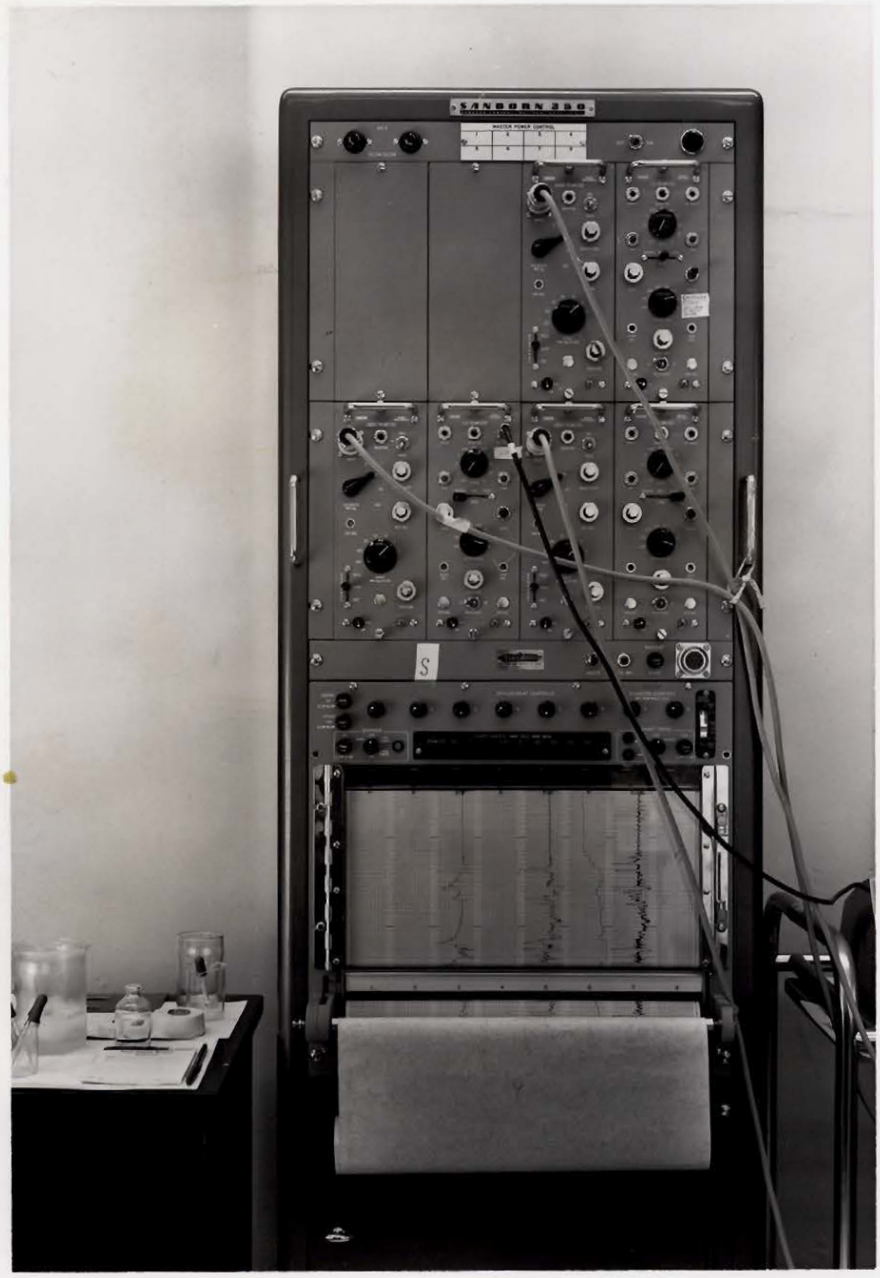

Fig. 6: The multichannel recorder (Sanborn 350) which is used for recording results.

on the high pressure zone and Hill had found the technique dependable as a means of locating the esophageal hiatus. However, as reported by others, and as was soon learned, intra-esophageal pressure tracings were not always reproducible. The pressure inversion point was usually evident and continued to serve as an accurate method of locating the level of the diaphragmatic esophageal hiatus. The high pressure zone, however, was not often present. At first its presence appeared to be significantly related to the presence of a competent sphincter. However, it was then discovered that its presence or absence was not dependably duplicated on a repeat determination. This was finally explained in a rather simple manner. In order to activate a pressure transducer, there must be a certain minimal displaceable volume of fluid. However, the esophagus has only a potential lumen and perhaps the necessary minimal displaceable volume of fluid is not always present. The high pressure zone with its apparent sphincteric action probably squeezes out what little fluid would normally be present in the esophageal lumen and, thus, very often there will not be enough fluid present to activate the transducer. The high pressure zone is then evident at one time and manometrically not demonstrable just a few minutes later.

Others have reported the more accurate and reproducible demonstration of the high pressure zone by means of tiny balloons at the ends of the catheters. With balloons, a minimal displaceable volume is always present for activation of the transducer. However,

the balloon occupies a much greater volume and may stimulate the esophageal musculature. Quite possibly, more than normal resting intra-esophageal muscle tone is being measured. The balloon probably stimulates the esophageal musculature to respond with greather than normal muscular contraction. Other difficulties with esophageal balloons include the manufacture and attachment of these tiny devices, the complete filling of the hydraulic system, including elimination of air bubbles, and maintenance of a filled system with a constant base-line pressure and volume.

The chief objection to the use of a balloon rather than an open-ended catheter for these esophageal pH studies is a theoretical one. With a balloon adjacent to the electrode, the head of the sensing device is quite large. As it is withdrawn from the stomach up through the gastro-esophageal sphincter, it may allow significant amounts of acid to flow into the esophagus behind the balloon.

The acquisition of an 8-channel Sanborn recording machine in February, 1962, made it possible to investigate the use of methods other than those depending on balloons for accurately detailing the presence of the high pressure zone. Two additional open-ended catheters were placed at 4 centimeters and 8 centimeters, respectively, above the pH electrode and the first pressure catheter tip. The chances of detecting the high pressure zone were therefore theoretically considerably increased without the inherent disadvantages of the balloon system. In addition, the staged pressure-

monitoring catheters could be employed for motility studies of the esophagus, should this ever be desired.

(2) Inclusion of Esophageal Motility Studies:

A pneumotachogram is now included to help differentiate peristaltic pressure changes from pressure variations caused by respiratory movements. An elastic cylindrical bellow is placed around either the patient's chest at the nipple line or the abdomen below the costal margin. Pressure changes are recorded using a sensitive transducer, d.c. amplifier and a direct-writing D'Arsenval galvanometer.

(3) Simultaneous Electrocardiography:

To aid in the differential diagnosis of chest pain, simultaneous esophageal pH and electrocardiographic recordings were obtained in several patients. ECGs were taken using only the left arm and leg and the right arm electrodes, because the patient-ground electrode was found to interfere with pH recording.

PROCEDURE

I The Development and Description of a Standard Test for Detection of Gastroesophageal Reflux

(1) The Multiphased esophageal pH Test for Reflux:

The first procedure used was simple determination of pH in the stomach and esophagus. With the patient sitting, the data-gathering nasogastric device was passed into the stomach via the nasogastric route. Care was taken not to induce gagging or vomiting since this could cause regurgitation of acid into the esophagus of a normal person and thereby cause completely misleading esophageal pH readings. A minimal amount of ice chips was used to aid the passing of the nasogastric device because the accurate functioning of the pH meter is dependent on the pre-selected temperature range setting. An arbitrary setting of 35°C. was employed in all tests. No premedications were given and no anaesthetic spray was used in the nasopharynx. After checking the pressure recording for a gastric-type tracing, indicating that the nasogastric device had reached the stomach, the patient was placed in the supine position. The transducers were usually set at the level of the posterior axillary line close to the actual level of the esophagus in the mediastinum. The location of the pH electrode in the stomach was again confirmed from pressure and pH readings and simultaneous recordings of pH and pressure were started. The distance of the tip of the electrode from the nares was marked at the bottom of the portion of the simultaneous

recording chart taken from that level. The data-gathering naso-gastric device was then withdrawn approximately 1 centimeter every 20 seconds, and the distance of the tip of the electrode from the nares was noted under the appropriate part of the simultaneous pressure and pH recording at every 1-centimeter change in level of the electrode.

Cinefluoroscopic studies confirmed the presence of the pH electrode in each of the three areas which could be distinguished from the pressure studies. The electrode was seen in the vestibule during the high pressure zone recording and in the ampulla after passing the pressure inversion point.

This technique was first used in a group of patients who met the criteria of normal. A normal patient was arbitrarily designated as one admitted to the hospital for a disease unrelated to the gastrointestinal tract and in whom functional enquiry concerning the gastrointestinal tract revealed normal findings.

The technique was then employed in several patients with radiologically demonstrated hiatus hernia. The only occasional finding of a low esophageal pH in cases where this was expected raised doubts about the adequacy of the procedure. Two serious objections to the procedure as it then existed were considered:

(1) If the stomach happened to be empty at the time of examination, even if the esophagogastric junction was incompetent to such an extent that minimal resistance to backflow occurred, it would

be quite possible for the terminal esophagus to show normal pH values simply because there was insufficient fluid to flow back into the esophagus.

To overcome this objection, i.e., the possibility of insufficient fluid for gastroesophageal reflux to occur, several steps were evaluated. First, histamine chloride was used to stimulate acid gastric secretion, but a case of achlorhydria demonstrated the inadequacy of this step if the test was to be strictly for gastroesophageal reflux. It was finally decided that the most certain way to insure the presence of gastric fluid at the time reflux could occur was to add 200 to 300 cc 0.1 N.HCl to the stomach through the monitoring tubes. By introducing the acid through the monitoring tubes, the esophageal pH was not disturbed. The monitoring catheter was then flushed with water so that no acid from it could flow from it over the pH electrode. If acid did flow over the pH electrode as it was drawn into the esophagus, this would give false positive evidence of an acid esophagus.

Next, it had to be proven that 200 to 300 cc of 0.1 N.HCl remained in the stomach for an adequate period of time. Fluoroscopic studies using acidified $BaSO_4$ demonstrated that 200 to 300 cc volume of acid medium was retained in the stomach for at least 20 minutes.

(2) The second objection to the procedure was related to the fact that patients with hiatus hernia and esophagitis or pregnant females complaining of heartburn during the third trimester (and

these groups include the majority of cases of reflux esophagitis) generally only complain of symptoms at certain times such as during bending over, lying in bed or after heavy meals. Quite possibly these patients would have a normal pH change at the esophagogastric junction and lower esophagus under ordinary conditions. A pH test done during a normal period would, of course, be normal. But, under conditions which cause symptoms, they would experience gastroesophageal reflux and an esophageal pH test at this time would show acid conditions in the esophagus.

