DYSPHAGIA AND BELCHING DIFFICULTIES

AFTER NISSEN FUNDOPLICATION

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ABSTRACT

Dysphagia and belching difficulties are not uncommon after Nissen fundoplication. Many studies have relied on subjective reports and have not undertaken objective measurements to define the pathophysiology.

To investigate the effect of fundoplication on oesophageal motor function and its relationship to dysphagia, we studied 11 volunteers and 15 patients with gastro-oesophageal reflux disease pre-fundoplication. Thirteen patients returned for a post-operative study; 6 of whom experienced dysphagia. Twelve other patients complaining of dysphagia post-fundoplication were also studied. The severity of dysphagia was graded numerically and all subjects underwent oesophageal manometry and videofluoroscopy.

Patients with reflux disease had lower oesophageal sphincter hypotension and wider sphincter opening compared with volunteers but primary peristaltic amplitude and ramp pressure were not significantly different. After fundoplication, primary and secondary peristalsis did not improve but the ramp pressure, lower oesophageal sphincter basal and nadir pressure increased. Patients with post-fundoplication dysphagia did not differ from patients without dysphagia in primary or secondary peristalsis, or the maximum opening diameter of the lower oesophageal sphincter but had a significantly higher ramp pressure, basal and nadir lower oesophageal sphincter pressure than patients without dysphagia. The numerical dysphagia score was significantly correlated with ramp pressure, basal and nadir lower oesophageal sphincter pressure.

To study the effect of fundoplication on the ability to belch, 11 volunteers and 20 patients after fundoplication were interviewed and the ability to belch graded numerically. During oesophageal manometry, common cavities were measured as objective markers of gas gastro-oesophageal reflux. None of the patients had any belches that corresponded with common cavities. Also, there was no correlation between the reported ability to belch and the belch urges and common cavities measured during oesophageal manometry.

An experimental porcine model was used in the study of variables influencing the effect of fundoplication on oesophageal motor function. Three groups of 6 pigs underwent tight, loose and floppy fundoplications respectively. Fundoplication increased the peristaltic amplitude, ramp pressure, basal and nadir lower oesophageal sphincter pressure in all 3 groups but there was no difference between the 3 groups.

In conclusion, dysphagia after fundoplication was related to the ability to relax the newly constructed lower oesophageal sphincter. The ramp pressure is a useful parameter which reflects the physiological obstruction at the lower oesophageal sphincter imposed by a fundoplication. After fundoplication, patients do not experience gas reflux from the stomach to the oesophagus. Using an experimental porcine model, there was no relationship between the tightness of the fundoplication and manometric parameters that were found to correlate with post-fundoplication dysphagia in patients.

DECLARATION

I declare that this thesis contains no material
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Sawjin Tew **Date**

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LITERATURE REVIEW

CHAPTER 1: OESOPHAGEAL ANATOMY AND PHYSIOLOGY

The pathophysiology of dysphagia and belching difficulties after fundoplication has not been investigated in detail and it is possible that these clinical sequelae are related to mechanical disturbances at the gastro-oesophageal junction. A review of normal oesophageal anatomy and physiology sets the scene for considering the abnormalities associated with gastro-oesophageal reflux, the changes in oesophageal motility after Nissen fundoplication and the relationship of motility to bolus transit.

1.1 OESOPHAGEAL MUSCULATURE AND INNERVATION

Oesophageal Body

The body of the human oesophagus is 20 to 22 cm in length. Proximally, striated muscle is found in both the inner circular and outer longitudinal layers, but this is replaced by smooth muscle beginning about 4 cm from the inferior border of the cricopharyngeus. Mixed smooth and striated muscle is present in the middle third. The distal one-third to one-half, including the gastro-oesophageal junction, is entirely smooth muscle, with rare exceptions (Goyal *et al* 1981, Ingelfinger 1958). A poorly developed oblique layer, the bracket fibres of Laimer, may be present internal to the circular layer in the distal oesophagus. The circular fibres are mostly arranged in ellipses in the upper two-thirds and in helices in the terminal part (Ingelfinger 1958). Smooth muscle cells of the human oesophagus have 3 types of cellular connections, namely specialized plaque junctions, sharply defined plasmalemmal contacts and protoplasmic bridges that facilitate the coordinated spread of excitation and equilibration of intercellular tension (Harman *et al* 1962). The oesophageal lumen is collapsed in the resting state.

Research into the digestive tract has been carried out most often in the dog, opossum and cat although pigs have also been used successfully (Mount *et al* 1971). The muscle distribution is similar among primates, cats and opossum. In the dog, rabbit, guinea pig, rat, mouse, cow, sheep, bat, elephant and giraffe, the oesophagus consists entirely of striated muscle while birds, amphibia and reptiles have an entirely smooth muscled oesophagus (Ingelfinger 1958). The porcine distal oesophagus from just above the diaphragm to the gastro-oesophageal junction consists of smooth muscle (Landers *et al* 1987). Histologically comparable muscle behaves with remarkably similarity although one has to be cautious when extrapolating physiological data between species.

Lower Oesophageal Sphincter

A physiological sphincter with characteristic behavioural patterns exists at the lower end of the oesophagus and this is identified manometrically as a high pressure zone (Fyke *et at* 1956). This barrier is 2 to 4 cm long and straddles the hiatus (Atkinson *et al* 1957, Botha *et al* 1957).

The anatomy of the closing mechanism at the gastro-oesophageal junction has been the subject of much debate. If an anatomic sphincter is defined as a ring of circular muscle separated from adjoining muscles by connective tissue septa, then a sphincter does not exist (Vantrappen *et al* 1960). However, there are other structures around the cardia, a word first used by Hippocrates (Friedland 1978), that are of interest. Willis in 1679 and Helvetius in 1719 described an oblique gastric muscle bundle which invests posterior, lateral and anterior aspects of the cardia like a horse-shoe shaped sling. This "collar of Helvetius" is also known as Willis' loop, constrictor cardia and spiral constrictor (Jackson 1978). Liebermann-Meffert *et al* (1979) described this structure as an asymmetrical muscle thickening approximately 3 cm wide on the greater curvature and 2.3 cm wide on the lesser curvature. This region is covered by columnar mucosa, with the squamo-columnar junction, as determined by potential difference measurement (Eckhardt *et al* 1980), being located 2.5 cm more proximally (Goyal *et al* 1981). Botha *et al* (1957), Byrnes *et al* (1963) and Samelson *et al* (1983) believed in a role for the muscular thickening at the cardia whereas Lendrum (1937), Adler *et al* (1958), Belsey (1952), Higgs *et al* (1965) and Oglesby (1975) denied any role for it.

Innervation

The striated muscle is innervated by somatic motor fibres that make direct contact with individual muscle fibres at motor end-plates (Weisbrodt 1976). Their cell-bodies are located in the nucleus ambiguus and the myelinated efferent fibres are carried in the vagus nerves (Ingelfinger 1958). Acetylcholine is the neurotransmitter involved at the neuromuscular junction and its effects are mediated by nicotinic receptors.

The smooth muscle is supplied by autonomic nerves. The extrinsic nerves are vagal and sympathetic. Cell bodies of preganglionic parasympathetic fibres to the oesophageal body are in the dorsal motor nucleus of the vagus in the floor of the fourth ventricle of the medulla oblongata (Andrew 1956). Parasympathetic nerves are contained entirely in the vagal fibres (Mitchell 1938) which distribute themselves over the oesophageal body in a plexiform arrangement, and branches from this plexus innervate the oesophageal body and lower oesophageal sphincter. Vagal fibres regroup

between 1 to 4 cm above the diaphragm forming the anterior and posterior gastric nerves (Goyal *et al* 1981). The sympathetic nerve supply to the oesophageal body arises from cell bodies in the intermediolateral cell columns of spinal columns of T5 and T6 (Weisbrodt 1976). Cell bodies from T6 to T10 supply the lower oesophageal sphincter. Preganglionic fibres destined for the oesophageal body enter the ganglia in the cervical and thoracic sympathetic chain. Those destined for the lower oesophageal sphincter travel in the greater splanchnic nerves synapsing in the coeliac ganglion with postganglionic nerves (Mitchell 1938). Postganglionic fibres accompany blood vessels; a few fibres join the vagus and reach the oesophagus. Most of the parasympathetic and sympathetic axons terminate in the myenteric or Auerbach's plexus but a supply to the submucosal or Meissner's plexus has also been demonstrated. Very few are distributed directly to the muscle layers (Goyal *et al* 1981).

The intrinsic innervation of the oesophagus consists of intramural neurons and their extensions. Intramural neurons may be classified on the basis of morphologic, histochemical, functional and electrical differences (Goyal *et al* 1981). Axons make contact with smooth muscle cells at varicosities which are filled with neurotransmitter granules such as acetylcholine and noradrenaline (Zfass *et al* 1970). Noncholinergic nonadrenergic neurotransmitters are present and may be related to ATP, purine, neuropeptide or nitric oxide.

Afferent fibres from the upper oesophagus are carried by vagal nerves while those from the lower oesophagus follow sympathetic nerves (Weisbrodt 1976). Indirect evidence suggests that mechanoreceptors (Paintal 1973), osmoreceptors and free nerve endings may be present in the human oesophagus and lower oesophageal sphincter (Goyal 1981).

1.2 NORMAL OESOPHAGEAL MOTILITY

Our understanding of the physiology of the oesophagus and lower oesophageal sphincter depends on the measurement techniques available. In 1899, Meltzer used balloons attached to catheters to record intraluminal pressure of the oesophagus. Open tipped unperfused catheters have also been used (Langley 1898, Atkinson *et al* 1957) but these resulted in underestimation of pressures compared to measurements using newer techniques. High compliance water-perfused catheters were used in the 1960's (Winans *et al* 1967). A high rate of infusion is necessary to enable the measurement of pressures that are changing rapidly and this causes some patients to gag or swallow constantly.

In 1977, Arndorfer *et al* introduced a low compliance hydraulic capillary infusion system with a flow rate of 0.6 ml/min per side-hole of the catheter. Occlusion of the sidehole due to direct circumferential squeeze by oesophagus causes a pressure

rise in the system which reflects the tension that is developed in the circular muscle. A pressure rise of 844 mmHg/sec can be achieved for a catheter with a diameter of 0.8 mm with high fidelity recording systems (Dodds 1976). Today's catheters with multiple lumina around a central core allow simultaneous recording of pressures from multiple sites. The measurement of lower oesophageal sphincter pressure with a single sidehole is unsatisfactory because of the axial movement of the sphincter with swallowing and respiration. Basal or resting lower oesophageal sphincter pressure can measured by rapid or station pull-through (Csendes *et al* 1989, Welch *et al* 1980) but a sleeve device (Dent 1976) is necessary for prolonged recording. Pressure transducers are located in series a distance away and damping of the pressure wave is a function of catheter length and internal diameter. Currently, catheter tip miniature transducers are available (Humphries *et al* 1977) and are useful for ambulatory oesophageal manometry.

1.2.1 Primary peristalsis

Primary peristalsis is a propagated oesophageal contraction that follows oropharyngeal activity. Swallowing is initiated voluntarily beginning with mylohyoid activity but primary peristalsis is involuntary. Our understanding is derived from manometry, radiology and electromyogram studies.

Basal oesophageal pressure ranges from +2 to -20 mmHg relative to atmospheric pressure. The initial pressure change in peristalsis is a negative deflection, 5 to 10 mmHg in amplitude, beginning around 0.2 sec after the onset of a swallow and lasting 0.3 to 0.5 seconds (Vantrappen *et al* 1967). Then a small positive pressure change occurs. This small positive wave is best seen in the proximal oesophagus and is attributed to the transmission of pharyngeal pressures through the swallowed bolus. It occurs 0.5 to 1 second after the onset of swallowing. This wave may plateau into a second positive pressure wave in approximately 33% of swallows which is best seen in the distal oesophagus. Its incidence can be increased by obstructing the gastro-oesophageal opening with a tube before swallowing (Vantrappen *et al* 1967). It begins 1-2 seconds after the onset of swallowing. This observation, along with its site of occurrence, is felt to be evidence that the wave is produced by compression of the lower oesophageal segment between the advancing bolus and the lower oesophageal sphincter (Goyal *et al* 1981). The third or terminal positive deflection is the main peristaltic wave, corresponding to oesophageal contraction. Peristaltic velocity is approximately 3 cm/sec in the upper oesophagus, 5 cm/sec in the mid oesophagus before slowing down again to 2.5 cm/sec just above the lower oesophageal sphincter (Humphries *et al* 1977).

Recorded amplitude and propagation speed are influenced by bolus volume (Dodds *et al* 1973, Hollis *et al* 1975, Richter *et al* 1987), bolus temperature (Winship *et al* 1970), bolus viscosity (Ingelfinger 1958), body position (Kaye *et al* 1981), intra-abdominal pressure (Dodds *et al* 1974), inotropic state of the muscle (Cohen *et al* 1973) and recording fidelity (Dodds *et al* 1976). Wet swallows have a higher amplitude and lower velocity compared to dry swallows (Dodds *et al* 1973, Hollis *et al* 1975). Within the same individual, peristaltic amplitude remains reasonably constant when examined serially (Nagler *et al* 1961, Russell *et al* 1987). Amplitude may be diminished in the elderly (Hollis *et al* 1974, Richter *et al* 1987).

When a person swallows in a supine position, peristalsis advances the column of liquid causing moderate bulging of the oesophageal lumen (Ingelfinger 1958, Kahrilas *et al* 1986). Peristalsis generally traverses the entire oesophagus even in the absence of a bolus (Dodds *et al* 1973, 1981). During peristalsis, the oesophagus shortens by 26 to 46% of its resting length (Dodds *et al* 1973).

From electromyographic studies, mylohyoid activity is the first recordable event of a swallow (Mittal *et al* 1989). Electrical activity in the smooth muscle precedes the mechanical activity by a short latency interval (Hellemans *et al* 1968, Goyal *et al* 1981). Spike activity ceases at or near the peak of muscle contraction so the descending phase of the peristaltic contraction is not associated with spike activity. Sequential activation of longitudinal muscle is dependent upon an intact vagal innervation (Sugarbaker *et al* 1984), whereas activation of circular muscle is less so (Gidda *et al* 1984, Dodds *et al* 1978, Sugarbaker *et al* 1984).

1.2.2 Secondary peristalsis

Secondary peristalsis may be defined as the oesophageal response initiated by transient oesophageal distension (Meltzer *et al* 1906, Dornhurst *et al* 1954, Fleschler *et al* 1959, Winship *et al* 1967) without an oropharygeal component (Ingelfinger 1958, Christensen 1970). Early experiments by Meltzer and Auer (1906) showed that secondary peristalsis triggered by oesophageal distension did not jump a gap in the canine oesophagus that had been transected and rejoined, so they concluded that secondary peristalsis is due to local reflexes and is different from primary peristalsis. This finding is not supported by later experiments (Hwang 1954, Siegel *et al* 1961). Acid, saline or balloon was found to elicit secondary peristalsis equally by Thompson *et al* (1988) suggesting that the stimulus is distension not pH. However, less volume was needed with liquids of pH 4, 3 and 2. In another study in healthy subjects, balloon distension was not as effective in triggering secondary peristalsis as 10 ml air boluses and 10 ml water boluses (Schoeman *et al* 1994).

The response observed in the striated muscle of the canine oesophagus is a centrally mediated response that is abolished by vagotomy (Hwang 1954). Secondary peristalsis in the smooth muscle part of the opossum oesophagus is mainly a local reflex (Christensen 1970, 1982). In humans, a central reflex involving the vagus sometimes participate in the response (Paterson *et al* 1991).

In contrast to the findings of Siegel *et al* (1961) that secondary peristalsis is similar to primary peristalsis in amplitude and velocity, Paterson *et al* (1991) and Schoeman *et al* (1994) found that the amplitude and velocity were lower in secondary peristalsis.

1.2.3 Rapid swallows

If swallows are taken in rapid succession, no peristaltic wave appears until the last swallow. Both primary and secondary peristalsis may be interrupted when the person swallows repetitively, when observed by fluoroscopy (Stewart 1981). Each swallow exerts an inhibitory effect and the oesophageal musculature is in a refractory phase (Dornhurst *et al* 1954, Fleschler *et al* 1959, Meyer *et al* 1981, Vanek *et al* 1987). Inhibition is avoided if the minimum interval between swallows is 1 to 2 seconds for the upper oesophagus, 3 seconds in the mid oesophagus and 5 to 6 seconds in the distal oesophagus (Ingelfinger 1958, Ask *et al* 1980, Meyer *et al* 1981, Vanek *et al* 1987). At intervals of more than 10 seconds between swallows, 2 separate peristaltic waves occur. Kronecker and Meltzer believed this inhibition to be the result of sensory impulses mediated by the glossopharyngeal nerve because electrical stimulation prevented the response (Ingelfinger 1958).

1.2.4 Lower oesophageal sphincter function

Resting tone

Early investigators refer to the "constriction of the cardia" where swallowed mass is detained before it is carried into the stomach (Meltzer 1897). The resting or basal lower oesophageal sphincter high pressure zone is identified manometrically (Fyke *et al* 1956).

The lower oesophageal sphincter is asymmetrical (Kaye *et al* 1971) and highest pressures are recorded when the recording channel faces the left side of the sphincter (Winans *et al* 1972). The recorded pressure is also affected by catheter diameter (Lyndon *et al* 1975). Body position has an effect in that the basal lower oesophageal sphincter pressure is lower when measured in the right decubitus, left decubitus and

standing positions, compared with supine (Babka *et al* 1973). Lower oesophageal sphincter pressure is not affected by age (Csendes *et al* 1989).

Lower oesophageal sphincter pressure shows fluctuations with respiration as well as rhythmic pressure changes that occur at a slow rate of 3 to 4 per min (Goyal *et al* 1981). The pressures in the upper and lower halves of the lower oesophageal sphincter are affected by respiration in opposite ways as they are related to the diaphragm which separates thoracic from abdominal cavities that provides opposing pressure environments during respiration (Goyal *et al* 1981). Inspiration causes an increase in pressure in the lower part and a fall in pressure in the upper part of the sphincter. The point at which this respiratory pressure transition occurs is called the pressure inversion point.

Resting lower oesophageal sphincter tone exhibits temporal variation (Winans *et al* 1967, Pope 1976, Dent *et al* 1980), such as minute to minute variation (Dent *et al* 1980) and variation during phase III interdigestive activity (Dent *et al* 1978). This variability diminishes during sleep (Dodds *et al* 1980). The degree of tonic contraction seems to be modified reflexly by changes in intra-abdominal pressure (Fyke *et al* 1956, Lind *et al* 1966, Dodds *et al* 1975), intragastric pressure (Winans *et al* 1967, Pope 1970, Haddad 1970) and intragastric pH (Muller-Lisner *et al* 1982, Reynolds *et al* 1984).

The basic mechanism that sustains resting lower oesophageal sphincter tone is believed to be a low membrane potential of lower oesophageal sphincter smooth muscle (Daniel *et al* 1976, Fox *et al* 1979) which is calcium dependent (Dent *et al* 1988, Goyal *et al* 1980, Hongo *et al* 1984). Acetylcholine (Dodds *et al* 1981) and myogenic factors (Goyal *et al* 1976) both contribute to the genesis of sphincter tone. Abdominal truncal vagotomy does not change basal lower oesophageal sphincter pressure (Crispin *et al* 1967, Mann *et al* 1968, Adam *et al* 1977) which is consistent with the observation that vagal fibres destined for the lower oesophageal sphincter enter the oesophageal body as a plexiform arrangement. It is difficult to understand why abdominal truncal vagotomy abolishes the increase in tone in response to increase in gastric pressure (Crispin *et al* 1967, Lind 1966).

Circular smooth muscle of the lower oesophageal sphincter demonstrates specialized responses to drugs, enteric hormones, passive stretch and electrical stimulation that differ from the adjacent oesophageal body or stomach (Christensen *et al* 1970, 1973, Lipschutz 1971, Cohen *et al* 1973). Pharmacologic studies show that bethanecol increases lower oesophageal sphincter pressure. Atropine (Lind *et al* 1968, Dodds *et al* 1981) and Propranolol (Thorpe 1980) decreases lower oesophageal sphincter pressure. Enkephalin may be a modulator of adrenergic transmission (Uddman 1980). Hormones such as gastrin (Castell *et al* 1970, Cohen *et al* 1971, Nebel *et al* 1973) increase sphincter tone while secretin, cholecystokinin, glucagon

lower it. Nifedipine and Verapamil lower sphincter tone (Hongo *et al* 1984) which suggests a role for calcium.

Cohen *et al* (1970) proposed that the basal lower oesophageal sphincter pressure correlates with sphincter strength. From in-vitro models, increasing diameter of the cardia reduces sphincter competency but the overall effect is reversed by increasing sphincter length (Bonavina *et al* 1986). Gastric wall tension contributes to sphincter opening and the importance of this contribution is reduced by the length of the sphincter (Petterson *et al* 1980). In any case, these studies are of questionable value and may not be relevant to the in-vivo situation.

Relaxation

Langley (1898) observed that the passage of fluid from the oesophagus to the stomach is due to inhibition of the cardiac sphincter. Deglutition causes relaxation of the lower oesophageal sphincter which starts at the onset or about 2 to 3 seconds after the onset of deglutition (Edwards 1961). Relaxation may last 5 to 10 seconds. The lower oesophageal sphincter then shows an after-contraction that lasts 7 to 10 seconds(Kelley *et al* 1960). Cold temperature does not affect the frequency of lower oesophageal sphincter relaxation (Winship *et al* 1970). Balloon distension of the oesophageal body may induce lower oesophageal sphincter relaxation unaccompanied by a peristaltic wave (Fleschler 1959). In a pig model, balloon distension of the oesophageal body induces lower oesophageal sphincter relaxation that is not altered by truncal vagotomy or cervical vago-sympathetic nerve section, but is abolished by transection of the gastro-oesophageal junction distal to the lower oesophageal sphincter which suggests the importance of intramural mechanisms (Lundell *et al* 1992). The lowest pressure that the lower oesophageal sphincter relaxes to is called the residual relaxation pressure or nadir pressure. Normally, it varies from 2mmHg to -2mmHg, relative to intragastric pressure at the time of relaxation (Kiroff *et al* 1984). The measurement of nadir pressures is only possible with a sleeve device that allows continuous monitoring of the lower oesophageal sphincter during deglutition because if a single channel is used, the cephalo-caudad movement of the lower oesophageal sphincter during deglutition relative to the side-hole would render the pressure measured from that channel unrepresentative of nadir pressure. Swallow induced lower oesophageal sphincter relaxation is mediated through vagal non-cholinergic non-adrenergic inhibitory nerves (Goyal *et al* 1975).

From radiological studies in healthy subjects, the lower oesophageal sphincter is a relatively narrow 2 cm channel which connects the oesophagus above the diaphragm to the stomach (Wolf 1960). Wolf called this the "submerged" segment which is collapsed at rest but distended by the passage of barium through it. Lower

oesophageal sphincter opening is determined mainly by pulsive forces transmitted via a swallowed bolus (Dodds 1989). The lumen widens until just before the peristaltic wave reaches it and is obliterated at the end of the peristaltic wave (Edwards 1961, Stewart 1981). This segment moves through the hiatus for a short distance during swallowing and only returns to its rest position following the passage of barium into the stomach. The top of this channel corresponds to the pressure inversion point (Botha *et al* 1957).

1.2.5. Gas gastro-oesophageal relux and belching

The sequence of events during spontaneous belching consists of transient lower oesophageal sphincter relaxation (McNally *et al* 1964, Wyman *et al* 1984), with gas gastro-oesophageal reflux occurring during the period when the oesophagus becomes a common cavity with the stomach (McNally *et al* 1964, Cohen *et al* 1972). This is followed by upper oesophageal sphincter relaxation (Kahrilas *et al* 1986) and oesophago-pharyngeal gas reflux. The contraction of somatic musculature is superimposed on this sequence of events. However, upper oesophageal sphincter relaxation can also occur independent of lower oesophageal sphincter relaxation (Kahrilas *et al* 1986). The common cavity is terminated by primary peristalsis (Wyman *et al* 1984) or secondary peristalsis (McNally *et al* 1964).

Transient lower oesophageal sphincter relaxations occur more often after gastric distension and more frequently in the sitting position compared to the recumbent position (Wyman *et al* 1990). A number of experiments in dogs have shed light on the control of the triggering of transient lower oesophageal sphincter relaxations.

Oesophageal common cavities during transient lower oesophageal sphincter relaxations are associated with gas venting in dogs (Martin *et al* 1986). Mechanoreceptors located in gastric segments that include the cardia, but not the fundus are primarily responsible for the transient lower oesophageal sphincter relaxations reflex produced by gastric distension (Martin *et al* 1988, Franzi *et al* 1990). Fundectomy did not abolish eructation of gas (Strombeck *et al* 1988) but placement of a band around the gastro-oesophageal junction and the first few centimetres of the cardia did (Strombeck *et al* 1989). This suggests that distension of the cardia along the lesser curve is adequate to trigger transient lower oesophageal sphincter relaxations leading to eructation.

Evidence for neural mediation of this reflex in humans comes from the observation that gastric distension failed to elicit transient lower oesophageal sphincter relaxations in patients with achalasia (Holloway *et al* 1989). Healthy people tolerate gastric distension by air insufflation without considerable increase in intragastric pressure whereas vagotomized patients experience a marked increase in intragastric

pressure during gastric distension (Jahnberg *et al* 1977). Sham fundoplication reduces the triggering of transient lower oesophageal sphincter relaxations by gastric distension, which suggests that mobilisation of the cardia interrupts afferent vagal fibres (Martin *et al* 1988). Atropine does not block the occurrence of transient lower oesophageal sphincter relaxations so muscarinic receptors are not important (Martin *et al* 1986).

The frequency of transient lower oesophageal sphincter relaxations decreases in the recumbent position, and is not related to the pooling of gastric fluid in proximity to the gastro-oesophageal junction (Little *et al* 1989). General anaesthesia (Cox *et al* 1987), truncal vagotomy (Jahnberg *et al* 1977, Strombeck *et al* 1987) and vagal cooling abolishes transient lower oesophageal sphincter relaxations in dogs (Martin *et al* 1986).

By definition, transient lower oesophageal sphincter relaxations are not swallow related. However, mylohyoid electromyogram signals accompany them (Mittal *et al* 1987) although the appearance of this complex is different from those associated with swallows.

1.3 RELATIONSHIP OF MOTILITY TO TRANSIT

Concurrent manometry and videofluoroscopy is useful in the study of the relationship of motility to bolus transit. This technique was first used by Dornhurst *et al* in 1954 and it is useful for relating pressures to deformations of the oesophageal wall. When the measuring port is within the bolus that is present in the oesophageal lumen, intrabolus pressures are recorded. During the contractile period, the peak amplitude measured represents the contracting wall squeeze which is much higher than the pressure required hydrodynamically to maintain complete luminal occlusion (Brasseur 1987).

Cook *et al* (1992) used this technique to study the upper oesophageal sphincter during swallowing. They described elevated hypopharyngeal intrabolus pressures proximal to a non-compliant cricopharyngeus muscle at the time of trans-sphincteric flow in patients with Zenker's diverticulum. Massey *et al* (1992) used the same technique to study the lower oesophageal sphincter in patients with oesophageal pulsion diverticula.

A single normal peristaltic wave results in complete clearance of barium from the oesophagus (Kahrilas *et al* 1986). Little clearance is achieved by regional hypotensive waves or incomplete peristaltic sequences (Kahrilas *et al* 1988). Primary peristalsis that is too feeble to maintain oesophageal luminal occlusion allows retrograde escape of barium. In the distal oesophagus, peristaltic amplitude necessary for lumen occlusion in the supine position is 30 mmHg and peristaltic velocities more

than 6.25 cm/sec usually result in abnormal bolus transit (Kahrilas *et al* 1986). Nearly complete barium clearance from the oesophagus can be accomplished by generalised oesophageal contraction and sequential tertiary activity whether they are isobaric or non-isobaric waves (Ott *et al* 1989, Hewson *et al* 1990, Massey *et al* 1991). Different patterns of bolus clearance may be seen in the same person (Ott *et al* 1989).

Simultaneous oesophageal manometry and radiology demonstrated that there is delay of about 1 second from deglutition to the passage of barium at the level of the hiatus (Creamer *et al* 1957). A liquid bolus reaches the lowest segment of the oesophagus in about than 1 second (Meltzer 1899, Ingelfinger 1958) as little resistance is offered by the oesophageal body. This mass is then squeezed through the cardia about 5 seconds after the beginning of deglutition by the peristaltic wave (Meltzer 1899, Humphries *et al* 1977). Barium streams across the cardia while the pressure in the oesophagus maintains a plateau. The normal cardia exerts little resistance to forward flow but is resistant to regurgitant flow during inspiration or Valsalva manouevres (Dornhurst *et al* 1954). In an experiment in cats, crural myotomy abolished the increase in gastro-oesophageal junction pressure associated with Valsalva manoeuvre (Mittal *et al* 1993).

Solid bolus transit was first assessed radiologically by Cannon in 1896 (Curtis 1986). More recently, barium tablets, bagel bread spheres (Curtis 1986) and marshmallows (Kelly 1961, Stewart 1981, Ott *et al* 1991) have been used. The marshmallow is an elastic solid that is advanced by peristalsis. When it impacts, it can reproduce the patient's symptoms. It is safe because it dissolves and eventually passes through the obstruction. Factors determining solid transit include oral thrust, adequate pharyngeal orifice and upper oesophageal sphincter, gravity, oesophageal body relaxation and lower oesophageal sphincter relaxation (Kelly 1961, Curtis *et al* 1986). Curtis *et al* (1986) defined as normal solid swallowing when there is no delay along the oesophagus, no additional swallows are necessary, and it takes less than 10 seconds for completion. In another study in 1987, he defined solid swallowing as abnormal if initial impaction occurs. When impaction occurs, gravity alone will not overcome a delay but additional liquid is most effective in clearing the bolus. Only a quarter of the people tested were aware of the initial arrest (Curtis *et al* 1987).

Bolus transport may also be assessed by radionuclide techniques (Russell *et al* 1981, Richter *et al* 1987). Bolus transit may be considered in 2 phases, the initial rapid dissemination of a bolus which depends on the pharyngeal ejection force and the second phase which depends on the oesophageal motor function, gravity and resistance to flow.

Using simultaneous radionuclide transport and oesophageal manometry, Richter *et al* (1987) showed that above a threshold of 30 mmHg, liquid transport is equally effective for peristaltic amplitudes between 33 and 500 mmHg and for the

duration of contraction between 3 and 15 seconds. There is an inverse correlation between liquid transit time and peristaltic velocity.

Oesophageal propulsive force has been studied using an intraluminal fixed balloon attached to a device that measures pull. This force of 4 to 200 grams-force appears soon after distension of the fixed balloon. If the balloon is allowed to dislodge this force is converted to a propagated propulsive force which propels the distending balloon aborally at 4 to 8 cm/sec (Winship *et al* 1967). Russell *et al* (1992) showed that the propulsive force and manometric pressure waves had a simultaneous onset and were of similar duration. Peak values of propulsive force are greatest in the distal oesophagus. However the correlation between manometric pressure and propulsive force is only moderately strong ($r = 0.61$).

CHAPTER 2: GASTRO-OESOPHAGEAL REFLUX DISEASE

Peptic oesophagitis was first recognised as a clinical entity by Winkelstein in 1935 (Dodds *et al* 1981) although it was Allison (1951) who first introduced the term "reflux oesophagitis". Oesophagitis is caused by abnormal reflux of gastric contents into the oesophagus. Gastro-oesophageal reflux disease is typically characterised by symptoms such as heartburn and regurgitation. In a survey of healthy hospital employees, 7% reported experiencing heartburn daily while 36% experience it once a month and have not sought any medical attention (Nebel *et al* 1976).

The defense mechanisms of the oesophagus include a competent anti-reflux barrier such as lower oesophageal sphincter tone; oesophageal mucosal resistance, efficient oesophageal clearing of refluxed contents and normal gastric emptying (Richter *et al* 1982, Jamieson *et al* 1986).

The association of gastro-oesophageal reflux disease with hiatus hernia is unclear (Wankling *et al* 1965, Olsen *et al* 1965, Lind *et al* 1966, Haddad 1970, Cohen *et al* 1972, Olsen 1965). In one study of 1011 patients, only 8.9% of the 786 patients with hiatus hernia were symptomatic (Palmer 1968).

2.1 OESOPHAGEAL MOTOR DYSFUNCTION

2.1.1 Lower oesophageal sphincter dysfunction

A hypotensive lower oesophageal sphincter pressure was more common in patients with oesophagitis compared to healthy people (Wankling *et al* 1965, Winans *et al* 1967, Kramer 1969, Cohen *et al* 1971, Dodds *et al* 1982). Basal lower oesophageal sphincter hypotension has been ascribed to dysfunction of circular smooth muscle or defective tonic neural control (Higgs *et al* 1976). The association of lower oesophageal sphincter hypotension with oesophagitis has been interpreted as lower oesophageal sphincter dysfunction being the cause of oesophagitis. However, experimentally induced oesophagitis in cats (Eastwood *et al* 1975, Higgs *et al* 1976) and baboons (Sinar *et al* 1981) led to lower oesophageal sphincter hypotension suggesting that sphincter hypotension may be the result rather than the cause of oesophagitis.

Substances that decrease lower oesophageal sphincter pressure include atropine (Lind *et al* 1968, Skinner *et al* 1968), secretin (Cohen *et al* 1971), cholecystokinin (Resin *et al* 1973), glucagon (Jennewein *et al* 1973), prostaglandin E1, E2, A2 (Goyal *et al* 1973), isoproterenol, a beta-agonist (DiMarino 1970), phentolamine, an alpha-blocker (DiMarino *et al* 1974), caffeine (Dennish *et al* 1971), gastric acidification

(Castell *et al* 1970, Farrell *et al* 1973), fat meal (Nebel *et al* 1973), chocolate (Babka *et al* 1973), cigarettes (Dennish *et al* 1971) and ethanol (Hogan *et al* 1973).

