Clinical Measurement in Gastroenterology

Volume 1/The Oesophagus

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Foreword

Everyone is familiar with respiratory or cardiac dysfunction such as wheezing in asthma or an irregular heartbeat. The gut is just as complex as the airways or heart, and we have all experienced unpleasant aspects of its function such as vomiting, colic or diarrhoea. However, dysfunction has been difficult to study and measure; as a result, at least half the people who attend a gastroenterological out-patient clinic leave without any abnormality being detected. This is largely because up to now the search in diagnosis has been for abnormalities of structure. Routine tests of secretion and absorption exist but, in fact, help few patients. Study of visceral sensation and muscle function has lagged behind advance in other areas.

This situation is now being redressed. New experts are making a contribution to clinical diagnosis. They are clinical scientists, trained in measurement of gastrointestinal function. Many of the techniques they employ were developed as research methods and have now shown their usefulness in routine practice. These tests have usually been developed in several laboratories using methods that vary in detail and in the expression of results. The time has now come to standardize techniques, normal ranges and the results to be expected in various clinical conditions. This book fulfils that need.

It has been prepared by a group of clinical scientists who are recognized and welcomed by the British Society of Gastroenterology as Clinical Measurement Associates. They work in specialist gastroenterological units throughout the country and their role is increasing. Within these pages they seek to explain investigation of oesophageal function, define the methods used, standardize analysis of results and indicate their clinical relevance. Several methods included are still at a stage of development such as the measurement of oesophageal propulsive force.

This book should be of international importance because it is the first of its kind. The two editors and all the clinical measurement scientists who have collaborated with them are to be congratulated on its production. The field is expanding and I look forward to their contribution on other aspects of function as well as to updates of this book in subsequent editions.

JOHN E. LENNARD-JONES
Former President of the British Society of Gastroenterology
Patron of the Clinical Measurement Associates
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Preface

The investigation of the oesophagus has seen major advances in the second half of the 20th Century as technology has developed and our understanding of the physiology and pathophysiology of oesophageal diseases has increased. In the wake of these changes, research and development of oesophageal function tests have lead to a new breed of specialists in medicine to provide for the needs of the clinician in diagnosis and management of patients with oesophageal diseases.

The development of investigations has been progressing steadily. Radiology was the mainstay of oesophageal function in the first half of the century. In the 1950s, oesophageal manometry was developed to investigate motor function. Flexible fibreoptic endoscopy revolutionized the investigation and treatment of oesophageal disease from the mid-1960s and has become a specialty of medicine in its own right. pH monitoring has made a huge impact in the diagnosis of gastro-oesophageal reflux disease and the management of this common disorder has changed dramatically in the past 20 years since its early development.

Modern electronic and computer technology now allows us to investigate patients' oesophageal function in their home environment with small, sophisticated, portable, computerized recorders. Other technology has enabled clinicians to investigate oesophageal function in ways not previously possible.

This technology requires the services of a new breed of healthcare professionals, highly trained in the field of physiology and technology with special skills in clinical science. These people are drawn from all disciplines in medicine. Academic clinicians, nurses, clinical scientists and technologists have been attracted to this specialized field of investigative medicine and now form an important group in healthcare in gastroenterology.

The British Society of Gastroenterology have recognized the importance of this subspecialty and have inaugurated a new group, 'The Clinical Measurement Associates'. This group is growing in number and importance and has initiated a series of handbooks dedicated to raising the standards of the techniques and interpretation of results of the multitude of investigations now available.

This handbook is the first of a series dedicated to different areas of the gastro-intestinal tract. Future volumes will cover the stomach, small intestine, colon and ano-rectum. It is hoped that the reader will use this volume as a reference guide to help them to undertake the investigations to the best of their ability and to the

highest possible standards. This will ensure that patients will receive a higher standard of healthcare in both diagnosis and treatment of gastrointestinal conditions.

1 Introduction to oesophageal structure and function

Josephine D. Barlow & David F. Evans

Structure

The oesophagus is a muscular tube 23–25 cm in length joining the mouth and the stomach and lies mainly within the thoracic cavity. It begins at the terminus of the laryngo-pharynx where a high pressure zone, the upper oesophageal sphincter (UOS), provides a barrier to oesophago-pharyngeal reflux and also prevents aerophagia. The oesophagus then passes through the mediastinum between the trachea and the vertebral column before traversing the diaphragm at the oesophageal hiatus to terminate at the gastro-oesophageal junction. A region of higher pressure is found at the level of the diaphragmatic hiatus and is referred to as the lower oesophageal sphincter (LOS). This region provides a barrier to gastro-oesophageal reflux.

Histologically, the oesophagus is composed of four tissue layers.

1 The innermost layer, the mucosa, consists of non-keratinized stratified epithelium, lamina propria and muscularis mucosae. Mucus-secreting glands are also present close to the border with the stomach.