To produce the circumstances most likely to result in a breach of the obviously impaired gastroesophageal barrier mechanism and to produce reflux of acid into the esophagus, several additions were made to the procedure:

(a) A special corset was prepared. Many women experience their symptoms of esophagitis while wearing a corset and this, therefore, seemed to offer a possible technique for more readily causing reflux in the hiatus hernia patient. The corset consisted of an abdominal binder which contained a balloon in the part fitting over the rectus muscles. The balloon could be inflated to specific pressures, using a monometer for control.

(b) Manoeuvres which commonly result in gastroesophageal reflux were also added to the test in an attempt to

breach the weakened barrier with a well-defined effort that would not exceed the limits of a normal mechanism. With the pH electrode about 5 or 10 centimeters above the esophagogastric junction, the patient was asked to roll from the supine position onto the right side. After about 10 to 15 seconds, the patient returned to the supine position. This was repeated several times. The same procedure was carried out again, only the roll was changed to the left side. Then the patient was asked to raise his ankles off the bed with the knees straight in order to increase intra-abdominal pressure. One or more Valsalva manoeuvres were included. Finally, the patient was asked to stand and to touch his toes, bend at the waist or even stoop down. A head-down position was included after the acquisition of an electric bed. If the pH meter indicated reflux at any point in the series of reflux-inducing manoeuvres, the test was stopped after the esophageal pH had been given some time to return to normal.

In this form, the one used in testing the majority of patients, the procedure was thus carried out in several steps:

Phase (1): With the patient in the supine position, the data-gathering tip of the nasogastric device was withdrawn

over the esophagogastric junction and up the esophagus. This step was retained to provide information on the actual pH conditions in the stomach and esophagus. It would detect those cases of achlorhydria, casting doubt on the chance of symptoms being secondary to reflux esophagitis. It would also demonstrate the presence of acid conditions in the esophagus which existed as such before the addition of acid to the stomach for the second step in the test.

Phase (2): The data-gathering tip of the nasogastric device was again passed into the stomach and 200 cc of 0.1 N.HCl added as previously described. The nasogastric device was then withdrawn as described and the pH and pressure studies simultaneously recorded with the presence of intragastric acid which could, when afforded the opportunity, reflux into the esophagus.

Phase (3): The data-gathering tip of the apparatus was stationed at an arbitrary level in the esophagus 5 to 10 centimeters above the pressure inversion point and the patient was put through reflux-inducing manoeuvres. The pressure corset was occasionally inflated to various levels in order to subject the esophagogastric barrier mechanism to every conceivable realistic force likely to make it incompetent.

Channel

(1) pH

(2) Low Catheter

(3) Middle Catheter

(4) High Catheter

(5) Respirations

(6) Distance from Nares

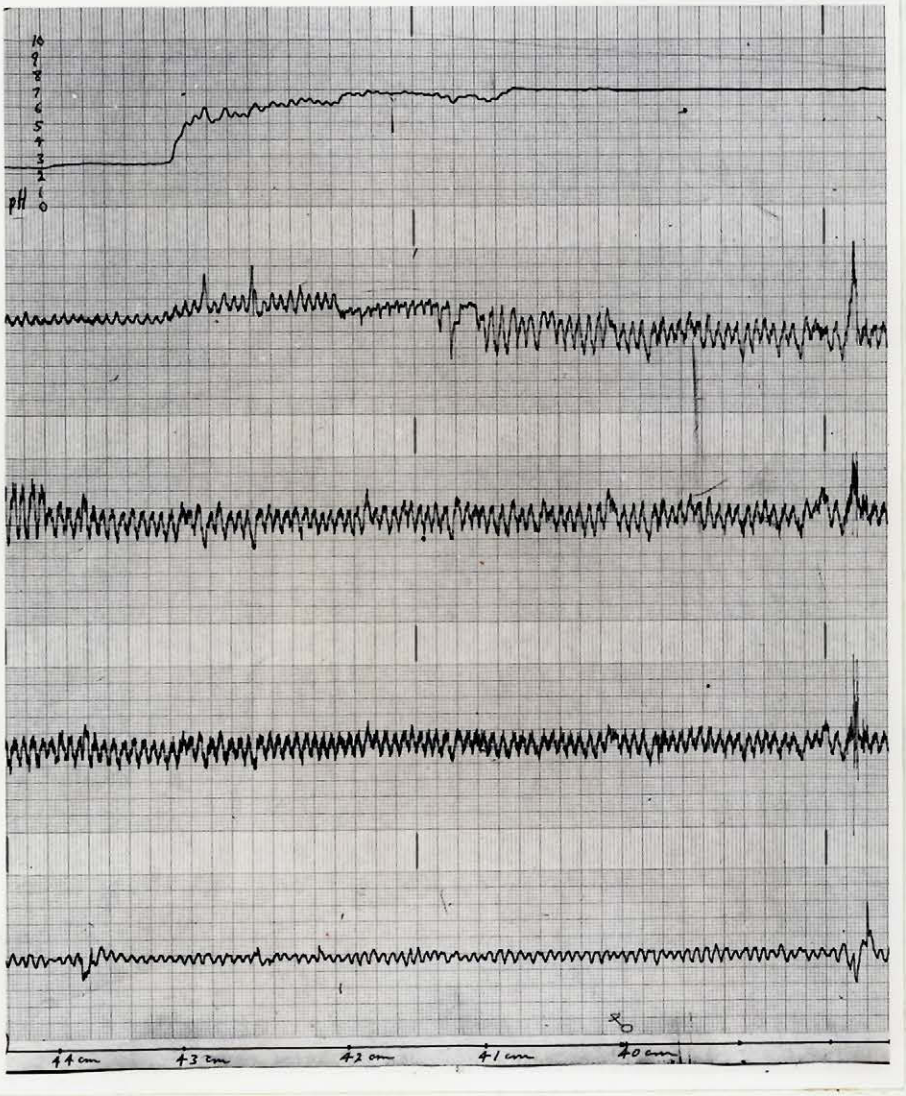

Fig. 7: A tracing showing the usual change in pH at the gastro-esophageal junction as the pH electrode is drawn over the area. Channel (1) shows the pH change at the level of the high pressure zone seen in channel (2), and compare this with Fig. 4. This change is seen to occur at 44 centimeters from the nose. Such a tracing is seen in phases (1) and (2) of the multiphase esophageal pH test when performed in normal subjects.

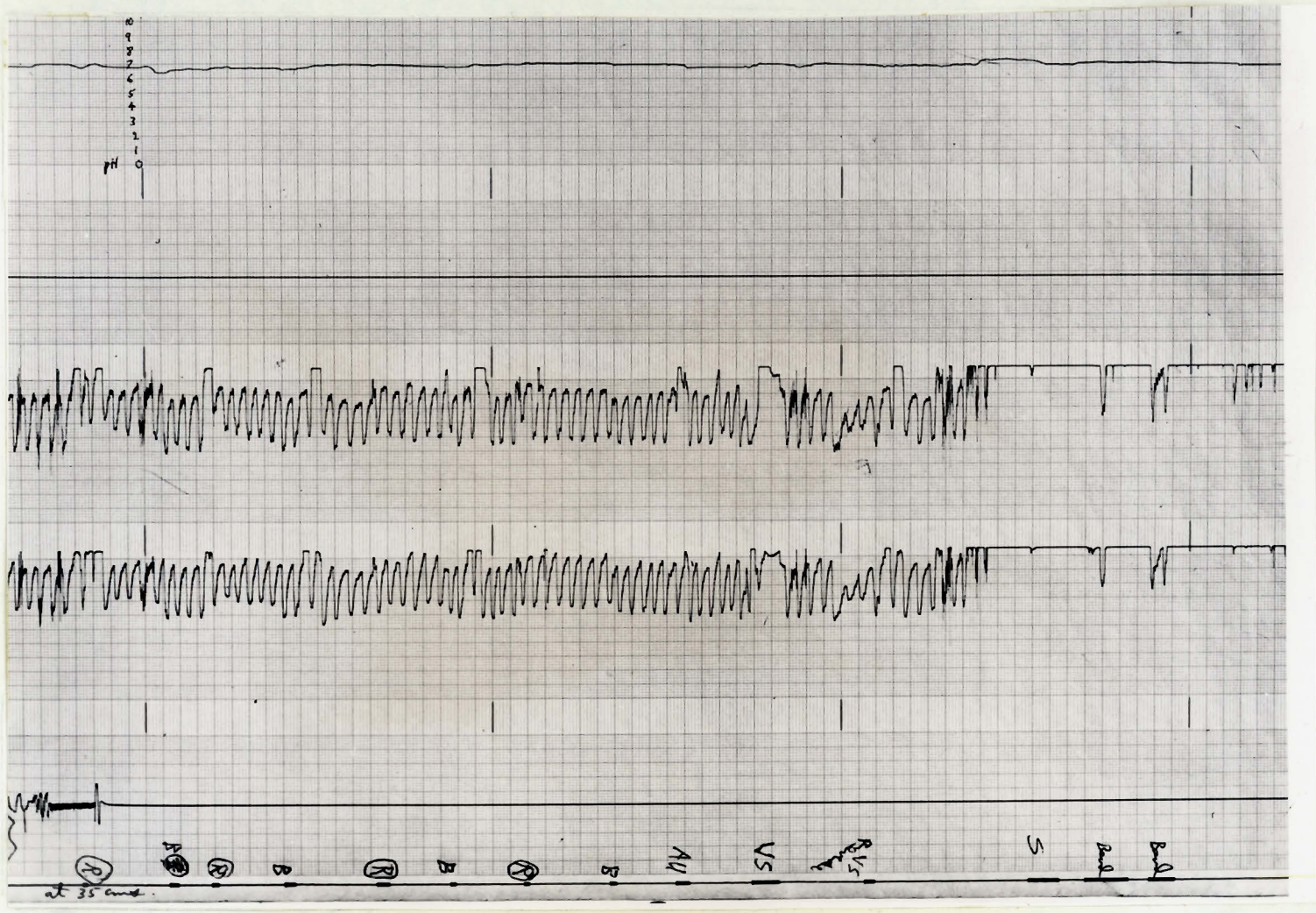

Fig. 8: Phase (3) of the Esophageal pH Test

The pH electrode is stationed at 35 centimeters (6 centimeters above the gastroesophageal junction. The patient performs reflux-producing manoeuvres which are marked on the bottom line with the marker stylus. The type of manoeuvre is indicated by abbreviations. The pH tracing is in channel (1). This tracing is from a normal subject and shows that no reflux of acid from the stomach has occurred during the test.