It has been reported that the competence of the lower oesophageal sphincter depends not only on its tone but also the length of the sphincter that is exposed to the abdominal environment (DeMeester *et al* 1979, Zainotto *et al* 1988, Stein *et al* 1992). A short sphincter is less able to protect against reflux when progressive gastric dilatation occurs (Bonavina *et al* 1986). A combination of a lower oesophageal sphincter pressure less than 6 mmHg, overall length less than 2 cm and abdominal length less than 1 cm was associated with gastro-oesophageal reflux disease (Bonavina *et al* 1986, Zainotto *et al* 1988). However, 40% of patients with gastro-oesophageal reflux disease have a competent sphincter by this definition (Zainotto *et al* 1988).

How does one explain reflux in patients with normal lower oesophageal sphincter pressure (Pope *et al* 1981, Edwards *et al* 1961)? Prolonged recording of lower oesophageal sphincter pressure and direct measurement of the lower oesophageal sphincter pressure at the moment gastro-oesophageal reflux occurs using concurrent oesophageal manometry and pH measurements lead to a better understanding than inferences derived from indirect evidence of sphincter function.

Prolonged recording of lower oesophageal sphincter pressure is possible with the invention of a sleeve device that straddles the lower oesophageal sphincter (Dent 1976). A minimum of 5 mmHg basal lower oesophageal sphincter pressure is sufficient to prevent reflux in recumbent healthy subjects (Dent *et al* 1980). Physiological reflux occurs in healthy individuals, 94% of the episodes being due to transient lower oesophageal sphincter relaxations. In patients with gastro-oesophageal reflux disease, it was found that 82% of reflux episodes were due to transient lower oesophageal sphincter relaxations, and 23% were due to absent basal lower oesophageal sphincter pressure which was more common in severe oesophagitis.

The timing of 69% of lower oesophageal sphincter relaxations were not related to swallowing. Transient lower oesophageal sphincter relaxations may be spontaneous, post-swallow which is the most common or post-secondary contraction (Lundell *et al* 1992). Mittal *et al* (1989) found that the frequency of transient lower oesophageal sphincter relaxations was the same in patients and controls, but the proportion of transient lower oesophageal sphincter relaxations accompanied by acid reflux was 36% in controls and 65% in patients. Even in patients with severe oesophagitis, 65% of reflux episodes were due to transient lower oesophageal sphincter relaxations, 17% were due to strain and 18% were due to free reflux (Dodds *et al* 1982). Incomplete transient lower oesophageal sphincter relaxations are not associated with reflux in the absence of straining (Dodds *et al* 1982). Straining became important in patients with absent basal lower oesophageal sphincter tone (Marchand *et al* 1957, Dent *et al* 1988). The frequency of transient lower oesophageal sphincter

relaxations and the proportion of transient lower oesophageal sphincter relaxations accompanied by acid reflux was increased in the post prandial period (Holloway *et al* 1991). Delayed gastric emptying may be responsible for the increased frequency of transient lower oesophageal sphincter relaxations in patients with gastro-oesophageal reflux disease through the mechanism of proximal gastric distension (Lundell *et al* 1992).

Transient lower oesophageal sphincter relaxations during gastro-oesophageal acid reflux resemble the transient lower oesophageal sphincter relaxations associated with the occurrence of common cavities (Dent *et al* 1980).

2.1.2 Oesophageal body

Gastro-oesophageal reflux of acid is most frequently cleared by primary peristalsis (Dent *et al* 1980, Corazziari *et al* 1984, Baldi *et al* 1985, Bremner *et al* 1992), although secondary peristalsis and non-peristaltic contractions have a role (Corazziari *et al* 1984).

Abnormalities of primary peristalsis are found in gastro-oesophageal reflux disease. Failed primary peristalsis or hypotensive peristalsis in the distal oesophagus for over half the test swallows occur in 25% of patients with mild oesophagitis and 48% with severe oesophagitis compared to 3% of controls (Kahrilas *et al* 1986). This finding of primary peristaltic dysfunction is supported by others (Heddle *et al* 1984, Corazziari *et al* 1984, Baldi *et al* 1985). Peristaltic waves have a lower amplitude (Bombeck *et al* 1973, Marshall *et al* 1982, Gill *et al* 1986, Kahrilas *et al* 1986, Katz *et al* 1986, Grande *et al* 1991, Singh *et al* 1992) and slowed propagation compared with healthy controls (Kahrilas *et al* 1986, Singh *et al* 1992). The duration of contraction was found to be shortened by Kahrilas *et al* (1986) but more prolonged by Singh *et al* (1992). The amplitude is not correlated with the severity of oesophagitis (Bombeck *et al* 1973, Gill *et al* 1986, Grande *et al* 1991) or the severity of dysphagia (Grande *et al* 1991).

It is not known if these abnormalities are primary or secondary to reflux. Experimentally induced oesophagitis in cats (Eastwood *et al* 1975, Higgs *et al* 1976) and baboons (Sinar *et al* 1981) show similar peristaltic changes. Primary peristalsis has been reported to improve with medical therapy by some (Marshall *et al* 1982, Kahrilas *et al* 1986, Moses 1987) but not by others (Baldi *et al* 1985, Eriksen *et al* 1985, Katz *et al* 1986, Singh *et al* 1992).

Clearance of a radioactively labelled liquid (Russell *et al* 1981) and solid (Eriksen *et al* 1985, Maddern *et al* 1986) have been shown to be delayed in patients with reflux oesophagitis. Acid clearance is poor in 50% of patients with gastro-oesophageal reflux disease (Skinner *et al* 1970, Stanciu *et al* 1973). The observation

that a fall in pH due to acid reflux is more often normalised by primary peristalsis does not mean that secondary peristalsis has no role. Secondary peristalsis can act by clearing the bulk of the volume of refluxate from the oesphagus but the pH may not rise until primary peristalsis delivers bicarbonate rich saliva to the oesophagus (Joelsson *et al* 1982, Helm *et al* 1984). Acid volume as small as 0.05 ml is recorded as a significant drop in pH. Minute amounts of acid injected 6 cm above the lower oesophageal sphincter that was not detected 1 cm above the sphincter which suggests that the acid is neutralized rather than cleared.

In a study of secondary peristalsis by Schoeman, 10 ml air and water boluses have a median of 0% success in triggering secondary peristalsis in these patients compared with healthy subjects where 10 ml air boluses triggered secondary peristalsis with a median response rate of 70% and 10 ml water boluses were successful 50% of the time (Schoeman 1993). The majority of patients with defective secondary peristalsis in this study had normal primary peristalsis. The distension threshold may also be higher in patients compared to controls (Williams *et al* 1992).

Other motility disturbances that have been reported include non progressive oesophageal contractions occur during periods of acid induced heartburn (Creamer 1955, Siegel *et al* 1963, Olsen *et al* 1965, Corazziari *et al* 1984). Scleroderma-like aperistalsis is also associated with oesophagitis, in such cases, tight anti-reflux procedures may compromise a borderline oesophageal pump (Joelsson *et al* 1982, Richter *et al* 1982).

2.1.3 Diaphragm and other factors

The role of the diaphragm as a "pinchcock" was put forward by Jackson in 1978. Byrnes *et al* (1963) suggested a role for the crura in the closing mechanism at the gastro-oesophageal junction. Food and liquid are held up at the diaphragm and this arrest is prolonged during inspiration (Creamer *et al* 1957). Mittal *et al* (1989) showed that graded voluntary contractions of the diaphragm induced proportional increases in gastro-oesophageal junction pressure during sustained lower oesophageal sphincter relaxation by balloon distension. In an experimental model in cats, there was a significant increase in spontaneous acid reflux after crural myotomy but no increase in acid reflux associated with abdominal compression. Abdominal compression caused a reflex contraction at the gastro-oesophageal junction that was not affected by crural myotomy (Mittal *et al* 1993). However, when the diaphragm is paralysed or transposed in humans, sphincter function is satisfactory. A normal high pressure zone at the gastro-oesophageal junction can exist in patients with hiatus hernia where the contribution of the diaphragm to the closing mechanism is negligible (Atkinson *et al* 1957, Lind *et al* 1966, Cohen *et al* 1971). Furthermore, when muscle layers of the

gastro-oesophageal junction is excised, reflux oesophagitis occurs even if the hiatus is carefully repaired (Meltzer 1899).

The terminal oesophagus is said to act as a flaccid tube passing from a low to a high pressure zone (Dornhurst *et al* 1954). A segment of the terminal oesophagus exposed to the positive environment of the abdominal cavity is otherwise referred to as the abdominal length of the lower oesophageal sphincter and may contribute to its competence (O'Sullivan *et al* 1982). Simple positioning of a hypotensive lower oesophageal sphincter below the diaphragm results in increase in basal lower oesophageal sphincter pressure whereas replacement of a normal lower oesophageal sphincter did not (Katz *et al* 1974). The sling of oblique gastric muscle fibres which invests the cardia may be important in maintaining the acute angle of His, contributing to the valve mechanism (Dornhurst et al 1954, Gahagan 1962). When the oesophagus is divided and joined to the posterior stomach in a canine model in such a way that a mucosal lip is the only mechanism capable of preventing reflux, competence is maintained (Jamieson et al 1988). However, Wald et al (1982) denied the importance of the angle of His as this angle can vary from acute to obtuse in normals.

Galen in the year 200 first described the phreno-oesophageal membrane (Friedland 1978), which was subsequently named after Laimer (1883). This membrane is a fibro-elastic sleeve that arises from transversalis and subdiaphragmatic fascia; its upper leaf maintains the gastro-oesophageal junction in the abdomen during periods of raised intra-abdominal pressure (Bombeck *et al* 1966). Displacement of its insertion at the lower oesophagus inferiorly may contribute to gastro-oesophageal junction incompetence (Byrnes *et al* 1963, Dillard *et al* 1966, Eliska 1973). In operations enhancing lower oesophageal sphincter function, there are those who regard it as important (Allison 1951, Hill 1967, Bombeck *et al* 1966) and those who ignore it (Daniel *et al* 1976). Division of the phreno-oesophageal membrane failed to result in a change in the high pressure zone (Bremner 1992).

Magendie advocated a role for the mucosa rosette which Dornhurst *et al* (1954) and Botha *et al* (1957) described as a valve formed by the action of the muscularis mucosae on the mucosa.

It is possible that all the above factors contribute to gastro-oesophageal junction competence as excision of this junction results in oesophagitis (Ellis *et al* 1973).

CHAPTER 3: ANTI-REFLUX SURGERY

3.1 HISTORICAL ASPECTS

Anti reflux surgery is recommended for 5-20% of patients with reflux disorder who have troublesome symptoms in spite of 8 to 12 weeks of vigorous medical treatment (Richter *et al* 1982, Stein *et al* 1992) or if complications such as a stricture or a columnar-lined oesophagus supervene. According to Stein *et al* (1992), patients with a mechanically defective sphincter such as lower oesophageal sphincter pressure less than 6 mmHg, overall length less than 2 cm and abdominal length less 1 cm, are more likely to benefit from anti-reflux surgery. Mortality associated with surgery is 0.2 to 1.6% (Richter *et al* 1982).

Until Allison's paper in 1951, surgical attention was aimed at the anatomic defect of the hiatus hernia (Behar *et al* 1975), not the physiological defect of incompetence of the cardia. This change in focus after Allison's paper was important because operations in which an anatomical repair was carried out without incorporating technical features designed to restore competence to the cardia did not succeed in curtailing reflux (Woodward *et al* 1971).

Naumann in 1888, Mayo in 1911 (Hill 1967) and Soresi in 1919 were pioneers in the repair of the hiatus hernia. Hiatal hernia repairs by Berg, Harrington (1928) and Allison (1948) advocated fixing the curvature of the stomach to maintain their correct positions. Other operations for reflux may involve invaginating, plicating or wrapping the cardia.

In the Allison repair, the diaphragm is incised and the anterior part of the phreno-oesophageal ligament is used to fix the stomach (Allison 1951). The Belsey Mark VI (Skinner *et al* 1967) consists of wrapping the greater curvature of the fundus of the stomach around the anterior two-thirds of the circumference of the distal oesophagus followed by transdiaphragmatic sutures to anchor the abdominal oesophagus in the abdomen. The Nissen fundoplication is described in some detail in the following section. In the Hill operation (1967), a posterior gastropexy is carried out and the use of intra-operative manometry with this procedure improves the results. Other anti-reflux procedures (Jamieson *et al* 1986) include anterior gastropexy, Ligamentum teresopexy, the Collis operation, combined gastro-plasty and fundoplication or the Collis-Nissen procedure, the Angelchik prosthesis and Watson's operation (Watson *et al* 1991).

The incidence of recurrent reflux after the Allison repair is 20 to 25% (Woodward *et al* 1971), the Belsey repair 7 to 10% (DeMeester *et al* 1974), Nissen fundoplication 0% to 12% (Woodward *et al* 1971, DeMeester *et al* 1974, Cordiano *et*

al 1976, Negre *et al* 1983, Donahue *et al* 1985, O'Hanrahan *et al* 1990). Long term follow-up of more than 20 years reveal that the recurrence rate after the Allison repair is 40%, Belsey 30% and Nissen 28% (Jamieson 1993).

Experiments in dogs showed that constructing the angle of His alone allowed flow from the oesophagus to the stomach and vice versa. Creating a tunnel for the cardia out of the fundus of the stomach or placing a plastic sling around the cardia creates a one way gastro-oesophageal valve that is independent of the diaphragm (Adler *et al* 1958).

3.2 NISSEN FUNDOPLICATION

Rudolf Nissen reported the technique of fundoplication of the stomach around the lower oesophagus for reflux oesophagitis in the German literature in 1956 and in the English literature in 1961. He had serendipitously discovered that fundoplication prevented reflux when he reviewed a patient 16 years after he performed a partial oesophagectomy and wrapped the fundus of the stomach around the anastomosis. The technique involves the construction of a peri-oesophageal fundic ring around the gastroesophageal junction, buttressing the sphincter.

Nissen mobilised the lesser curve of the stomach and pushed the anterior and posterior walls of the stomach around the oesophagus. The posterior wall was then sutured to the anterior wall and the oesophageal wall was included in the suture. A "pseudotumour" of the fundus is often seen after fundoplication. This is usually located anterior to a subdiaphragmatic oesophagus. It is a smoothly demarcated and well circumscribed filling defect. It is quite large in the immediate post-operative period but subsides 3 months later (Teixidor *et al* 1973, Feigin *et al* 1974). Moran *et al* (1971) considered the presence of a pseudotomour as indicative of a good result but this is controversial to say the least.

A variation of the technique for the obese patient is to wrap the anterior wall of the stomach around the lower oesophagus, stitching the stomach to itself (Jamieson *et al* 1984). The use of the anterior wall of the stomach minimises dissection around the cardia and is also known as Rosetti's modification of the Nissen fundoplication or the Nissen II operation (Rossetti *et al* 1977).

Other modifications to the original technique include mobilisation of the greater curve by dividing the short gastric vessels (Donahue *et al* 1985), full mobilisation of the fundus and stomach (Kiroff *et al* 1984), closure of the oesophageal hiatus, anchoring the fundoplication to the pre-aortic fascia, addition of highly selective vagotomy (Jamieson *et al* 1984), making an incomplete wrap (Guarner *et al* 1975, Menguy 1978, Lundell *et al* 1991), double plication and constructing a floppy wrap

(Rohr 1991) and anchoring the fundoplication to the right crus of the diaphragm (Cordiano *et al* 1976).

The Nissen fundoplication offers relief in 91% in follow-up studies of more than 10 years (Stein *et al* 1991).

Laparoscopic fundoplication

Minimally invasive surgery is rapidly gaining acceptance. The laparoscopic Nissen fundoplication is the most commonly performed of the laparoscopic anti-reflux procedures, although the Toupet (Lundell *et al* 1991) and Watson operations (Watson *et al* 1991) are also amenable to laparoscopic techniques (Branicki 1993).

Laparoscopic fundoplication was first reported by Dallemagne *et al* in 1991. Since then follow-up of patients ranges from 12 (Dallamagne *et al* 1991), 14 (Bagnato 1992), 21 (Cregan 1993), 36 (Falk *et al* 1993), 37 (Cadiere *et al* 1992), 40 (Hinder *et al* 1992) to 150 patients (Jamieson *et al* 1994).

It is well tolerated by elderly patients (Cuschieri *et al* 1992) and the advantage of a fast post-operative recovery and early discharge from hospital has encouraged surgeons to offer the operation more readily. In the 1970's, the persistence of oesophagitis and the presence of complications despite intensive medical treatment was a secure indication for surgery but whether patients with reflux but no oesophagitis should be operated on was a contentious issue (Polk *et al* 1971). More recently, open fundoplication became an option for those with troublesome symptoms in spite of 8 to 12 weeks of vigorous medical treatment if reflux was objectively proven by pH monitoring even in the absence of oesophagitis. The indications for laparoscopic Nissen fundoplication was similar to the above, but also included those who respond to medical management but choose not to take tablets for the rest of their lives.

The experience at the Royal Adelaide Hospital with the first 150 cases was that 83% had good to excellent results from their surgery (Jamieson *et al* 1994). Experienced surgeons warn of the need to achieve equal or better results to the open operation with a low incidence of side effects (Stein *et al* 1992, Jamieson 1993). Hence long term follow-up is important and there may be a role for prospective trials.

3.3 EFFECT ON OESOPHAGEAL MOTILITY

3.3.1 Effect on the gastro-oesophageal junction

Fundoplication increases basal gastro-oesophageal junction pressure (Lind *et al* 1965, Moran *et al* 1971, Csendes *et al* 1972, Ellis *et al* 1973, Pope *et al* 1973, Bahadorzadeth *et al* 1975, Behar *et al* 1975, Lipshutz *et al* 1974, Ellis *et al* 1973,

Bushkin *et al* 1977, De Meester *et al* 1974, Fisher *et al* 1978, Brand *et al* 1979, Papp 1979, Goodall *et al* 1980, Russell *et al* 1981, Kiroff *et al* 1984, Kozarek *et al* 1983, Matikainen *et al* 1984, Ellis *et al* 1984, Johnsson *et al* 1987, Stuart *et al* 1989, O'Hanrahan *et al* 1990, Ortiz Escandell *et al* 1991, Lundell *et al* 1991, 1992 & 1993, Little *et al* 1992, Ireland *et al* 1993).

Chambers *et al*, (1972) suggested that the addition of an external cuff to the region of the lower oesophageal sphincter is responsible for the increase in gastro-oesophageal junction pressure. In dogs who have had a myomectomy to resect the lower oesophageal sphincter junction, fundoplication still imposes a high pressure zone on the gastro-oesophageal junction (Samelson *et al* 1983). It allows the maximal influence of gastric pressure on the lower oesophageal sphincter. It also serves as a conduit in which the intra-abdominal pressure is transmitted directly to the terminal oesophagus (Matikanen *et al* 1984, DeMeester *et al* 1979) so it is effective even when the wrap is in the chest (Woodward *et al* 1971). However, the new gastro-oesophageal junction pressure is more than the sum of the pre-operative lower oesophageal sphincter pressure and intragastric pressure in the wrap around it (Behar *et al* 1975) so perhaps fundoplication increases the gastro-oesophageal junction pressure independent of simple transmission of abdominal pressure.

Fundoplication also creates a mechanical compression of the lower oesophageal sphincter (Dent *et al* 1982, Ogorek *et al* 1989, Ireland *et al* 1993, Lundell *et al* 1993). Application of an extrinsic weight of as little as 50 g narrows the oesophagus and results in a zone of elevated pressure (Bowes *et al* 1975).

Healing of oesophagitis may also contribute to the increase in lower oesophageal sphincter pressure (Higgs *et al* 1975) although Katz *et al* (1986) found that there was no significant difference between lower oesophageal sphincter pressures obtained during exacerbations and remissions of the disease. In humans, histologic improvement in oesophagits was not correlated with the increase in gastro-oesophageal junction pressure (Pope *et al* 1973).

In dogs, the magnitude of the gastro-oesophageal junction high pressure zone depends on how tightly the fundus is drawn around the terminal oesophagus (Siewert *et al* 1974). A study of the relationship of bougie diameter to basal gastro-oesophageal junction pressure and yield pressure showed that the smaller the bougie, the tighter the wrap and the higher the basal and yield pressures. Yield pressure was obtained by perfusing the distal oesophagus while occluding the proximal oesophagus till the gastro-oesophageal junction pressure opens. Regardless of the size of the bougie, however, all the fundoplications prevented the transmission of fluid from the stomach to the oesophagus (Bergeron *et al* 1985).

In randomised control trials, basal gastro-oesophageal junction pressure is also increased when a partial fundic wrap is performed but this is lower than the increase

achieved by a total wrap (DeMeester *et al* 1974, Lundell *et al* 1991). An anterior 180 degrees fundoplication or Dor patch is also associated with an increase in basal gastro-oesophageal junction pressure (Mir *et al* 1986). The increase in basal gastro-oesophageal junction pressure could be reproduced by placing rods and dilators behind the gastro-oesophageal junction in baboons suggesting that posterior padding of the gastro-oesophageal junction changes length tension relationships of the muscle at the junction and causes an increase in basal pressure (Benjamin *et al* 1983).

During water swallows, the relaxation of the post-fundoplication gastro-oesophageal junction is incomplete (Bowes *et al* 1975, Dent *et al* 1982, Kiroff *et al* 1984, Jamieson *et al* 1992, Lundell *et al* 1993, Ireland *et al* 1993) with a nadir pressure of 4 to 6.5 mmHg.

Patients with tight fundoplication have a lower rate of gastro-oesophageal junction relaxation. Experimental studies in cats when a gortex band was placed around the gastro-oesophageal junction showed that the rate of gastro-oesophageal junction relaxations decreased at 4 weeks after banding (Little *et al* 1986). There is a 50% decrease in transient lower oesophageal sphincter relaxations after fundoplication, and decrease in the proportion of transient lower oesophageal sphincter relaxations accompanied by reflux from 47% to 17% (Ireland *et al* 1993). Fundoplication changes the distensibility of the cardia which is the trigger zone for transient lower oesophageal sphincter relaxations (Ireland *et al* 1993). It prevents distraction of the cardia by limiting gastric wall tension in the region of the gastro-oesophageal junction (Samelson *et al* 1983, Little *et al* 1992) and changes the gastric wall tension response to increase in intra-gastric pressure (Petterson *et al* 1980). Interestingly, sham fundoplication in dogs decreased the occurrence of transient lower oesophageal sphincter relaxations suggesting that mobilisation of the cardia interrupts neural mechanisms involved in the reflex (Martin *et al* 1988). After fundoplication, the gastro-oesophageal junction has improved response to pentagastrin (Lipschutz *et al* 1974, Siewert *et al* 1974) and Tensilon (Farrell *et al* 1973). However, it fails to generate an increase in pressure in response to abdominal compression (Behar *et al* 1975) and protein meal (Farrell *et al* 1973).

It has been suggested that control of reflux by fundoplication does not necessarily depend on increasing the gastro-oesophageal junction pressure (Bancewicz *et al* 1987, Maddern *et al* 1991). Fundoplication narrows the angle of His re-creating a flap valve effect (Bowes *et al* 1975, Fisher *et al* 1978, Butterfield 1971, Matikainen *et al* 1984, Little 1992). The Nissen fundoplication can be competent in the absence of myogenic influence as demonstrated by post-mortem studies in humans (Butterfield 1971). An effective flap-valve need not exert any increase in resting gastro-oesophageal junction pressure (O'Hanrahan *et al* 1990), and surgical correction of reflux need not be directly related to the new gastro-oesophageal junction pressure

(Bowes *et al* 1975, Fisher *et al* 1978, Bancewicz *et al* 1987). Excision of the cardia in dogs and replacing it with a flap valve constructed from the stomach wall was successful in preventing oesophagitis (Dillard *et al* 1954).

3.3.2 Oesophageal body

Fundoplication has been found to restore normal oesophageal motility to patients with gastro-oesophageal reflux disease and poor pre-operative motility independent of any increment in gastro-oesophageal junction pressure (Moses 1987, Grande *et al* 1991, Ortiz Escandell *et al* 1991) and some investigators believe that motor abnormalities are the consequence of reflux induced oesophageal damage.

After fundoplication, increase in amplitude of contraction has been observed (Bowes *et al* 1975, Kozarek *et al* 1983, Ortiz Escandell *et al* 1991). Stein *et al* (1992) identified a subgroup of patients with pre-operative peristaltic amplitude less than 35 mmHg who did not show any improvement after fundoplication. Improvement in contraction amplitude may be a response to obstruction (Jamieson 1993), an effect that has been demonstrated experimentally in cats (Mittal *et al* 1990). The correlation between distal oesophageal amplitude and basal or nadir gastro-oesophageal junction pressure is poor (Gill *et al* 1986). Bowes *et al* (1975) found that the duration of contraction was less after fundoplication.

The effect of fundoplication on secondary peristalsis is unknown. However, tertiary contractions were unchanged (Ortiz Escandell *et al* 1991, Stein *et al* 1992) or increased (Gill *et al* 1986). Patients with tight fundoplication have the same frequency of tertiary contractions as patients with strictures suggesting that a tight fundoplication is a form of oesophageal outflow obstruction. Experimental studies in cats where a gortex band was placed around the gastro-oesophageal junction showed that there was mild dilatation of the oesophagus at 4 weeks. The frequency of tertiary contractions increased from 0% before banding to 85% at 4 weeks post banding. Little *et al* (1986) suggested that abnormal oesophageal function is caused by partial distal oesophageal obstruction, which is mechanical and fixed in strictures but functional and apparently related to inability of the gastro-oesophageal junction to relax fully after fundoplication.

Massey *et al* (1992) found that patients with oesophageal pulsion diverticula have either hypertensive lower oesophageal sphincter pressure or incomplete lower oesophageal sphincter relaxation. This was associated with a high ramp intrabolus pressure compared to normals which suggests that the ramp pressure may be a useful parameter indicative of oesophageal obstruction.

The effect of outflow obstruction on oesophageal motility was studied in detail in a feline model using synchronous oesophageal manometry and videofluoroscopy

(Mittal *et al* 1990). A specially designed pressure cuff was placed at the gastro-oesophageal junction. The degree of inflation of this cuff was adjusted to control the degree of outflow obstruction. Secondary peristalsis was triggered using 3, 6 and 9 ml boluses of barium. The amplitude of contraction increased with increasing obstruction at low volumes but decreased with larger bolus volumes. Increasing outflow obstruction decreased the velocity of peristalsis but had no effect on the duration of contraction. With increasing outflow obstruction, contractions fail to traverse the entire length of the oesophagus and the incidence and site of failure was directly related to cuff pressure and bolus volume. Retrograde escape occurred at the site of failure. Ramp intrabolus pressures were seen in the distal oesophagus; its amplitude and duration increased with increasing outflow obstruction. The ramp intrabolus pressure can merge into the amplitude at some degrees of outflow obstruction, making it difficult to identify the upstroke of the contraction manometrically. As long as the amplitude of the contraction exceeded the intrabolus pressure, aboral movement of the bolus occurred and there was progression of peristalsis. With extreme obstruction, isobaric waves were seen, representing intrabolus pressures only. This study suggests that an isolated lower oesophageal sphincter abnormality can induce oesophageal contraction dysfunction.

The effect of fundoplication on bolus transport is unclear. Stanciu *et al* (1973), Maddern *et al* (1985) and Hinder *et al* (1992) observed that fundoplication improved solid and liquid emptying but Russell *et al* (1981) disagreed.

CHAPTER 4: CLINICAL SEQUELAE OF FUNDOPLICATION

4.1 DYSPHAGIA AFTER FUNDOPLICATION

Incidence

Dysphagia is defined as the subjective sensation of solid or liquid sticking at the level of the mouth, neck or chest when a person swallows (Ravich *et al* 1989).

The incidence of non-obstructive dysphagia in unoperated patients with gastroesophageal reflux disease varies from 28% to 52% in different patient series (Bombeck *et al* 1972, Postlethwait 1979, Henderson 1980, Triadafilopoulos 1989, Grande *et al* 1991). These patients have no organic lesion secondary to reflux, such as strictures, no local structural lesions or neuromuscular disorders. Non-obstructive dysphagia is associated with the presence of oesophagitis (Dakkak *et al* 1993) although it is related more to peristaltic dysfunction than to the severity of oesophagitis (Russell *et al* 1981, Maddern *et al* 1986, Grande *et al* 1991). Dysphagia can improve following surgery even if peristaltic dysfunction as measured by radionuclide transit does not (Russell *et al* 1981, Maddern *et al* 1986). Henderson (1980) noted pharyngoesophageal dysphagia in 51% of 1000 consecutive patients evaluated and treated for gastroesophageal reflux disease. Anti-reflux surgery improved pharyngoesophageal dysphagia in 90%. Conversely, if dysphagia occurs as a new symptom after fundoplication, then that dysphagia is a complication of fundoplication.

The goal of anti-reflux surgery is not solely the control of reflux (Menguy 1978). It must improve the quality of life (Pope 1992). In one study, 7% of patients considered their operation a failure because of post-operative dysphagia (MacIntyre *et al* 1990). Yet, some surgeons view the presence of side-effects such as dysphagia and gas-bloat as testimony to the effectiveness of the fundoplication (Menguy 1978)!

Transient post-operative dysphagia occurs from the second post-operative day and usually settles by the sixth post-operative week in 85% to 100% (DeMeester *et al* 1974, Negre *et al* 1983). This may be due to the increase in gastro-oesophageal junction pressure (Grande *et al* 1991) and post-traumatic oedema around the cardia (Polk *et al* 1971, Ellis *et al* 1984, Shirazi *et al* 1987). DeMeester *et al* (1992) reported that Nissen fundoplication carried out by the intrathoracic route resulted in less post-operative dysphagia compared to the abdominal approach and suggested that stretching of the lower oesophagus may be a cause. Dodds *et al* (1973) showed that the axial excursion of the oesophagus during swallowing is greatest in the distal oesophagus so dysphagia may be related to the inability of the oesophagus to maintain its axial

movement initially. He speculated that when tissues accommodate to this new length, dysphagia resolves.

The incidence of post-operative dysphagia after 3 months ranges from 0 to 43% (Woodward *et al* 1971, Bahadorzadeh *et al* 1974, DeMeester *et al* 1974, Fisher *et al* 1978, Negre *et al* 1983, Gear *et al* 1984, Kiroff *et al* 1984, Deakin *et al* 1989, Stuart *et al* 1989, Kmiot *et al* 1991, Eyre-brook *et al* 1993, Luostarinen 1993).

Dysphagia has been classified as mild if it is noticeable and occurs occasionally, moderate if solids required liquids to clear or severe if it requires medical attention. In a study by Johanssen *et al* (1993), mild dysphagia was present in 24% of his patients at 3 months and 5 years whereas moderate dysphagia was present in 14% at 3 months, decreasing to 0.3% at 5 years. In another study by Lundell *et al* (1991), mild dysphagia was present in 50% of his patients at 3 months, decreasing to 11% at 6 months, moderate dysphagia was present in 17% at 3 months which resolved by 6 months. None of the patients in these 2 studies experienced severe dysphagia.

Laparoscopic fundoplication is also complicated by dysphagia. The incidence ranged from 0% to 6% at 3 months (Dallemange *et al* 1991, Cuche *et al* 1992, Weerts *et al* 1993). Mild dysphagia was present in 3%, moderate dysphagia in 2% and severe dysphagia in 1%, requiring re-operation at 9 months (Weerts *et al* 1993). In Mitchell's follow-up of the first 100 patients who underwent laparoscopic fundoplication in Adelaide, 32% reported some dysphagia, at least 7 patients had dilatations and 3 were re-operated for dysphagia (personal communication).

Some advocate division of short gastric vessels as a routine to minimise dysphagia (Cregan 1993) while others deem it unnecessary (Watson *et al* 1993). This is an important and yet unresolved issue.

Post-fundoplication dysphagia is managed by dilatation (Bahadorzadeh *et al* 1974, Rossman *et al* 1979, Stirling *et al* 1989) but severe cases may require re-operation (Henderson *et al* 1979, Siewert *et al* 1989). Tight wraps account for 0.8 to 43% of all cases of re-operations for gastro-oesophageal reflux (Hill *et al* 1979, Leonardi *et al* 1981, Henderson *et al* 1985, Siewert *et al* 1989, Stirling *et al* 1989, Rieger *et al* 1993).

Other complications such as a slipped fundoplication can also present with dysphagia (Leonardi *et al* 1981). In this case, the gastro-oesophageal junction pressure cannot be identified manometrically (Mattox *et al* 1990).

Objective correlates

Information on objective findings associated with post-fundoplication dysphagia is sparse.

Woodward *et al* (1971) found that patients with dysphagia post-fundoplication have normal peristaltic amplitude and normal lower oesophageal sphincter relaxation with deglutition although no values were quoted. Gill *et al* (1986) and Breumelholf *et al* (1991) reported that there was no significant difference in the amplitude, duration of contraction and velocity in patients with dysphagia post-fundoplication compared with those without dysphagia post-fundoplication. Increase in tertiary waves have been noted in patients with post-fundoplication dysphagia (Skinner 1967).

When conventional techniques such as barium meal, oesophageal manometry and endoscopy are unable to find a cause for post-fundoplication dysphagia in patients who have no pre-operative dysphagia; and when dilations are ineffective but the dysphagia is relieved by refashioning a loose wrap, dysphagia is assumed to be due to the tightness of the original wrap (Leonardi *et al* 1981, Donahue *et al* 1985).

Duranceau *et al* (1982) and Orringer *et al* (1980) both constructed fundoplications around large size bougies. Duranceau *et al* found no significant post-operative dysphagia while Orringer *et al* found significant post-operative dysphagia in his patients who had longer fundoplications.

Del Genio (Jamieson *et al* 1988) carried out intraoperative manometry on patients who had total fundoplication after myotomy and found that when they tightened the fundoplication to 18 mm Hg, dysphagia post-operation became a greater problem than with a looser wrap of 13 mm Hg. Basal gastro-oesophageal junction pressure measured intraoperatively and at 6 months after fundoplication showed no significant correlation with dysphagia (Jamieson *et al* 1992) although the number of patients was only 4. It was hypothesised that the ability of the oesophageal body to propel a bolus distally may depend on the ability of the gastro-oesophageal junction to open which bears no direct relationship to the basal gastro-oesophageal junction pressure.