2 The submucosa contains connective tissue, blood vessels and mucous glands.

3 The muscularis layer is striated muscle fibres in the most proximal 5% of the oesophageal length. The next 35–40% is mixed striated and smooth muscle with an increasing proportion of smooth to striated muscle moving distally. The most distal 35–40% is composed entirely of smooth muscle fibres only [1,2]. The muscularis layer is composed of an inner circular ring of fibres and an outer longitudinal layer of fibres. The outer adventitial layer is loose connective tissue which merges with the connective tissue of adjacent structures. Figure 1.1 is a schematic diagram of a transverse section of the oesophagus and the relationship of the nerve and muscle layers. Figure 1.2 is an endoluminal ultrasound picture of the oesophageal body showing the layered structure *in vivo* and the different tissue layers can again be seen as hyperechoic and hypoechoic images in section.

4 Innervation of the oesophagus is both extrinsic via the vagus [3,4] and intrinsic via ganglionated neural plexuses [5–7]. Two plexi of intramural nerve networks complete the layers within the oesophagus. The submucosal or Meissner's plexus lies between the submucosal and circular muscle layer and the myenteric or Auerbach's plexus lies between the circular and longitudinal muscle layers. The role of the submucosal plexus is mainly in control of secretion and blood flow in

Circular muscle
Sub-mucosal plexus
Longitudinal muscle
Mucosa
Lumen
Serosa (adventitia)
Myenteric plexus
Sub-mucosa

Tissue layers
– Mucosa
– Sub-mucosa
– Circular muscle
– Longitudinal muscle

Nerve plexi
– Sub-mucosal (Mesissner's)
– Myenteric plexus (Auerbach's)
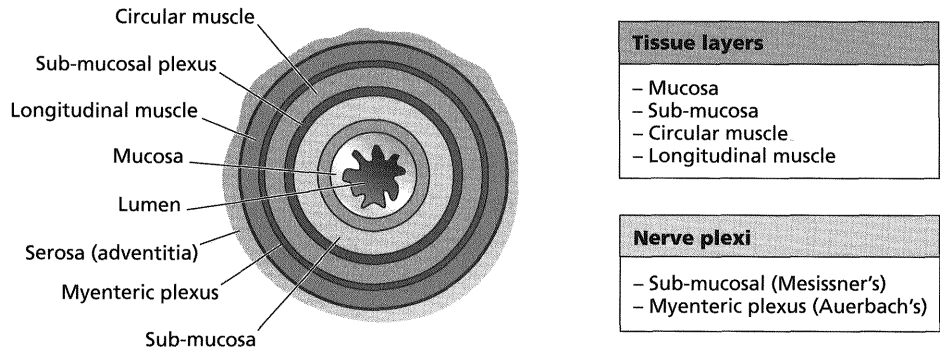
Fig. 1.1 Schematic transverse section of the tissue layers through the wall of the gastrointestinal tract.

the mucosal layers. The role of the myenteric plexus is the control of muscular function including sphincter activity during the act of deglutition (swallowing). The nerve plexi also modulate neural input from the extrinsic system and regulate reflex activity during swallowing [8,9].

Function

The main function of the oesophageal body is to maintain a state of emptiness. The lumen is normally in a collapsed state and a swallowed bolus entering the oesophageal body via the oro-pharynx and upper oesophageal sphincter is rapidly transported down the oesophagus into the stomach through the LOS [10]. Swallow activity in the pharynx initiates a sequence of activity in the oesophageal body that consists of longitudinal muscle shortening and a ring of aborally propagating contraction in the circular muscle layer [11,12] that is preceded by a wave of inhibition [13–15] so allowing aboral progression of the swallowed bolus. The ring of contraction can be measured and recorded via an intra-oesophageal catheter containing several longitudinal and radial pressure sensors.

Pressures within the oesophageal lumen and sphincters are important and contribute towards normal function. The UOS is normally a tight junction maintained by the tonic contraction of the cricopharyngeus muscle and the surrounding structures. Oesophageal resting body pressure normally varies between –5 mmHg, on inspiration to +5 mmHg on expiration. During contractions, this pressure can rise briefly to over 200 mmHg, as a peristaltic wave sweeps a bolus before it. The LOS is a relatively weak sphincter with a tonic pressure of 15–20 mmHg, this is maintained by smooth muscle tonicity and other important structural features at the gastro-oesophageal junction.