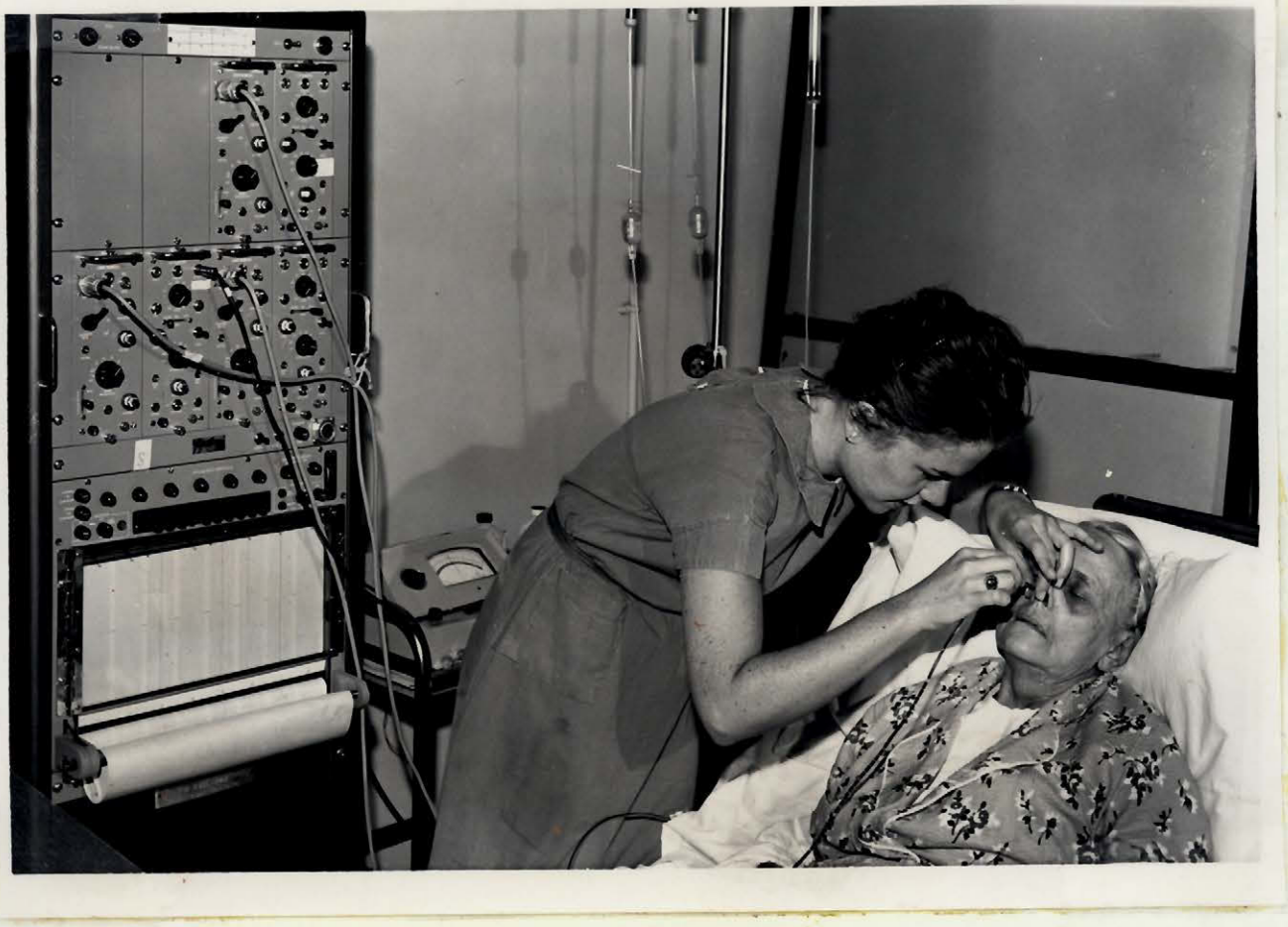

Fig. 9: The nasogastric device is being passed into the patient's stomach as described. The recorder and pH meter are visible behind Miss FitzPatrick.

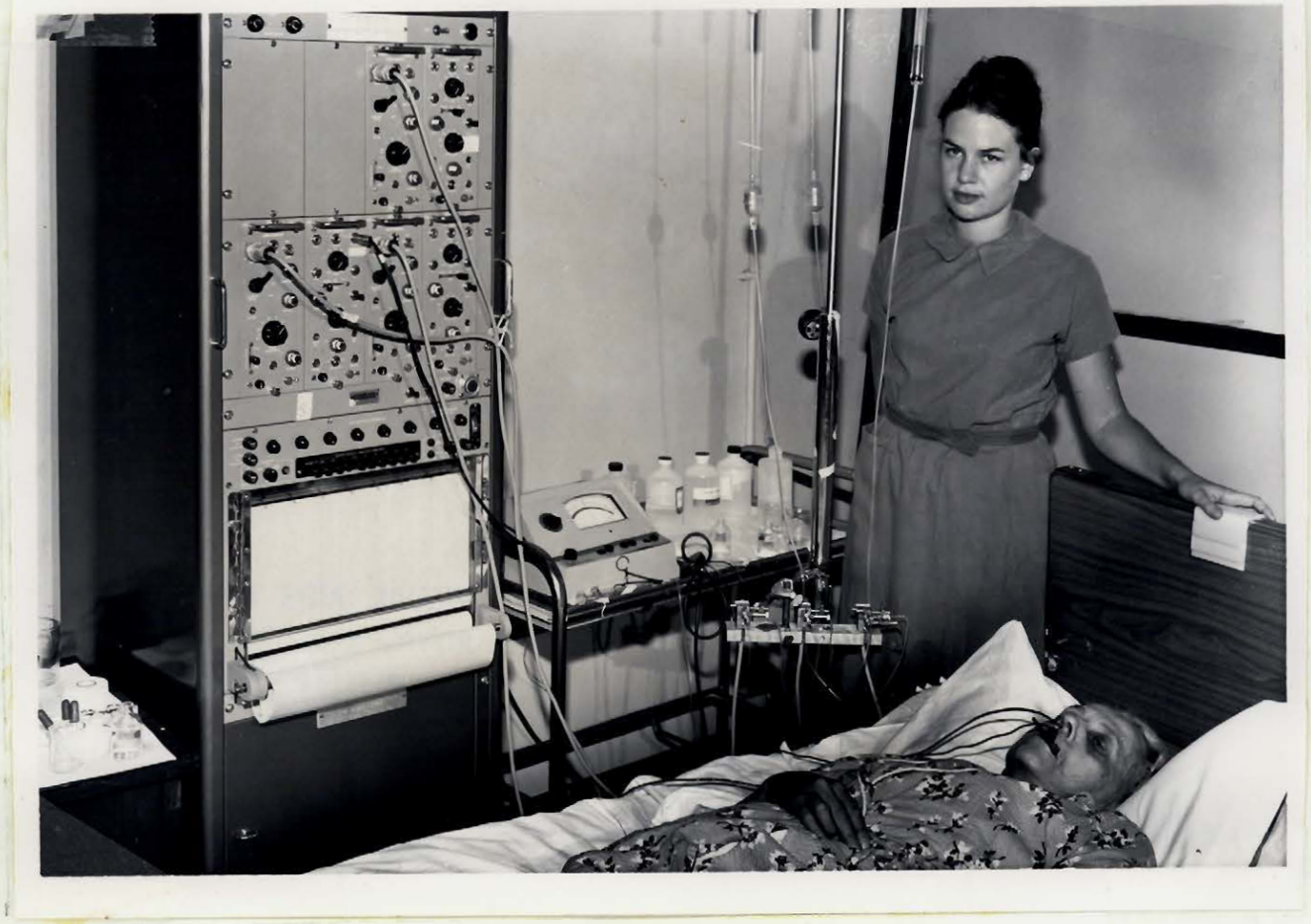

Fig. 10: The nasogastric data-gathering tip is now in the stomach and the reference electrode is under the tongue. The patient is supine and ready for the test.

Phase (1) was for the detection of pH conditions in the stomach and esophagus.

Phase (2) was to record pH conditions in the terminal esophagus with gastric acid (which could, during an instant of barrier break-down, gush into the esophagus) known to be present.

Phase (3) was intended to demonstrate the ability of the gastroesophageal barrier mechanism to withstand a deliberate and objectively defined attempt to breach its competency.

II Selection of Clinical Material

The groups of patients studied were:

(a) Normal patients.

(b) Patients with complaints suggestive of a diagnosis of hiatus hernia and/or reflux esophagitis.

(c) Patients who had a hiatus hernia repair and who pre-operatively showed objective evidence of hiatus hernia and gastroesophageal reflux. Among this group were patients who had anterior and posterior transabdominal repairs and Allison repairs.

(d) Previous Heller's procedure complicated by reflux esophagitis.

(e) Angina-like chest pain with or without hiatus hernia radiologically demonstrated.

(f) Women in the third trimester of pregnancy who complained of heartburn.

III The Theoretical Advantages of Including Motility Studies with the Esophageal pH Test

Consideration of the expected pH recording while the gastric pouch of a hiatus hernia protrudes above the diaphragm suggests an advantage in integrating esophageal motility studies with the multiphased esophageal pH test. The gastric pouch protruding above the diaphragm will, of course, show acid pH values. The pH test must be done with the electrode in the esophagus above this gastric pouch or a false positive test will be obtained. During these studies, the electrode was placed higher in the esophagus if the hernia was larger than the usual small variety. However, greater accuracy may well be obtained by combining the esophageal motility test with the multiphased esophageal pH test. Peristaltic waves are found in the esophagus but not in the stomach during motility studies. If the peristaltic waves ceased above the pressure inversion point, an acid pH should be expected in the zone between the pressure inversion point below and the point at which peristaltic waves stopped above, since this represents stomach which is herniated. An acid pH at a level above the point where the peristaltic waves ended would indicate actual esophageal

acidity.

With the acquisition of a large multichannel recorder and the use of staged pressure catheters to increase the accuracy with which the high pressure zone is located, the technical set-up for the performance of simultaneous pH and esophageal motility studies was complete. It would therefore seem very more definitive to use both tests together.

IV Simultaneous Esophageal Acidity and ECG Studies to Aid in the Differential Diagnosis of Chest Pain

In using the multiphased esophageal pH test on patients with chest pain of angina-like quality and hiatus hernia, the finding of acid reflux and concomitant pain was very suggestive that the complaints should be ascribed to esophagitis rather than to myocardial ischemia. However, it was felt that a simultaneous ECG showing no ischemic change would be diagnostic. Therefore, in this series of patients, simultaneous ECGs were done with the multiphased esophageal pH test.