Dysphagia is a prominent symptom if the Nissen fundoplication is too long or too tight (Negre *et al* 1983, Mattox 1990, Loustarinen *et al* 1993). Woodward *et al* (1971) contends that post-fundoplication dysphagia is not the result of making a tight wrap as all his patients had fundoplications constructed around bougies of the same size but dysphagia was present in 24 %.

Since the 1970's, a loose wrap has been favoured (Ellis *et al* 1973, Bjerkeset *et al*, 1980, Siewert *et al* 1992) and it is said that it is impossible to make the wrap too loose. Loose wraps in dogs eliminated reflux, no matter how loose (Donahue *et al* 1985). Increasing the bougie size from 36 F to 60 F and decreasing the length of fundoplication from 4 cm to 1 cm reduced the incidence of transient dysphagia from 83% to 39% and the incidence of permanent dysphagia from 21% to 3%, without any loss in reflux control (DeMeester *et al* 1985). Dysphagia was decreased from 4.5% to 0.6% when the technique of fundoplication was changed from a snug wrap to a floppy

wrap (Shirazi *et al* 1987). A tight wrap could be due to a small fundus or an inadequately mobilised fundus (Wald *et al* 1982).

4.2 BELCHING DIFFICULTIES AFTER FUNDOPLICATION

Incidence

The reported incidence of the inability to belch as a new symptom after fundoplication varies from 1.5% to 100% in different patient series (DeMeester *et al* 1976, Negre *et al* 1983, Ellis *et al* 1984, Kiroff *et al* 1984, Johnsson *et al* 1987, Breumelhof *et al* 1991, Johansson *et al* 1993). Inability to vomit ranged from 31% to 63% (DeMeester *et al* 1974, Negre *et al* 1983). Many studies have relied on subjective reports and have not undertaken objective measurements.

Woodward *et al* (1971) introduced the phrase "gas-bloat" to describe early satiety, fullness in the epigastrium and left upper quadrant, decreased ability to eructate, increased boborygmi and flatus. Gas-bloat is also known as abdominal meteorism. The incidence ranges from 13% to 67% (Woodward *et al* 1971, Ellis *et al* 1973, DeMeester *et al* 1974 & 1986, Bushkin *et al* 1976, Menguy *et al* 1978, Negre *et al* 1983, Thor *et al* 1989, Lundell *et al* 1993). In one study, 17% of patients considered their operation a failure because of post-operative gas-bloat (MacIntyre *et al* 1990). In one study by Bushkin *et al* (1977), 2% of patients had their fundoplication taken down because of gas-bloat. The few follow-up studies of laparoscopic fundoplication have not reported any gas-bloat or inability to belch (Dallemagne *et al* 1991, Cuche *et al*, 1992, Weerts *et al* 1993).

Objective correlates

A widely accepted explanation for gas bloat is that swallowed air is trapped in the fundus and cannot be released through the one-way valve of the fundoplication (Woodward *et al* 1971).

Gas-bloat has been linked with increase in gastro-oesophageal junction pressure (Bushkin *et al* 1976, Strombeck *et al* 1989, Lundell *et al* 1993). The inability of the gastro-oesophageal junction to relax fully during water swallows is also correlated with gas bloat (Lundell *et al* 1993). Basal gastro-oesophageal junction pressure measured intraoperatively and at 6 months after fundoplication showed no significant correlation with gas-bloat (Jamieson *et al* 1992).

In Papp's (1979), 2 patients were relieved of their gas-bloat symptoms after dilatation suggesting that the tightness may be partly responsible. Gas-bloat has been attributed to tightness of fundoplication by Menguy *et al* (1978) and Shirazi *et al*

(1987). Yet other investigators suggest that inability to belch occurs in a random fashion that is not related to the tightness of the wrap (Henderson 1985). Crural repair alone does not result in gas-bloat (Woodward *et al* 1971).

Donahue *et al* (1985) reported that only 1.5% of patients were unable to belch at all after a floppy Nissen fundoplication, but there were other patients who said that they could belch but not "as freely as before the operation". Others advocated incomplete fundoplication which are as effective as total fundoplication but allows the patient to belch (Guarner *et al* 1975, Menguy 1978, Lundell *et al* 1991).

After a floppy fundoplication, the incidence of gas-bloat range from 1.5% (Donahue *et al* 1985) to 29% (Stuart *et al* 1989). Shirazi *et al* (1987) found an 8% incidence of gas-bloat with a long, snug fundoplication and 4% incidence after a short, floppy fundoplication. An incidence of 2% is associated with incomplete wraps (Menguy *et al* 1978). This complication is also seen in patients who have undergone an insertion of the Angelchik prosthesis (Stirling *et al* 1982, Wale *et al* 1982, Kozarek *et al* 1985, Stuart *et al* 1989). Watson *et al* (1991) reported that none of his patients experienced gas-bloat or difficulty belching or vomiting after his physiological anti-reflux operation.

Distension of the cardia is necessary for gas gastro-oesophageal reflux so any fundoplication that surrounds more than half the terminal oesophagus may prevent belching (Rasche *et al* 1973). A wrap encircling two-third of the terminal oesophagus functions as well as a total wrap in preventing vomiting. Fundoplication may prevent distension of the cardia by decreasing the diameter of the gastro-oesophageal junction (Strombeck *et al* 1989).

Belch volume has been studied post fundoplication in 12 patients after gastric distension. Compared to healthy volunteers, the patients had lower volumes for individual belches and belched less gas in one hour. The incidence and severity of belching difficulty and gas-bloat was unrelated to belch volume (Smith *et al* 1991). This experiment measures total gas expelled from the pharynx rather than gastro-oesophageal gas reflux specifically.

In summary, the literature suggests that the inability to belch, gas-bloat and dysphagia may reflect the production of a supercompetent sphincter (DeMeester *et al* 1979, Bjerkeset *et al* 1980) by fundoplication. The separation of patients with dysphagia post-fundoplication from those without dysphagia using conventional manometric techniques is difficult. In fact, Brand *et al* (1979) reasoned that the results of anti-reflux surgery are best evaluated by subjective findings because of the discordance of objective findings!

METHODS

CHAPTER 5: OESOPHAGEAL MANOMETRY AND VIDEOFLUOROSCOPY

The project comprised (i) a study of the effect of fundoplication on oesophageal motor function and the relationship to dysphagia (ii) a study of the effect of fundoplication on belching and (iii) an investigation of the effect of fundoplication on oesophageal motor function in a pig model.

To determine if patients with post-fundoplication dysphagia differed from post-operative patients without dysphagia in any of the measured parameters using questionnaire, oesophageal manometry and concurrent videofluoroscopy.

The patients' inability to belch after fundoplication was examined by questionnaire and oesophageal manometry.

Experiments in a porcine model were carried out to determine if the tightness of the Nissen fundoplication was related to changes in oesophageal motility.

The human studies were undertaken in the Departments of Surgery, Gastroenterology and Radiology at the Royal Adelaide Hospital while the animal operations and studies were carried out in the Institute of Medical and Veterinary Science. Ethical approval for the human studies and animal studies were obtained from the Royal Adelaide Hospital Human Ethics Committee and the Institute of Medical and Veterinary Science Animal Ethics Committee respectively.

5.1 STUDIES IN HUMAN SUBJECTS

5.1.1 Subjects

(1) Healthy volunteers:

11 age-matched healthy volunteers: 7 males, 4 females ranging in age from 20 to 53 years, median age 42 years, (designated "healthy") took part in both the study on the effect of fundoplication on oesophageal motor function and the effect of fundoplication on the ability to belch

(2) Patients with reflux oesophagitis:

15 patients with reflux oesophagitis: 5 males and 10 females ranging in age from 23 to 65 years (median age 45 years) before their anti-reflux operation (designated "reflux") were recruited for the study on the effect of fundoplication on oesophageal motility only

(3) Patients after fundoplication:

13 of the 15 patients with reflux oesophagitis returned for a post-operative study at 3 months, 7 had no dysphagia post-fundoplication (designated "post-op no dysphagia") and 6 had dysphagia (designated "post-op dysphagia").

12 patients who have previously undergone fundoplication and who complain of dysphagia after their anti-reflux operation: 7 males, 5 females ranging in age from 32 to 62 years (median age 45 years) were studied retrospectively (also designated "post-op no dysphagia")

20 of the patients also participated in the study on the effect of fundoplication on belching

Healthy subjects were free of symptoms of reflux disease and had not been exposed to radiation for research purposes in the last 12 months.

All patients who were referred to the Professorial Surgical Unit for Nissen fundoplication complained of symptoms of gastro-oesophageal reflux disease such as heartburn or regurgitation. Of the 15 patients, 11 had erosive or ulcerative oesophagitis on endoscopy, 3 had oesophageal acid exposure more than 6% of the time during 24 hour ambulatory pH monitoring and 1 had a positive Bernstein test and positive standard acid reflux tests. Fundoplication was completed laparoscopically in 13 and open in 2 because of obesity. A 52 F bougie was used in 14 patients.

Patients who complained of dysphagia for solids or liquids more than 3 months after laparoscopic fundoplication who came to the attention of the Department of Surgery Oesophageal Manometry Laboratory also were invited to participate in a retrospective study. The same surgical unit had operated on 10 of the 12 patients who responded to the invitation, 2 were referred from surgeons outside the unit. These 12 patients were studied between 3 and 12 months post-fundoplication. The results of their pre-operative investigations indicated that 6 had erosive or ulcerative oesophagitis on endoscopy and 3 had excessive acid exposure on 24 hour pH monitoring. No pre-operative information was available on 3 patients. Fundoplication was completed laparoscopically in all 12, a 52 F bougie having been used in 7, 50 F in 1 patient, 46 F in 1 patient and no bougie in 3 patients.

Subjects were excluded if they had a history of oesophageal or gastric surgery apart from simple procedures such as oversewing of perforation, primary connective tissue disease e.g. scleroderma, significant central nervous system disease, significant cardiac disease, diabetes mellitus, pregnant females or were using medications such as anti-cholinergics, tricyclic anti-depressants, neuroleptics, prokinetics which could not be stopped for at least 24 hours before the study

All subjects gave written informed consent.

5.1.2 Interview and questionnaire

Assessment

Each subject was interviewed by the investigator and asked questions about their reflux symptoms, medical treatment, and anti-reflux surgery according to a pre-planned questionnaire. Specific details included the severity, frequency and duration of symptoms.

The subject who took part in the study on the effect of fundoplication on gas gastro-oesophageal reflux was also interviewed regarding the ability to belch, relieve bloating by belching and ability to vomit was recorded according to a pre-planned questionnaire. Other symptoms such as nausea, stomach pains during a meal, the ability to eat a normal size meal and flatulence were recorded. The severity of each symptom was noted.

Grading

Symptoms such as heartburn, regurgitation, dysphagia, painful swallowing, retrosternal pain, aspirations, haemetemesis, fullness during eating were noted. The severity was recorded on a scale from 0 to 10 where 0 indicates no symptoms and 10 severe symptoms. The frequency of the symptoms was noted, whether it was once a month, a few times a week or daily.

In the patients with gastro-oesophageal reflux disease before their operation, factors that might aggravate heartburn such as tobacco, coffee, chocolate, alcohol and obesity were noted. The use of medications, for example antacids, H2 blockers, omeprazole and prokinetics was also recorded.

In the post-fundoplication patients, details of their anti-reflux surgery, date of the surgery, surgeon involved, and the hospital where it was performed were noted.

Coding the questionnaire

Post-fundoplication dysphagia was coded according to the severity and frequency. Severity was originally recorded on a scale of 0 to 10. This was coded as "1" if the analogue score was 1 to 3 (noticeable but no change in eating), "2" if 4 to 6 (occasional sticking) and "3" from 7 to 10 inclusive (could swallow liquids only). Frequency of dysphagia was coded as "1" if it occurred less than once every 2 weeks, "2" if it occurred more than once every 2 weeks but less than daily and "3" if it occurred at least once a day (Pope 1992).

The severity and frequency scores were multiplied to obtain a score for dysphagia for solids and a separate score for liquids. To obtain a total dysphagia score, the score for solids and that for liquids were added. Wtih this scoring system, a person with no dysphagia would have a total score of 0, mild dysphagia a total score of 1 to 5,

moderate dysphagia a total score of 6 to 14 and severe dysphagia a total score of 15 to 18.

Overall, dysphagia was considered mild if it was noticeable but no interference with eating, moderate if dietary habits are changed and severe if led to weight loss or failure to eat solid foods.

The ability to belch was coded as "0" if it was normal, "1" if the subject could belch sometimes, "2" if the subject could only belch with difficulty, and "3" if the subject was unable to belch at all.

The ability to relieve bloating by belching was coded as "0" if relief was complete with each belch, "1" if relief was possible sometimes, "2" if relief was rarely possible and "3" if there was no relief at all.

5.1.3 Manometry

Manometric assembly

The design incorporated features that allow it to be used in both the studies of the effect of fundoplication on oesophageal motor function and on belching.

A sleeve device (Dent 1976) recorded lower oesophageal sphincter pressure. The sleeve was attached to a multilumen silicone rubber extrusion, 1.5 m long. The rubber extrusion consisted of 10 lumina of 0.75 mm internal diamter around a central core of 1.5 mm internal diameter. The outer diameter of the assembly was 4.4 mm. One side hole was located 1 cm beyond the distal end of the sleeve and another at the proximal margin of the sleeve. 4 other side holes were located 4 cm apart starting from the proximal margin of the sleeve. Two side holes were located at 27 and 30 cm respectively from mid sleeve, either of which were used to record the pharyngeal signal depending on the length of the oesophagus. Tantalum wire markers, 0.6 mm diameter and 5 mm long were inserted into the channels distal to each side hole opening. These wires were visible during video fluoroscopy and were used for indicating the position of the catheter and acting as magnification markers. An oesophageal infusion channel led to side hole at 15 cm from mid sleeve which was used in the secondary peristalsis section of the standard manometry. The central core was used as a gastric infusion channel during the belch study.

To measure pressure, each lumen was connected in series with a pressure transducer (Statham P231D, Gould Inc, Oxnard, California, USA) and was constantly perfused with degassed distilled water at 0.6 ml/min by a low compliance pneumohydraulic pump (Arndorfer Medical Specialities, Greendale, Wisconsin). Pressure signals from the transducers were recorded on a polygraph chart recorder (Grass Instrument Company, Model 7D, Massachusetts, USA).

For the investigation of the variables influencing the effect of fundoplication on oesophageal motor function in pigs, a separate manometric assembly was constructed from a polyvinylchloride tube with 8 lumen of 0.75 mm internal diamter around a central core of 1.5 mm internal diameter attached to a Dentsleeve. The outer diameter of the assembly was 4 mm. One side hole was located 1 cm beyond the distal end of the sleeve and another at the proximal margin of the sleeve. 5 other side holes were located 1 cm, 2 cm, 4 cm, 8 cm and 16 cm from the proximal margin of the sleeve. The central core was used as a oesophageal infusion channel leading to a sidehole 13 cm from the proximal margin of the sleeve.

Technique

The manometric assembly was inserted via the nose of the patient. The lower oesophageal sphincter was located by station pull through and the sleeve was then positioned straddling the lower oesophageal sphincter. Hence, the side hole 1 cm below the distal margin of the sleeve measured the intragastric pressure. Side holes at the proximal end of the sleeve and at 4, 8, 12 and 16 cm proximal to the upper margin of the sleeve monitored the motor activity of the oesophageal body. A side hole located in the pharynx monitored swallows.

5.1.4 Videofluoroscopy

Equipment

Images of swallows in the lateral and postero-anterior projections were obtained with Shimadzu image intensifiers (Shimadzu UD150, Tokyo, Japan) and recorded on videotape (Hitachi E180 HR VHS system, Hitachi, Tokyo, Japan) at 25 frames per second using a video cassette recorder (Panasonic AG 7350, Japan) to give an impression of continuous motion (Dengel *et al* 1991). Included in the field were the gastro-oesophageal junction and the distal 8 cm of the oesophagus.

Technique

Patients and volunteers were studied standing to minimise the risk of aspiration in patients with dysphagia. They swallowed boluses of barium (250% wt/vol, E-Z-HD, E-Z-EM Inc, Westbury, New York) delivered into the mouth by a syringe and half a marshmallow. The marshmallow was injected with barium to obtain sufficient opacity. The total radiation burden for videofluoroscopy was calculated to be 2.8 mSv. The tantalum wires located 4 cm apart in the manometric assembly were seen during each swallow and they served as magnification markers.

Linkage to manometry

A video digital timer unit (Practel Sales International, Holden Hill, South Australia) imprinted simultaneously elapsed time on the video images in hundredths of a second and a signal on the polygraph tracing each whole second. This allowed temporal correlation of video images with pressure measurements. (Figure 1)

5.1.5 Protocol

Oesophageal manometry

Subjects were instructed to fast for 6 hours before the test. Anti-cholinergic, anti-secretory and anti-dopaminergic drugs were discontinued 48 hours before the study.

Measurements were taken during the following periods: (i) 5 minute rest period, (ii) primary peristalsis and lower oesophageal sphincter relaxation during 5 ml, 10 ml, 15 ml water swallows, each done 5 times (iii) lower oesophageal sphincter relaxation during 5 clusters of rapid swallows and (iv) secondary peristalsis triggered 10 times with 10 ml air boluses and 5 times with 10 ml water boluses.

Subjects swallowed boluses of water delivered into the mouth with a syringe. Each swallow was separated by at least a 20 second interval. Rapid swallows were done in 5 clusters. Each cluster consisted of 5 swallows in 10 seconds or a swallow every 2 seconds and the patient was given about 3 ml of water per swallow. During the study of secondary peristalsis, air and water boluses were injected rapidly by hand in order to distend the mid oesophagus. Air was injected within 0.5 seconds and water was injected within 1.5 seconds. The distending stimulus was given at least 20 seconds after the preceeding stimulus and 20 seconds was allowed after each stimulus for any response to occur, during which time subjects were instructed not to swallow. At the end of 20 seconds, subjects performed a dry swallow to ensure clearance of residual air or water before the next injection and to reduce the desire to swallow during distension (Schoeman *et al* 1993). The chart speed was set at 5 mm/sec.

For the study on the effect of fundoplication on gas gastro-oesophageal reflux, the subject was studied sitting and asked to indicate the urge to belch with a hand-held event marker. After a 10 minute baseline recording, the stomach was distended with 750 ml of carbon dioxide. The carbon dioxide was generated in the stomach from a 2-part radiological mixture called Field's Negative C. The 2 parts of the mixture, namely, a food grade acid and an alkali-metal bicarbonate was instilled into the stomach within 10 seconds via the core of the manometric assembly. the chart recorder was run at 5 mm/sec for 10 minutes of recording. Measurements included transient lower oesophageal sphincter relaxations, common cavities and belch urges.

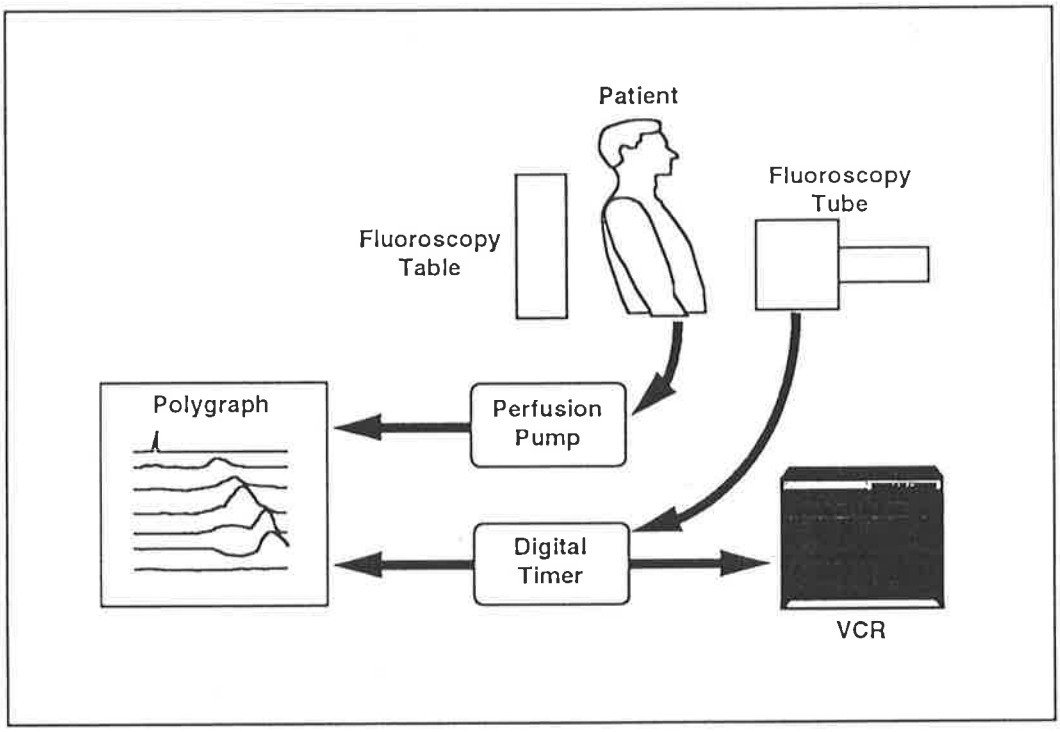

Figure 1: The set-up for concurrent oesophageal manometry and videofluoroscopy. The fluoroscopy tube focussed on the distal oesophagus and lower oesophageal sphincter region of a subject in the upright position and images were recorded on videotape. Signals from the trans-nasal manometric assembly were transduced and recorded on a polygraph. A digital timer unit imprinted simultaneously elapsed time on the video-tape and the polygraph.

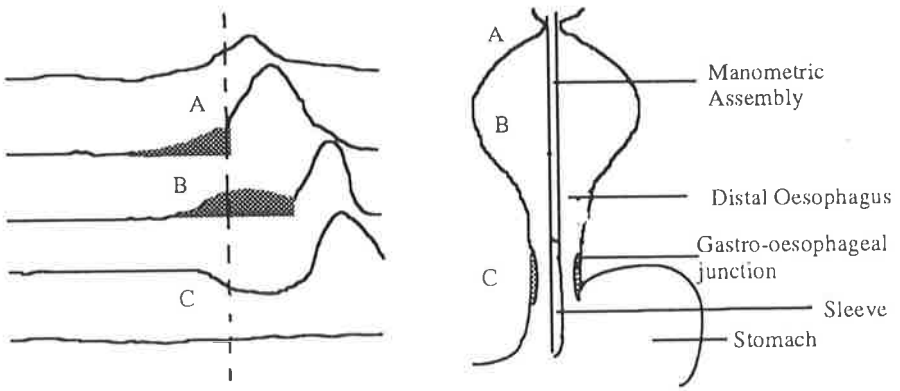

Figure 2: Radiologic correlates of ramp pressure

Videofluoroscopy

An identification tag was imaged before the subject stood in front of the image intensifier. For each barium swallow, the polygraph speed was switched to 25 mm/sec. Measurements were made in the lateral and postero-anterior projections. In the lateral projection, subjects swallowed in duplicate 5 ml, 10 ml, 15 ml barium boluses to assess lower oesophageal sphincter opening. Single swallows of each bolus were obtained in the postero-anterior projection. Solid swallows were assessed with half-marshmallows. If a half-marshmallow was arrested at any point along the oesophagus, the subject was asked to swallow every 30 seconds, with the help of water until the half-marshmallow traversed the lower oesophageal sphincter or until 2 minutes had elapsed from the first pharyngeal signal whichever was earlier. The fluoroscope was switched off intermittently to minimise radiation exposure.

5.1.6 Data analysis

Manometric measurements

Oesophageal body motor function

The resting pressure of the proximal and distal oesophagus during the 5 minute rest period was measured.

From the manometric tracing, each oesophageal motor response was classified as primary peristalsis, secondary peristalsis, isobaric waves or non-isobaric synchronous contractions. Peristalsis was regarded as complete if a propagated pressure wave was > 12 mmHg in the proximal oesophageal body side-holes and more than 25 mmHg in the distal oesophageal body side-holes. The minimum latency between 2 recording sites was 0.5 seconds (Kahrilas *et al* 1988, Hewson *et al* 1990).

For complete primary peristalsis, the success of propagation of primary peristalsis, peristaltic amplitude of the proximal and distal oesophagus, propagation velocity of the peristaltic wave in the distal oesophagus and duration of contraction in the distal oesophagus. The amplitude of contraction was measured from basal end-expiratory intra-oesophageal pressure to the peak of the pressure wave. The onset of the major upstroke of the pressure wave was used as the reference point for determination of wave latency. Velocity was calculated from the time taken for the wave to traverse 8 cm in the distal oesophagus. The duration of contraction was measured from the onset of the major upstroke to the return of the contraction to baseline

For secondary peristalsis, the percentage response in initiation of secondary peristalsis, propagation of the peristaltic wave and lower oesophageal sphincter

relaxation was recorded. Lower oesophageal sphincter relaxation was deemed a successful response if the nadir pressure was within 2 mmHg of the nadir pressure obtained with the dry swallow after each bolus. The peristaltic amplitude of the proximal and distal oesophagus was measured for propagated secondary peristalsis.

The primary peristaltic waves that resulted in incomplete clearance of barium were analysed for their amplitude.

Synchronous waves, whether iso-baric or non-isobaric that were associated with some barium clearance were analysed for the pressure gradient between the most distal oesophageal side-hole and the lower oesophageal sphincter pressure at the time of flow. Isobaric waves are waves of the same amplitude measured from all the oesophageal channels.

Ramp pressures

The ramp pressure is one of the manometric measures of flow across the gastro-oesophageal junction. Using the video data in conjunction with the manometric record, the ramp pressure is the highest plateau pressure recorded on manometric studies before the major upstroke of the peristaltic contraction, best seen in the distal channels. By the above definition, ramp pressure can be measured for healthy volunteers and patients with reflux disease, although it resembles the appearance of a "ramp" only in post-fundoplication patients. It began 1 to 2 seconds after the onset of swallowing. (Figure 2)

For each successful peristaltic wave, the time at which the peak ramp pressure occurs and the magnitude of ramp pressure was measured. The peak ramp pressure was measured from basal end-expiratory intra-oesophageal pressure.

Lower oesophageal sphincter pressure

The basal lower oesophageal sphincter pressure was measured relative to intragastric pressure at 20 second intervals during swallow free periods of the recording and a median of 10 readings was calculated.

Nadir lower oesophageal sphincter pressure otherwise known as residual relaxation pressure was the lowest pressure that the sphincter relaxes to during single or multiple rapid water swallows or in response to oesophageal distension. In complete sphincter relaxation, it is 0 mmHg relative to intragastric pressure. (Figure 3)

Gas gastro-oesophageal reflux

The chart recordings were analysed manually for the number of spontaneous transient lower oesophageal sphincter relaxations, and total number of common cavities, total number of belch urges, the number of belch urges associated with common cavities and the number of belch urges without common cavities, in the 10

minute rest period and the 10 minutes post distension. Transient lower oesophageal sphincter relaxxations were scored if the nadir pressure during relaxation was on or below the nadir pressure determined during water swallows, not preceeded by a pharyngeal swallow within the previous 5 seconds and lasting longer than 5 seconds (Ireland *et al* 1993). A common cavity episode was defined as an abrupt increase in intra-oesophageal body pressure to intragastric pressure in at least 2 lower oesophageal body manometric recording sites, which was an accepted marker of gas or liquid reflux from the stomach to the oesophagus (Wyman *et al* 1990).

Concurrent videofluoroscopy and oesophageal manometry

Video data were analysed by slow motion playback of the videotape without reference to the manometric record. The correction factor for magnification was determined using the tantalum markers in the manometric assembly which were located 4 cm apart. Each barium swallow was classified as complete or incomplete, depending on the clearance of the barium bolus from the oesophagus.

For boluses that were cleared completely by a single primary peristaltic wave, the maximum lower oesophageal sphincter opening and distal oesophageal diameter were measured The moment of opening of the lower oesophageal sphincter. was taken as the time the bolus head first entered the sphincter. The moment the lower oesophageal sphincter closed was noted. Transit time for the bolus to pass through the lower oesophageal sphincter was taken as the time from the opening to the closing of the lower oesophageal sphincter. Trans-sphincteric flow was calculated from the volume of the bolus divided by the transit time.

The maximum distal oesophageal diameter at the time of maximum lower oesophageal opening was measured. The time at which the tail of the stripping wave arrived at the 2 most distal recording orifices and the time of the upstroke of the peristaltic wave in the distal 3 channels were noted.

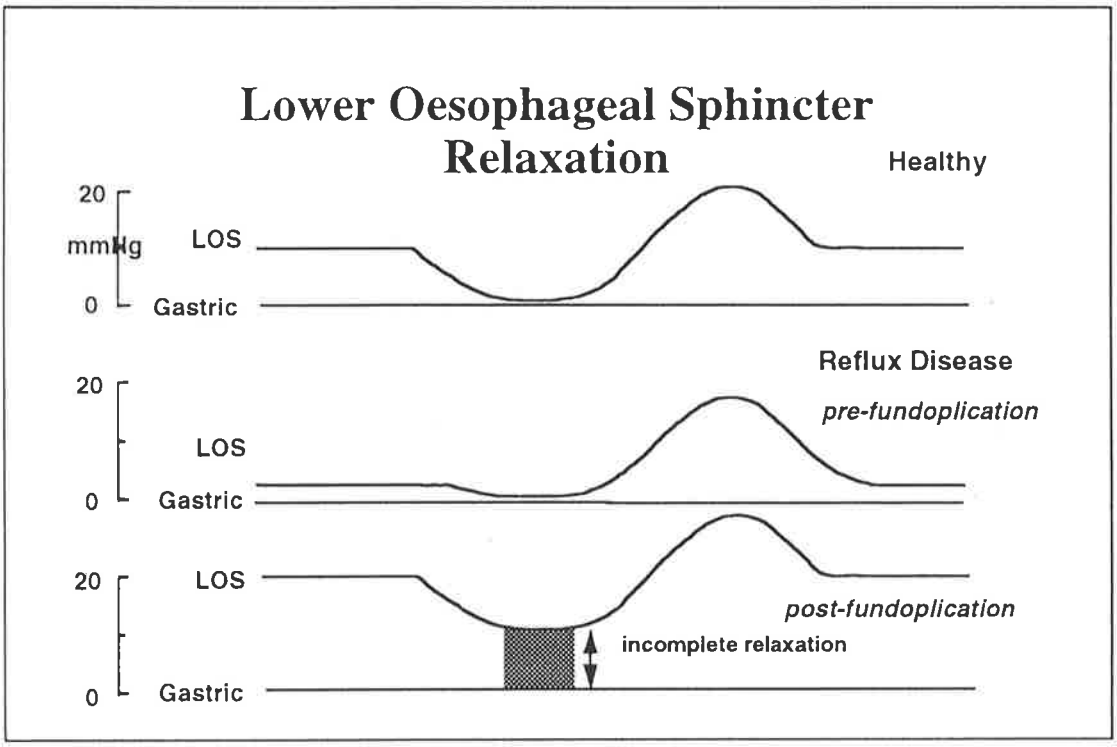

Figure 3: Residual relaxation pressure or nadir pressure of the lower oesophageal sphincter

5.1.7 Statistical analyses

The data was entered into Excel spreadsheet (Microsoft Corporation, Bellevue, Washington, USA) and then analysed by the SAS program (SAS Institute Inc, Cary, North Carolina, USA). Statistical significance was set at $p < 0.05$ for all the tests.

Age

Age matching of healthy volunteers to patients was examined by one way analysis of variance.

Primary peristalsis

For complete primary peristalsis, the peristaltic amplitude of the proximal and distal oesophagus, propagation velocity of the peristaltic wave and duration of contraction was analysed by repeated measures analysis of variance (ANOVA). Subject median data was first calculated for swallows that were repeated. The group data was normally distributed so group values are expressed as mean $\pm$ SEM. Statistical inferences were made regarding the group effect, the swallowed volume effect, and the group/volume interaction using an analysis of variance (ANOVA) for repeated measures with mixed design.

Patients with gastro-oesophageal reflux disease before their fundoplication (designated "reflux") were compared with healthy volunteers (designated "healthy") for the effect of reflux disease.

Of the 15 patients studied pre-operatively, only 13 post-operative studies were obtained. These 13 could be subdivided into 7 without dysphagia post-fundoplication (designated "post-op no dysphagia") and 6 who experienced dysphagia post-fundoplication (designated "post-op dysphagia"). The "reflux" group was compared with "post-op no dysphagia" and "post-op dysphagia" groups using tests for paired data, to examine for the effect of fundoplication.

The 12 patients with dysphagia post-fundoplication from the retrospective study were combined with the 6 patients with dysphagia post-fundoplication from the prospective study. This group is designated "all post-op dysphagia". The "all post-op dysphagia" group was compared with "post-op no dysphagia" group looking for parameters that separate the two. The "all post-op dysphagia" group was compared with "post-op no dysphagia" group looking for parameters that separate the two.

Finally, within the "all post-op dysphagia" group, patients were classified as having mild, moderate or severe dysphagia according to the criteria used in coding the questionnaire. Groups designated "mild dysphagia", "moderate dysphagia" and "severe dysphagia" were compared with "post-op no dysphagia" group.

Secondary peristalsis

Using data from the study of secondary peristalsis, the response rate in initiation, propagation of peristaltic wave and lower oesophageal sphincter relaxation by air or water boluses were compared. The Wilcoxon rank sums test was used for "reflux" versus "healthy", "post-op no dysphagia" versus "healthy", "all post-op dysphagia" versus "post-op no dysphagia" as they were unpaired comparisons. In addition, "mild dysphagia", "moderate dysphagia" and "severe dysphagia" were compared with "post-op no dysphagia" group, using the Wilcoxon rank sum test. The Friedman's test was used for the "reflux" group compared with "post-op no dysphagia" and "post-op dysphagia", which were paired comparisons. When the Wilcoxon, Friedman and Spearman tests were used for non-parametric data, group values are expressed as medians (interquartile ranges).

Statistical inference regarding the group effect on secondary peristaltic amplitude of the proximal and distal oesophagus was made using an analysis of variance.

Ramp pressure

Statistical inferences were made regarding the group effect, the swallowed volume effect, and the group/volume interaction with regards to ramp pressure using an analysis of variance (ANOVA) for repeated measures.

Subject median data was first calculated for swallows that were repeated. In the ANOVA tests and linear regression tests, the group data was normally distributed so group values are expressed as mean $\pm$ SEM.

For all subjects, ramp pressure was compared with intrabolus pressure, maximum lower oesophageal sphincter opening diameter, distal oesophageal diameter, flow and nadir pressure and distal oesophageal peristaltic amplitude in the standard oesophageal manometry, using linear regression and Pearson correlation.

The time of the peak ramp pressure in the 2 most distal channels were compared with the instant of the upstroke of the peristaltic wave in the channel above using T tests. The time of the peak ramp pressure was also compared with the time of lower oesophageal sphincter opening and closing using T tests.

Lower oesophageal sphincter

Statistical inferences were made regarding the group effect for basal lower oesophageal sphincter pressure and rapid swallows nadir lower oesophageal sphincter pressure, using an ANOVA test.

Statistical inferences were made regarding the group effect, the swallowed volume effect, and the group/volume interaction using an analysis of variance (ANOVA) for repeated measures with mixed design for nadir lower oesophageal

sphincter pressure, maximum lower oesophageal sphincter opening, maximum distal oesophageal diameter at the time of maximum lower oesophageal opening, transit time and trans-sphincteric flow.

Subject median data was first calculated for swallows that were repeated. In the ANOVA tests, the group data was normally distributed so group values are expressed as mean ± SEM.

Radiologic correlates of manometric variables

In all subjects who underwent concurrent oesophageal manometry and videofluoroscopy, the instant the tail of the stripping wave arrived at the 2 most distal recording orifices was compared with the instant of the major upstroke of the peristaltic wave in the distal 2 channels, using T-tests.

Subjective dysphagia scores

For the post-operative subjects from both the prospective and retrospective study, the post-fundoplication total score for dysphagia was correlated with all the parameters from concurrent oesophageal manometry and videofluoroscopy and standard oesophageal manometry using Spearman correlation.

Gas gastro-oesophageal reflux

The 20 post-fundoplication patients (designated "post-op") who underwent the belch study were compared with the 11 healthy volunteers (designated "healthy").

The 10 minute rest period and the 10 minute post distension was compared using Generalized Estimating Equations (Zeger SL, Liang K-Y 1986) with respect to spontaneous transient lower oesophageal sphincter relaxations, total number of common cavities, total number of belch urges, the number of belch urges associated with common cavities and the number of belch urges without common cavities. Results were expressed as median (interquartile range).

The occurrence of transient lower oesophageal sphincter relaxations was correlated with the total number of common cavities using Spearman correlation.

Subjective belch scores

The belch scores and the scores for the ability to relieve bloating by belching were correlated with the total number of common cavities, total number of belch urges, the number of belch urges associated with common cavities and the number of belch urges without common cavities, in the 10 minutes post distension using Spearman correlation. The scores were correlated with basal and nadir lower oesophageal sphincter pressures.

The belch scores were also correlated with the post-fundoplication total score for dysphagia in the 20 patients who underwent the belch study; 15 of whom were dysphagic and 5 who were not dysphagic, using Spearman correlation.

5.2 STUDIES IN A PORCINE MODEL

Laparoscopic fundoplication (Jorgensen *et al* 1993) and laparoscopic insertion of Angelchik prosthesis have been carried out in pigs (Berguer *et al* 1991) although worldwide, dogs were used most often in experiments on the gastro-oesophageal junction. In Adelaide, only dogs which have been bred for research are allowed to be used and these animals were expensive. Moreover, dogs are regarded as companion animals so it is more socially acceptable to use pigs. The anatomy of the pig's digestive tract was similar to humans and their biochemical and haematological profiles are also similar (Pond *et al* 1978). The muscle of the porcine distal oesophagus from just above the diaphragm to the gastro-oesophageal junction consists of smooth muscle (Landers *et al* 1987).

Domestic large white pigs about 18 - 30 kg in weight were used for this study. This size is suitable for investigating the mechanical effects of fundoplication by oesophageal manometry. The operations were performed at the Institute of Medical and Veterinary Science and the pigs were housed there while recovering from their operations. Oesophageal manometry was carried out in a laboratory that was set up in the Institute of Medical and Veterinary Science. The fitness and vigour of the commercial pig is somewhat suspect (McIntosh *et al* 1981) but these were the only animals available for this study.

5.2.1 Acute studies

Lower oesophageal sphincter behaviour has been studied in anaesthesized pigs (Landers *et al* 1987, Lundell *et al* 1992). Chloralose and urethane anaesthesia was used successfully by Malbert (personal communication) and Ketamine anaesthesia was used by Lundell *et al* (1992) in this department. The investigators were able to obtain lower oesophageal sphincter relaxation by balloon distension of the oesophagus or the gastric fundus.

Animal preparation

A 50 kg and a 20 kg domestic pig were used. After fasting for at least 12 hours, the pig was injected with intramuscular Ketamine injection (100 mg/ml Parnell Laboratories, Australia), followed by inhalation of 5% Halothane. An intravenous line was set up so that anaesthesia could be maintained by injection of 2 ml per kg of a mixture of 3 g Chloralose and 28 g of Urethane in 100ml water. Manometry was delayed for 30 min to allow the halothane was allowed to "wash out" of the pig's system.

Manometry

The manometric assembly was inserted via the an incision in the cervical oesophagus of the pig. Each lumen was connected in series with a pressure transducer (Transpac 42582-01, Abbott Critical Care Systems, Abbott Lab, North Chicago, Illinois, USA) and was constantly perfused with degassed distilled water at 0.6 ml/min by a low compliance pneumohydraulic pump (Arndorfer Medical Specialities, Greendale, Wisconsin). The lower oesophageal sphincter was located by station pull through. The sleeve was positioned straddling the lower oesophageal sphincter.

One side hole 1 cm below the distal margin of the sleeve measured the intragastric pressure. Side holes at the proximal end of the sleeve and at 1, 2, 4, 8, and 16 cm proximal to the upper margin of the sleeve monitored the motor activity of the oesophageal body. Signals from the pressure transducers were recorded on a chart recorder (model 7D, Grass Instrument Company, Quincy, Massachusetts) at a speed of at least 2.5 mm/sec.

Protocol

A baseline manometry was carried out. 10 ml of water was delivered into the pig's mouth 10 times. Then 10 ml of water was injected into the pig's oesophagus through the oesophageal infusion channel 10 times. Through a midline incision, a Nissen fundoplication was done by wrapping the anterior wall of the stomach snugly around the gastro-oesophageal junction with a 34 F bougie placed within the oesophagus. The fundoplication was sutured with 2/0 prolene starting with the cranial suture which included the anterior wall of the oesophagus. Then, 2 more sutures were placed 1 cm apart, creating a 2 cm long wrap in. The pig was allowed to stabilise for 15 min before manometry was repeated. Then a right thoracotomy was carried out. Without moving the manometric assembly, the proximal oesophagus was tied off. Water was infused through the oesophageal infusion channel in attempt to relax the lower oesophageal sphincter so that yield pressure could be measured.

The pig was killed with intravenous pentothal at the end of the experiment.

5.2.2 Chronic studies

Three groups of pigs were studied with 6 pigs in each group. They were all female, weighing between 18 and 30 kg (median weight 25 kg). One group underwent tight fundoplications which was carried out around a 20 F rod, the second group underwent loose fundoplications which was carried out around a 40 F rod. The last group underwent a floppy fundoplication around two rods which were 50 F and 56 F respectively, with division of the short gastric vessels to allow full mobilisation of the fundus of the stomach. The pigs were not randomised into the 3 groups; the group that underwent tight fundoplication was studied first, followed by loose fundoplication and finally, floppy fundoplication.

Cervical oesophagostomy

Most of the experimental animal studies of a similar nature in the English literature have been done on dogs, opossums and cats. Oesophageal and gastric fistulae (Zeller *et al* 1936) and operations on the cardia (Adler *et al* 1958) have been done successfully in dogs. The pig's neck was thick and its oesophagus was deep so it was not possible to create a fistula by suturing the oesophagus to the skin directly.

Studies on unaesthesized pigs using cannulae have been carried out (Mount *et al* 1971, Treacy 1991). The plastic T-shaped cannula used in this study was a modification of Treacy's cannula (1991). It consisted of a long flange of 3 cm and a short flange of 1.5 cm arranged at right angles to a cylindrical stem. The uneven flanges were important because the long end held the tube in the oesophagus while the short allowed for easy insertion. When inserted into the cervical oesophagus, part of the cylindrical stem protruded from the skin. A wide plastic ring that can be attached to the external cylindrical stem prevented the migration of the cannulae into the pig's neck. A cap was screwed onto the external end of the cannula to prevent loss of food during eating and drinking. The cannula was capped externally at all times except when the pig was undergoing oesophageal manometry. (See photograph).

After fasting for at least 12 hours, the pig was injected with intramuscular Ketamine (100 mg/ml Parnell Laboratories, Australia), followed by inhalation of 5 % halothane. The pig was positioned supine with its neck extended. It was intubated and anaesthesia was maintained by a Magill circuit containing a mixture of halothane and nitrous oxide with the pig breathing spontaneously.

A transverse incision was made on the left side of the pig's neck at the level of the cricoid cartilage. The identification of the oesophagus was made easy by having a bougie inserted through the pig's mouth into its oesophagus. A 3 mm incision was made in the cervical oesophagus with diathermy. It was stretched to 1 cm and a purse-string suture of 2/0 prolene was inserted. The long end of the oesophagostomy tube

was inserted into the incision and the incision was stretched to accommodate the short end of the tube. The purse-string was tightened around the tube. The tube was taken out through the skin via a separate incision 1 cm caudal to the transverse incision. The plastic ring and cap were then applied.

Baseline oesophageal manometry

A week after inserting the oesophagostomy, the pig was trained to stand in a cloth sling. This was not difficult once the initial struggle was overcome. The pig would stand quietly in the sling for an hour even during its first session in the sling. Any movement or grunt introduced noise into the manometric tracing hence efforts were made to quieten the pig. The pig was studied after fasting for at least 12 hours.

The perfused manometric assembly was inserted via the cervical oesophagostomy of the pig and each lumen was connected in series with a pressure transducer and a chart recorder as in the acute study With the pig standing quietly in the sling, the lower oesophageal sphincter was located by station pull through. The sleeve was positioned straddling the lower oesophageal sphincter. (Figure 5)

During the study of secondary peristalsis, water boluses were injected into the mid oesophagus by hand within 1.5 second to distend the oesophagus. During the injection of water boluses into the mid oesophagus, the pig was continually observed so that infusions were carried out when it was not swallowing. When the pig swallowed, there was a characteristic sharp ascent of the larynx which was palpated or observed. If the pig was observed to swallow, that bolus was not scored for analysis. The volume of the different boluses were written on the polygraph by the investigator. The distending stimulus was introduced 20 seconds after the preceeding stimulus and 20 seconds was allowed after each stimulus for any response to occur.

During the study of primary peristalsis, a syringe was used to draw up the volume and deliver it into the pig's mouth. Each swallow was separated by at least 20 second intervals.

Measurements included a 5 minute rest period, secondary peristalsis triggered by water boluses injected into the mid oesophagus in a random order that is 4 ml, 8 ml, 10 ml and 12 ml boluses each given 5 times and primary peristalsis during 10ml water swallows given 10 times.

Open Nissen fundoplication

The operation was supervised by a surgeon (P. Mitchell) and carried out under halothane and nitrous oxide general anaesthetic with the pig breathing spontaneously. A midline incision was made. The cardia was mobilised along the lesser and greater curves. Short gastric vessels were divided only in the group with floppy wraps. The diaphragmatic hiatus was closed with 2 2/0 prolene sutures such that it permitted the

surgeon to carefully put a finger between the oesophagus and the hiatus. Closure of the hiatus was done in all except the first 4 pigs, to minimise the risk of intrathoracic herniation of the stomach which has been found to lead to rapid death.

The anterior wall of the stomach was wrapped around the gastro-oesophageal junction and sutured to itself. Before suturing, a rod was placed external to the gastro-oesophageal junction and the wrap was constructed snugly around the rod. The size of the rod depended on which group the pig was assigned to. The rod was placed external to the oesophagus because it was found that the larger bougies could not be passed down the oesophagus with the cervical oesophagostomy tube in place. The fundoplication was sutured with 2/0 prolene starting with the cranial suture which included the anterior wall of the oesophagus. Then, 2 more sutures were put in 1 cm apart, creating a 2 cm long wrap in all pigs. (Figure 6)

The rod was then removed. The incision was closed in layers, using 1/0 Vicryl for the rectus muscles and 2/0 prolene for the skin.

Post-operative manometry

The pig was trained to stand in a sling again and post-operative manometry was carried out at 1 week using the same manometric assembly and following the same protocol as the baseline manometry. All 18 pigs underwent 1 week studies but only 14 underwent 2 week studies. 5 pigs also underwent 4 week studies to check for reproducibility of measurements.

Post-mortem examination

The pig was killed at completion of the experiments and an autopsy was carried out to confirm that the Nissen fundoplication was intact. Any pig that died unexpectedly underwent a post-mortem to determine the cause of death.

5.2.3 Data analysis

The 3 groups of pigs were "tight", "loose" and "floppy" fundoplication groups. The chart recordings were analysed manually for resting pressure of the proximal and distal oesophagus, and basal lower oesophageal sphincter pressure. Secondary and primary peristalsis were analysed with respect to the success of propagation of peristaltic wave, peristaltic amplitude of the proximal and distal oesophagus, nadir lower oesophageal sphincter pressure and ramp pressure.

5.2.4 Statistical analysis for chronic studies

Secondary and primary peristalsis

For the baseline manometry and the study at one week post-fundoplication, the peristaltic amplitude of the proximal and distal oesophagus, nadir lower oesophageal sphincter pressure, ramp pressure during secondary peristalsis were analysed by repeated measures analysis of variance (ANOVA). The reproducibility of secondary peristalsis at 1, 2 and 4 weeks was analysed with regards to the peristaltic amplitude of the proximal and distal oesophagus, nadir lower oesophageal sphincter pressure and ramp pressure by ANOVA.

Subject median data was first calculated for swallows that were repeated. The group data was normally distributed so group values are expressed as mean ± SEM. Statistical inferences were made regarding the group effect, the swallowed volume effect, and the group/volume interaction using an analysis of variance (ANOVA) for repeated measures with mixed design.

Statistical inferences were made regarding the group effect for basal lower oesophageal sphincter pressure, peristaltic amplitude of the proximal and distal oesophagus, nadir lower oesophageal sphincter pressure and ramp pressure for primary peristalsis (10 ml water swallows) and secondary peristalsis (10 ml water boluses) at baseline and 1 week post-fundoplication. Statistical inferences were also made regarding the group effect on the reproducibility of peristaltic amplitude of the proximal and distal oesophagus, nadir lower oesophageal sphincter pressure and ramp pressure for primary peristalsis (10 ml water swallows) and secondary peristalsis (10 ml water boluses) at 1, 2 and 4 weeks.

Ramp pressure correlations

Ramp pressure was correlated with nadir pressure, proximal and distal oesophageal amplitude using linear regression and Pearson correlation.

RESULTS AND DISCUSSION

CHAPTER 6: FUNDOPLICATION AND OESOPHAGEAL MOTOR FUNCTION

6.1 FUNDOPLICATION AND OESOPHAGEAL MOTILITY

6.1.1 Findings in unoperated patients with reflux oesophagitis and volunteers

Age

There was no significant difference in age between the healthy volunteers and patients.

Successful primary peristalsis

Pre-operative patients with reflux had a mean proximal amplitude of 53.64 ± 7.20 mmHg which was not significantly different from healthy volunteers with a mean amplitude of 70.73 ± 21.35 mmHg; patients with reflux had a lower mean distal amplitude of contraction of 68.46 ± 7.72 mmHg compared with healthy volunteers who had a mean amplitude of 105.36 ± 16.3 mmHg, but this difference did not reach statistical significance.

Pre-operative patients with reflux had a mean peristaltic velocity of 7.06 ± 1.45 cm/sec which was not significantly different from healthy volunteers with a mean peristaltic velocity of 6.69 ± 1.08 mmHg and mean duration of contraction of 3.49 ± 0.18 sec which was not significantly different from healthy volunteers who had a mean duration of contraction of 3.67 ± 0.23 sec.

Increasing the volume of the swallowed bolus did not have any effect on peristaltic amplitude, propagation velocity or duration of contraction.

Secondary peristalsis: Initiation, Propagation and Lower oesophageal sphincter relaxation

In the initiation of secondary peristalsis the median response rate with air injection was 100% in healthy volunteers and 60% in patients with reflux disease pre-fundoplication (NS) and with water was 80% and 20% respectively (NS). For propagated peristaltic waves triggered by air boluses, the median response rate was 80% in the healthy subjects and 40% in patients with reflux disease ($p < 0.02$). For propagated peristaltic waves triggered by water boluses, the median response rate was

40% in the healthy subjects and 0% in patients with reflux disease ($p < 0.006$). The median response rate for lower oesophageal sphincter relaxation triggered by air boluses was 70% in both healthy subjects and reflux patients. The median response rate for lower oesophageal sphincter relaxation triggered by water boluses was 60% in healthy volunteers and 80% in patients with reflux (NS).

Secondary Peristalsis: Proximal amplitude

Air boluses triggered secondary peristalsis with proximal amplitude of 26.27 $\pm$ 5.14 mmHg for the patients with reflux disease and it was not significantly different from healthy subjects was 36.70 $\pm$ 17.99 mmHg. Water boluses triggered secondary peristalsis with a mean proximal amplitude of 22.63 $\pm$ 4.68 mmHg in the patients with reflux and it was not significantly different from 41.00 $\pm$ 14.14 mmHg in healthy volunteers.

Secondary peristalsis: Distal amplitude

For secondary peristalsis triggered by air boluses, the distal amplitude for the group with reflux was 49.60 $\pm$ 11.74 mmHg and it was not significantly different from healthy subjects was 81.30 $\pm$ 18.19 mmHg. Water boluses triggered secondary peristalsis with a mean proximal amplitude of 45.40 $\pm$ 10.31 mmHg in the patients with reflux and it was not significantly different from 66.10 $\pm$ 13.01 mmHg in healthy volunteers.

However, air and water boluses triggered significantly lower ($p < 0.005$) amplitudes of contraction in both the proximal and distal oesophagus than wet swallows.

6.1.2 Effect of fundoplication on oesophageal motility

Peristaltic amplitude of the proximal oesophagus

Fundoplication had no effect on proximal primary peristaltic amplitude.

Patients with dysphagia post-fundoplication had a mean proximal contraction amplitude of 50.53 $\pm$ 6.54 mmHg which was not significantly different from patients without dysphagia post-fundoplication who had a mean proximal amplitude of 58.33 $\pm$ 21.44 mmHg.for successful primary peristalsis. There was a wider range of amplitudes for those without dysphagia. Increasing the volume of the swallowed bolus did not have any effect on the proximal contraction amplitude.

There was no significant difference between the patients with mild, moderate and severe dysphagia and patients without dysphagia in the proximal peristaltic amplitude. Increasing the volume of the swallowed bolus did not have any effect .

Peristaltic amplitude of the distal oesophagus

Fundoplication had no effect on distal primary peristaltic amplitude.

Patients with dysphagia post-fundoplication had a mean distal contraction amplitude of 70.76 ± 8.31 mmHg which was not significantly different from patients without dysphagia post-fundoplication who had a mean distal amplitude of 69.60 ± 23.68 mmHg.for successful primary peristalsis. There was a wider range of amplitudes for those without dysphagia. Increasing the volume of the swallowed bolus did not have any effect on the distal contraction amplitude.

There was no significant difference between the patients with mild, moderate and severe dysphagia and patients without dysphagia in the distal peristaltic amplitude. Increasing the volume of the swallowed bolus did not have any effect.

Propagation velocity of the peristaltic contraction

Fundoplication decreased peristaltic velocity measured in the upright position in both patients who became dysphagic post-fundoplication ($p < 0.0001$) and those who did not ($p < 0.007$). In the supine position, fundoplication decreased peristaltic velocity in patients who became dysphagic post-fundoplication ($p < 0.007$) but not in those without dysphagia post-fundoplication.

Patients with dysphagia post-fundoplication had a mean peristaltic velocity of 2.64 ± 0.15 cm/sec which was not significantly different from patients without dysphagia post-fundoplication who had a mean peristaltic velocity of 3.62 ± 1.18 cm/sec for successful primary peristalsis (Figure 7). Increasing the volume of the swallowed bolus did not have any effect on the peristaltic velocity.

There was no significant difference between the patients with mild, moderate and severe dysphagia and patients without dysphagia in peristaltic velocity. Increasing the volume of the swallowed bolus did not have any statistically significant effect on the peristaltic velocity but there was a trend with 5 ml boluses which separated the groups according to the severity of dysphagia. For 5 ml boluses, the peristaltic velocity for those without dysphagia was 4.03 ± 0.89 cm/sec, mild dysphagia 3.63 ± 0.57 cm/sec, moderate dysphagia 2.58 ± 0.24 cm/sec and severe dysphagia 2.04 ± 0.19 cm/sec.

Duration of contraction in the distal oesophagus

Fundoplication increased the duration of contraction in patients who became dysphagic post-fundoplication ($p < 0.0001$) but not in those who did not become dysphagic. This effect was observed in the upright position but not supine.

Patients with dysphagia post-fundoplication had a mean duration of contraction of 4.22 ± 0.29 sec which was not significantly different from patients without dysphagia post-fundoplication who had a mean duration of contraction of 3.10 ± 0.41 sec. Increasing the volume of the swallowed bolus did not have any effect on the duration of contraction.

There was no significant difference between the patients with mild, moderate and severe dysphagia and patients without dysphagia in the duration of contraction. Increasing the volume of the swallowed bolus significantly increased the duration of contraction ($p < 0.01$). For 15 ml boluses, the duration of contraction for those without dysphagia was 3.45 ± 0.37 sec, mild dysphagia 3.76 ± 0.39 cm/sec, moderate dysphagia 3.51 ± 0.31 cm/sec and severe dysphagia 5.61 ± 0.81 cm/sec.

Secondary peristalsis: Initiation, Propagation and Lower oesophageal sphincter relaxation

Effect of Fundoplication - prospective study

Fundoplication had no effect on the median initiation rate and propagation rate in response to air and water injections.

The median response rate for lower oesophageal sphincter relaxation triggered by air boluses was 70% in reflux patients pre-fundoplication and that triggered by water boluses was 80%. Fundoplication significantly decreased ($p < 0.03$) the median lower oesophageal sphincter relaxation rate with air injection to 45% in patients who were not dysphagic and 20% in those who became dysphagic. Fundoplication also significantly decreased ($p < 0.007$) the median lower oesophageal relaxation rate with water injection to 40% in patients who were not dysphagic and 20% in those who became dysphagic.

All Post-op Dysphagia compared with Post-op No Dysphagia

As a group, patients with dysphagia post-fundoplication were not significantly different from patients without dysphagia post-fundoplication in the initiation, propagation and lower oesophageal sphincter relaxation in response to air and water boluses. For air boluses, patients with dysphagia have a median initiation rate of 20%, propagation rate of 10% and lower oesophageal sphincter relaxation rate of 30% while patients without dysphagia have a median initiation rate of 20%, propagation rate of

15% and lower oesophageal sphincter relaxation rate of 45%. For water boluses, patients with dysphagia have a median initiation rate of 0%, propagation rate of 0% and lower oesophageal sphincter relaxation rate of 20% while patients without dysphagia have a median initiation rate of 10%, propagation rate of 10% and lower oesophageal sphincter relaxation rate of 40%.

Mild Dysphagia, Moderate Dysphagia, Severe Dysphagia compared with Post-op No Dysphagia

There was no significant difference in any of the comparisons in the initiation, propagation and lower oesophageal sphincter relaxation in response to air and water boluses.

Secondary Peristalsis: Proximal Amplitude

Effect of fundoplication

Air boluses triggered secondary peristalsis with a mean proximal amplitude of 27.67 $\pm$ 3.75 mmHg that was significantly lower ($p < 0.0001$) than wet swallows which had a mean proximal amplitude of 47.95 $\pm$ 2.93 mmHg. Water boluses triggered secondary peristalsis with mean proximal amplitude of 23.17 $\pm$ 5.62 mmHg which was significantly lower ($p < 0.001$) than wet swallows.

All Post-op Dysphagia compared with Post-op No Dysphagia

For secondary peristalsis triggered by air boluses, the respective values for patients with dysphagia was 36.22 $\pm$ 10.06 mmHg and it was not significantly different from patients without dysphagia was 41.25 $\pm$ 19.09 mmHg. Water boluses triggered secondary peristalsis with a mean proximal amplitude of 28.33. $\pm$ 7.88 mmHg in the patients with dysphagia and it was not significantly different from 10.5 $\pm$ 3.77 mmHg in patients without dysphagia.

Compared with wet swallows, air and water boluses triggered significantly lower ($p < 0.0007$) amplitudes of contraction in both groups.

Mild Dysphagia, Moderate Dysphagia, Severe Dysphagia compared with Post-op No Dysphagia

Air and water boluses triggered lower amplitudes of contraction than wet swallows in all groups ($p < 0.0007$ for air, $p < 0.007$ for water).

Secondary Peristalsis: Distal Amplitude

Effect of fundoplication

Air boluses triggered secondary peristalsis with mean proximal amplitude of 47.65 ± 5.64 mmHg that was significantly lower ($p < 0.003$) than wet swallows with mean proximal amplitude of 61.68 ± 4.79 mmHg. Water boluses triggered secondary peristalsis with mean proximal amplitude of 34.36 ± 8.70 mmHg that was significantly lower ($p < 0.02$) than wet swallows.

All Post-op Dysphagia compared with Post-op No Dysphagia

For secondary peristalsis triggered by air boluses, the respective values for patients with dysphagia was 58.44 ± 15.22 mmHg and it was not significantly different from patients without dysphagia was 50.00 ± 7.38 mmHg. Water boluses triggered secondary peristalsis with a mean proximal amplitude of 46.13 ± 10.31 mmHg in the patients with dysphagia and it was not significantly different from 52.00 ± 9.50 mmHg in patients without dysphagia.

Compared with wet swallows, air and water boluses triggered significantly lower ($p < 0.01$) amplitudes of contraction in both groups.

Mild Dysphagia, Moderate Dysphagia, Severe Dysphagia compared with Post-op No Dysphagia

Water boluses triggered lower amplitudes of contraction than wet swallows in all groups ($p < 0.01$). Distal amplitudes triggered by air boluses were not significantly different from wet swallows.

6.2 FUNDOPLICATION AND RAMP PRESSURE

6.2.1 Findings in patients with reflux oesophagitis and volunteers

Pre-operative patients with reflux had a mean ramp pressure of 7.54 ± 0.76 mmHg and were not significantly different from healthy volunteers with a mean ramp pressure of 7.55 ± 1.12 mmHg during successful primary peristalsis.

Increasing bolus volumes had no effect on ramp intrabolus pressure.

6.2.2 Effect of fundoplication on ramp pressure

Fundoplication increased ramp pressure in both patients who became dysphagic post-fundoplication ($p < 0.0001$) and those who did not ($p < 0.03$) in both the upright and supine position (Figure 4).

Patients with dysphagia post-fundoplication had a mean ramp pressure of 24.15 ± 1.49 mmHg which was significantly greater ($p < 0.01$) in patients without dysphagia post-fundoplication who had a mean ramp pressure of 14.4 ± 2.52 mmHg during successful primary peristalsis. Increasing bolus volumes had no effect on ramp intrabolus pressure (Figure 5).

Patients with severe dysphagia had a mean ramp pressure of 28.04 ± 3.52 mmHg that was significantly greater ($p < 0.009$) than those without dysphagia post-fundoplication with mean ramp pressure of 14.07 ± 3.22 mmHg. Patients with mild dysphagia had a mean ramp pressures of 23.42 ± 2.78 mmHg that was significantly higher ($p < 0.04$) than those without dysphagia. Patients with moderate dysphagia had mean ramp pressures of 21.11 ± 3.48 mmHg that was higher than those with no dysphagia but did not reach significance. Increasing the volume of the swallowed bolus did not have any consistent effect on ramp pressure (Figure 6).

Ramp Pressure - Correlations

The ramp pressure was not significantly correlated with maximum lower oesophageal sphincter opening, $r = 0.337$, $p = 0.051$ (Figure 7). Ramp pressure was significantly correlated with maximum distal oesophageal diameter at the time of maximum lower oesophageal sphincter opening, $r = 0.636$, $p < 0.0001$ (Figure 8). Ramp pressure increased with increasing oesophageal diameter and 40 % ($r^2 = 0.40$) of the variation in ramp pressure was explained by changes in oesophageal diameter.

The ramp pressure was significantly correlated with nadir lower oesophageal sphincter pressure, $r = 0.817$, $p < 0.0001$ (Figure 9). Ramp pressure increased with increasing nadir lower oesophageal sphincter pressures. Ramp pressure was not significantly correlated with distal oesophageal peristaltic amplitude.

Relationship of ramp pressure to transit through the lower oesophageal sphincter

The time of the peak ramp pressure occurs after the upstroke of the mid oesophageal peristaltic contraction ($p < 0.0001$). The time of the peak ramp pressure also occurs between the time of the sphincter opening and closing ($p < 0.0001$). This timing corresponded to the period of trans-sphincteric flow.

If the intrabolus pressure is defined as the pressure recorded by the most distal oesophageal side-hole during mid oesophageal luminal occlusion, the ramp pressure is significantly correlated with the oesophageal intrabolus pressure ($r = 0.968$. $p < 0.0001$). Ramp pressure increases as intrabolus pressure increase.

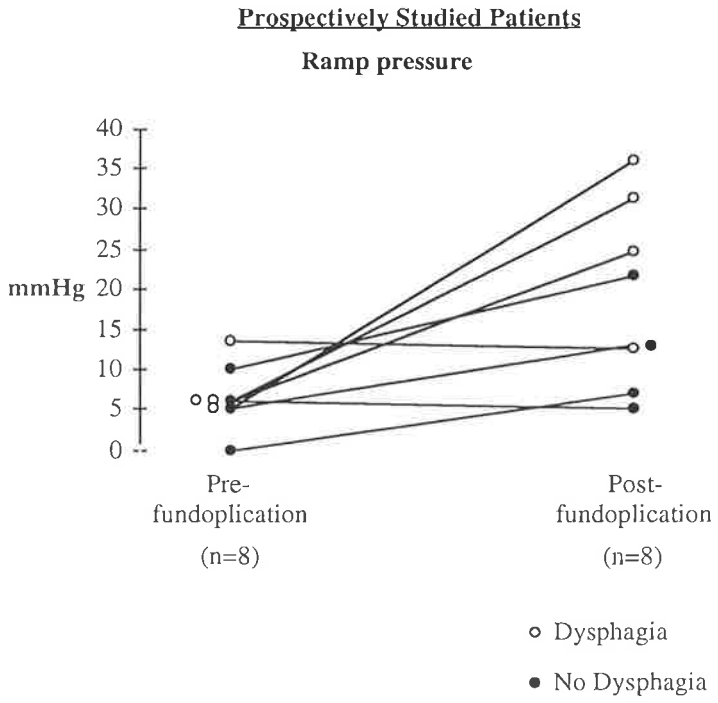

Figure 4: Effect of fundoplication on ramp pressure

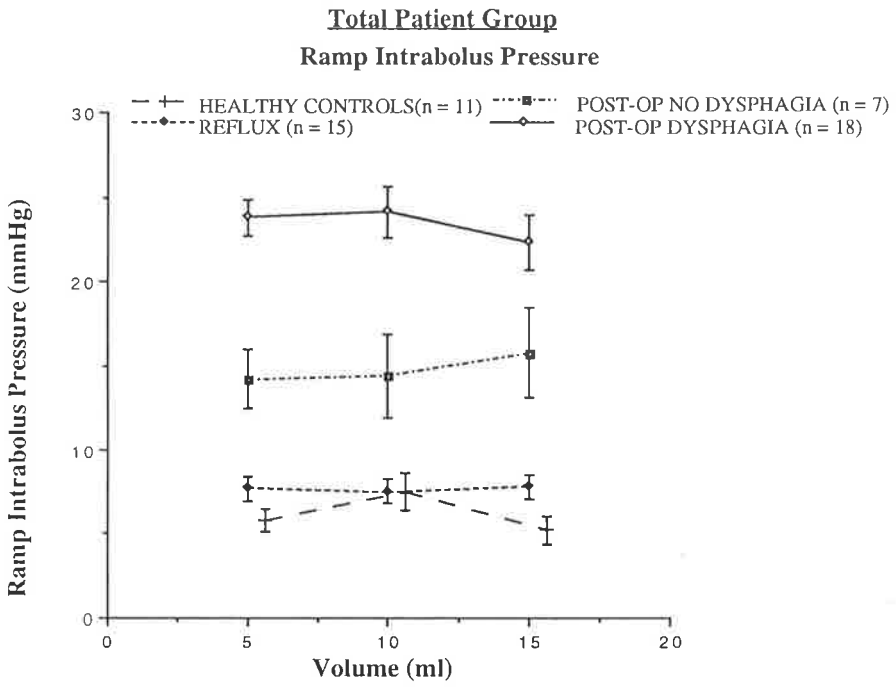

Figure 5: Ramp intrabolus pressure for 5 ml, 10 ml and 15 ml boluses in healthy subjects, patients with gastro-oesophageal reflux disease, patients without dysphagia and patients with dysphagia post-fundoplication.