RESULTS

TABLE I. GASTRIC AND ESOPHAGEAL PRESSURE STUDIES IN NORMAL SUBJECTS

Ptn.	Determination	Mean Gastric Pressure (cm. H_2O) Approximate Values	Gastric Amplitude Change (cm. H_2O)	PIP	Intrathoracic Pressure (cm. H_2O)	Intrathoracic Amplitude Change (cm. H_2O)	HPZ Length cm.	pH Change cm.
I.Z.	1	∠10	14	41	-10	25	2	46
	2	∠10	20	41	-15	40	1	42
D.Y.	1	∠10	15	41	-15	15	3	44
	2	∠10	10	42	-15	20	2	44
T.S.	1	∠10	15	41	-5	60	3	--
	2	∠10	15	41	-10	35	2	--
P.R.	1	∠10	10	41	-5	25	2	42
	2	∠10	10	41	-10	25	2	43
	3	∠10	10	41	-10	25	3	42
A.M.	1	∠10	12	44	-15	25	3	--
	2	∠10	15	44	-15	25	4	47

TABLE I CONTINUED

Ptn.	Determination	Mean Gastric Pressure (cm. H_2O) Approximate Values	Gastric Amplitude Change (cm. H_2O)	PIP	Intrathoracic Pressure (cm. H_2O)	Intrathoracic Amplitude Change (cm. H_2O)	HPZ Length cm.	pH Change cm.
W.K.	1	≠10	12	43	-10	25	3	47
J.K.	1	≠10	10	47	-10	20	0	50
	2	≠10	10	47	-15	25	2	50
	3	≠10	10	48	-10	20	3	50
K.G.	1	≠10	12	40	-10	25	3	42
	2	≠10	12	40	-10	25	3	41
E.M.	1	≠10	12	44	-10	20	1	46
	2	≠10	10	44	-10	20	0	--
	3	≠10	12	43	-5	20	0	45
	4	≠10	10	43	-5	15	0	--
P.B.	1	≠10	7	43	-20	20	2	46
	2	≠10	7	43	-20	25	2	46

I Gastric and Esophageal Pressure Studies in Ten Normal Subjects

1. Gastric pressure was in the low positive range in all individuals tested. The mean pressure in ten subjects was about 10 centimeters of water. The exact pressure was not noted in all cases since the change in the shape of the curve, and not the exact pressures, constituted the purpose of the pressure determinations.

2. Low amplitude pressure changes occurred in the stomach and these coincided with respiratory movements as demonstrated in the pneumotachogram. A rise in pressure always occurred with inspiration and a pressure decrease with expiration. The amplitude of these changes in ten patients was an average of 12 centimeters of water.

3. There was a sharp change from slightly positive mean pressure to definitely negative mean pressure as the tip of the nasogastric device was slowly withdrawn. Combined cineradiographic and manometric determinations in one patient confirmed the reports of others that this change occurred at the level of the diaphragmatic hiatus. This change in mean pressure is generally a clear feature of the pressure curve. It was called the pressure inversion point (P.I.P.) by Hill and the term was retained in this study. The P.I.P. was evident in all of 23 tests in the ten normal subjects. On repeat determinations in the same patient it was

within 1 centimeter of the other determinations in all instances. As seen in table I, as many as four determinations were done in some patients. Actually, some of the normal patients not included in this sampling of ten patients had up to six determinations with a 1-centimeter variation.

4. Intrathoracic esophageal pressure was slightly negative in all individuals tested. The mean pressure in 10 subjects was -11 centimeters of water. The exact pressure was not noted in all cases because the change in the shape of the curve was used as a determinant of electrode location and actual pressures therefore had no significance.

5. The amplitude of the pressure changes in the intrathoracic esophagus was much greater than in the stomach. The average amplitude of the changes in ten subjects was 25 centimeters of water. The pressure changes coincided with respiratory movements but were opposite in phase from the gastric pressure variations; i.e., inspiration produced a pressure fall and expiration produced a pressure rise.

6. The pressure inversion point in normal subjects was always preceded by a 2 to 3-centimeter zone of higher mean pressure (see figure 4). The amplitude of the pressure variations in this portion of esophagus was usually greater than that in the gastric portion of the tracing and less than that of the intrathoracic

esophageal tracing. Amyl nitrate was given to one patient while the monitoring catheter was in the high pressure zone and the amplitude was then considerably increased. On one patient combined cineradiographic and manometric studies were performed and in these the high pressure tracing was encountered when the pressure catheter was in the radiologically demonstrated esophageal vestibule.

II Gastric and Esophageal pH Studies in Normal Subjects

1. Ten randomly selected normal patients' pH tracings were examined. These patients had no upper gastrointestinal symptoms and were admitted to hospital for complaints not related to the gastrointestinal tract. They were selected at random with regard to age groups.

2. Simultaneous pH and pressure determinations as the tip of the nasogastric device was withdrawn from the stomach into the esophagus showed a change from highly acid gastric values to less acid esophageal values in the high pressure zone of all normal subjects.

The upper and lower limits of gastric pH encountered were 2.8 and 1.0, and the average value was 1.98.

The upper and lower limits of pH for the terminal 5 centimeters of esophagus were 7.2 and 3.0, and the average was 5.78.

TABLE II. GASTROESOPHAGEAL pH STUDIES IN NORMAL INDIVIDUALS

Ptn.	Determination	Gastric pH	pH in Terminal 5 cm. Esophagus	pH in Next 5 cm. Esophagus
L.D.	2	1.8	1.8 - 5.2	5.2 - 6.0
G.M.	2	2.0	2.0 - 7.2	7.2 - 7.2
L.F.	1	2.0	2.2 - 6.8	6.8 - 6.8
M.M.	3	1.8	1.8 - 3.0	3.0 - 6.0
P.B.	3	2.0	2.0 - 5.0	5.0 - 6.0
D.Y.	3	1.8	1.8 - 6.6	6.6 - 6.8
P.R.	3	2.4	2.4 - 7.0	7.0 - 7.2
W.K.	1	2.2	2.2 - 6.5	6.5 - 6.5
J.K.	3	2.8	2.8 - 5.0	5.0 - 5.5
E.M.	2	1.0	1.0 - 5.5	5.5 - 5.5

The terminal 5 centimeters of esophagus was that portion of the tracing beginning at the high pressure zone and extending 5 centimeters upward.

The average rise in pH in the terminal esophagus as the electrode was moved out of the stomach and into the esophagus was 3.78 pH units. The upper and lower limits were 5.2 and 1.2 pH units.

The average pH difference between the average value of the terminal 5 centimeters of esophagus and the next 5 centimeters of esophagus was 0.57 pH units.

3. After 200 to 300 cc of 0.1 N.HCl were added to the stomach and the pressure-monitoring catheters were then withdrawn from the stomach into the esophagus, results similar to those described under the previous section (simple withdrawal of the pH electrode from stomach to esophagus) were obtained. Under these conditions, the stomach pH closely approximated that of the 0.1 N.HCl. Essentially, there was always a change from low gastric pH values to relatively higher esophageal pH values, the change beginning at the high pressure zone.

4. Performance of reflux-inducing manoeuvres (with the pH electrode stationed approximately 5 centimeters above the esophagogastric junction) in normal subjects never resulted in reflux. Reflux was judged to have occurred when there was a drop in pH to near gastric

levels during any portion of the period during which the electrode was in the test position. (In two young volunteer subjects, the pH dropped during this period and subsequent barium swallows demonstrated suspected hiatus hernias in both individuals.) In none of the ten normal subjects was there shown a pH change of any sort during the test period. There was no belching accompanied by a pH change which could be confused with actual reflux.

III Gastric and Esophageal Pressure Studies in Patients with Hiatus Hernia

1. Gastric pressure patterns were unchanged.

2. While the esophageal pressure far above the pressure inversion point was generally unchanged, it was often altered in the lowest portion. The mean pressure was often quite elevated, nearly to gastric levels or even to that of the high pressure zone. In these cases, identification of the level of the diaphragmatic hiatus rests more with the amplitude changes than with the change in mean pressure. However, the pressure inversion point was often evident by the usual change in mean pressure to lower values.

Swallow waves were often not evident in the first few centimeters of viscus above the hiatus.

3. The high pressure zone was often not evident. This area was more frequently evident after the adoption of two additional

staged pressure-monitoring catheters. In some cases it seemed to extend into the area above the hiatus, the hiatus again being identified by the amplitude changes.

IV Gastric and Esophageal pH Studies in Patients with Hiatus Hernia

Three basic pH patterns were found in patients with hiatus hernia:

1. A normal pattern, with a change from acid gastric readings to higher esophageal levels at the high pressure zone.
2. A long duration acidity pattern.
3. A short duration acidity pattern.

1. The normal pattern was seen in three patients.

2. The long duration acidity pattern was found in fifteen patients. Ten of these patients had no change in pH as the electrode was withdrawn from the stomach into the esophagus; the esophageal pH was noted to closely approximate that of the stomach. Three of these ten patients did not have a stomach pH in the high acid range but, after this was ensured by the addition of acid to the stomach, simple withdrawal of the pH electrode from the stomach into the esophagus showed the esophageal pH to be in the same acid range as the stomach contents. In 5 patients there was a change from low gastric to

higher esophageal values on simple withdrawal of the electrode from the stomach. The change was not quite normal because the decrease in acidity came after the high pressure zone rather than simultaneously with it. After the addition of 200 to 300 cc of 0.1 N.HCl to the stomach and repeat withdrawal of the electrode, the pH of the esophagus was found to be consistently acid at pH levels closely approximating those of the stomach.

The common feature of the above patterns was the tendency of the esophagus to remain acid for the duration of the test once acid had succeeded in entering it. The long duration of acid conditions in the esophagus in this group was a reproducible event; similar pH tracings could be obtained on subsequent examinations. In all of these cases the pH of the esophagus was acid, not only in the terminal 5 centimeters but even up to 15 centimeters above the esophagogastric junction. During no part of the test did the esophageal pH rise to normal levels.