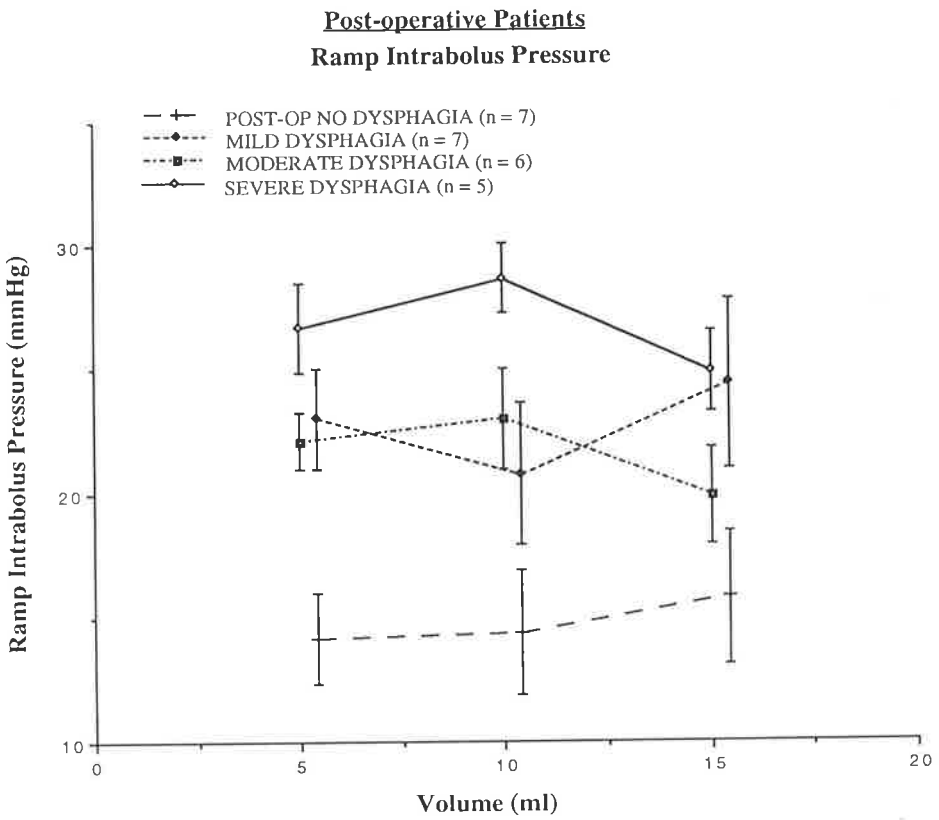

Figure 6: Ramp intrabolus pressure for 3 volumes in patients without dysphagia and patients with mild, moderate and severe dysphagia.

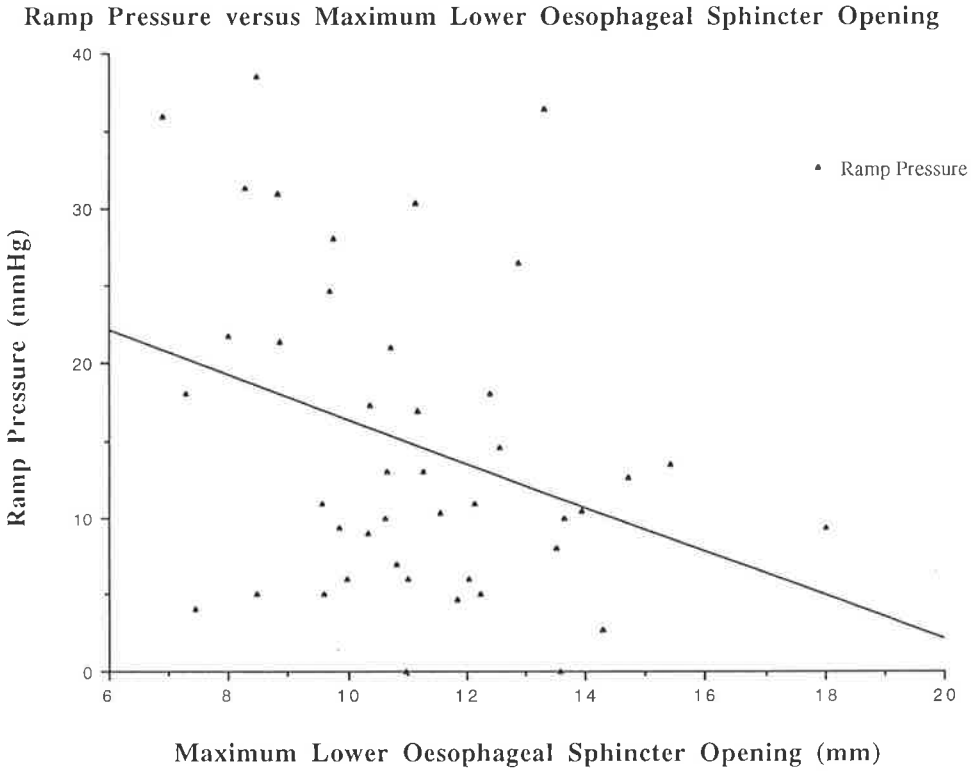

Figure 7: Regression model for ramp pressure versus maximum lower oesophageal sphincter opening

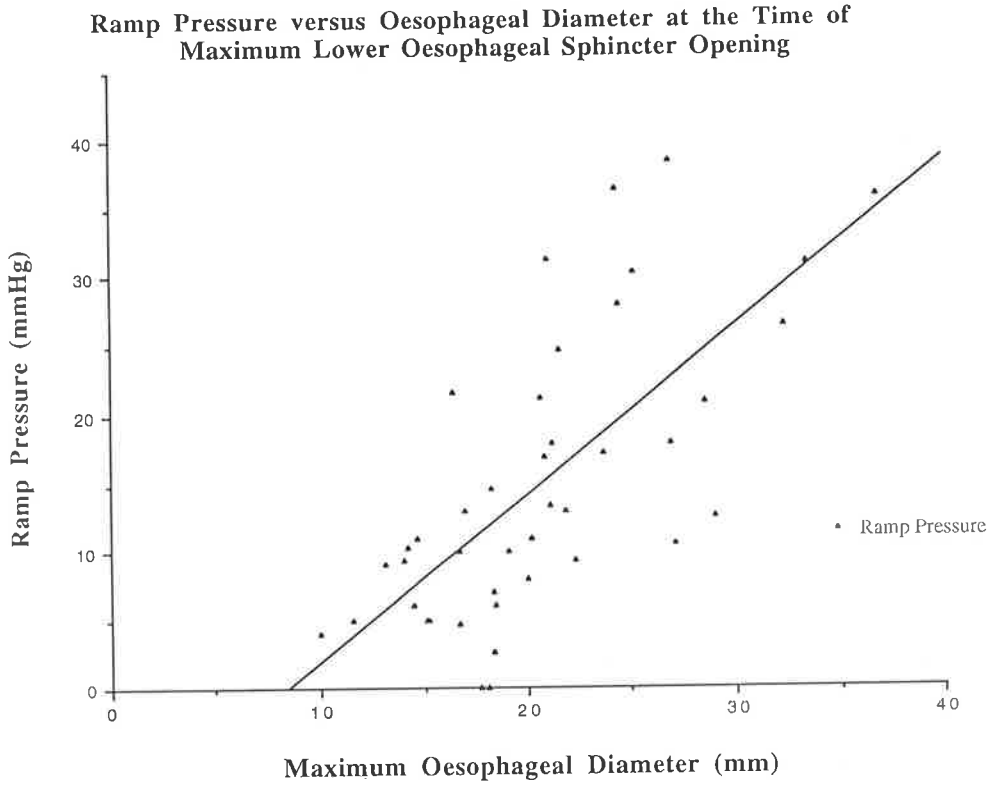

Figure 8: Regression model for ramp pressure versus distal oesophageal diameter at the time of maximum lower oesophageal sphincter opening

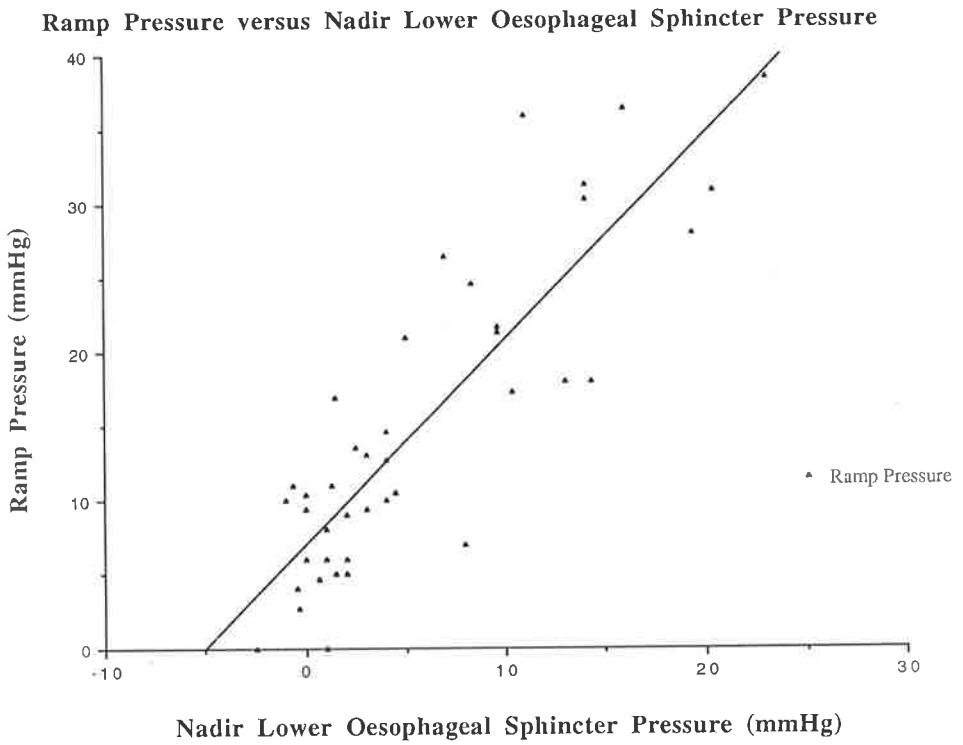

Figure 9: Regression model for ramp pressure versus nadir lower oesophageal sphincter pressure

6.3 FUNDOPLICATION AND LOWER OESOPHAGEAL SPHINCTER

6.3.1 Findings in patients with reflux oesophagitis and volunteers

A: Manometry

Basal lower oesophageal sphincter pressure

Posture did not have a statistically significant effect on the measurement of basal lower oesophageal sphincter pressure.

Pre-operative patients with reflux had a mean basal lower oesophageal sphincter pressure of 7.03 $\pm$ 0.49 mmHg which was significantly lower ($p < 0.03$) than healthy volunteers who had a mean basal lower oesophageal sphincter pressure of 12.49 $\pm$ 0.61 mmHg.

Nadir lower oesophageal sphincter pressure

Posture did not have a statistically significant effect on the measurement of nadir lower oesophageal sphincter pressure.

Pre-operative patients with reflux had a mean nadir lower oesophageal sphincter pressure of 0.58 $\pm$ 0.38 mmHg which was not significantly lower than healthy volunteers with a mean nadir lower oesophageal sphincter pressure of 0.77 $\pm$ 0.29 mmHg. This was true with both single swallows and repetitive rapid swallows and also with secondary peristalsis using 10 ml air and water boluses.

The median nadir pressure obtained with rapid swallows was lower than that obtained for single swallows but the difference was not statistically significant. In healthy volunteers, the lower oesophageal sphincter relaxation in response to air and water boluses was not as complete as sphincter relaxation due to wet swallows ($p < 0.001$). In patients with reflux disease, lower oesophageal sphincter relaxation in response to air and water boluses were not significantly different from wet swallows.

Increasing the volume of the swallowed bolus did not have any effect on the nadir lower oesophageal sphincter pressure.

B: Videofluoroscopy

Maximum distal oesophageal diameter at the time of maximum lower oesophageal sphincter opening

Pre-operative patients with reflux had a mean distal oesophageal diameter of 16.68 ± 0.72 mm which was not significantly different from healthy volunteers with a mean distal oesophageal diameter of 16.76 ± 0.90 mm during successful primary peristalsis.

Increasing the volume of the swallowed bolus did not have any effect on distal oesophageal diameter.

Maximum lower oesophageal sphincter opening

For the healthy volunteers, the mean diameter of lower oesophageal sphincter opening measured in the lateral projection was 11.47 ± 0.81 mm which was not statistically different from the diameter in the postero-anterior projection which was 11.32 ± 1.00 mm. For the patients with reflux disease, the mean diameter measured in the lateral projection was 13.77 ± 0.74 mm which was significantly higher ($p < 0.02$) than the diameter in the postero-anterior projection which was 10.80 ± 1.04 mm. It was difficult to estimate the area of the lower oesophageal sphincter from the lateral and postero-anterior diameters because one cannot assume that these diameters represent the longest and shortest diameters of an ellipse and calculate the area from a standard formula. The diameter measured in the lateral projection was used for all comparisons. Pre-operative patients had significantly higher values than healthy volunteers ($p < 0.05$).

Volumes of 15 ml resulted in greater lower oesophageal sphincter opening than 10 ml and 5 ml, 15 ml versus 5 ml was significantly different for reflux compared with healthy ($p < 0.006$).

C: Manometric observations relevant to transit

Transit time through the lower oesophageal sphincter

Pre-operative patients with reflux had a mean transit time of 5.80 ± 0.46 sec which was not significantly different from healthy volunteers with a mean ratio 4.88 ± 0.37 sec.

There was a direct volume effect. Volumes of 15 ml versus 5 ml was significantly different for reflux compared with healthy ($p < 0.0003$).

Trans-sphincteric flow

There was no correlation between trans-sphincteric flow and ramp intrabolus pressure (r = -0.2482, NS).

The data was not normally distributed so results were expressed as medians with interquartile ranges. Pre-operative patients with reflux who had a median trans-sphincteric flow of 1.77 ml/sec (1.57 - 2.07) was not significantly different from healthy volunteers with a median trans-sphincteric flow of 2.26 ml/sec (1.72 - 2.39). There was a direct volume effect. Volumes of 15 ml versus 5 ml was significantly different for reflux compared with healthy ($p < 0.0001$).

6.3.2 Effect of fundoplication on lower oesophageal sphincter

A: Manometry

Basal lower oesophageal sphincter pressure

In the upright position, fundoplication increased basal lower oesophageal sphincter pressure. This only reached significance ($p < 0.005$) in those who became dysphagic post-fundoplication. Pre-operative values were not significantly different in the 2 groups.

In the supine position, fundoplication increased basal lower oesophageal sphincter pressure in both the group who became dysphagic post-fundoplication ($p < 0.01$) and those without dysphagia post-fundoplication ($p < 0.04$).

Patients with dysphagia post-fundoplication had mean basal gastro-oesophageal junction pressure of 33.74 $\pm$ 1.37 mmHg which was significantly greater ($p < 0.02$) than in patients without dysphagia post-fundoplication with mean basal gastro-oesophageal junction pressure of 16.94 $\pm$ 2.62 mmHg. (Figure 10)

Patients with severe dysphagia had a mean basal lower oesophageal sphincter pressure of 40.70 $\pm$ 3.21 mmHg, patients with moderate dysphagia had a mean basal lower oesophageal sphincter pressure of 31.86 $\pm$ 2.71 mmHg, patients with mild dysphagia had a mean basal lower oesophageal sphincter pressure of 29.91 $\pm$ 2.06 mmHg while patients without dysphagia post-fundoplication had a mean basal lower oesophageal sphincter pressure of 14.07 $\pm$ 3.22 mmHg. There was a trend for those with severe dysphagia to have higher pressures although none of the comparisons reached a level of significance.

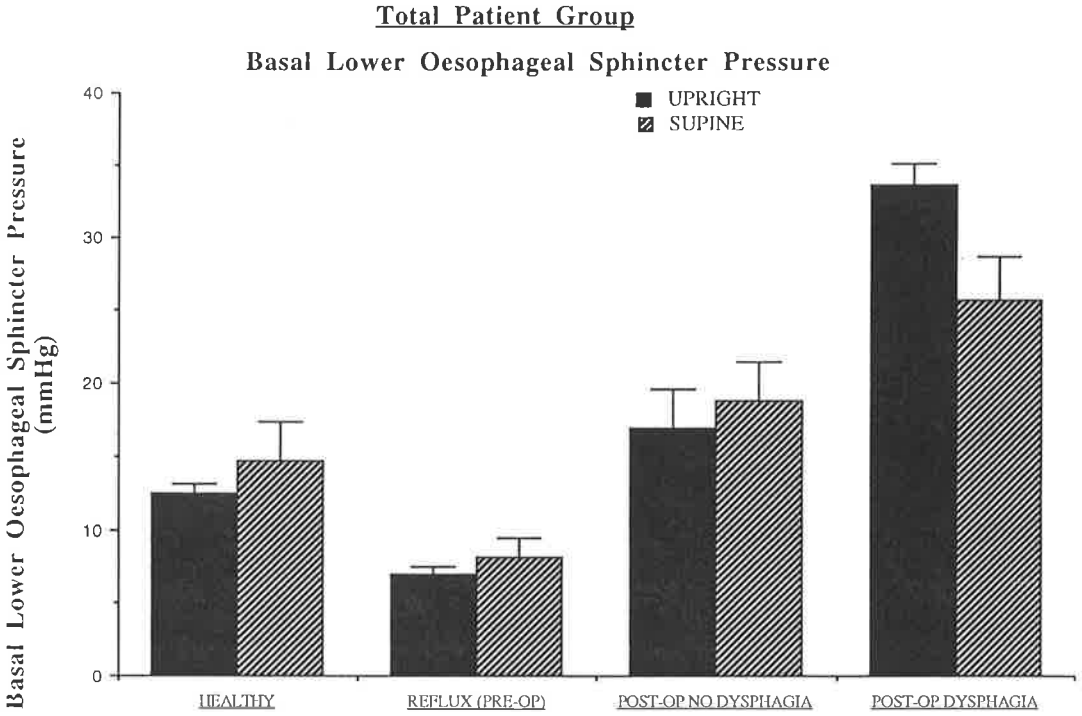

Figure 10: Basal lower oesophageal sphincter pressure in healthy subjects, patients with gastro-oesophageal reflux disease, patients without dysphagia and patients with dysphagia after fundoplication.

Nadir lower oesophageal sphincter pressure

Fundoplication increased nadir lower oesophageal sphincter pressure in both patients who became dysphagic post-fundoplication ($p < 0.0001$) and those who did not ($p < 0.02$), in the upright and supine positions. This effect was seen, not only with single swallows but also with repetitive rapid swallows and in the study of secondary peristalsis using 10 ml air ($p < 0.04$) and water boluses ($p < 0.007$). Air and water boluses did not relax the lower oesophageal sphincter as well as wet swallows ($p < 0.03$) in post-fundoplication patients (Figure 11).

Patients with dysphagia post-fundoplication had a mean nadir gastro-oesophageal junction pressure of 12.00 ± 0.99 mmHg which was significantly greater ($p < 0.04$) than in patients without dysphagia post-fundoplication who had a mean nadir pressure of 6.10 ± 1.78 mmHg (Figure 12). This trend was seen with repetitive rapid swallows and with air and water boluses in the study of secondary peristalsis, but it was not statistically significant (Figure 13).

The median nadir pressure with rapid swallows was lower than that obtained for single swallows but the difference was not statistically significant. Air and water boluses did not relax the lower oesophageal sphincter as well as wet swallows in both groups of post-fundoplication patients ($p < 0.0004$) (Figure 13).

Increasing the volume of the swallowed bolus did not have any effect on the nadir lower oesophageal sphincter pressure.

Patients with severe dysphagia had a mean nadir lower oesophageal sphincter pressure of 14.33 ± 2.52 mmHg, patients with moderate dysphagia had a mean nadir lower oesophageal sphincter pressure of 14.38 ± 0.90 mmHg, patients with mild dysphagia had a mean nadir lower oesophageal sphincter pressures of 7.57 ± 1.36 mmHg while patients without dysphagia post-fundoplication had a mean nadir lower oesophageal sphincter pressure of 6.10 ± 1.78 mmHg. Patients with severe dysphagia and moderate dysphagia had a nadir lower oesophageal sphincter pressures that were significantly higher than those with no dysphagia ($p < 0.03$). None of the other comparisons were significantly different (Figure 14). Increasing the volume of the swallowed bolus did not have an effect on nadir lower oesophageal sphincter pressure.

Nadir lower oesophageal sphincter pressure correlated significantly with basal lower oesophageal sphincter pressure ($r = 0.8945$, $p < 0.0001$).

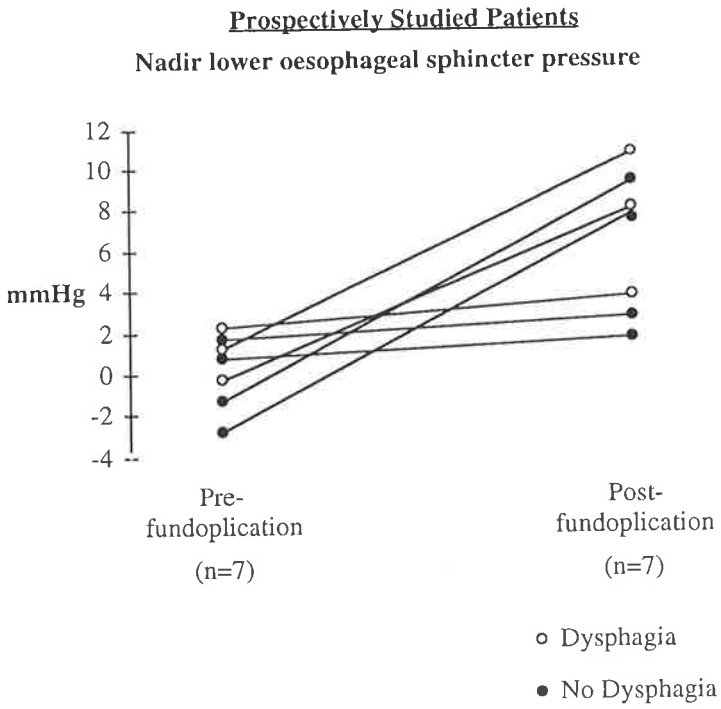

Figure 11: Effect of fundoplication on nadir lower oesophageal sphincter pressure

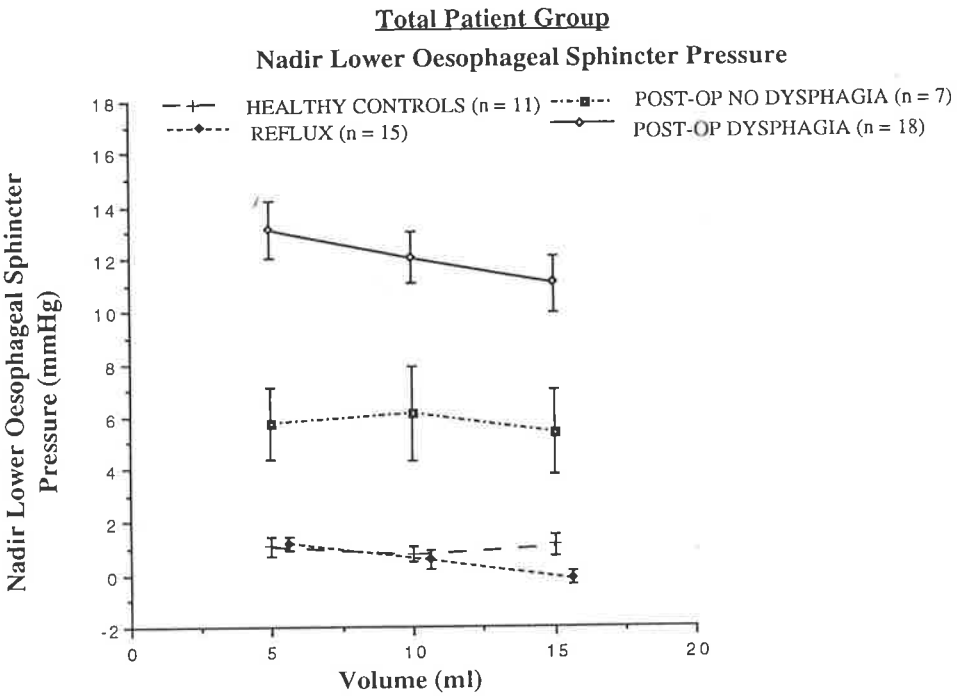

Figure 12: Nadir lower oesophageal sphincter pressure for 5 ml, 10 ml and 15 ml boluses, in healthy subjects, patients with gastro-oesophageal reflux disease before their operation, patients without dysphagia and patients with dysphagia post-fundoplication.

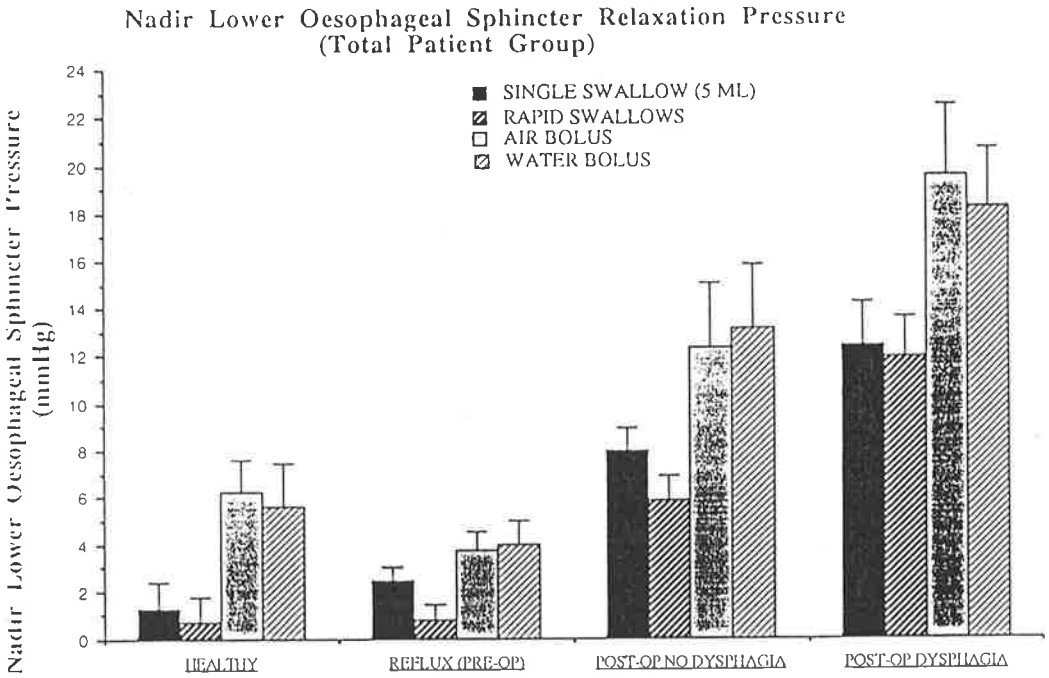

Figure 13: Nadir lower oesophageal sphincter pressure for single swallows, rapid swallows, injected air boluses and injected water boluses in healthy subjects, patients with gastro-oesophageal reflux disease, patients without dysphagia and patients with dysphagia after fundoplication

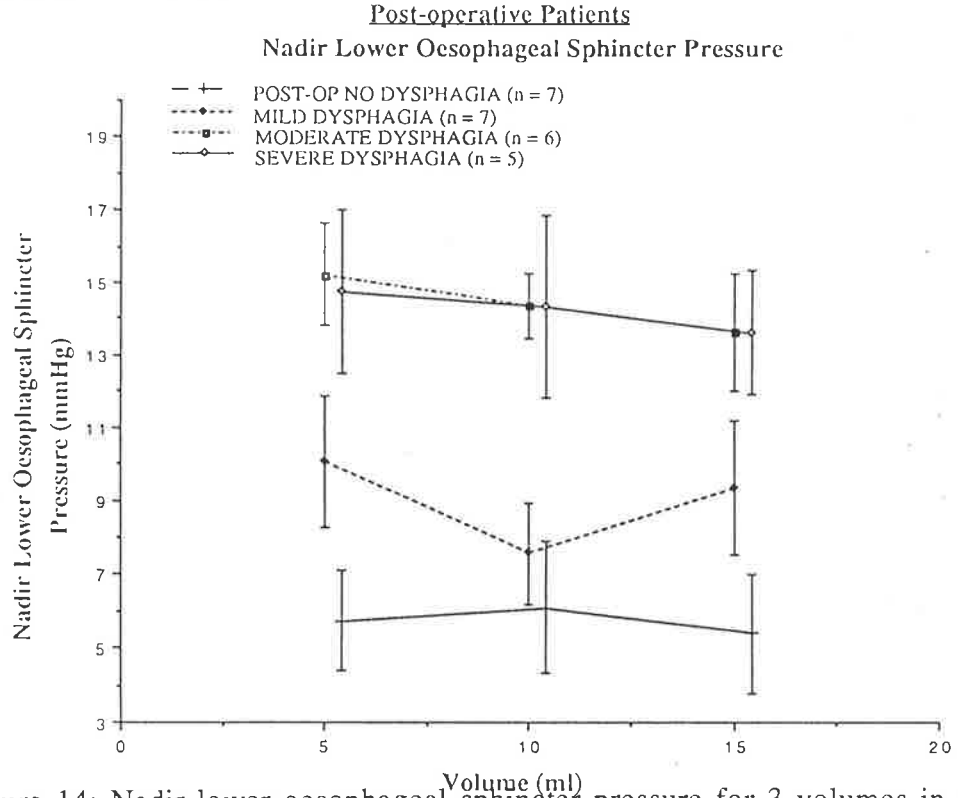

Figure 14: Nadir lower oesophageal sphincter pressure for 3 volumes in patients without dysphagia and patients with mild, moderate and severe dysphagia

B: Videofluoroscopy

Maximum distal oesophageal diameter at the time of maximum lower oesophageal sphincter opening

Fundoplication did not lead to an increase in the maximum distal oesophageal diameter at the time of maximum lower oesophageal sphincter opening in those who were not dysphagic post-fundoplication.

Patients with dysphagia post-fundoplication who had a mean distal oesophageal diameter of 25.27 $\pm$ 0.83 mm which was significantly greater ($p < 0.05$) than in patients without dysphagia post-fundoplication who had a mean distal oesophageal diameter of 18.57 $\pm$ 0.89 mm during successful primary peristalsis (Figure 15). Volumes of 15 ml were associated with greater oesophageal diameter than 5 ml, in patients post-fundoplication ($p < 0.0001$).

Patients with severe dysphagia had a mean oesophageal diameter of 26.44 $\pm$ 1.80 mm which was significantly larger ($p < 0.002$) than those without dysphagia post-fundoplication who had a mean oesophageal diameter of 18.57 $\pm$ 0.89 mm. None of the other comparisons were significantly different. Increasing the volume of the swallowed bolus increased distal oesophageal diameter ($p < 0.0001$).

Maximum lower oesophageal sphincter opening

Fundoplication decreased lower oesophageal sphincter opening ($p < 0.006$).

Patients with dysphagia post-fundoplication who had a mean lower oesophageal sphincter opening diameter of 10.78 $\pm$ 0.40 mm which was not significantly different from patients with no dysphagia post-fundoplication who had a mean lower oesophageal sphincter opening of 9.74 $\pm$ 0.65 mm (Figure 16). Volumes of 15 ml resulted in greater lower oesophageal sphincter opening than 10 ml and 5 ml, 15 ml versus 5 ml was significantly different for post-fundoplication compared with pre-fundoplication ($p < 0.05$).

Patients with severe dysphagia have mean sphincter opening of 8.83 $\pm$ 0.65 mm that was not significantly from those with no dysphagia post-fundoplication who had a mean sphincter opening of 9.74 $\pm$ 0.65 mm. Patients with mild dysphagia had a mean sphincter opening of 12.40 $\pm$ 0.64 mmHg that was significantly higher ($p < 0.04$) than those with no dysphagia. Patients with moderate dysphagia had a mean sphincter opening of 10.64 $\pm$ 0.57 mm that was not significantly different from those with no dysphagia. Increasing the volume of the swallowed bolus did not have a consistent effect on lower oesophageal sphincter opening.

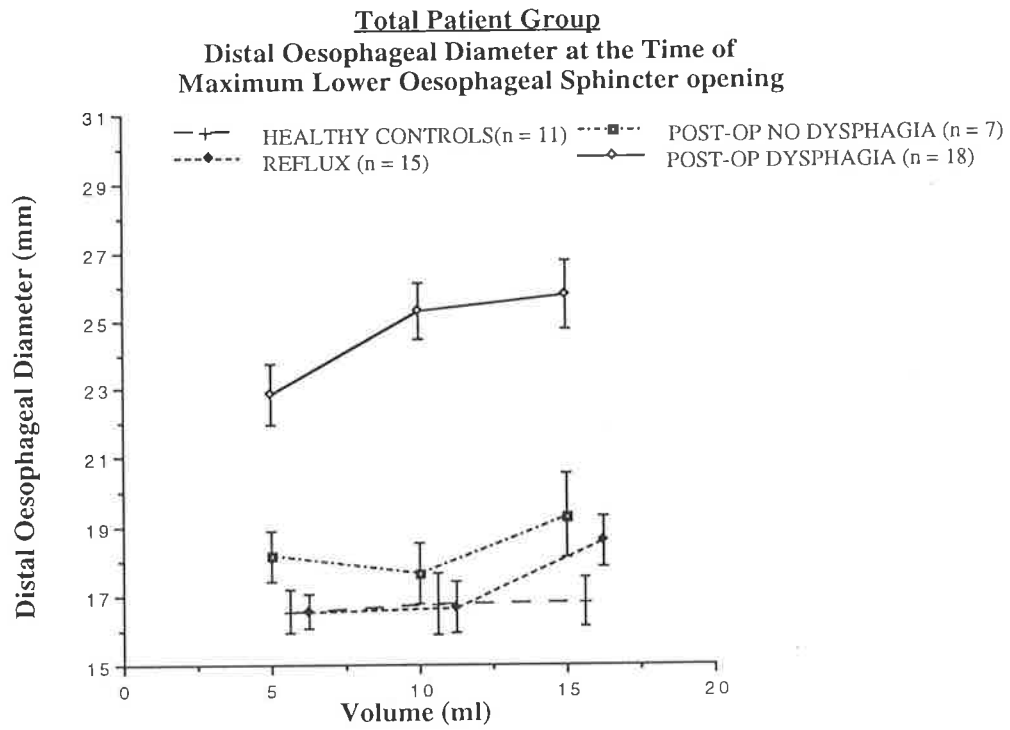

Figure 15: Maximum distal oesophageal diameter for 5 ml, 10 ml and 15 ml boluses, in healthy subjects, patients with gastro-oesophageal reflux disease before their operation, patients without dysphagia and patients with dysphagia post-fundoplication.

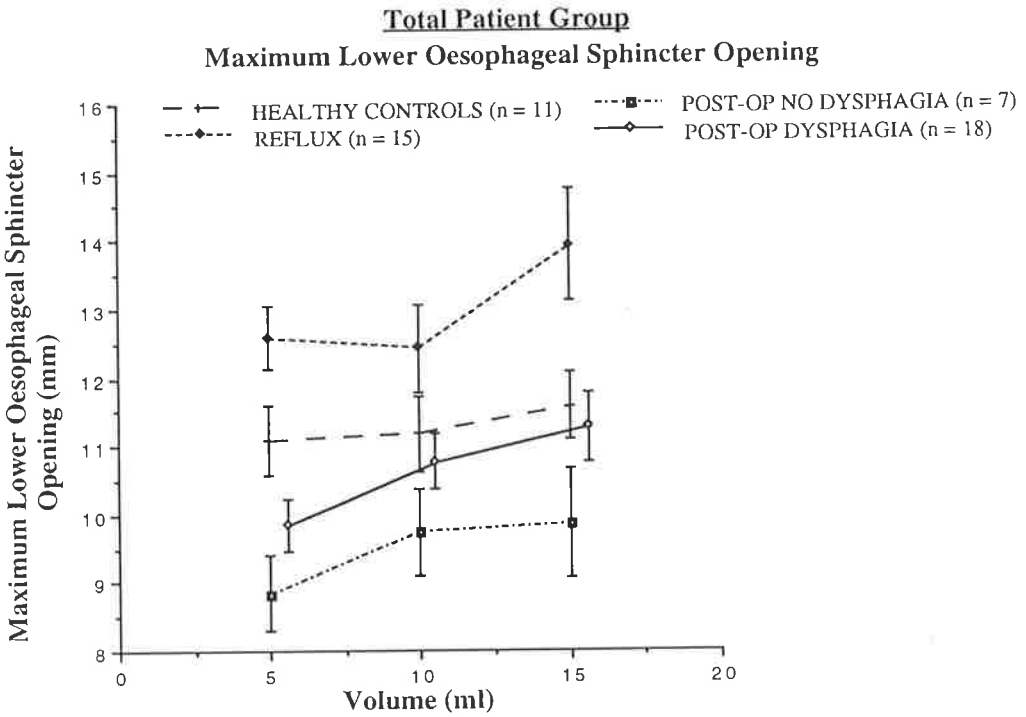

Figure 16: Maximum lower oesophageal sphincter opening for 5 ml, 10 ml and 15 ml boluses, in healthy subjects, patients with gastro-oesophageal reflux disease before their operation, patients without dysphagia and patients with dysphagia post-fundoplication.

C: Manometric observations relevant to transit

Transit time through the lower oesophageal sphincter

Fundoplication had no effect on transit time.

Patients with dysphagia post-fundoplication had a mean transit time of 5.60 $\pm$ 0.34 sec which was not significantly different from patients without dysphagia post-fundoplication who had a mean transit time of 4.58 $\pm$ 0.36 sec.

There was a direct volume effect. Volumes of 15 ml versus 5 ml was significantly different for patients with post-fundoplication dysphagia compared with patients without dysphagia ($p < 0.0001$).

Patients with severe dysphagia have median transit time of 5.63 sec (4.46 - 8.09), patients with moderate dysphagia have median transit time of 5.06 sec (4.42 - 5.92), patients with mild dysphagia have median transit time of 4.89 sec (3.96 - 5.78), while patients without dysphagia post-fundoplication with median transit time of 4.12 sec (3.64 - 4.95). The data was not normally distributed so results are expressed as medians with interquartile ranges.

Patients with severe dysphagia have transit times that were significantly longer than those without dysphagia ($p < 0.03$) and mild dysphagia ($p < 0.02$). None of the other comparisons were significantly different.

Increasing the volume of the swallowed bolus increased transit time across the lower oesophageal sphincter ($p < 0.0001$) for patients with dysphagia of varying severity.

Trans-sphincteric flow

Fundoplication had no effect on trans-sphincteric flow.

The data was not normally distributed so results are expressed as medians with interquartile ranges. Patients with dysphagia post-fundoplication with median trans-sphincteric flow of 2.02 ml/sec (1.73 - 2.36) was not significantly different from patients without dysphagia post-fundoplication with median trans-sphincteric flow of 2.26 ml/sec (1.77 - 2.46).

There was a direct volume effect. Volumes of 15 ml versus 5 ml was significantly different for patients with dysphagia compared with patients without dysphagia ($p < 0.0001$).

Patients with severe dysphagia had median trans-sphincteric flow of 1.39 ml/sec (0.87 - 2.06), patients with moderate dysphagia had median trans-sphincteric flow of 1.91 ml/sec (1.50 - 2.18), patients with mild dysphagia had median trans-sphincteric flow of 2.16 ml/sec (1.82 - 2.43), while patients without dysphagia post-

fundoplication had median trans-sphincteric flow of 2.09 ml/sec (1.75 - 2.65). The data was not normally distributed so results are expressed as medians with interquartile ranges.

Patients with severe dysphagia had trans-sphincteric flows that were significantly slower than those without dysphagia ($p < 0.03$) and mild dysphagia ($p < 0.02$). None of the other comparisons were significantly different. Increasing the volume of the swallowed bolus led to higher trans-sphincteric flow ($p < 0.0001$).

Complete emptying

After fundoplication, 68% of the liquid swallow sequences in the group with no dysphagia post-fundoplication, and 77% in those with dysphagia post-fundoplication were associated with complete clearance of barium.

In the healthy volunteers, 76% of the liquid swallow sequences were primary peristalsis associated with complete clearance of barium. The corresponding values were 68 % in the group with reflux disease.

The instant the tail of the bolus passed the side-hole was not significantly different from the instant of the major upstroke of the peristaltic contraction ($p < 0.05$).

Partial emptying

None of the peristaltic sequences in patients without dysphagia post-fundoplication resulted in incomplete emptying. In patients with dysphagia post-fundoplication, 6% of the 177 primary peristaltic sequences were associated with incomplete emptying of barium.

Of the 102 primary peristaltic sequences analysed in healthy subjects, 2% of them resulted in partial emptying of the barium bolus from the oesophagus.

Synchronous waves

Complete clearance of barium boluses from the oesophagus was accomplished by 14.2% of 133 synchronous waves in the 4 groups of patients. In 81.2% of the 133 synchronous waves, the pressure in the distal oesophagus was higher than the lower oesophageal sphincter pressure at the time of flow across the sphincter. This positive pressure gradient may have contributed to the flow.

The incidence of synchronous waves was fairly even across the four groups of subjects: healthy, patients with reflux disease before fundoplication and those with or without dysphagia after fundoplication.

One patient in this study who had normal peristalsis before the fundoplication had only synchronous waves after a total fundoplication and experienced dysphagia as a new symptom after fundoplication.

Marshmallows

The mean in vivo diameter of the half-marshmallow bolus was 13 mm. Of the total of 131 half-marshmallows swallowed, 21% of the half-marshmallows impacted at the level of the aortic arch, and 17% had impacted at the level of the thoracic inlet. The mean time taken for the half-marshmallow to pass through the oesophagus was 32 seconds in the healthy group, 42 seconds in the group with reflux disease before fundoplication, 40 seconds in the group without dysphagia and 32 seconds in the group with dysphagia. The mean lower oesophageal sphincter opening diameter that accommodated the passage of the half-marshmallow was 14.4 mm in the healthy group, 15.6 mm in the reflux group, 9.6 mm in the group with no post-operative dysphagia and 10.3 mm in the group with post-fundoplication dysphagia. Even though the mean in vivo diameter of the half-marshmallow bolus was 13 mm, it was elastic enough to squeeze through the post-fundoplication sphincter.

Symptoms of dysphagia was reproduced in only 5.6% of swallows in the dysphagic group, in other words, most of the subjects were not aware of the arrest of the half-marshmallow.

Healthy subjects experienced arrest of the half-marshmallow in 64% of swallows but none of them were aware of the impaction. The half-marshmallow was then cleared by an additional swallow and the mean time taken was 32 seconds.

6.4 SUBJECTIVE DYSPHAGIA SCORE

The total dysphagia score was not correlated with peristaltic velocity, duration of contraction, proximal amplitude or distal amplitude of contraction.

The total dysphagia score was directly correlated with the ramp intrabolus pressure for 5 ml ($r = 0.540$, $p < 0.02$), 10 ml ($r = 0.608$, $p < 0.003$) and 15 ml ($r = 0.568$, $p < 0.02$) measured in the upright position. In the supine position, this correlation was not seen.

The total dysphagia score was directly correlated with the basal lower oesophageal sphincter pressure ($r = 0.626$, $p < 0.001$).The total dysphagia score was also directly correlated with the nadir lower oesophageal sphincter pressure for 5 ml ($r = 0.484$, $p < 0.02$), 10 ml ($r = 0.677$, $p < 0.0005$), 15 ml ($r = 0.538$, $p < 0.02$) swallows and rapid swallows ($r = 0.551$, $p < 0.007$). It was correlated with the nadir pressure associated with secondary peristalsis triggered by air injections ($r = 0.422$, p

= 0.05) but not with nadir pressure associated with water injections (r = 0.1129, NS).

The total dysphagia score was not correlated with transit time through the lower oesophageal sphincter and transphincteric flow

6.5 DISCUSSION

Information on the pathophysiology of dysphagia post-fundoplication is scarce and conflicting. A better understanding of the sequelae of Nissen fundoplication such as dysphagia and gas-bloat may lead to modifications of the operation to reduce the side-effects, because the quality of life after fundoplication is as important as the control of gastro-oesophageal reflux (Pope 1992).

The introduction of laparoscopic anti-reflux procedures promises to reduce the morbidity associated with the open operation but it has yet to stand the test of time and rigorous evaluation with respect to side-effects and reflux control. The laparoscopic Nissen fundoplication is the most commonly performed of the laparoscopic anti-reflux procedures.

In 1963, Siegel *et al* (1963) found no correlation between the intensity of dysphagia and oesophageal motility findings when the oesophagus is studied empty with perfusion manometry. Breumelhof *et al* (1991) found that neither conventional nor ambulatory pressure recordings of the oesophageal body revealed abnormalities that could be held responsible for dysphagia so they concluded that their data did not support the concept that post-fundoplication dysphagia is a major complication of Nissen fundoplication. Their conclusions are illogical and the lower oesophageal sphincter was not studied. The incidence of post-operative dysphagia in reported series is high and more sophisticated techniques may reveal differences that objectively characterise patients with dysphagia post-fundoplication.

Dysphagia as a new symptom occurs in up to 40% of patients after Nissen fundoplication. Woodward *et al* (1971) noted post-operative dysphagia in 24% of patients after fundoplication, notwithstanding the fact that surgery was done with a large bougie of 36 to 42 F in position. However Woodward *et al* did not comment on how tightly the fundoplication was constructed around the bougie. Luostarinen (1993) in a follow up study of 109 patients over a mean of 77 months, found that dysphagia increased or began after fundoplication in 43%. This included mild cases where information about the dysphagia was only brought out by direct questioning. In his study, the Nissen-Rossetti anterior wall fundoplication was carried out around a 32 F tube without mobilisation of the lesser curvature or ligation of the short gastric vessels, and the surgeon was able to place one or two fingers under the plicated wrap. In Mitchell's follow-up of the first 100 patients who underwent laparoscopic fundoplication in Adelaide, 32% reported some dysphagia, at least 7 underwent oesophageal dilatations and 3 were re-operated for dysphagia (personal communication).

The total incidence of dysphagia, of varying severity, in our prospective study was 6 out of 13 patients or 46%. The incidence of severe dysphagia was 2 out of 13 patients or 15% at 3 months.

Dysphagia is not a static symptom. The incidence of mild dysphagia after open Nissen-Rossetti fundoplication was 30% at 3 months decreasing to 10% at 6 months in one study of 38 patients (Lundell *et al* 1991) and 18% at 6 months and also 18% at 5 years in another study of 40 patients (Johansson *et al* 1993). The incidence of moderate dysphagia was 10% at 3 months and 0% at 6 months in the first study (Lundell *et al* 1991) and 10% at 6 months decreasing to 2.5% at 5 years (Johansson *et al* 1993). None of the patients in these studies experienced severe dysphagia.

Dysphagia is a subjective symptom and many studies assess it by patients' complaints (Woodward *et al*, 1971, DeMeester *et al* 1975, Negre *et al* 1983, Gill *et al* 1986, Triadafilopoulos 1989, Mattox 1990, Breumelholf *et al* 1991, Luostarinen *et al* 1993). Dakkak *et al* (1992) used a clinical test of dysphagia by giving 9 items of food of increasing solidity to patients. The patients' ability to swallow was assessed using a standard form administered by a research assistant. Patients' accounts of their eating capacity correlated well with their observed performance ($r = 0.793$, $p < 0.001$). Hence it seems reasonable to rely on the patients' subjective accounts of dysphagia.

Grading the severity of dysphagia is arbitrary. Most studies use "mild", "moderate" or "severe". Mild dysphagia has been defined as occasional, short duration (Johansson *et al* 1993) or noticeable but not interfering with eating habits (Pope 1992). Moderate dysphagia occurred when solids required liquids to clear (Johansson *et al* 1993) or when dietary habits were changed (Pope 1992). Dysphagia was classified as severe if there were episodes of oesophageal obstruction requiring medical attention (Johansson *et al* 1993) or if it led to weight loss and failure to eat solid foods (Pope 1992). Lundell *et al* (1991) did not elaborate on how scoring was done except to say that the patient was evaluated by 2 independent observers, and the more unfavourable score was registered if there was disagreement between observers. Csendes *et al* (1989) recorded the incidence of severe dysphagia by noting the number of patients who required dilatations for dysphagia.

Instead of just coding for intensity of the dysphagia, it would seem useful to incorporate frequency into the score. Thus the scoring system suggested by Pope (1992) but slightly modified, has been useful. A score was derived for solids and liquids separately by multiplying the severity score by the frequency score. The scores for liquids and solids were then summated to give a total score.

The hypothesis that inability to belch, gas-bloat and dysphagia may reflect the production of a supercompetent sphincter (DeMeester *et al* 1979, Bjerkeset *et al* 1980) which relaxes imperfectly on swallowing has not been the subject of much investigation.

Dysphagia post-fundoplication has been attributed to the tightness of the wrap (Luostarinen 1993). In our study, almost all wraps were constructed around large bougies of 46 to 52 F. Yet the incidence of dysphagia, of varying severity, in my prospective study was 6 out of 13 patients or 46 % and the incidence of severe dysphagia was 2 out of 13 patients or 15 % at 3 months.

The short gastric vessels had been divided in 2 open and 2 laparoscopic operations in our prospective study and these 4 patients experienced no dysphagia post-fundoplication. It is possible that division of the short gastric vessels lessens the tension that the gastrosplenic ligament exerts on the greater curve of the stomach. However, Weerts *et al* (1993) reported that even when short gastric vessels were divided routinely in 132 patients who underwent laparoscopic Nissen fundoplication around a 36 F bougie, 9 patients required dilatations for dysphagia.

Crural sutures were used in 2 patients in the prospective study and one had mild dysphagia while the other had moderate dysphagia. In the retrospective study of 12 patients with dysphagia, crural sutures were placed in 4 patients. These 6 patients have varying degrees of dysphagia.

Scarring at the hiatus was responsible for severe dysphagia in one patient in our prospective study. Clinically she only developed dysphagia at 2 months after fundoplication and was symptom free prior to that.

Slippage or gastric pull-through is another mechanism for dysphagia, though this was not the cause of dysphagia in any of our patients.

Negre (1983) postulated a mechanical or motility disturbance as a cause for post-fundoplication dysphagia.

Radiologic correlates of manometric variables

Each subject swallowed the same volume of liquid 3 times. This was a balance of the intra-individual variability against the negative effects of radiation exposure (Lof *et al* 1990).

Studies in the supine position (Kahrilas *et al* 1988, Mittal *et al* 1990, Hewson *et al* 1990, Massey *et al* 1991) would have eliminated the effect of gravity and demonstrated retrograde flow better. However, concurrent oesophageal manometry and videofluoroscopy were performed in the upright position in our study, first, to minimise aspiration in those with gastro-oesophageal reflux disease, second, to aid swallowing in those with dysphagia and third, because it was a more natural position in which to undertake studies.

Kahrilas *et al* (1988) observed that a single normal peristaltic wave results in complete clearance of barium from the oesophagus, whereas little clearance is achieved by regional hypotensive waves or incomplete peristaltic sequences. It is surprising that

only 76% of the liquid swallows in the healthy controls were primary peristaltic waves associated with complete clearance of barium unlike Kahrilas' *et al* (1988) findings that successful peristalsis occurred in 97% of controls. The incidence of successful primary peristalsis for liquid swallows in the group with reflux disease was 68%, contrasts this with the reported 75% successful peristalsis in patients with mild oesophagitis and 52% successful peristalsis in patients with severe oesophagitis.(Kahrilas *et al* 1988). In the group without dysphagia post-fundoplication, 68% of liquid swallows was associated with primary peristalsis, and for those with dysphagia post-fundoplication, the corresponding value was 77% which suggests that post-operative dysphagia is not a motility problem.

The tail of the bolus seen radiologically has been observed to correspond to the major upstroke of the pressure complex qualitatively (Kahrilas *et al* 1988, Mittal *et al* 1990, Hewson *et al* 1990, Massey *et al* 1991) that is, the bolus travels in front of the peristaltic wave as might be expected. Our study confirmed quantitatively that the time of the tail passing a recording channel was not statistically different from the time of the major upstroke of the peristaltic complex.

Proximal and distal amplitude

It has been established that severe oesophagitis is associated with peristaltic dysfunction (Bombeck *et al* 1973, Marshall *et al* 1982, Corazziari *et al* 1984, Heddle *et al* 1984, Baldi *et al* 1985, Gill *et al* 1986, Kahrilas *et al* 1986, Katz *et al* 1986, Grande *et al* 1991). Unlike other studies, patients with reflux in this study did not have lower oesophageal peristaltic amplitude than healthy subjects. This is surprising considering that this subgroup has relatively severe disease requiring surgery. It may be a Type II statistical error because of the small numbers of patients in this study.

Primary peristalsis has shown improvement with medical therapy as reported by Marshall *et al* (1982), Kahrilas *et al* (1986), and Moses (1987). In contrast to studies by Bowes *et al* (1975), Kozarek *et al* (1983), Gill *et al* (1986), Ortiz Escandell *et al* (1991) which showed that fundoplication led to an increase in peristaltic amplitude, Baldi *et al* (1985), Eriksen *et al* (1985), and Katz *et al* (1986) did not.

Stein *et al* (1992) found that peristaltic amplitude also increased after fundoplication and proposed that it is secondary to the healing of oesophagitis. In reviewing that paper, Jamieson (1993) suggested that the increase in amplitude may simply be a response to obstruction at the lower oesophageal sphincter imposed by fundoplication. Mittal's *et al* (1990) study in cats demonstrated that the amplitude of contraction increased with increasing obstruction at low volumes but this effect was not seen with larger bolus volumes.This experiment showed that an isolated lower

oesophageal sphincter abnormality could induce oesophageal contraction dysfunction. In patients after anti-reflux surgery, abnormal oesophageal body function caused by distal obstruction is functional and apparently related to incomplete lower oesophageal sphincter relaxation , unlike the obstruction in patients with strictures which is mechanical and fixed (Little *et al* 1986).

There was no difference in oesophageal amplitude between those with and without dysphagia and fundoplication did not lead to an increase in amplitude in either group. However, in the group without dysphagia after fundoplication, there was a greater range of amplitude than in the group with dysphagia. One may have expected the amplitude to increase in response to greater functional obstruction at the lower oesophageal sphincter in patients with dysphagia. Peristaltic amplitude was reported to be in the normal range in patients with dysphagia post-fundoplication by Woodward *et al* (1971) although no values were quoted. Gill *et al* (1986) and Breumelholf *et al* (1991) also reported that there was no significant difference in the amplitude, duration of contraction and velocity in patients with dysphagia post-fundoplication compared with those without dysphagia post-fundoplication.

Increasing the volume of the bolus in our study did not affect amplitude, which is similar to Hollis' *et al* (1975) finding that 2 ml boluses produced the same amplitude as 20 ml boluses. Two ml boluses would seem inadequate to cause local stretch to alter the force-velocity characteristics of oesophageal muscle and thus altering peristaltic amplitude so a myogenic mechanism seems unlikely. Instead, a neural mechanism could be responsible for determining amplitude. Peristalsis in oesophageal striated muscle is determined by a descending sequence of efferent neural discharges generated by a central swallowing program (Diamant *et al* 1977). Sequential activation is more prominent in the striated than smooth muscle part of the oesophagus (Higgs *et al* 1963, Mann *et al* 1968, DiMarina *et al* 1973, Rattan *et al* 1974). Within each muscle type, sequential activation of longitudinal muscle is dependent on an intact vagal innervation (Sugarbaker *et al* 1984) whereas circular muscle less so (Gidda *et al* 1984, Dodds *et al* 1978, Sugarbaker *et al* 1984).

Propagation Velocity

The propagation velocity of swallowing waves in controls and preoperative patients in our study were greater than 2 - 4 cm/second similar to Ingelfinger (1958) and Dodds *et al* (1973). Other studies (Kahrilas *et al* 1986, Gill *et al* 1986) showed that the propagation velocity was faster in patients with reflux compared with healthy subjects.

The decrease in propagation velocity of swallowing waves post-fundoplication in our study supports the observation by Gill *et al* (1986) and Mittal *et al* (1990) and

may again suggest that a fundoplication acts as a relative obstruction . However, there was no difference between patients with dysphagia and those without dysphagia, again similar to Gill's findings (Gill *et al* 1986). This is surprising as patients with dysphagia may be expected to have more oesophageal outflow obstruction.

Larger volumes were not associated with slowing down of peristalsis, a similar finding to that of Dodds *et al* (1973) who found that dry swallows propagate faster than wet swallows. and Hollis *et al* (1975) who reported that volumes from 2 to 20 ml result in similar amplitude.

Duration of contraction

For patients with reflux disease, the duration of contraction was similar to controls. This differs from the findings of Gill *et al* (1986) and Kahrilas *et al* (1986) where the duration of contraction was shorter in patients with reflux disease.

The duration of contraction was increased in those patients with dysphagia post-fundoplication. Bowes *et al* (1975) found that the duration of contraction was less after fundoplication whilst Gill *et al* (1986) found that fundoplication increased the duration of contraction but found no difference between patients with dysphagia and patients without dysphagia. Mittal *et al* (1990) found that increasing outflow obstruction had no effect on the duration of contraction in cats.

Increasing the volume of the bolus had no effect on the duration of contraction.

Secondary peristalsis

In our study, 10 ml of injected air triggered secondary peristalsis with a median response rate of 100% and 10 ml of injected water had a median response rate of 80% in healthy subjects. The corresponding values from Schoeman's study (Schoeman *et al* 1994) were 70% and 50%. In patients with reflux disease in our study, air boluses triggered secondary peristalsis with a response rate of 60% and water boluses triggered secondary peristalsis 20% of the time. This contrasts with Schoeman's study where the median response rate was 0% for both air and water. Schoeman found that the response to water boluses discriminated between patients with reflux disease and healthy controls. In our study, the initiation rate and the lower oesophageal sphincter relaxation rate were not significantly different between patients with reflux disease and healthy subjects for both air and water boluses. However, the propagation rate was lower in patients with reflux disease compared with healthy subjects for both air and water boluses.

In our study of secondary peristalsis, injected air boluses triggered significantly lower proximal and distal amplitudes than wet swallows in all groups except healthy

volunteers. In patients with reflux disease, distal oesophageal amplitudes triggered by injected air boluses were significantly less than the amplitudes obtained with wet swallows similar to the findings of Schoeman *et al* (1993).

Fundoplication had no effect on the median initiation and propagation rates with air and water injections. In the post-operative patients, distal oesophageal amplitude triggered by injected air boluses was also not significantly different from wet swallows. In our study, secondary peristalsis did not return to normal in post-fundoplication patients in the period of follow up. Fundoplication decreased the rate of lower oesophageal sphincter relaxation response to oesophageal distension. It has been shown that fundoplication decreases the rate of transient lower oesophageal sphincter relaxations and reflux episodes associated with these relaxations (Ireland *et al* 1993). From this study, it appears that fundoplication also abolishes lower oesophageal sphincter relaxations from the aboral direction which in theory would explain side-effects such as dysphagia.

It is contentious whether the motility disorder associated with poor clearance is a primary abnormality or is secondary to reflux disease which is reversed when reflux is cured (Jamieson 1993). The observation that fundoplication did not improve secondary peristalsis could mean (1) the motility disturbance is primary or (2) fundoplication introduced an obstruction at the lower oesophageal sphincter leading to failure of improvement of secondary peristalsis or (3) not enough time had elapsed for improvement to occurred.

However, in this study, patients with dysphagia post-fundoplication whatever the severity were not significantly different from those without dysphagia. Whether this is a type II error due to small patient numbers is not known.

Ramp pressure

Ramp intrabolus pressure is best seen in the distal oesophagus (Goyal 1981). Dornhurst *et al* (1954) alluded to a gentle rise in pressure accompanying the passive expansion of the oesophagus as the contents are forced ahead of the peristaltic wave. In this study, the ramp intrabolus pressure occurs after occlusion of the mid oesophagus and during lower oesophageal sphincter opening, an obsesrvation which has not been recognised before. The ramp intrabolus pressure does not reflect the peristaltic wave pushing against a closed sphincter in an attempt to open it, but is related to the lower oesophageal sphincter residual relaxation pressure since it coincides with sphincter opening. This does not support Goyal's *et al* (1981) suggestion that it is produced by compression of the lower oesophageal segment between the advancing bolus and the lower oesophageal sphincter.

In the healthy controls and patients with gastro-oesophageal reflux before their surgery, ramp pressures were 7.55 ± 1.12 and 7.54 ± 0.76 mmHg respectively. The respective nadir lower oesophageal sphincter pressure for 10 ml swallows was 0.77 ± 0.29 and 0.58 ± 0.38 mmHg. This minimum ramp pressure above basal oesophageal pressure is probably due to the mere presence of the bolus.

Patients with reflux and controls therefore had minimal ramp pressures. Fundoplication resulted in higher ramp pressures in those who developed dysphagia compared to those who did not. Those with severe dysphagia had the highest ramp pressures.

Ramp intrabolus pressure might be expected to increase with increasing bolus volume. However, in our study, increasing the volume of the swallowed bolus had no effect on the intrabolus pressure. Larger volumes were associated with wider sphincter opening and it may be hypothesised that increased flow is possible due to wider sphincter opening, so there was no difference in the ramp pressure. Moreover, larger volumes were associated with wider distal oesophageal diameter in post-fundoplication patients and this may explain the lack of a direct volume effect on ramp pressure.

Ramp correlations

Vantrappen *et al* (1967) described a second positive wave which occurred in 33% of swallows in the distal oesophagus and its incidence was increased by obstructing the gastro-oesophageal opening. This contraction began 1 to 2 seconds after the onset of swallowing.

Our hypothesis is that ramp intrabolus pressure is the result of resistance at the gastro-oesophageal junction when the sphincter is open and the bolus is being squeezed from above by the peristaltic wave. The magnitude of ramp intrabolus pressures might be expected to increase with increasing outflow obstruction.

Since the timing is such that ramp pressure occurs when the lower oesophageal sphincter is open, outflow obstruction may manifest itself in the form of residual relaxation pressure of the lower oesophageal sphincter (nadir pressure). In our study, the ramp pressure correlated directly with nadir lower oesophageal sphincter pressure and distal oesophageal diameter. In the presence of incomplete lower oesophageal sphincter relaxation, the ramp pressure increased and this probably caused the distal oesophageal diameter to increase. There was no correlation with maximum lower oesophageal sphincter opening diameter.

Richter *et al* (1987) showed that above a threshold of 30 mmHg, liquid transport through the oesophagus in healthy subjects is equally effective at amplitudes from 33 to 500 mmHg. It is therefore not surprising that there is no correlation between ramp pressure and distal amplitude in this study and as long as distal

oesophageal amplitude is above lumen occlusion pressure, increases in the amplitude are not associated with increases in the ramp pressure (Gill *et al* 1986, Richter *et al* 1987, Kahrilas *et al* 1986). The ramp intrabolus pressure can merge into the amplitude of the contraction at some degrees of outflow obstruction, making it difficult to identify the upstroke of the contraction manometrically (Mittal *et al* 1990). Massey *et al*, (1992) found that patients with oesophageal pulsion diverticula had either a hypertensive lower oesophageal sphincter pressure or incomplete lower oesophageal sphincter relaxation. These findings were associated with higher ramp intrabolus pressures than in normals.

The pathophysiology of increased ramp intrabolus pressure in post-fundoplication patients appears to be different from hypopharyngeal ramp pressures in patients with Zenker's diverticulum. In those patients, the upper oesophageal sphincter relaxes completely but the sphincter opening is incomplete. This incomplete sphincter opening causes the marked increase in hypopharyngeal pressures during the phase of trans-sphincteric flow (Cook *et al* 1992) which is directly proportional to bolus volume. The distal oesophageal ramp pressure in this study was correlated with nadir lower oesophageal sphincter pressure but not the sphincter opening, and there was no volume effect.

Distal oesophageal ramp pressures does not reflect bolus volume. It may reflect oesophageal stretch or the physical work necessary to move the bolus into the stomach against the lower oesophageal sphincter pressure.

Basal lower oesophageal sphincter pressure

The finding in our study that patients with reflux disease have a lower basal lower oesophageal sphincter pressure than healthy volunteers is consistent with previous studies (Wankling *et al*, 1965, Olsen *et al* 1965, Lind *et al*, 1966, Haddad 1970, Cohen *et al* 1972, Olsen 1965). Dent *et al* (1980) found that 5 mmHg basal lower oesophageal sphincter pressure is probably sufficient to prevent reflux in recumbent healthy subjects, although a hypotensive lower oesophageal sphincter pressure is not the only mechanism by which reflux occurs (Dent *et al* 1988). Even in patients with reflux disease, 65 to 82% of reflux episodes were found to be due to transient lower oesophageal sphincter relaxations and only 18 to 23% due to absent lower oesophageal sphincter pressure (Dodds *et al* 1982, Dent *et al* 1988).

Fundoplication increased basal lower oesophageal sphincter pressure of patients in this study, a finding similar to other studies. Basal lower oesophageal sphincter pressure is said to reflect sphincter strength (Cohen *et al* 1970). Ogorek *et al* (1989) suggested that patients with a hypotensive lower oesophageal sphincter will respond favourably to surgery whereas patients with normal pressures usually will not

require surgery. This view would be regarded by many as controversial at the very least! This increase in basal lower oesophageal sphincter pressure may not be the mechanism by which fundoplication works (Jamieson 1987) as there is no direct relationship between an increase in gastro-oesophageal junction pressure and successful fundoplication (Kiroff *et al* 1984, O'Hanrahan *et al* 1990).

It has been suggested that fundoplication increases basal lower oesophageal sphincter pressure by mechanically compressing the lower oesophageal sphincter (Dent *et al* 1982, Ogorek *et al* 1989, Ireland *et al* 1993, Lundell *et al* 1993). However, the restoration of normal anatomical relationships in the Allison repair for hiatus hernia (Allison 1951), overcorrection of the spatial relationships between the oesophagus, stomach and diaphragm in the Belsey Mark IV repair (Skinner *et al* 1967) and Hill's posterior gastropexy (Hill 1967) all lead to an increase in basal lower oesophageal sphincter pressure (Jamieson *et al* 1988). Additionally, insertion of an Angelchik prosthesis (Angelchik *et al* 1979) increases sphincter pressure and the effect appears to be due to posterior padding of the gastro-oesophageal junction (Benjamin *et al* 1983). Siewert *et al* (1974) used evidence from in-vitro studies, animal experiments and follow-up studies in humans to show that the wall of the fundus next to the cardia shows a reactivity to gastrointestinal hormones similar to that of the lower oesophageal sphincter. When the original lower oesophageal sphincter was eliminated in dogs, the fundus cuff formed by a fundoplication set up its own pressure zone which was demonstrated by manometry and this pressure zone was subjected to similar hormone regulations to the normal lower oesophageal sphincter. This is unusual but interesting.

In our study, patients with dysphagia had higher basal lower oesophageal sphincter pressure than patients without dysphagia. There was a trend for patients with severe dysphagia to have the highest basal lower oesophageal sphincter pressure. Patients without dysphagia had basal lower oesophageal sphincter pressures which were similar to healthy unoperated volunteers.

It has been hypothesised that a supercompetent valve is a one way valve that allows food and drink into the stomach but causes dysphagia and gas-bloat (Bjerkerset *et al* 1980). A previous study by Jamieson *et al* (1992) showed that basal gastro-oesophageal junction pressure measured intraoperatively and at 6 months after fundoplication showed no significant correlation with dysphagia, although the number of patients with dysphagia in this study was only four.