3. The short duration acidity pattern was found in 34 patients. These patients usually showed a normal pH change on simple withdrawal of the pH electrode from the stomach into the esophagus. After the addition of acid to the stomach, withdrawal of the electrode again showed the normal change from acid gastric to higher esophageal values. However, with the pH electrode at approximately 5 centimeters above the esophagogastric junction, reflux-inducing

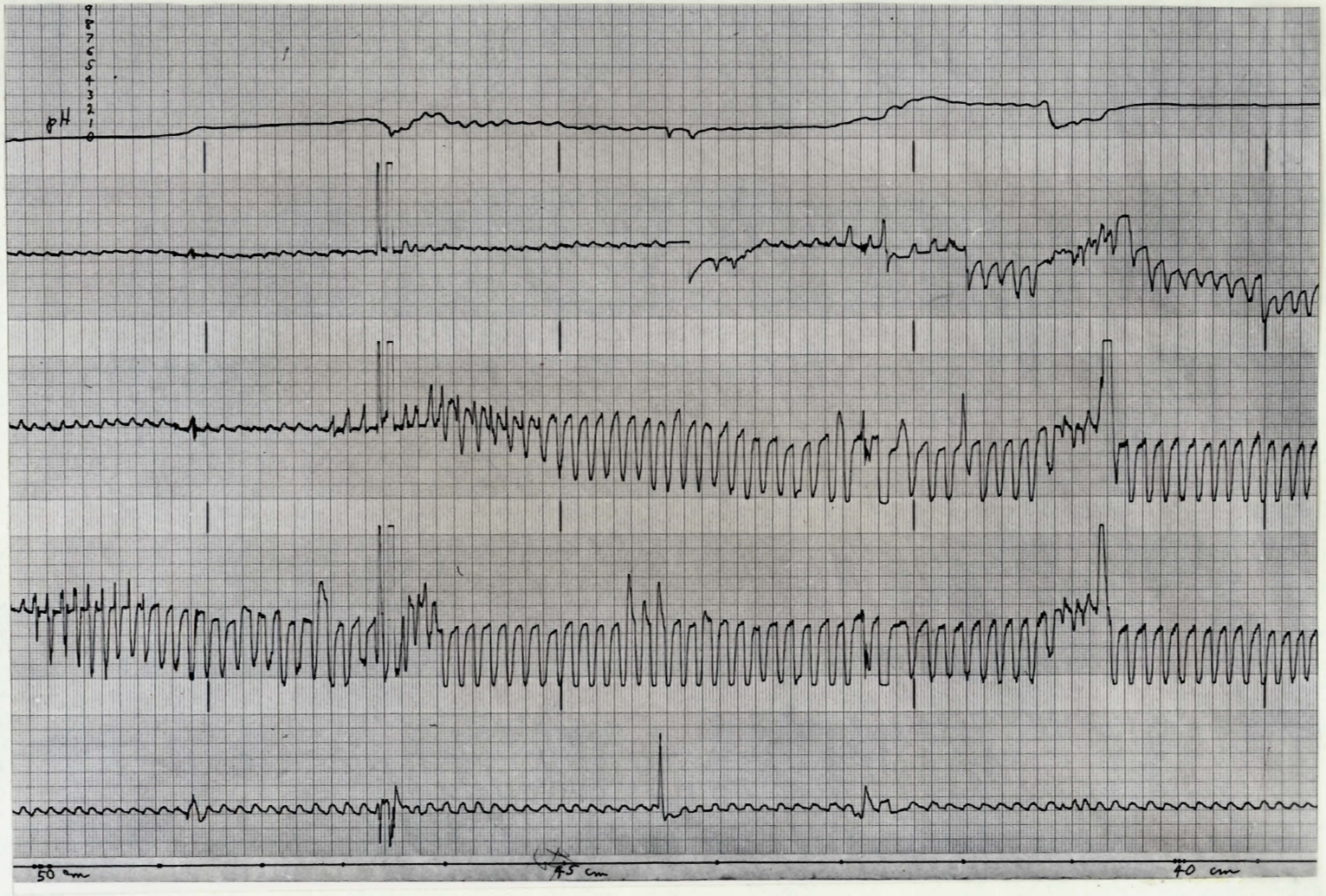

Fig. 11: The Long Duration Acidity Pattern

At 42 centimeters from the nares, the long catheter passes into the intrathoracic esophagus and the esophageal pH remains low at close to gastric values. The same result occurred in this patient (J.M.) when the test was repeated two months later. A normal tracing was obtained after hernia repair.

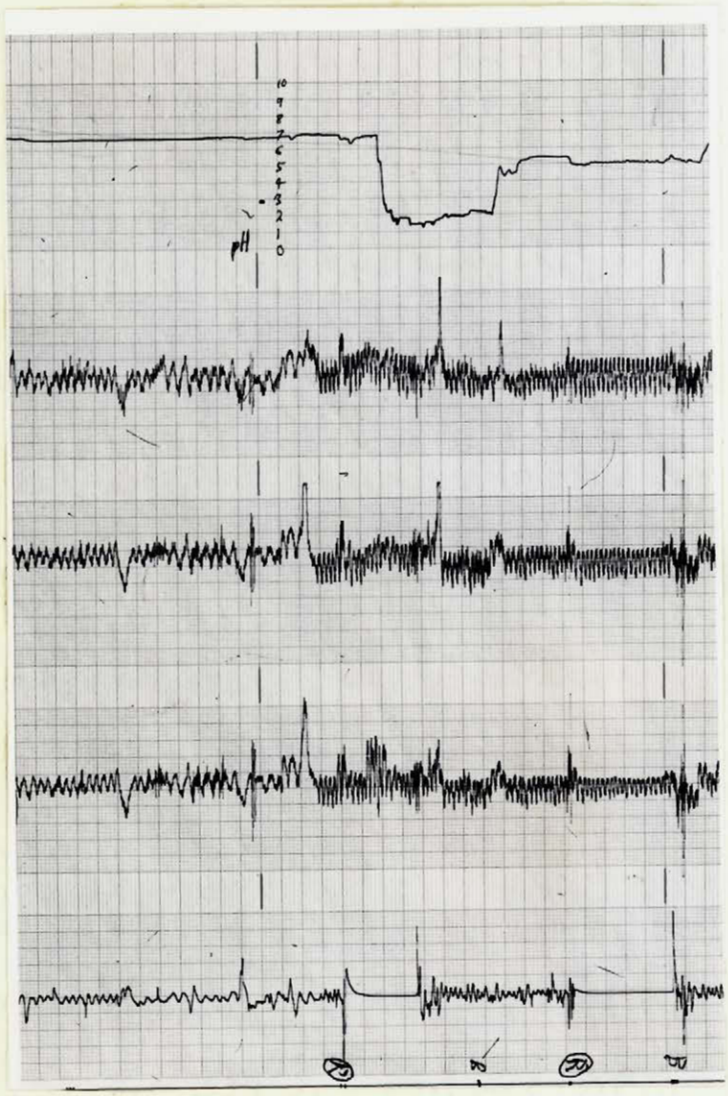

Fig. 12: The Short Duration Acidity Pattern

The first two phases of the esophageal pH test showed a change of pH from low gastric to higher esophageal values. In the third phase, with the electrode about 6 centimeters above the gastroesophageal junction and appropriate reflux-inducing manoeuvres being performed, the pH suddenly and for a short time drops to acid (gastric) values indicating reflux. The pH channel (1) has dropped from 6.8 to 2.5 just after the patient rolled on her right side (bottom line).

manoeuvres produced a sharp change from normal esophageal pH to low acid gastric levels. The pH then rapidly returned to normal esophageal values. The acid condition was a very short-lived event in this group--in sharp contrast with the long duration of acidity in the previously described group. Again, the results were reproducible. On subsequent examinations the same reflux pattern was obtained.

V Gastric and Esophageal pH and Pressure Studies Following Hiatus Hernia Repair

Gastric and esophageal pressure tracings were of the normal variety in all patients following surgical repair of the hiatus hernia.

Gastric and esophageal pH tracings were made in 11 patients before and after hiatus hernia repair. The post-operative pH tracings were normal in 10 patients, all of whom had acid reflux preoperatively. No reflux was evident even with the reflux-inducing manoeuvres. The change from acid gastric pH values to relatively higher esophageal ones was readily evident (see fig.13) and, in most cases, the change was somewhat sharper than in normal subjects. The number of pH units' change at the esophagogastric junction was 5.0 compared with 3.7 in controls, and the change took place over a shorter zone.

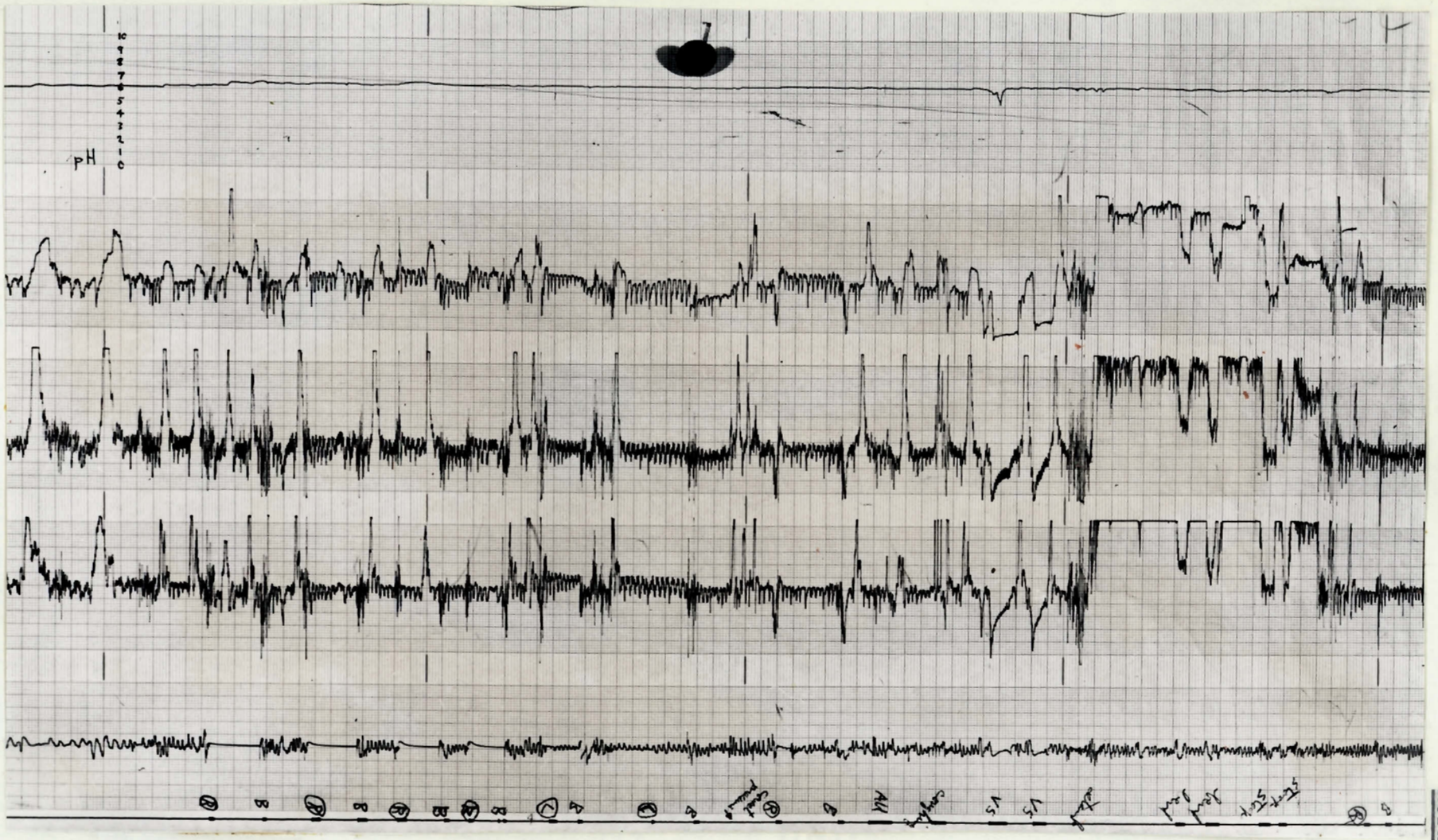

Fig. 13: Phase Three of the Multiphased Esophageal pH Test after Hiatus Hernia Repair