Myogenic mechanisms have been proposed for the increase in basal sphincter pressure, such as (a) muscle re-alignment and (b) muscle tension that is not dependent on neural mechanisms (Goyal *et al* 1976). This re-alignment of the muscle places the lower oesophageal sphincter muscle at its optimal degree of stretch to allow the sphincter to respond normally to both neural and humoral stimulation restoring lower oesophageal sphincter tone (Lipschutz *et al* 1974, Kozarek *et al* 1985) and enhancing

valvular activity of the lower oesophageal sphincter (Libermann-Meffert *et al* 1979). Fundoplication changes the length-tension relationship of the muscle at the gastro-oesophageal junction (Lipschutz *et al* 1974, Behar *et al* 1975). According to length-tension curves for muscle, tension rises steeply during stretch and thus could serve as a force to restore sphincter closure (Christensen *et al* 1970, 1973, Lipschutz 1971, Cohen *et al* 1973, Biancani *et al* 1975). Against the myogenic view is the observation that the Nissen fundoplication can be competent in the absence of myogenic influence as demonstrated by a post-mortem study in humans (Butterfield 1971).

It has been suggested that the vagus nerve is not responsible for sphincter tone as abdominal vagotomy has no effect on sphincter tone (Crispin *et al* 1967, Mann *et al* 1968, Agorn *et al* 1977). This suggests either (a) the lower oesophageal sphincter is supplied by nerves that left the vagal trunk before reaching the sphincter or (b) a neural mechanism is not responsible.

Since an increase in basal lower oesophageal sphincter pressure is not the only explanation for the mechanism of fundoplication, a flap valve effect and the length of the abdominal oesophagus have been proposed as possible mechanisms.

Bowes *et al* (1975), Fisher *et al* (1978), Butterfield (1971), Matikenen *et al* (1984) and Little (1992) suggest that fundoplication narrows the angle of His to produce the flap valve effect.

Fundoplication also restores a length of abdominal oesophagus when constructed in the abdomen (DeMeester *et al* 1979), and Bonavina *et al* (1986) used a sphincter model to document the importance of this in providing sphincter competence. The length of the sphincter contributes to sphincter competence by diminishing the importance of gastric wall tension in sphincter opening and by improving the mucosal seal according to Petterson *et al* (1980). However Bancewicz *et al* (1987) were unable to find any relationship between the intra-abdominal length of the oesophagus and the effectiveness of fundoplication in preventing reflux.

A more important function may be changes in the distensibility of the cardia which is the trigger zone for transient lower oesophageal sphincter relaxations (Ireland *et al* 1993). Fundoplication may prevent the distraction of the cardia by limiting gastric wall tension in the region of the gastro-oesophageal junction (Samelson *et al* 1983, Maddern *et al* 1985, Little *et al* 1992). A greater increase in intra-gastric pressure must be present to increase gastric wall tension sufficiently to open the lower oesophageal sphincter (Petterson *et al* 1980). Another theory is that fundoplication may serve as a conduit in which the intra-abdominal pressure is transmitted directly to the terminal oesophagus (DeMeester *et al* 1979, Matikanen *et al* 1984) so it is effective even when the wrap is in the chest (Woodward *et al* 1971).

Hence, a hypotensive lower oesophageal sphincter is associated with gastro-oesophageal reflux and the increase in sphincter tone after fundoplication improves

reflux control, even though it is not the full explanation. However, a supercompetent lower oesophageal sphincter results in dysphagia.

Nadir lower oesophageal sphincter pressure

Patients with reflux disease and control subjects were able to fully relax their lower oesophageal sphincter pressure to gastric pressure with wet swallows. The nadir lower oesophageal sphincter pressure is the lowest pressure that the lower oesophageal sphincter relaxes to, and this is achieved by wet swallows.

Following fundoplication, however, the gastro-oesophageal junction does not relax to intragastric pressure during water swallows, but has a residual pressure (Bowes *et al*, 1975, Dent *et al* 1982, Kiroff *et al* 1984, Jamieson *et al* 1992, Lundell *et al* 1993, Ireland *et al* 1993). This residual relaxation pressure or nadir pressure has a mean of about 4 to 6.5 mmHg and this may be a further mechanism by which fundoplication works.

Woodward *et al* (1971) observed that patients with dysphagia post-fundoplication had "normal" lower oesophageal sphincter relaxation with deglutition but did not provide data to substantiate their statement. DeMeester *et al* (1979) hypothesised that dysphagia reflects the production of a supercompetent sphincter that relaxes imperfectly on swallowing. In our study, the nadir pressure was higher in those with dysphagia post-fundoplication and this is different from the findings of Jamieson *et al* (1992) although there were only 4 patients in their dysphagia group. We found that patients with severe dysphagia had the highest nadir lower oesophageal sphincter pressure. Mittal *et al* (1990) observed that increasing pressure in the region of the gastro-oesophageal junction experimentally in cats resulted in obstruction.

Nadir lower oesophageal sphincter pressure in patients without dysphagia was still higher than healthy volunteers, which is similar to the findings of Gill *et al* (1986). There is no volume effect. Little *et al* (1986) similarly found that patients with tight fundoplication had a lower rate of complete gastro-oesophageal junction relaxation and that cats with a gortex band placed around the gastro-oesophageal junction showed a lower rate of complete gastro-oesophageal junction relaxation at 4 weeks after banding.

Nadir pressure may reflect the permanent tension which is imposed on the lower oesophageal sphincter. Biancani *et al* (1975) found that pressure within the competent sphincter was highest near closure. When the lower oesophageal sphincter was passively distended by a probe, there was an initial decline and then an increase in pressure with increasing probe diameter. Force of closure and circular muscular tension also increased with increasing probe diameter. An incompetent sphincter exhibited lower pressures at all diameters. Fundoplication changed the shape of the

incompetent pressure - diameter curve to a competent one, and increased the force of closure. The tension is possibly largely due to the gastric muscle used to construct the wrap. A small fundus wrapped around a large bougie may result in increased tension in the gastric muscle (Wald *et al* 1983) which may be reflected in higher nadir pressure. From past experience it is likely that most of the patients with dysphagia in this study who were studied between 3 to 6 months post-operatively will either lose their dysphagia, or at the very least will get improvement in their dysphagia. This improvement in dysphagia may be the result of gastric muscle adapting over time. Transient dysphagia is probably different from permanent dysphagia for instance, as in constructing a wrap around a small bougie, or from scarring at the diaphragmatic hiatus. Dysphagia is sometimes improved by dilatation of the gastro-oesophageal junction and this is equivalent to stretching the elastic muscle until it gives. However the relief may be short-lived because the elasticity allows the muscle to return to its previous length.

Vagotomy does not abolish the relaxation of the lower oesophageal sphincter which occurs at high levels of gastric distension (Jennewein *et al* 1976). However, sham fundoplication in which the oesophagus and fundus were mobilised was associated with a decrease in the frequency of transient lower oesophageal sphincter relaxation, supporting the view that denervation has a role (Martin *et al* 1988). Hence denervation of the cardia may be responsible for impaired relaxation even when the vagi are intact, as speculated by Negre (1983).

In our study, rapid swallows led to a nadir lower oesophageal sphincter pressure that was less than that of wet swallows in all groups of patients, although this difference did not reach statistical significance. Previous studies have looked at inhibition of the oesophageal body (Meyer *et al* 1981) but not at the lower oesophageal sphincter. It is believed that inhibition of the lower oesophageal sphincter occurs along with inhibition of the oesophageal body. The inhibition may be due to the refractoriness of oesophageal smooth muscle or neural inhibitory discharge. There is simultaneous inhibition of both myoelectric activity and oesophageal contraction (Hellemans *et al* 1968). Rapid swallows are the best known stimulus for complete relaxation, but in spite of this, the lower oesophageal sphincter in our subjects still showed a residual relaxation pressure.

Air and water boluses did not trigger the same degree of lower oesophageal sphincter relaxation as wet swallows in all groups except patients with reflux who already had a hypotensive lower oesophageal sphincter pressure. In humans, oesophageal distension is not as reliable or as effective in stimulating sphincter relaxation as wet swallows.

Distal oesophageal diameter

Distal oesophageal diameter in patients with reflux disease, healthy subjects and patients who did not experience any dysphagia post-fundoplication were similar. However, those who experienced dysphagia post-fundoplication showed an increase in their lower oesophageal diameter compared to those without dysphagia. Moreover, patients with severe dysphagia had the largest oesophageal diameters.

Dilatation of the oesophagus and a narrow gastro-oesophageal junction on barium swallow has been observed after a tight fundoplication (Rossman *et al* 1979) and these patients presented with dysphagia. Ramp intrabolus pressure is the pressure in the oesophageal segment contained between the proximally occluded region and the open sphincter distally and this pressure correlated with distal oesophageal diameter. The dilatation in the lower oesophagus could be due to the higher ramp pressures in the distal oesophagus in those with dysphagia, and in particular severe dysphagia. The higher ramp intrabolus pressure is generated in order to push the bolus through the sphincter. The resistance of the gastro-oesophageal junction is high compared to the resistance of the distal oesophagus (Kahrilas *et al* 1988) so when the lower oesophageal sphincter cannot be opened beyond a maximum diameter, the pressure generated in the distal oesophagus ahead of the advancing peristaltic wave causes the compliant oesophagus to "balloon out" to a larger diameter.

Maximum lower oesophageal sphincter opening

Lower oesophageal sphincter maximum opening diameter has not been studied quantitatively before. Dodds *et al* (1989) suggested that lower oesophageal sphincter opening is determined mainly by pulsive forces transmitted via a swallowed bolus. In this study, there was a direct volume effect on lower oesophageal sphincter opening which may be the result of gravity on the bolus generating an additional force to open the sphincter, as measurements were taken in the upright position. There was no volume effect on peristaltic amplitude but peristaltic amplitude is not a direct measure of the strength of peristaltic squeeze.

Patients with reflux had lower oesophageal sphincters which opened more widely than healthy subjects. Csendes *et al* (1989) found that the circumference of the cardia correlated with oesophagitis, being 13 to 14 cm in patients and 6 cm in normals. However an incompetent sphincter has been observed at endoscopy independent of oesophagitis. Fundoplication narrowed this opening diameter, which concurs with Strombeck *et al* 's observation (1989) and also the findings of Little (1992). In patients who experienced no dysphagia post-fundoplication, lower oesophageal sphincter opening was not as wide as healthy volunteers. It is appropriate to consider the

physiological ramifications of the law of LaPlace in considering how fundoplication contributes to gastro-oesophageal reflux control. The smaller the radius of a tube, the greater the pressure required to distend it as P (distending pressure) is proportional to T (wall tension) / R(radius). Thus the intragastric pressure required to open the cardia to its maximum "physiological" opening diameter and perhaps initiate a reflux episode, is increased.

In the group with dysphagia post-fundoplication, lower oesophageal sphincter opening was not significantly different from patients with no dysphagia. This finding does not support the hypothesis (Jamieson *et al* 1992) that dysphagia may be related to the ability of the gastro-oesophageal junction to open. Yet sphincter opening in patients with mild dysphagia was larger than in patients with severe dysphagia. One can postulate that patients with mild dysphagia are able to generate greater pulsive forces in the bolus to open the sphincter, patients with severe dysphagia are unable to generate the necessary force whilst patients without dysphagia do not need to generate such a large force because of larger sphincter opening. However, we did not measure oesophageal propulsive force in this study and peristaltic amplitude is not a direct measure of peristaltic squeeze.

Dysphagia is a prominent symptom if the Nissen fundoplication is considered too long or too tight (Negre *et al* 1983, Mattox 1990, Luostarinen *et al* 1993), although "tightness" is difficult to quantify. Woodward *et al* (1971) contended that post-fundoplication dysphagia was not the result of making a tight wrap as all his patients had fundoplications constructed around bougies of the same size but dysphagia was present in 24%. However, it must be noted that a wrap can be made tight or loose around a bougie and this was not quantified by Woodward *et al* (1971).

In our study, all patients had fundoplications constructed around large bougies (46 - 52 F) suggesting that a large bougie alone is not protection against the development of dysphagia. DeMeester *et al* (1985) showed that increasing the bougie size from 36 F to 60 F and decreasing the length of fundoplication from 4 cm to 1 cm reduced the incidence of transient dysphagia from 83% to 39% and the incidence of permanent dysphagia from 21% to 3%, without loss in reflux control. Shirazi *et al* (1987) found that severe dysphagia was decreased from 4.5% to 0.6% when the technique of fundoplication was changed from a snug wrap to a floppy wrap.

Thus it seems that the tightness of fundoplication is only partly related to the bougie diameter. It seems likely that the pressure exerted on the lower oesophageal sphincter muscle from the gastric muscle comprising the wrap prevents the lower oesophageal sphincter from opening fully even though a large bougie is able to stent the region open during operation. Any fundus that is inadequate in size or an inadequately mobilised fundus may lead to a tight wrap (Wald *et al* 1982). Division of short gastric vessels allowing the fundus to be more fully mobilised seems an attractive

option. However, as discussed previously (Weerts *et al* 1993), even when short gastric vessels are divided, dysphagia can still occur in the post-operative period.

Transit Time and Flow

Bolus transit across the lower oesophageal sphincter has not been investigated before. In those who developed severe dysphagia after fundoplication, the time taken for the bolus to traverse the lower oesophageal sphincter was significantly longer. Conversely, flow was slower in those with severe dysphagia, but not significantly different in those with reflux, healthy controls, and no dysphagia post-fundoplication. According to Poiseuille's law, flow is directly proportional to the fourth power of the radius and it is likely that small differences in flow are not reflected in changes in the lower oesophageal sphincter opening.

Partial emptying

Of the 102 primary peristaltic sequences analysed in healthy subjects, 2% of them resulted in partial emptying of the barium bolus from the oesophagus. For patients with reflux disease and patients without dysphagia post-fundoplication, there were no primary peristaltic sequences that resulted in incomplete emptying. In patients with dysphagia post-fundoplication, 6% of the 177 primary peristaltic sequences were associated with incomplete emptying of barium.

The distal oesophageal amplitude of the primary peristaltic waves associated with partial emptying were above the threshold of 30 mmHg (Richter *et al* 1987) known to be necessary for oesophageal lumen occlusion and complete emptying in healthy volunteers. Moreover, retrograde oesophageal flow was associated with peristaltic waves that resulted in partial emptying, especially in the patients with dysphagia post-fundoplication. A higher threshold pressure may be necessary for complete emptying in those patients with dysphagia post-fundoplication.

Synchronous waves

It has been observed that nearly complete barium clearance from the oesophagus can be accomplished by sequential tertiary activity whether they are isobaric or non-isobaric waves (Ott *et al* 1989, Hewson *et al* 1990, Massey *et al* 1991). In our study, 81.2% of the 133 synchronous waves were associated with pressure gradients between the distal oesophagus and the lower oesophageal sphincter pressure with higher pressure in the distal oesophagus. Massey *et al* (1991) also found that some clearance occurred if a pressure gradient was created between the

oesophagus and the stomach. Complete clearance of barium boluses from the oesophagus was accomplished by only 14.2% of 133 synchronous waves in the 4 groups of patients. The majority of the synchronous waves were associated with partial emptying.

Several studies have regarded tertiary waves as abnormal. Non-progressive oesophageal contractions have been observed during periods of acid induced heartburn (Creamer 1955, Siegel *et al* 1963, Olsen *et al* 1965, Corazziari *et al* 1984). Scleroderma-like aperistalsis is also associated with oesophagitis (Joelsson *et al* 1982, Richter *et al* 1982). Extreme obstruction to the lower oesophageal sphincter can result in isobaric waves representing intrabolus pressures only (Mittal *et al* 1990). An increase in tertiary waves has been noted in patients with post-fundoplication dysphagia (Skinner 1967). In our study, the incidence of synchronous waves was fairly evenly distributed across the four groups of subjects: controls, patients with reflux disease before fundoplication and those with or without dysphagia after fundoplication. We did not therefore find tertiary waves to be pathognomonic of post-fundoplication dysphagia or reflux disease.

One patient in this study with normal motility before the fundoplication lost his peristalsis and had only synchronous waves after a total fundoplication. Demonstration of abnormal pre-operative oesophageal motility has been attended by less desirable post-operative results than if pre-operative motility was normal (Pope *et al* 1978). Another patient with an aperistaltic oesophagus regained peristalsis after a Dor patch. The former patient had dysphagia but the latter patient had no dysphagia after fundoplication.

It is difficult to know what degree of fundoplication causes dysmotility (Branicki 1993). It has been suggested that Nissen fundoplication should not be used in patients with ineffective peristalsis due to scleroderma, achalasia with Heller myotomy, diffuse spasm, and presbyoesophagus because it may cause obstruction (Skinner *et al* 1967). However, no objective data has been produced to support this contention.

Marshmallows

The solid swallows in this study were performed after the liquid swallows to allow the oesophagus to "warm-up" as recommended by Curtis *et al* (1986). Sufficient bolus opacity was obtained by injecting a half-marshmallow with barium. The mean in vivo diameter of a half-marshmallow bolus was 13 mm. Of the total of 131 marshmallow swallows, impaction occurred 38% of the time, 21% of the impaction occurring at the level of the aortic arch, and 17% at the level of the thoracic inlet. The mean time taken for the half-marshmallow to pass through the oesophagus was 32

seconds in the healthy group, 42 seconds in the group with reflux disease before fundoplication, 40 seconds in the group with no dysphagia and 32 seconds in the group with dysphagia. The mean lower oesophageal sphincter opening diameter when distended by the half-marshmallow in the healthy group was 14.4 mm, in the reflux group 15.6 mm, in the group with no post-operative dysphagia 9.6 mm and in the group with post-fundoplication dysphagia 10.3 mm. Although the mean in vivo diameter of the half-marshmallow bolus was 13 mm, it was elastic enough to squeeze through the post-fundoplication sphincter even when associated with dysphagia.

Kelly (1961) found that 25% of his subjects were aware of the initial arrest along the oesophagus. In a study of impaction at Schatzki rings, 41% of test marshmallows between 13 and 20 mm reproduced symptoms (Ott *et al* 1991). Schatzki rings less than 13 mm often are symptomatic but those greater than 20 mm rarely cause problems. Symptoms of dysphagia was reproduced in only 5.6% of swallows in the group of patients with dysphagia, in other words, most of the subjects were not aware of the initial arrest of the half-marshmallow. The patients in this study experienced episodic dysphagia, not aphagia, so the test conditions may not have captured the dysphagic episodes. Moreover, marshmallow is much softer than some solid foods that might have been responsible for dysphagia.

Factors determining solid transit include oral thrust, adequate pharyngeal orifice and upper oesophageal sphincter, gravity, oesophageal body relaxation and lower oesophageal sphincter relaxation (Kelly 1961, Curtis *et al* 1986). Curtis *et al* (1986) defined normal solid swallowing as swallowing that involves no delay along the oesophagus, requires no additional swallows and takes less than 20 seconds for completion. Kelly (1961) found that even marshmallows greater than 20 mm are readily transported into the stomach with liquid swallows.

Contrary to the studies of Kelly (1961) and Curtis *et al* (1986), the healthy subjects in our study experienced arrest of the half-marshmallow in 64 % of swallows. The half-marshmallow was then cleared by an additional swallow and the mean time taken was 32 seconds. Gravity alone did not overcome the delay and the arrest occured most frequently at the level of the aorta, supporting Curtis *et al*'s findings (1986). Unlike Kelly's (1961) findings, the second most common site of arrest the thoracic inlet, not the lower oesophageal ampulla. The level of the aortic arch approximates the transition from striated to smooth muscle in the oesophagus. The thoracic inlet is a level where the oesophagus is physically narrowed as it traverses a somewhat restrictive bony ring. It is also where the oesophagus changes direction as it passes into the posterior mediastinum. Nuclear medicine studies of oesophageal transit showed arrest in similar areas (McCallum *et al* 1982).

In other words, the marshmallow proved to be a relatively useless test for dysphagia after fundoplication when, on a priori ground, it might have been expected to be an excellent test.

Total dysphagia score - correlations

None of the parameters of oesophageal body function distinguish patients with dysphagia from patients without dysphagia after fundoplication.

The dysphagia score was also directly correlated with ramp pressure and it is possible that changes in the nadir lower oesophageal sphincter pressure (see next section) is reflected in the ramp pressure.

Previous studies have not found any correlation between sphincter relaxation and symptoms of dysphagia. In our study, a post-fundoplication dysphagia score correlated significantly with both basal lower oesophageal sphincter pressure, and nadir lower oesophageal sphincter pressure.

Most authors do not regard dysphagia as a long term problem following this procedure. Transient post-operative dysphagia occurs from the second post-operative day and usually settles by the sixth post-operative week in 85% to 100% of patients (DeMeester *et al* 1974, Negre *et al* 1983, Csendes *et al* 1989). This may be due to the initial increase in gastro-oesophageal junction pressure (Grande *et al* 1991) reflecting gastro-oesophageal junction compression by the plicated fundus or post-traumatic oedema around the cardia (Polk *et al* 1971, Ellis *et al* 1984, Shirazi *et al* 1987, Weerts *et al* 1993). The Angelchik prosthesis results in transient dysphagia in up to 80% of patients and is associated with an early re-operation of approximately 10% to remove the Angelchik prosthesis when moderate to severe dysphagia continues (Jamieson *et al* 1985). One reason for such persistence is that although both fundoplication and the Angelchik prosthesis push the lower oesophagus forward, the Nissen wrap is a muscular structure that may attenuate with time whereas the prosthesis does not.

DeMeester *et al* (1992) reported that Nissen fundoplication carried out by the intrathoracic route resulted in less post-operative dysphagia compared to the abdominal approach but did not provide any data to substantiate his statement. He suggested that stretching of the lower oesophagus may be a cause of dysphagia. Dodds *et al* (1973) showed that the cranio-caudad excursion of the oesophagus during swallowing is greatest in the distal oesophagus so dysphagia may be related to the inability of the oesophagus to maintain its axial movement initially. When tissues accommodate to this new length, dysphagia resolves.

Some studies suggest that division of the short gastric vessels lessens the risk of dysphagia especially if a total fundoplication is contemplated (Branicki 1993). In

this study, short gastrics were divided in 4 patients, none of whom experienced post-fundoplication dysphagia. This is a very important and as yet unresolved issue.

Dakkak *et al* (1992) found that patients accounts of their eating capacity correlated well with their observed performance ($r = 0.793$, $p < 0.001$) but did not match each other exactly. The imperfect correlation can be attributed to the inconstant nature of dysphagia on different occasions or inaccuracies of self-estimation of eating ability.

The finding from this study that the post-fundoplication dysphagia score correlated significantly with basal lower oesophageal sphincter pressure, and nadir lower oesophageal sphincter pressure may be useful if a reproducible method for intra-operative calibration of tension in the fundoplication can be devised (Johnsson *et al* 1993).

Summary

For peristaltic waves associated with complete emptying, parameters of oesophageal body function such as peristaltic amplitude, propagation velocity and duration of contraction did not differentiate patients with gastro-oesophageal reflux disease from healthy volunteers or patients with post-fundoplication dysphagia from those without dysphagia. However, distal oesophageal diameter was widest in patients with severe dysphagia.

The dysphagia score was not significantly correlated with any of the above-mentioned parameters.

Fundoplication decreased the triggering of secondary peristalsis by air and water boluses and the frequency of lower oesophageal sphincter relaxations.

Partial oesophageal emptying was not due to subthreshold amplitudes. Synchronous waves can result in complete oesophageal emptying, were equally distributed in all groups of patients and were not pathognomonic of reflux or dysphagia. Marshmallow swallows were useless tests for post-fundoplication dysphagia, as impaction did not reproduce symptoms and was just as common in healthy volunteers.

Ramp intrabolus pressure is a novel parameter that was found to be useful for differentiating between patients with dysphagia and patients without dysphagia, and also correlated with subjective dysphagia score. Ramp pressure occurs in the distal oesophagus when the lower oesophageal sphincter is open and is related to functional outflow obstruction in the form of incomplete lower oesophageal sphincter relaxation.

Patients with gastro-oesophageal reflux disease have hypotensive lower oesophageal sphincters that relax to intragastric pressure with swallowing. Fundoplication increases basal and nadir lower oesophageal sphincter pressure, more

so in patients with dysphagia compared with patients without dysphagia. Lower oesophageal sphincter opening was largest in the pre-operative patients. Fundoplication narrowed the sphincter opening but to our surprise, sphincter opening did not discriminate between patients with severe dysphagia and patients without dysphagia.

The subjective dysphagia score correlated with basal and nadir lower oesophageal sphincter pressures and ramp pressures. There is potential in the application of these parameters in the assessment of post-fundoplication dysphagia and perhaps in the intraoperative calibration of the fundoplication to prevent the creation of a supercompetent sphincter.

CHAPTER 7: GAS GASTRO-OESOPHAGEAL REFLUX

7.1 OESOPHAGEAL MANOMETRY

Spontaneous transient lower oesophageal sphincter relaxations

During the rest and gastric distension periods, healthy subjects had a median of 0.5 (0 - 1) transient lower oesophageal sphincter relaxations which was significantly different ($p < 0.05$) from the post-fundoplication patients who did not have any transient lower oesophageal sphincter relaxations (Figure 17).

Common cavities

Healthy subjects had a median of 2 (0 - 6) common cavities during the gastric distension period which was significantly different ($p < 0.05$) from post-fundoplication patients, none of whom had any common cavities (Figure 18).

Total belch urges

Healthy subjects had a median of 4 (2 - 7) belch urges during the gastric distension period which was not significantly different from post-fundoplication patients with a median of 1 (0 - 2) belches, although the difference did not reach statistical significance (Figure 19).

Belch urges not associated with common cavities

Healthy subjects had a median of 2 (1 - 3) belch urges without common cavities during the gastric distension period which was significantly different ($p < 0.05$) from post-fundoplication patients with a median of 3 (0 - 3) belches without common cavities during the gastric distension period (Figure 19).

Belch urges with common cavities

Healthy subjects had a median of 1 (0 - 4) belch urges with common cavities during the gastric distension period which was significantly different ($p < 0.05$) from post-fundoplication patients none of whom had any common cavities associated with belch urges during the gastric distension period (Figure 19).

Correlation of transient lower oesophageal sphincter relaxations with common cavities

During the 10 minute rest period, the total transient lower oesophageal sphincter relaxations was correlated with the number of common cavities ($r = 0.503$, $p < 0.005$) and the spontaneous transient lower oesophageal sphincter relaxations was also correlated with the number of common cavities ($r = 0.520$, $p < 0.003$).

Moreover, during the 10 minutes post distension, the total transient lower oesophageal sphincter relaxations was correlated with the number of common cavities ($r = 0.378$, $p < 0.04$) and the spontaneous transient lower oesophageal sphincter relaxations was also correlated with the number of common cavities ($r = 0.454$, $p < 0.01$).

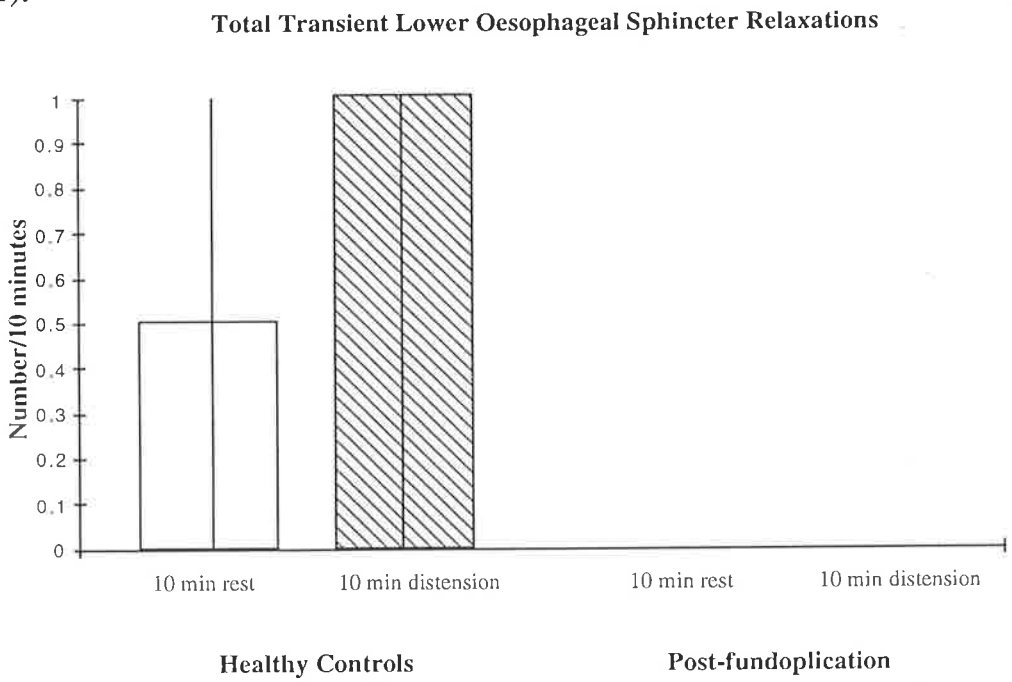

Figure 17: Total transient lower oesophageal sphincter relaxations in the 10 min rest period compared with 10 min post distension for healthy volunteers and post-fundoplication patients.

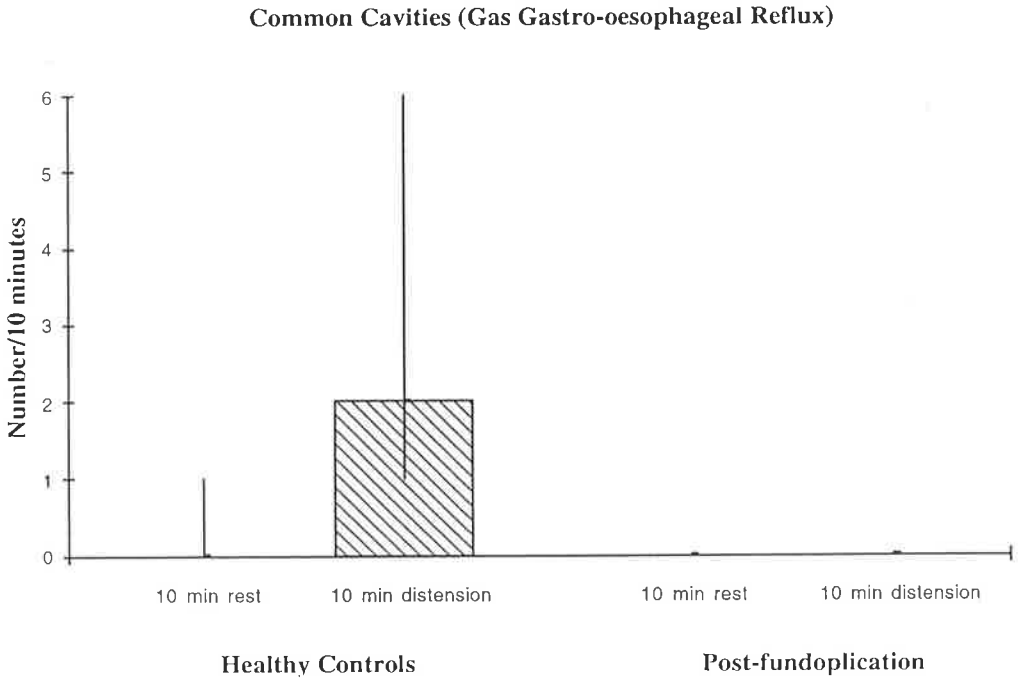

Figure 18: Common cavities in the 10 min rest period compared with 10 min post distension, for healthy volunteers and post-fundoplication patients

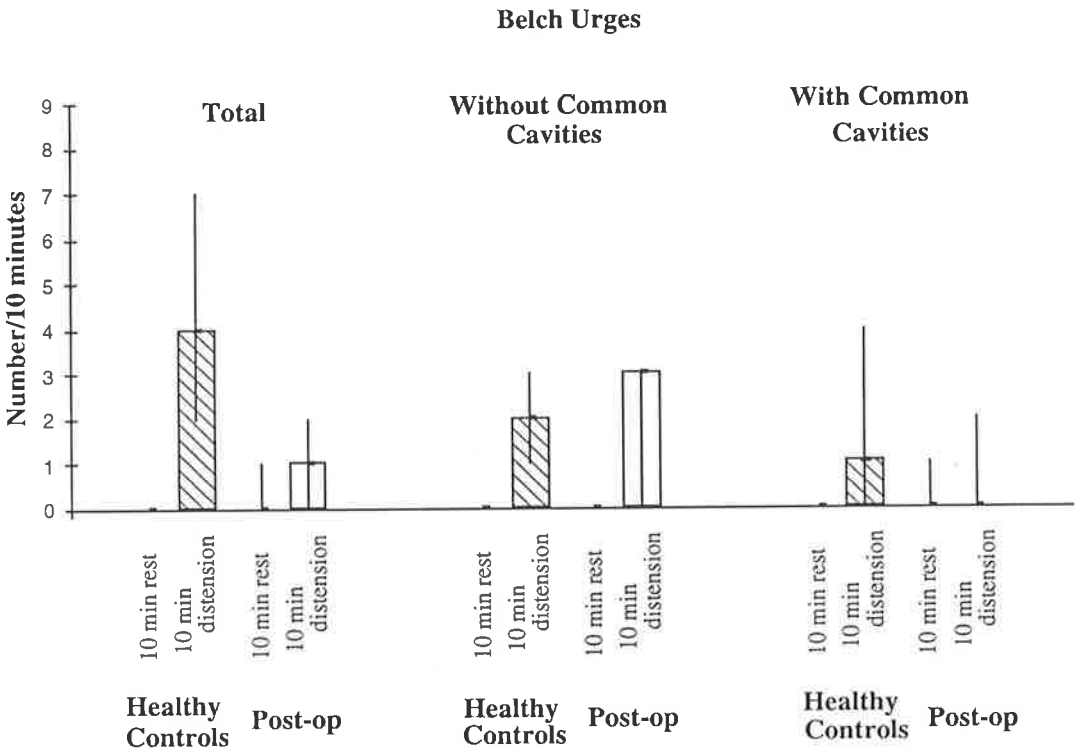

Figure 19: Total belch urges, belch urges without common cavities and belch urges with common cavities in the 10 min rest period compared with 10 min post distension, for healthy volunteers and post-fundoplicaiton patients

7.2 BELCH SCORES

Belch scores and common cavities

There was no correlation between post-fundoplication belch scores and the number of common cavities in the 10 minutes after gastric distension. There was no correlation between post-fundoplication belch scores and the total number of belch urges and the number of belch urges without common cavities in the 10 minutes after gastric distension. None of the patients had common cavities associated with belch urges.