The top channel shows the esophageal pH and the lowest line has the time and abbreviation of the reflux-inducing manoeuvre which was performed. It is readily apparent that 25 separate manoeuvres were not able to bring about a single episode of reflux. This is a totally different situation from the pre-operative recording.

The tracings continued to show reflux in one post-operative patient. In this patient a pre-operative test had been done and it also showed reflux. The reflux was less pronounced postoperatively.

Five patients were repaired by transabdominal approximation of the crura anterior to the esophagus and reconstruction of the esophagogastric angle. None showed persistent reflux.

Two patients were repaired by transabdominal approximation of the crura posterior to the esophagus and reconstruction of the esophagogastric angle. Neither showed persistent reflux.

One patient had a transabdominal hernia repair but the operative note did not state how the crura had been reapproximated. This patient had persistent reflux. Three patients were repaired by the classical Allison technique. None showed persistent reflux.

VI Gastric and Esophageal pH and Pressure Studies Following a Heller Procedure

Two patients were studied following Heller procedures.

The first, J.M., had phase one and phase two of the reflux detection test performed on him. These showed acid pH conditions were present in the lower 20 centimeters of esophagus, the pH ranging from 1.0 to 2.0 units.

The gastric and esophageal pressure studies in phase one showed a normal gastric mean pressure, elevated amplitude in the

gastric tracing, a probable high pressure zone 46 centimeters from the nares, a change to thoracic amplitude tracing at 42 centimeters, but no decrease in mean intrathoracic esophageal pressure below the 30-centimeter level.

The gastric and esophageal pressure studies in phase two showed a normal gastric mean pressure, elevated amplitude in the gastric tracing, no high pressure zone, a change to thoracic amplitude tracing at 43 centimeters, but no decrease in mean intrathoracic esophageal pressure at all.

The second patient, .H., also showed acid pH conditions in the esophagus. This, unfortunately, was the only information which could be obtained. The nasogastric device could not be passed through the esophagus beyond the level of the diaphragmatic hiatus and the pressure studies showed only the pressure and amplitude results for the intrathoracic esophagus.

VII Gastric and Esophageal pH and Pressure Studies for Complaints of Heartburn during the Third Trimester of Pregnancy

Three patients were studied. Of these, only one patient tolerated passage of the nasogastric apparatus.

The patient was examined before the development of the second and third phases of the reflux detection test. Simple

withdrawal of the electrode from the stomach into the esophagus was performed twice. Pressure tracings showed a normal mean gastric pressure and changes in amplitude, the high pressure zone was present from 42 to 40 centimeters on both occasions, the pressure inversion point occurred at 40 centimeters both times, and the intrathoracic esophageal tracing showed the usual decrease in mean pressure and more marked amplitude changes.

The pH studies showed a somewhat sluggish rise in the first tracing. The gastric pH was 3.0, there was a transient rise in the high pressure zone to 5.0, and the pH rose to between 5.0 and 7.0 in the lower six centimeters of esophagus. During the second pH determination there was a much earlier and smoother pH shift from a gastric pH of 2.0 to an esophageal pH of 6.0 in the lower esophagus.

VIII The Need for a Multiphased pH Test as Described under "Procedure"

Forty-eight patients had a positive reflux test if all phases of the test are included. Only 5 of all these subjects showed acid conditions in the esophagus on simple withdrawal of the electrode from the stomach into the lower half of the esophagus. By the addition of acid to the stomach and simple withdrawal of the electrode from the stomach into the esophagus, 13 positive tests resulted. The 5 patients with a positive first phase also showed

a positive second phase. Thirty-five patients showed no reflux on the simple withdrawal of phase (1) or with the added acid of phase (2) but did show reflux during certain previously described manoeuvres.

IX Correlation of Gastroesophageal Reflux Indicated by the pH Test with other Means of Objectively Determining Reflux

Forty-eight patients had a positive reflux test.

Twenty-five of the patients with a positive reflux test had a hiatus hernia and reflux on x-ray examination.

Nine of the patients with a positive reflux test had a hiatus hernia on x-ray examination but no radiologically demonstrated reflux. However, 5 of these patients had some other objective evidence of gastroesophageal reflux. In 3 patients the esophageal acid perfusion test showed that their complaints were probably of esophageal origin. In 2, the hiatus hernia was demonstrated at laparotomy, then repaired, and the post-operative pH studies no longer showed reflux. No patients were esophagoscoped and showed reflux. Four patients had a positive reflux test, a hiatus hernia but no reflux on x-ray examination and, because of circumstances, were never exposed to a substantiating test other than x-ray examination. One of the last 4 patients complained strongly of heartburn.

Five of the patients with a positive reflux test had no hiatus hernia or reflux on x-ray examination. All of these 5 patients showed some other objective indication of reflux. One patient had reflux on esophagoscopy. Two patients had esophagitis seen at esophagoscopy and a biopsy in one case revealed esophagitis. Two other patients had hiatus hernias found at operation. One of the two with a hernia found at operation was tested for reflux postoperatively and the pH test was then normal.

Two of the patients had no signs of hiatus hernia on x-ray examination but reflux was demonstrated. This confirmed the finding of reflux with the pH test.

Three patients who had a positive reflux test had no hiatus hernia and no reflux demonstrated on x-ray examination. Unfortunately, these three patients were not available for repeat barium swallows or other tests which might objectively determine the presence or absence of gastroesophageal reflux.

Two patients who had a positive reflux test were achalasia patients who had a Heller procedure performed. X-ray studies confirmed the presence of reflux.

Conversely, there were two patients with a negative pH reflux test who had a hiatus hernia shown by x-ray examination. Neither of these patients had fluoroscopically demonstrated reflux. Reflux was not demonstrated by other means in these patients.

X Use of the Multiphased Esophageal pH Reflux Test and ECG to Determine the Origin of Chest Pain

One patient (F.D.) had chest pain previously treated as angina pectoris and was undergoing more complete investigation prior to a possible cardiac revascularization procedure. Reflux was demonstrated with the multiphased esophageal pH test and a hiatus hernia demonstrated subsequently on x-ray examination. Pain during pH electrode-demonstrated reflux strongly suggested that the chest pain was of esophageal origin. A hiatus hernia repair was later performed but no post-operative evaluation could be carried out. Simultaneous ECGs could not be done with the esophageal pH test because the technical means were not yet available.

A second patient with chest pain of an undifferentiated nature was examined simultaneously with the pH electrode and the ECG. However, electronic difficulties prevented simultaneous recording. This difficulty has now been corrected and the technical capacity for simultaneous testing is now available.

DISCUSSION

I Gastric and Esophageal Pressure Studies in Normal Subjects

The purpose of studying gastric and esophageal pressures in normal individuals was to determine: (1) if predictable and dependable pressure patterns could be located in the esophagus and stomach at various distances from the external nares, (2) if these patterns were typical of certain important anatomical structures, and (3) if these pressure reference points on simultaneously obtained pressure and pH readings at the same level of stomach or esophagus could be used to locate precisely the pH electrode.

First, it is readily seen that there is a very predictable pressure profile in the stomach and lower esophagus. Three distinct pressure zones are generally evident. There is a zone of slightly positive mean pressure with low amplitude waves caused by respiratory movements which is followed by a zone of increased mean pressure with slightly increased amplitude waves and then by a zone of negative mean pressure with sharply increased wave amplitude. The first two zones show an increased pressure on inspiration but the third zone has a decreased pressure on inspiration. The same pressure zones are always found at the same distance from the nares in any one individual.

Simultaneous cineradiographic, pressure and pH studies

of the stomach and esophagus in one individual confirmed the previously reported correlation of various reference points in the pressure profile with definite anatomical landmarks. The zone of slightly positive mean pressure, low amplitude waves and positive pressure rise during inspiration was obtained when the x-ray image intensifier showed the electrode to be in the stomach. The high pressure zone corresponded to the radiologic esophageal vestibule. The pressure inversion point was probably at the level of the diaphragmatic hiatus. However, because the diaphragm is actually dome-shaped and only a silhouette of the highest cross-section of the dome is seen at fluoroscopy, it is difficult to determine just where the electrode is in the plane of the diaphragm through which the hiatal opening is found. It is therefore only a reasonable assumption which locates the pressure inversion point at the level of the diaphragmatic hiatus. The zone of mean negative pressure and high amplitude waves is seen radiologically to be located definitely in the intrathoracic esophagus. The lowest portion of the zone of negative pressure and high amplitude waves corresponds to the radiologically demonstrated ampulla.

It is therefore seen that there is a definite and reproducible pressure profile in the stomach and esophagus in normal individuals. Furthermore, clearly defined reference points on the pressure profile correspond to definite anatomical structures. By

knowing the distance from the external nares to a pre-selected reference point and the distance from the external nares to the tip of the pH electrode, the location of the pH referable to the various anatomical structures is readily obtained. This, of course, merely substantiates the reported findings of others.

The accuracy of detecting the high pressure zone in normal subjects and those described in other sections is greatly increased by the utilization of staged pressure monitoring catheters. Three open-ended catheters, 5 centimeters apart, were finally employed as described in the section on modification of apparatus. It is impossible to conclude from these studies whether this apparent increased accuracy in the detection of the high pressure zone is due to the possibility of insufficient fluid to activate the pressure transducer, in a sphincteric area with no actual lumen, or to the possibility that the high pressure zone is not always maintained at the same pressure but is characterized by a rhythmicity or variation in its pressure.

The pressure inversion point reported in this study can probably be correlated with the biphasic wave of the esophageal motility studies. The biphasic wave is caused by the pressure monitor passing the moving diaphragm during a single downward or upward movement. If the diaphragm is moving downward and the monitor is below the diaphragm, a positive pressure develops on the recorder. As the monitor tip is drawn upward, it, at one point, passes the

downward moving diaphragm and immediately registers a quick change from a positive to a negative pressure. The diaphragm continues to contract, negative intrathoracic pressure is increased and the recorder continues its downward swing far below the lowest intragastric pressure. As the diaphragm returns to its resting position, the recorded pressure increases again. This biphasic complex replaces the usual simple pressure wave. However, with a decrease in paper speed from the 2.5 mm/sec. used for esophageal motility to the 1.0 mm/sec. speed employed in these studies, each pressure wave is squeezed into 40 percent of the space. The biphasic wave is therefore not nearly so evident on the pressure patterns in this study as it is in the motility tests.

No conclusion about the lower esophageal sphincter can be drawn from these studies. The cause of the high pressure zone in the pressure profile was not investigated. The sole reason for these pressure studies was to confirm the usefulness of pressure determinations in locating a glass pH electrode in the stomach or esophagus.

II Gastric and Esophageal pH Studies in Normal Subjects

There is a change from acid gastric pH values to higher esophageal pH values which begins in the lowest part of the high pressure zone and is mostly completed over the next few centimeters of esophagus. This change occurs before the pressure inversion point is reached and, therefore, before the level of the diaphragmatic hiatus. Whatever causes the high pressure effect in the lower esophagus could have a great deal to do with the prevention of gastroesophageal reflux since both occur at the same level of the esophagus.

In the second phase of the test, after the addition of 200 to 300 cc 0.1 N.HCl, the electrode is once again drawn over the gastroesophageal junction and into the lower esophagus. Thus, even with acid present in sufficient quantity to allow reflux if the reflux barrier should be exceeded, normal subjects still show the usual change from acid gastric pH values to higher esophageal ones.

With the pH electrode stationed at about 5 centimeters above the gastroesophageal junction, a normal subject could perform all the reflux-inducing manoeuvres without having the esophageal pH change. Certainly, most people have reflux at one time or another but no normal subject had this under test conditions. Two patients who were selected for normal group studies did have reflux during manoeuvres. However, subsequent barium meals demonstrated a hiatus

hernia in each of these subjects.

Normal subjects, then, had a definite change from acid gastric pH values to higher esophageal values at the esophagogastric junction and under test conditions did not have reflux of acid into the esophagus at any time, even with an abdominal corset inflated to 40 centimeters of water pressure.

III Gastric and Esophageal Pressure Studies in Patients with Hiatus Hernia

The interpretation of these tracings was the most difficult and uncertain part of the entire project.

While using a single monitoring tube for pressure recordings, it seemed that hiatus hernia patients without a high pressure zone had a long-duration acid esophageal pattern (see description in "Results of Gastric and Esophageal pH Studies in Patients with Hiatus Hernia") and those with an intermittent acidity pattern had a normal high pressure zone. However, when multiple pressure-monitoring tubes were employed, the high pressure zone was always detected in at least one tracing. One can only assume that if the multiple tubes had been used in the earlier cases tested with a single tube, more high pressure zones would have been detected.

Later, it seemed that the high pressure zone was transposed to a higher than normal position. The mean pressure above the pressure

inversion point was much higher than normal; in fact, the pressure inversion point had to be identified more by amplitude and phase changes than by mean pressure itself. The pressure changes described may have been caused because the hernia was not reduced during the moment the pressures were recorded. Thus no elevation in pressure was noted below the pressure inversion point because the sphincter was herniated into the thorax. The high pressure above the pressure inversion point also extended to an abnormally high level in the esophagus because the sphincter was herniated into the thorax.

It is also easy to understand why a normal pressure profile might be obtained moments after the abnormal pattern described above--when the hernia has become reduced. It must be remembered that during fluoroscopy it most often takes a considerable effort to demonstrate a sliding hiatus hernia and that the hernia is then immediately reduced. One may therefore speculate that a normal or abnormal pressure profile or both may be obtained in a hiatus hernia patient and this depends on whether the hernia is reduced or not. The fact that a pressure corset was applied to all these patients probably explains why the abnormal curves were seen as frequently as they were.

In those cases where the high pressure zone was found higher than usual and the high pressure zone did not occur lower than the pressure inversion point, swallow waves were not evident below the pressure inversion point. Again, the herniation was present at that

time and no esophagus extended below the hiatus.

However, all of this can only be classified as speculation on a firm basis of probability. With a technique having as many artifacts as intra-esophageal pressure studies, assigning significance to anything that is not a dependable, clear-cut pattern that is fairly simple to pick out, is a dangerous venture. A much more specially designed and accurate series of pressure studies would be needed to begin to sort the pressure changes in hiatus hernia into a meaningful pattern.

The recognizable points in the pressure profile which are necessary to locate the pH electrode are still present in hiatus hernia patients. It is therefore possible to use the esophageal pH test described above to objectively determine pH conditions in the lower esophagus in patients with hiatus hernia.

IV Gastric and Esophageal pH Studies in Patients with Hiatus Hernia

The patients with hiatus hernia on x-ray examination who did not have acid reflux during the pH test may be a demonstration of the well-known fact that not all people with hiatus hernia seem to have reflux. A second possibility is the lack of sufficient sensitivity of the test to detect all cases of reflux. It is reasonable to imagine that additional reflux-inducing manoeuvres or a repeat

test at a later date might have resulted in a demonstration of reflux. Certainly, at present, it is not evident why one individual with a hiatus hernia should have gastroesophageal reflux while another does not.

The reflux which occurred during the pH test in 39 patients with a radiological diagnosis of hiatus hernia was seen to form the two distinctly different pH patterns described in "Results". The long-duration acidity pattern was characterized by a tendency of the esophagus to remain acid throughout the remainder of the test once acid had entered the esophagus and occurred in 13 patients. The short-duration acidity pattern was characterized by a normal esophageal pH except for a brief change to acid pH brought on by certain manoeuvres which was followed by a prompt change to normal esophageal pH and occurred in 26 patients.

The finding of a long or short duration of acidity pattern was a reproduceable phenomenon in any one patient, indicating that it represents some basic difference between the two groups. Patients with a long-duration acidity pattern generally complained of heartburn during the entire period that acidity persisted, so that symptoms supported the pH electrode evidence that acid remained in the lower esophagus for a considerable period. Patients showing a short-duration acidity pattern generally complained of heartburn only for a minute or so after the pH electrode showed an acid change in the esophageal pH and stopped complaining as the pH returned to normal.

There was, therefore, evidence that symptoms appeared only while acid remained in the esophagus.

Indeed, reproducibility of the phenomena and symptomatic evidence both strongly support the idea that there are two basically different pH duration patterns in patients with proven hiatus hernia and gastroesophageal reflux.

Further definition of the difference in the two pH duration patterns was revealing. At first it was assumed that the two different patterns were caused by a slight incompetency of the gastroesophageal barrier mechanism and a more serious and complete incompetency of the barrier. The short-duration pattern was felt to be caused by a sudden reflux of gastric acid which was quickly cleared from the esophagus. The long-duration pattern was believed due to free back and forth movement of acid-peptic secretions across the gastroesophageal junction. However, cinefluoroscopy soon proved this concept to be totally incorrect. Only 5 out of 14 patients with the long-duration pH drop were shown to have free back and forth passage of barium past the gastroesophageal junction; 6 showed occasional reflux fluoroscopically and 3 had no reflux demonstrated on radiologic examination. Four patients with a short-duration pH drop were shown to have free reflux of barium at x-ray examination. Another point against the theory of sharply different degrees of incompetency being responsible for the two basic esophageal acid duration patterns is the finding of a high pressure zone in all

patients with the long-duration acid pattern. If this were missing, perhaps due to destruction by peptic esophagitis, it could provide a logical basis for free reflux.

If a relatively more complete degree of incompetency does not seem responsible for the difference between the short-duration acidity patern in one group of patients and the long duration of low esophageal pH values in a second group, then the actual time that any refluxed acid remains in the esophagus may be the answer. Usually the esophagus is stimulated to a series of secondary peristaltic waves until the acid is cleared out of the esophagus. The long-duration acidity pattern may be caused by a prolonged stay of acid gastric contents in the esophagus following reflux. Further studies, such as, combined pH, manometric and cinefluoroscopic studies with acidified barium sulfate and motility determinations in the lower esophagus, would be needed to elucidate the nature of these two different reflux duration patterns.

The importance of these two patterns may be considerable. Symptoms of reflux esophagitis were generally severe in the long-duration acidity group and there was marked relief after a successful hiatus hernia repair in these people. This indicates that the grouping of patients according to the type of acid duration pattern may be of considerable value in predicting the patient's result from a hiatus hernia repair. More important to the writer, however, is

the fact that, of the 13 patients with hiatus hernia and a long-duration acidity pattern, three suffered massive upper gastrointestinal hemorrhages. In addition, ulcers were demonstrated in the esophagus or herniated stomach of two of these patients. None of the 26 patients with a hiatus hernia and a short duration esophageal acid pattern ever had an upper gastrointestinal hemorrhage. The sequence of (1) longer exposure of esophageal mucosa to acid peptic secretions, (2) more severe esophagitis and perhaps ulceration, followed by (3) hemorrhage is not difficult to imagine. Certainly, there would seem to be a strong indication for further investigation of this matter.

V Gastric and Esophageal pH and Pressure Studies Following Hiatus Hernia Repair

While no obvious difference was noted in a rough comparison of the pre- and post-operative pressure studies, several points must be noted. First, these tests were of a qualitative rather than a quantitative nature. In this whole project many aspects were scanned for promising leads and, where present, these leads were followed by attempts to improve the data-gathering methods. Since there was no obvious change in the pre-and post-operative pressure tracings, especially the high pressure zone, no further attempt to quantitate the results was made.

The high pressure zone may have been more constantly located in the usual position than in the possibly altered positions described in "Results" under "Gastric and Esophageal Pressure Studies in Patients with Hiatus Hernia" (Page 3).