Belch scores and basal and nadir lower oesophageal sphincter pressure

There was no correlation between complaints of inability to belch and basal lower oesophageal sphincter pressure ($r = 0.125$, NS), nadir lower oesophageal sphincter pressure ($r = 0.228$, NS)

Belch scores and dysphagia scores

There was no correlation between complaints of inability to belch and dysphagia.

Ability to relieve bloating by belching scores and common cavities

There was no correlation between the ability to relieve bloating post-fundoplication scores and the number of common cavities in the 10 minutes after gastric distension. There was no correlation between the ability to relieve bloating post-fundoplication scores and the total number of belch urges and the number of belch urges without common cavities in the 10 minutes after gastric distension. None of the patients had belch urges associated with common cavities.

Ability to relieve bloating by belching scores and basal and nadir lower oesophageal sphincter pressure

There was no correlation between complaints of inability to relieve bloating and basal lower oesophageal sphincter pressure ($r = 0.231$, NS) and nadir lower oesophageal sphincter pressure ($r = -0.228$, NS)

Ability to relieve bloating by belching scores and dysphagia scores

There was no correlation between complaints of inability to relieve bloating and dysphagia.

7.3 DISCUSSION

The "belch" reflex is initiated by stretch receptors in the gastric fundus leading to afferent discharge to the dorsal nucleus of the vagus and subsequent efferent discharge to non-adrenergic, non-cholinergic inhibitory fibres to the lower oesophageal sphincter muscle (Wyman *et al* 1984). Belching is gaseous reflux with a mechanism similar to acid reflux so following fundoplication it would seem that some restriction in the ability to belch will be inevitable (Wyman *et al* 1990). Gastric distension facilitates belching and transient lower oesophageal sphincter relaxations occur more frequently in the sitting position compared to the recumbent position (Wyman *et al* 1990) and most common cavities occured in the first 10 minutes of gastric distension. We therefore studied our subjects sitting during a 10 minute rest period and in the first 10 minutes of gastric distension. Healthy volunteers tolerated gastric distension without any problems but half of the post-fundoplication patients experienced some epigastric discomfort

Common cavities are the only markers of gas gastro-oesophageal reflux. McNally *et al* (1964) confirmed by cineradiography that oesophageal body common cavities occurred concurrently with oesophageal distension caused by gas gastro-oesophageal reflux. Although post-fundoplication patients in our study had total belches that were not significantly different from healthy volunteers, the number of spontaneous transient lower oesophageal sphincter relaxations and common cavities were significantly less.

Smith *et al* (1991) was the first to attempt studying belching ability objectively by measuring belch volumes. He found no relationship between any abdominal symptoms and belch volume. The problem with measuring belch volumes is that it is difficult to know what components of the belch volume are gastro-oesophageal reflux and oesophago-pharyngeal reflux. In this study, the belch urges in post-fundoplication patients were not associated with common cavities. This would suggest that the belch results from distension of the proximal oesophagus, possibly by swallowed air that has not been cleared by peristalsis. Kahrilas *et al* (1986) found that upper oesophageal sphincter relaxation can occur voluntarily and independent of lower oesophageal sphincter relaxation. Wyman *et al* (1990) found that common cavities that are confined to the lower oesophagus were not associated with belch urges.

In dogs, Rasche *et al* (1973) found that fundoplication caused bloating, inability to vomit and problems with gastric dilatation if the plication surrounded more than 52 % of the oesophagus. Possible mechanisms by which fundoplication may modify the ability to belch include preventing distension of the cardia which may be necessary for eructation (Strombeck *et al* 1989), decreasing the diameter of the lower

oesophageal sphincter (Leonardi *et al* 1981), eliminating the role the fundus has in gastric filling and emptying and increasing basal lower oesophageal sphincter pressure (Strombeck *et al* 1989, Lundell *et al* 1993).

Sham fundoplication in dogs reduced the triggering of transient lower oesophageal sphincter relaxations by gastric distension, suggesting that mobilisation of the cardia had interrupted afferent vagal fibres (Martin *et al* 1988). Another possibility is that vagal trunks may not be clearly visualised or dissected during anti-reflux surgery. The vagal trunks might then be in danger of being cut or being included in the sutures applied for fundoplication. An unintended partial vagotomy might then be responsible for gastric distension post-fundoplication (Csendes *et al* 1989) in a minority of cases.

Impaired belching and aerophagy has logically been suggested to accentuate meteorism (Negre *et al* 1983, Luostarinen 1993). A widely accepted explanation is that swallowed air is trapped in the fundus and cannot be released through the one-way valve of the fundoplication (Woodward *et al* 1971). An inability to belch was associated with increasing flatus and Papp (1979) reported two patients in whom gas bloat was relieved by dilatation. Some investigators have stated that their patients are "able to belch" after total fundoplication with incidences quoted ranging from 43 % to 80 % (DeMeester *et al* 1975, Ellis *et al* 1984). Others contend that patients with partial fundoplication retain their ability to belch and have no postprandial bloating or increased flatus (DeMeester *et al* 1975, Guarner *et al* 1975, Menguy 1978, Lundell *et al* 1991).

Many investigators have relied on subjective accounts of belching ability (Woodward *et al* 1970, Polk *et al* 1971, Ellis *et al* 1973, DeMeester *et al* 1975, Menguy *et al* 1978, Henderson 1978, Bjerkeset *et al* 1980, Ellis *et al* 1984, Gear *et al* 1984, Donahue *et al* 1985, Thor *et al* 1989, Rohr *et al* 1991, Watson *et al* 1991). Without measuring common cavities, it is not possible to objectively compare the outcome of various anti-reflux procedures with regard to belching ability.

Subjective accounts of the ability to belch and relieve bloating by belching do not correlate with the number of belch urges or common cavities suggesting the unreliability of using patient's complaints to judge the outcome of an operation. Belch scores also do not correlate with dysphagia scores. Unlike dysphagia scores, belch scores did not correlate with basal or nadir lower oesophageal sphincter pressures, so a different mechanism such as a one way valve effect may be responsible. Bergeron *et al* (1985) and Butterfield (1971) showed that fundoplications were competent in preventing the transmission of gastric pressure.

In summary, common cavities are the only objective markers of gas gastro-oesophageal reflux. Post-fundoplication patients may report that they are able to belch but are experiencing oesophago-pharyngeal gas reflux only. To compare the outcome

of various anti-reflux operations with regard to the ability to belch, it is important not to rely on patient's complaints of belching difficulties which bear little relationship to objective markers.

CHAPTER 8: VARIABLES INFLUENCING THE EFFECT OF FUNDOPLICATION ON OESOPHAGEAL MOTOR FUNCTION: A PORCINE MODEL

8.1 ACUTE STUDIES

Water delivered into the mouth of the anaesthesized pig or injected into the oesophagus through the infusion channel did not cause relaxation of the lower oesophageal sphincter before or after fundoplication. Secondary peristalsis occurred intermittently and ramp pressures were seen only when there was a peristaltic wave.

When a large volume of water was infused into the mid oesophagus with the proximal oesophagus tied off and the manometric assembly straddling the lower oesophageal sphincter, there was no relaxation of the lower oesophageal sphincter. Instead, the oesophagus distended like a balloon usually leading to the water leaking out of the proximal oesophagus.

It was decided that the acute study was not worth pursuing.

8.2 CHRONIC STUDIES

8.2.1. Effect of fundoplication

Basal lower oesophageal sphincter pressure

Fundoplication increased basal lower oesophageal sphincter pressure for all 3 groups of pigs ($p < 0.02$). However, there was no significant difference between the 3 groups having tight, loose or floppy fundoplications.

Secondary peristalsis - nadir pressure

Fundoplication increased nadir pressure in all 3 groups ($p < 0.001$ in all groups). The 3 groups were not significantly different in their nadir pressure, for the 4 volumes used to trigger secondary peristalsis.

Secondary peristalsis - ramp pressure

Fundoplication increased ramp pressure in all 3 groups ($p < 0.0001$ in all groups). The 3 groups were not significantly different in their ramp pressure except for the ramp pressure for 8 ml and 10 ml boluses which were highest in the group with floppy fundoplication ($p < 0.04$).

Secondary peristalsis - proximal amplitude

Fundoplication increased peristaltic amplitude in the proximal oesophagus in all 3 groups ($p < 0.02$ in all groups). The group with tight fundoplications had greater proximal amplitudes than groups with loose or floppy fundoplications ($p < 0.003$). There was no significant difference between loose and floppy wraps. This effect was seen for all volumes used to trigger secondary peristalsis.

Secondary peristalsis - distal amplitude

Fundoplication increased peristaltic amplitude in the distal oesophagus in all 3 groups ($p < 0.03$ in all groups). The 3 groups were not significantly different in their distal amplitude. This effect was seen for all volumes used to trigger secondary peristalsis.

Primary peristalsis versus secondary peristalsis

Primary peristalsis for 10 ml water swallow was not significantly different from secondary peristalsis triggered by a 10 ml water bolus, in the nadir lower oesophageal sphincter pressure, ramp pressure, proximal amplitude or distal amplitude. Fundoplication also increased nadir lower oesophageal sphincter pressure, ramp pressure, proximal amplitude or distal amplitude across the 3 groups of pigs during primary peristalsis

8.2.2 Reproducibility

Basal lower oesophageal sphincter pressure

Basal lower oesophageal sphincter pressure was not significantly different between 1 week, 2 week and 4 week studies.

Secondary peristalsis

Nadir lower oesophageal sphincter pressure, ramp pressure, proximal and distal amplitude were not significantly different for 1,2 and 4 week studies in the 3 groups of pigs

Primary peristalsis versus secondary peristalsis

Primary peristalsis during a 10 ml water swallow was not significantly different to secondary peristalsis triggered by a 10 ml water bolus in the nadir lower oesophageal sphincter pressure, ramp pressure, proximal amplitude or distal amplitude for both 1, 2 and 4 week studies.

8.2.3 Ramp pressure correlations

The ramp pressure was significantly correlated with nadir lower oesophageal sphincter pressure for 8 ml ($r = 0.68$ $p < 0.004$), 10 ml ($r = 0.56$, $p < 0.02$) and for 12 ml ($r = 0.543$, $p < 0.03$) but not for 4ml boluses. Ramp pressure increased with increasing nadir lower oesophageal sphincter pressure. Ramp pressure was not significantly correlated with proximal or distal oesophageal amplitude for any of the volumes.

8.2.4 Morbidity and mortality

Of the 18 pigs who had a baseline study and a study at 1 week after a fundoplication, the morbidity and mortality is tabulated as follows:

Group	No of pigs	Complication
tight	1	rectal prolapse at 6 weeks - died
tight	1	pneumonia at 4 weeks - killed
tight	1	herniation of stomach into the chest at 2 weeks - died
tight	1	generally unwell possibly septic at 10 days - killed
tight	1	small bowel obstruction at 10 days - died
tight	1	killed- end of study at 6 weeks
loose	1	gastric and small bowel distension at 10 days - died
loose	3	killed- end of study at 2 weeks
loose	2	killed- end of study at 4 weeks
floppy	1	gastric and small bowel distension at 2 weeks - died
floppy	1	small bowel obstruction at 1 week - died
floppy	1	sepsis - died
floppy	2	killed-end of study at 1-2 week
floppy	1	killed-end of study at 4 weeks

The morbidity and mortality was high. After the occurrence of intrathoracic herniation of the stomach in 1 out the first 4 pigs, the hiatus was closed routinely in an attempt to prevent this complication in the latter 14 pigs.

8.3 DISCUSSION

Secondary peristalsis

In the pig model, balloon distension of the oesophageal body has been shown to cause relaxation of the lower oesophageal sphincter (Lundell *et al* 1992). The porcine lower oesophageal sphincter exhibits pressure variation at 3 to 4 cycles/min during basal recording (Landers *et al* 1987). In man, air and water boluses can trigger peristalsis and lower oesophageal sphincter relaxations more effectively than balloon distension (Schoeman *et al* 1993). To examine the effect of different volumes on peristaltic amplitude, ramp pressures and lower oesophageal sphincter relaxation, it was difficult to ensure that the same volume was swallowed in a single swallow when water was delivered into the pig's mouth. Hence boluses of different volumes were injected into the oesophagus to trigger secondary peristalsis.

Fundoplication increased basal lower oesophageal sphincter pressure, nadir lower oesophageal sphincter pressure and ramp pressure, which concurred with the human studies. The proximal oesophageal amplitude and distal oesophageal amplitude increased after fundoplication which differed from our findings in humans and may be a response to obstruction.

However, there was no significant difference between tight, loose or floppy fundoplications in basal lower oesophageal sphincter pressure, nadir lower oesophageal sphincter pressure and distal oesophageal amplitude. The tightness of the fundoplication did not have any effect on these parameters. It seems that fundoplications of different tightness can result in the same tension in the wrap and the same basal and nadir lower oesophageal sphincter pressure. Human studies quote the incidence of dysphagia as rare if bougie diameters greater than 42 F are used (Ellis *et al* 1984). Perhaps the bougie of 20 F used to calibrate the tight wrap in the pig was above the threshold for dysphagia, and may be equivalent to a moderately snug wrap in humans.

In anaesthetised dogs, Siewert *et al* (1974) found that the magnitude of the gastro-oesophageal junction high pressure zone depends on how tightly the fundus was drawn around the terminal oesophagus. In another study, Bergeron *et al* (1985) found that bougie diameter was related to basal gastro-oesophageal junction pressure and yield pressure obtained by perfusing the distal oesophagus while occluding the proximal oesophagus till the gastro-oesophageal junction opened. The smaller the bougie, the tighter was the wrap and the higher the basal and yield pressures recorded. Regardless of the size of the bougie, all the fundoplications prevented transmission of fluid from the stomach to the oesophagus (Bergeron *et al* 1985).

No other studies have measured basal and nadir lower oesophageal sphincter pressures in unsedated pigs using a sleeve device. We found that basal lower oesophageal pressures in unsedated pigs were not as useful as the yield pressure in anaesthesised dogs for assessing the tightness of the wrap.

The tight fundoplication was associated with a higher proximal amplitude. This may suggest that the tight fundoplication required a greater opening force. Once the sphincter was open, the ramp pressure needed to drive the bolus through the lower oesophageal sphincter was similar for all 3 groups.

The most surprising finding was that the ramp pressure was highest in the group with floppy fundoplication. The proximal stomach of the pig is extremely capacious and we noted in the floppy group that a very large amount of stomach was drawn behind the oesophagus. This may be responsible for the higher ramp pressure in this group. On the other hand the number of animals was small so it may be a type II error we are seeing. The ramp pressure post-fundoplication correlated with nadir lower oesophageal sphincter pressure but not proximal and distal oesophageal amplitude. When the Angelchik prosthesis was inserted laparoscopically into 10 pigs, 2 of the pigs experienced distal oesophageal obstruction (Berguer *et al* 1991). Berguer reasoned that this is due to the use of a large human prosthesis in small animals. Perhaps a floppy wrap behaved like a large prosthesis.

There was no difference between primary and secondary peristalsis in their amplitude, nadir lower oesophageal sphincter pressure and ramp pressure in this study. The post-fundoplication parameters were reproducibly measured over 1 to 4 weeks.

Morbidity and mortality

Domestic pigs did not do well with surgery. Large para-oesophageal hernia caused death when the intrathoracic stomach distended with air and compressed the heart and right lung. The porcine stomach is much more mobile than the human stomach. Small bowel obstruction secondary to adhesions was common.

In the early post-operative episode, massive gastric distension with air presenting as an increase in the girth and tension of the abdomen was probably due to a combination of ileus and the inability to belch after fundoplication. Early nasogastric decompression relieved the problem but if not done in time, the pigs often died. The anterior and posterior vagal trunks were clearly identified and were more obvious than the vagi in the human. None of the vagal trunks were inadvertently divided or included in the fundoplication sutures. However, sham fundoplication in dogs has been shown to reduce the triggering of transient lower oesophageal sphincter relaxations by gastric distension, suggesting that mobilisation of the cardia alone interrupts afferent vagal

fibres (Martin *et al* 1988). That may contribute to the inability to belch and subsequent gastric distension in pigs after Nissen fundoplication.

Incidental causes of death include rectal prolapse, pneumonia, and sepsis. The commercial pig has reduced fitness and vigour which is probably associated with selection pressure for size and high muscle to fat ratio (McIntosh *et al* 1981).

When anti-reflux surgery was carried out in dogs (Adler *et al* 1958), many lost weight in the first few weeks but all regained their pre-operative weight and had no difficulty eating. The pigs in this study lost an average of 5% of their baseline weight in the 2 weeks post-fundoplication. In the early post-operative period, the pigs were fasted until their ileus resolved which often took 2 days. Then they were introduced to milk. Pellets were added from the second post-operative week, and those pigs that were allowed to live to 4 to 6 weeks after the operation regained their pre-operative weight.

Summary

The unsedated domestic pig was a useful experimental model for measurement of peristaltic amplitude, ramp pressure, basal and nadir lower oesophageal sphincter pressure. Fundoplication increased all 4 parameters although none of the parameters discriminated between the wraps of different tightness.

SUMMARY AND CONCLUSIONS

Dysphagia of varying severity occurs in up to 40% of patients after Nissen fundoplication and the pathophysiology for this has not been defined. In addition, 1.5 to 100% of patients complain of inability to belch after fundoplication. Many studies have relied on subjective reports and have not undertaken objective measurements.

The aim of this thesis is to assess the effect of fundoplication on oesophageal motility, lower oesphageal sphincter competence and bolus transit so as to determine their relationship to dysphagia and belching difficulties. The studies will be considered in 3 sections.

First the investigation of the effect of fundoplication on oesophageal motor function and its relationship to dysphagia. We studied 11 healthy volunteers and 15 patients with gastro-oesophageal reflux disease before their operation. Of the 15 patients, 13 returned for a post-operative study; 6 experienced dysphagia while 7 did not. In addition, 12 other patients complaining of dysphagia post-fundoplication were studied. The fundoplication was carried out laparoscopically in 21 patients and open in 4 patients and almost all were constructed around a large bougie in the oesophagus.

The severity of dysphagia was given a numerical score at an interview. The subjects were studied by oesophageal manometry and videofluoroscopy to assess primary and secondary peristalsis, ramp pressure and lower oesophageal sphincter basal and residual relaxation pressure.

Primary peristaltic amplitude in patients with reflux disease was not significantly lower than healthy volunteers. In patients with reflux disease, secondary peristalsis was initiated at a median rate of 60%, propagation occurred in 40% and lower oesophageal sphincter relaxation in 70%. The ramp pressure, which was a positive deflection on manometry preceding the peristaltic contraction, correlated with the intrabolus pressure in the distal oesophagus when the mid oesophagus was occluded by a peristaltic wave and when the lower oesophageal sphincter was open. The ramp pressure in pre-fundoplication patients with reflux disease was similar to volunteers. Lower oesophageal sphincter hypotension and wider sphincter opening was found in patients with reflux disease compared with volunteers.

After fundoplication, primary and secondary peristalsis did not recover. Fundoplication did not improve the initiation or propagation rate of secondary peristalsis but it decreased the median lower oesophageal sphincter relaxation rate to 45%. The ramp pressure, lower oesophageal basal and nadir pressure increased after fundoplication. The lower oesophageal sphincter opening was narrower after fundoplication. Ramp pressure increased with increasing residual relaxation pressure but was not correlated with peristaltic amplitude or lower oesophageal sphincter opening.

Patients with post-fundoplication dysphagia did not differ from patients without dysphagia in primary or secondary peristalsis. However, patients with dysphagia had a significantly higher ramp pressure, basal and nadir lower oesophageal sphincter pressure compared to patients without dysphagia. There was no difference between the two groups in the maximum opening diameter of the lower oesophageal sphincter. The numerical dysphagia score was significantly correlated with the ramp pressure, basal and nadir lower oesophageal sphincter pressure.

The second study was the effect of fundoplication on the ability to belch. The development of a gastro-oesophageal common cavity is the only objective marker of gas gastro-oesophageal reflux, that is, a belch from the stomach. We interviewed 11 volunteers and 20 patients after fundoplication, regardless of the presence of dysphagia, and graded the ability to belch numerically. During oesophageal manometry, the occurrence of common cavities, transient lower oesophageal sphincter relaxations and belch urges were measured before and after distending the stomach with 750 ml of carbon dioxide gas. When belches not associated with common cavities were considered, patients averaged 3 whereas volunteers averaged 2 in the 10 minutes after gastric distension. However when belch urges coinciding with common cavities were measured, volunteers averaged 1 in the 10 minutes post gastric distension whereas none of the 20 patients had any. None of the patients had any transient lower oesophageal sphincter relaxations. Also, there was no correlation between the reported ability to belch and the belch urges and common cavities measured during oesophageal manometry.

The third study was on the variables influencing the effect of fundoplication on oesophageal motor function using an experimental porcine model. Three groups of 6 pigs underwent tight, loose and floppy fundoplications respectively. The fundus was wrapped around the gastro-oesophageal junction and a 20 F rod for the "tight" group, a 40 F rod for the "loose" group, and two 50 F rods for the "floppy" group. Short gastric vessels were divided in the group that underwent "floppy" fundoplication. Oesophageal manometry was carried out prior to and at 1 week after fundoplication in unaesthetised pigs. Fundoplication increased the peristaltic amplitude, ramp pressure and basal and nadir lower oesophageal sphincter pressure in all 3 groups but there was no difference between the 3 groups.

In conclusion, patients with more severe dysphagia were less able to relax their newly constructed lower oesophageal sphincter, as evidenced by the higher nadir pressure. The ramp pressure is a useful parameter which reflects the physiological obstruction at the lower oesophageal sphincter imposed by a fundoplication, and is directly correlated with nadir lower oesophageal sphincter pressure. Dysphagia is not related to the success of primary or secondary peristalsis. With respect to the ability to belch after fundoplication, patients do not experience gas gastro-oesophageal reflux as

evidenced by the absence of common cavities associated with belches. Using an experimental porcine model, we were unable to demonstrate any relationship between the tightness of the fundoplication and manometric parameters that correlated with post-fundoplication dysphagia in patients.

APPENDICES

Peristaltic amplitude of the proximal oesophagus (mmHg)

Volume (ml)	Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	63.09 ± 19.06	54.23 ± 6.75	44.86 ± 16.26	50.81 ± 5.53
10	70.73 ± 21.35	53.64 ± 7.2	58.33 ± 21.44	50.53 ± 6.54
15	64.73 ± 14.48	49.29 ± 6.74	62.33 ± 23.35	49.29 ± 6.14

Peristaltic amplitude of the distal oesophagus (mmHg)

Volume (ml)	Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	112 ± 13.26	70.33 ± 8.45	59.33 ± 8.19	77.13 ± 8.06
10	105.36 ± 16.3	68.46 ± 7.72	69.6 ± 23.68	70.76 ± 8.31
15	108.27 ± 16.91	59.46 ± 6.17	87.6 ± 21.49	75.19 ± 8.34

Propagation velocity of the peristaltic wave (cm/sec)

Volume (ml)	Healthy Controls (mean ± SEM)	Relux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	6.31 ± 0.84	6.18 ± 1.03	4.03 ± 0.89	2.83 ± 0.26
10	6.69 ± 1.08	7.06 ± 1.45	3.62 ± 1.18	2.64 ± 0.15
15	5.61 ± 0.92	5.86 ± 0.6	3.11 ± 0.45	2.76 ± 0.23

Duration of contraction in the distal oesophagus (sec)

Volume (ml)	Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	3.59 ± 0.33	3.44 ± 0.25	3.53 ± 0.2	3.88 ± 0.27
10	3.67 ± 0.23	3.49 ± 0.18	3.1 ± 0.41	4.22 ± 0.29
15	4.28 ± 0.53	3.57 ± 0.24	3.45 ± 0.37	3.97 ± 0.31

Ramp pressure (mmHg)

Volume (ml)	Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	5.79 ± 0.69	7.68 ± 0.71	14.19 ± 1.82	23.8 ± 1.03
10	7.55 ± 1.12	7.54 ± 0.76	14.4 ± 2.52	24.15 ± 1.49
15	5.24 ± 0.82	7.81 ± 0.71	15.8 ± 2.68	22.35 ± 1.64

Basal lower oesophageal sphincter pressure (mmHg)

Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
12.49 ± 0.61	7.03 ± 0.49	16.94 ± 2.62	33.74 ± 1.37

Nadir lower oesophageal sphincter pressure (mmHg)

Volume (ml)	Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	1.08 ± 0.39	1.21 ± 0.25	5.75 ± 1.36	13.07 ± 1.1
10	0.77 ± 0.29	0.58 ± 0.38	6.1 ± 1.78	12 ± 0.99
15	1.1 ± 0.4	-0.14 ± 0.24	5.4 ± 1.63	11.03 ± 1.07

Maximum distal oesophageal diameter at the time of maximum lower oesophageal sphincter opening (mm)

Volume (ml)	Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op Np Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	16.55 ± 0.61	16.55 ± 0.5	18.16 ± 0.72	22.85 ± 0.87
10	16.76 ± 0.9	16.68 ± 0.72	18.57 ± 0.89	25.27 ± 0.83
15	16.83 ± 0.72	18.59 ± 0.74	19.33 ± 1.22	25.76 ± 1.01

Maximum lower oesophageal sphincter opening diameter(mm)

Volume (ml)	Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	11.09 ± 0.51	12.59 ± 0.47	8.84 ± 0.55	9.85 ± 0.38
10	11.17 ± 0.54	12.42 ± 0.64	9.74 ± 0.65	10.78 ± 0.4
15	11.57 ± 0.49	13.93 ± 0.82	9.87 ± 0.8	11.28 ± 0.5

Transit time through lower oesophageal sphincter (secs)

Volume (ml)	Healthy Controls (mean ± SEM)	Reflux (mean ± SEM)	Post-op No Dysphagia (mean ± SEM)	Post-op Dysphagia (mean ± SEM)
5	3.07 ± 0.25	4.39 ± 0.33	3.64 ± 0.22	4.54 ± 0.28
10	4.88 ± 0.37	5.8 ± 0.46	4.58 ± 0.36	5.6 ± 0.34
15	5.33 ± 0.37	4.98 ± 0.34	5.73 ± 0.6	6.18 ± 0.38

Trans-sphincteric flow (ml/sec)

Volume (ml)	Healthy Controls median (quartile 1 & 3)	Reflux median (quartile 1 & 3)	Post-op No Dysphagia median (quartile 1 & 3)	Post-op Dysphagia median (quartile 1 & 3)
5	1.51 (1.31 - 2.34)	1.21 (0.865 - 1.48)	1.455 (1.215 - 2.1)	1.23 (1 - 1.55)
10	2.255 (1.72 - 2.39)	1.765 (1.57 - 2.07)	2.255 (1.765 - 2.455)	2.015 (1.73 - 2.36)
15	2.74 (2.27 - 3.23)	3.16 (2.59 - 3.97)	2.83 (2.26 - 3.47)	2.53 (2.12 - 3.18)

PRESENTATIONS
arising from the work done for this thesis

1. Tew S, Jamieson GG, Gabb M, Holloway R, Ferguson S, Tew P. What causes dysphagia after fundoplication? *Royal Australasian College of Surgeons Annual Scientific Meeting, Hobart* 1994; 461

2. Tew S, Jamieson GG, Holloway R, Ferguson S, Tew P. The effect of fundoplication on primary and secondary peristalsis in the oesophagus. *Surgical Research Society of Australasia Meeting, Sydney* 1994

3. Tew S, Jamieson GG, Holloway R, Gabb M, Ferguson S, Tew P. Ramp intrabolus pressure after Nissen fundoplication. *Surgical Research Society of Australasia Meeting, Sydney* 1994

4. Tew S, Jamieson GG, Holloway R, Ferguson S. Can patients belch after anti-reflux surgery? *Surgical Research Society of Australasia Meeting, Sydney* 1994

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WHAT CAUSES DYSPHAGIA AFTER FUNDOPLICATION?

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Dysphagia of varying severity occurs in up to 40% of patients after Nissen fundoplication and the pathophysiology for this has not been defined.

We have studied 25 patients following a Nissen fundoplication, 21 patients having a laparoscopic procedure and 4 patients having an open procedure all constructed around a large bougie in the oesophagus (40F-52F). Dysphagia was graded at a postoperative interview as none, mild, moderate or severe. Thirteen patients were studied before and after their operations and 6 had dysphagia, whereas 7 did not. Twelve patients complaining of dysphagia were also studied. We used concurrent videofouoroscopy and oesophageal manometry to study the diameter of lower oesophageal sphincter (LOS) opening as well as basal LOS pressure, residual relaxation pressure of the LOS and ramp intrabolus pressures. LOS opening diameter was not significantly different between the two groups. Patients with dysphagia had a significantly higher basal LOS pressure, higher residual relaxation pressure and ramp intrabolus pressure than those with no dysphagia.

(mean ± SEM)	Dysphagia	No Dysphagia	
Basal LOSP	33.7±1.4 mmHG	16.9±2.6 mmHg	$p < 0.02$
Residual LOSP	12.0±1.0 mmHg	6.1±1.8 mm Hg	$p < 0.04$
Ramp Pressure	24.2±1.5 mmHg	14.4±2.5 mm Hg	$p < 0.01$

The dysphagia score was correlated with the residual relaxation pressure ($r = 0.677$, $p < 0.05$). Thus patients with more severe dysphagia are less able to relax their newly constructed LOS. In conclusion, it appears that tightness of the fundoplication per se (opening diameter of the LOS) is not the factor causing dysphagia but the degree of permanent tension (residual relaxation pressure) which is imposed on the LOS which leads to dysphagia.

The Effect of Fundoplication on Primary and Secondary Peristalsis in the Oesophagus

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Fundoplication has been found to improve primary peristalsis and decrease the rate of transient lower oesophageal sphincter relaxations (TLOSR) responsible for gastro-oesophageal reflux. Secondary peristalsis is also defective in patients with reflux disease and the aim of this study is to ascertain if secondary peristalsis recovers after fundoplication.

We studied 13 patients before and after fundoplication. Oesophageal manometry was performed to assess the response rate, peristaltic amplitude and residual relaxation pressure of the lower oesophageal sphincter using 10ml air boluses injected into the mid oesophagus by hand. This was compared with primary peristalsis elicited by wet swallows.

In the pre-operative patients with GORD, secondary peristalsis was initiated at a median rate of 60%, propagation occurred in 40% and lower oesophageal sphincter relaxation in 70%. Fundoplication did not improve the initiation or propagation rate but it decreased the median lower oesophageal sphincter relaxation rate to 45% ($p < 0.03$). Moreover, fundoplication did not improve the amplitude of primary peristalsis in this study. In post-fundoplication patients, successful secondary peristalsis had significantly lower ($p < 0.003$) proximal and distal amplitude than primary peristalsis.

We conclude that secondary peristalsis did not recover after fundoplication. Fundoplication which is known to decrease the rate of transient lower oesophageal sphincter relaxations responsible for reflux, also lessens the rate of lower oesophageal sphincter relaxation induced by secondary peristalsis.

Ramp Intrabolus Pressure After Nissen Fundoplication

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Obstruction of the lower oesophageal sphincter has been observed to increase the magnitude of a positive deflection on manometry which precedes the peristaltic contraction and has the appearance of a plateau or ramp. The aim of this study is to define ramp pressure and relate it to the obstruction imposed on the lower oesophageal sphincter by a fundoplication.

We studied 11 healthy volunteers, 15 patients with reflux disease, 7 patients without dysphagia after fundoplication and 18 patients with post-fundoplication dysphagia, by concurrent oesophageal manometry and videofluoroscopy.

The ramp pressure correlated with the intrabolus pressure in the distal oesophagus when the mid oesophagus was occluded by a peristaltic wave and when the lower oesophageal sphincter was open. Ramp pressure increased with increasing residual relaxation pressure of the lower oesophageal sphincter ($r = 0.817$, $p < 0.0001$) and both parameters were highest in patients with dysphagia post-fundoplication. The dilatation of the distal oesophagus ahead of the advancing peristaltic contraction was directly correlated with ramp pressure ($r = 0.636$, $p < 0.0001$). However, ramp pressure was not significantly correlated with peristaltic amplitude or lower oesophageal sphincter opening.

It is possible that tension in the lower oesophageal sphincter region (residual relaxation pressure) results in high
ramp intrabolus pressure in the distal oesophagus which causes the relatively compliant distal oesophagus to dilate.

We conclude that ramp pressure is a useful parameter that reflects the physiological obstruction at the lower oesophageal sphincter.

Can Patients Belch After Anti-reflux Surgery?

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Determining a patient's ability to belch after anti-reflux surgery is not as simple as it sounds and many studies have relied on the patient's view and have not undertaken objective measurements. The development of a gastro-oesophageal common cavity is the only objective marker of gas gastro-oesophageal reflux, that is, a belch from the stomach.

We interviewed 11 healthy volunteers and 20 patients after their Nissen fundoplication regarding their ability to belch and relieve bloating by belching. During oesophageal manometry, the occurrence of common cavities, transient lower oesophageal sphincter relaxations and belch urges were measured before and after distending the stomach with 750ml of carbon dioxide gas. When belch urges not associated with common cavities were considered, patients averaged 3 whereas volunteers averaged 2 in the 10 min after gastric distension. However when belch urges coinciding with common cavities were measured, volunteers averaged 1 in the 10 min after gastric distension whereas none of the 20 patients had any ($p < 0.05$). None of the patients had transient lower oesophageal sphincter relaxations. Also, there was no correlation between the reported ability to belch or relieve bloating by belching, and the belch urges and common cavities measured during manometry.

In conclusion, post-fundoplication patients do not experience gas gastro-oesophageal reflux as their belch urges are not associated with common cavities. Instead, belch urges in these patients may be the result of upper oesophageal sphincter relaxation alone. Subjective reporting of belching ability is an inadequate method of assessment.

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