Careful quantitative pressure studies in the pre- and post-operative patient would have to be carried out. The small pressure variations to be evaluated would necessitate placement of the pressure transducers at exactly the esophageal level. This would necessitate a lateral x-ray view showing the barium-filled esophagus at the same level as the transducers. Since it was not possible to carry out this procedure in the present project, it would not be valid to quantitatively compare the pre- and post-operative high pressure zone values.

Post-operative gastric and esophageal pH tests were done in 11 patients who had had pre-operative studies. Ten of the 11 patients had normal post-operative pH tracings; all of the 10 had shown reflux pre-operatively. The hernia repair had obviously been effective in these patients.

On the basis of the few cases studied pre- and post-operatively, it is not possible to determine if any particular technique of repair is better than another in restoring an effective barrier to gastroesophageal reflux. Each method utilized seems to be effective in the hands of the particular surgeon

employing it.

Follow-up studies are being prepared for annual reassessment of these patients and will include x-ray, esophageal pH and other objective means of determining the duration of improvement.

VI Gastric and Esophageal pH and Pressure Studies Following a Heller Procedure for Achalasia

The gastric and esophageal pressure studies cannot be meaningfully interpreted for two reasons: First, the results are not the same in the two determinations on the same patient and secondly, more results are not available.

The pH studies, however, are interesting. The part of the esophagus normally giving a high pressure zone has been divided at the muscular level leaving pouting mucosa. The pH studies show an acid esophageal pH in both patients. This would seem to suggest that a physiological lower esophageal sphincter may play a prominent role in the prevention of gastroesophageal reflux. This could be studied still more accurately in patients with achalasia who have undergone hydrostatic dilatation with a Brown-McCarty bag. In these patients the gastroesophageal angle and hiatal structures are not disturbed so much as by a Heller operation, and the effect of destroying the hyperactive lower esophageal sphincter but leaving intact other factors supposedly responsible for the prevention of reflux could be studied.

VII Gastric and Esophageal pH and Pressure Studies for Complaints of Heartburn During the Third Trimester of Pregnancy

The effect of pregnancy on the reflux barrier mechanism has not been clarified by these studies. The effect of the naso-gastric apparatus on an already distressed woman was such that calm, detailed studies were impossible. A completely different approach will be necessary to study the heartburn of the third trimester.

However, the findings in the one patient studied must be briefly mentioned. A grossly normal high pressure zone indicated that the muscle tone of the physiological lower esophageal sphincter is not altered; i.e., gross loss of muscle tone does not seem to be responsible for weakening of the reflux barrier mechanism in the single patient studied.

The one patient studied showed a normal change from low acid gastric pH values to higher esophageal ones as the electrode was withdrawn from the stomach past the gastroesophageal junction and into the esophagus. The reflux-inducing manoeuvres had not yet been included as part of the test, and so no information on whether the patient could be made to have reflux is available.

VIII The Advantages of the Standard Multiphased pH Test Developed During This Project

Comparison of the results from the three different phases of the multiphased test clearly demonstrates the need for the inclusion of reflux-inducing manoeuvres and the addition of acid to the stomach. The Phase (2) addition of acid to the stomach tripled the number of positive tests and, with reflux-inducing manoeuvres, acid reflux into the esophagus was demonstrated seven times more frequently than by the use of simple withdrawal of the electrode from the stomach into the esophagus.

The multiphased pH test was designed by the writer and others associated with this project to take advantage of every conceivable method to increase the chance of reflux detection in a subject who seemed likely to exhibit this phenomenon. The addition of acid to the stomach insured the presence of intragastric fluid in a subject who would potentially have reflux under test conditions and provided a medium which could be detected by the pH electrode as reflux occurred. The reflux-inducing manoeuvres were included to promote the chance of reflux during the test period.

The in-situ pH electrode test developed by Tuttle and Grossman is similar to the Phase (2) of the test used at the Royal Victoria Hospital. In the test of Tuttle and Grossman there were

two patients who had a positive esophageal perfusion test and a negative in-situ pH electrode test. No patients in the R.V.H. series had a positive esophageal perfusion test and a negative pH test. In addition, as noted above, by adding the reflux-inducing manoeuvres, the incidence of detected reflux was seven times greater than that in the test done as described by Tuttle and Grossman.

Hill et al. described the use of reflux-inducing manoeuvres with and without HCl being added to the stomach but were concerned more with how high acid refluxed into the esophagus. The multiphased test was not concerned with the height of the reflux but rather with the acid duration pattern of the lower esophagus. It seemed more important to try to relate the duration of exposure to the severity of the disease.

The multiphased esophageal pH test developed at this institution is probably the most sensitive, systematized in-situ pH test for gastroesophageal reflux currently described in the literature.

IX Correlation of Gastroesophageal Reflux Indicated by the pH Test with Other Means of Objectively Determining Reflux

A. Comparison with radiology reveals that the multiphased R.V.H. reflux test is a considerably more sensitive indicator of reflux than x-ray methods. A critical review of the results shows that of 43 positive reflux pH tests only 26 of these patients had fluoroscopically-demonstrated reflux. The 17 subjects with pH-demonstrated reflux and no radiological evidence of reflux included 11 patients with other evidence of reflux, such as, a positive acid perfusion, endoscopic evidence of reflux or esophagitis or a negative pH test following a hiatus hernia repair. Three additional subjects had a radiologically-demonstrated hiatus hernia, reflux on the pH test, but no supporting objective evidence of reflux (because the necessary tests were not ordered). It seems reasonable to assume that in these three cases there was true reflux. The remaining three with a positive pH test and no x-ray evidence of reflux showed no hiatus hernia on x-ray and, unfortunately, the other necessary tests to objectively evaluate reflux could not be performed because the patients were semi-private and uncooperative. Because no normal subject showed a positive pH reflux test and only one post-operative patient with a hiatus hernia repair had a positive pH test, it seems more likely that, if other objective means

of detecting had been employed in the last three cases, the presence of reflux would have been substantiated. If this last assumption is true, it would mean that x-ray detection of reflux is only about 60 percent as sensitive as the pH test.

B. Comparison of the esophageal acid perfusion test and the multiphased esophageal pH reflux test is based on the results of studies in six subjects. In all six, the multiphased pH reflux test was positive. The esophageal acid perfusion test showed symptoms of heartburn produced by acid and relieved by antacids in 4 patients; the results were inconclusive in one patient, and in one patient the acid perfusion caused no symptoms. Actually, the acid perfusion test only indicates whether a patient's pain may be of esophageal origin or not. It is quite possible that someone with infrequent reflux and insufficient exposure to cause peptic esophagitis would have a positive pH reflux test and a negative acid perfusion test. Each test adds to the completeness of the evaluation in a patient with complaints of reflux esophagitis.

However, there can be little doubt that as far as reflux detection alone is concerned, the multiphased esophageal pH test is a more sensitive indicator than esophageal acid perfusion. While the number of patients studied is small, it must be stated that, (1) the results are similar to those of Tuttle, Bettarello and Grossman who used a less sensitive esophageal pH test than the one

developed here, (2) those patients with a negative or equivocal acid perfusion test but a positive esophageal pH test had reflux demonstrated by another objective method, and (3) subsequent studies in this laboratory but not included in this thesis fully support the finding that the multiphased esophageal pH test will detect reflux more frequently than the esophageal acid perfusion test will suggest reflux.

C. Endoscopy was done in ten patients who also had the multiphased esophageal pH test. Esophagoscopy showed seven patients to have visible esophagitis, biopsy evidence of esophagitis or reflux during endoscopy. Two subjects had a normal appearing mucosa but biopsy was not performed. In one patient the esophagoscope could not be passed. All of the patients demonstrated reflux on the multiphased esophageal pH test, once again demonstrating the marked sensitivity of this technique.

Where biopsy as well as visualization was carried out, both methods showed evidence of reflux. In the two cases in which a normal appearing mucosa was seen but no biopsy taken and in which reflux was demonstrated during the pH test, submucosal changes may well have been detected had a biopsy been done. The value of esophagoscopy is not to be minimized. Direct visual inspection of the involved mucosa, especially when combined with biopsy, remains

very useful. There is a good case for visualization of a lesion before encountering it at surgery.

D. Esophageal motility studies have been used successfully by Code, Schlegel and Ellis in establishing the diagnosis of hiatus hernia. In five subjects with reflux detection established by the multiphased esophageal pH test and at least one other method, the esophageal motility studies failed to detect a hiatus hernia. Four of these patients had radiologically demonstrated hiatus hernias.

In the patients who had esophageal motility studies, a hiatus hernia was often demonstrated on x-ray examination, but not detected by motility studies, and the reflux was in each instance detected by the multiphased esophageal pH test.

X Simultaneous Use of the Multiphased Esophageal pH Test and Electrocardiography to Differentiate Certain Types of Chest Pain

The advantages of simultaneous use of these tests is obvious. The technical difficulties have now been overcome. A serial study is now possible to actually determine the practicability and usefulness of this concept in appropriate patients.

CONCLUSIONS

1. Gastric and esophageal pressure studies in normal subjects confirm the reports of Code and Hill that there is a highly predictable pressure profile for the proximal stomach and the lower esophagus and demonstrate that reference points in this curve may be used to determine the position of a glass pH electrode.

2. Gastric and esophageal pH studies in normal subjects confirm the reports of others that there is a change from acid gastric to relatively higher esophageal pH values at the gastroesophageal junction. Under test conditions, acid reflux does not take place in normal subjects as indicated by a glass pH electrode stationed 5 centimeters above the esophagogastric junction.

3. No significant pressure differences were detected which could differentiate patients with hiatus hernias from normals. However, considerable improvement in methodology is needed and would possibly give very different results.

4. Gastric and esophageal pH studies in patients with hiatus hernia demonstrated two distinctly different esophageal acid duration patterns. The long duration acidity pattern was associated with severe symptoms, difficulty with medical regimens, a more marked beneficial result after hiatus hernia repair and, in 3 of 13

cases, with upper gastrointestinal bleeding. The short duration acidity pattern group of 35 patients had less severe symptoms and not one instance of upper gastrointestinal bleeding.

5. Gastric and esophageal pH and pressure studies after hiatus hernia repair demonstrated that the reflux barrier mechanism is usually and also effectively restored to normal. There was no recognized change in the pressure profile following repair but improvement in technique is necessary before a definite statement can be made.

6. A Heller procedure for achalasia may be complicated by gastro-esophageal reflux, as demonstrated by esophageal pH studies in two patients.

7. The multistage esophageal pH test for reflux is of no use in studying the cause of heartburn during the third trimester of pregnancy.

8. The multistaged esophageal pH test for reflux developed in this study is a most sensitive indicator of gastroesophageal reflux and may exceed the incidence of x-ray detection by as much as forty percent.

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