Patients presenting with oesophageal symptoms including chest pain, dysphagia, odynophagia and heartburn and reflux may be referred for investigation of
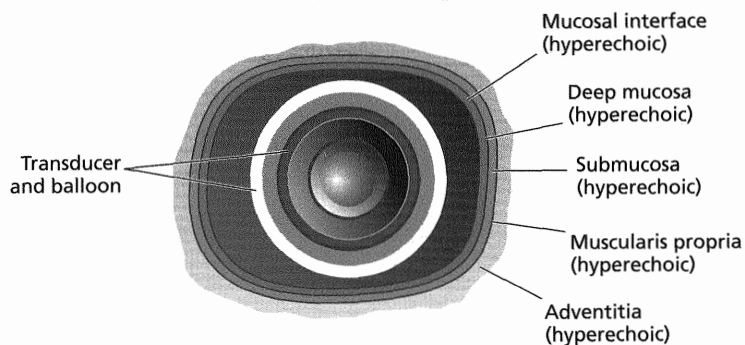
(a)
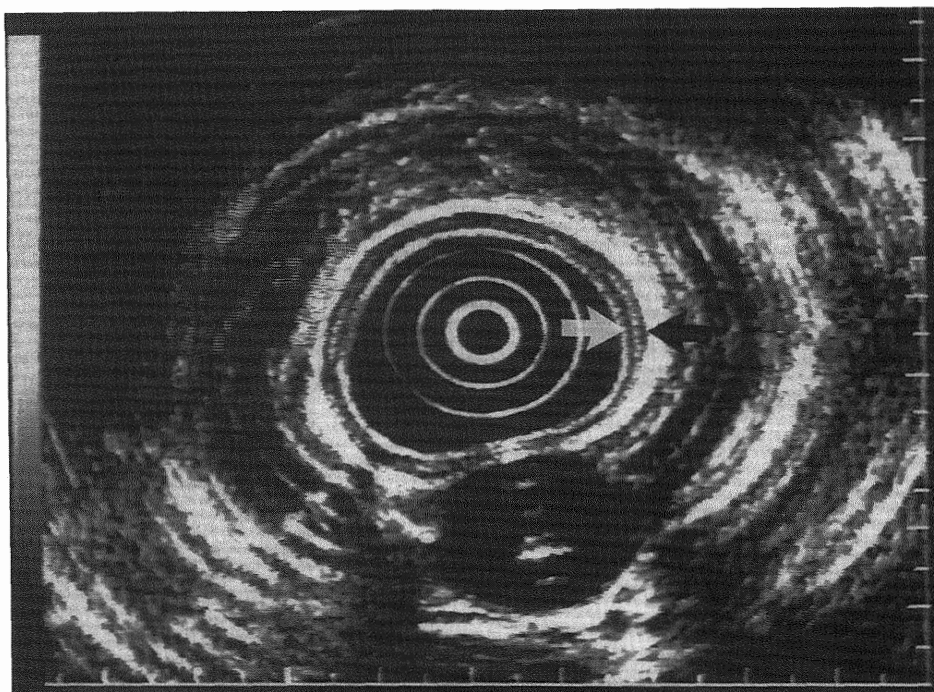
(b)

Fig. 1.2 (a) Schematic diagram of tissue layers through the gastro-intestinal tract depicted by endoluminal ultrasound. (b) Ultrasonogram of the tissue layers of the gastro-intestinal tract.

oesophageal function to establish the cause of their symptoms. The following chapters describe in detail the correct procedures to investigate these symptoms.

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2 Technical history and fidelity

Lene Wallin

History

The first description of oesophageal manometry was in 1883 by Kronecher & Meltzer [1] who used air-filled balloons connected to a manometer. In 1940 Ingelfinger & Abbott [2] used water-filled balloons and in 1957 Creamer & Pierce [3] used fluid-filled, but not continually perfused, catheters, with external transducers. Winans & Harris [4] showed improved fidelity with perfused tubes in 1967, and that the pressure recorded is a measure of the resistance of the sphincter to distension by the force acting within its lumen.

Measurement systems

The actual pressure at the measuring point in the oesophagus compresses the transducer membrane either directly or through the fluid-filled catheter. The signal is transformed to an electrical impulse, amplified and recorded. In sphincteric areas the pressure is a relationship between the circumference and muscle tension, the result dependent on probe diameter.

A pressure measuring unit is characterized by its natural frequency, the degree of damping, the rise time $\delta P/\delta T$ and the compliance of the system $\delta V/\delta P$, defined as the system's volume change for a given pressure increase. This should be less than $0.11 \, mm^3/cmH_2O$ for recording pressures up to $300 \, cmH_2O$.

The mechanical part of the pressure measuring unit (the transducer) depends on the movement of the membrane, caused by the external pressure at the measuring point in the oesophagus; mathematically it can be described as a second-order mechanical system, defined by its natural frequency and the degree of damping. The measuring unit has to be linear within the quoted measuring range. Modern transducers have a linear frequency up to 300–400 Hz, the upper limit of physiological frequencies is about 30 Hz.

Faithful recording of the pressure wave depends upon an accuracy of 8–10 harmonics of the fundamental wave, i.e. for a wave of 2 seconds duration with a 0.5 Hz frequency, a flat frequency response of about 4–5 Hz is required.

Rise rates of oesophageal waves are usually less than 300 mmHg/s, thus the system should have an inherent pressure rise rate to a minimum of 100 mmHg/s,

but to ensure correct measurement a value of 300 mmHg/s is recommended.

For pharyngeal waves, however, amplitudes are up to 600 mmHg with a duration of 0.2–1 s propagating at 9–25 cm/s. The harmonics can reach 50 Hz with rise rates of 2000 mmHg/s, hence perfused tubes can only give approximate timings.

Compliance

The pressure transmission from the distal opening in the catheter to the external transducer depends on the combined compliance of a catheter, the infusion system and the displacement of the transducer membrane, as well as the perfusion rate.

With water-perfused systems the compliance of the tubing must also be considered because compliant tubing will distend when occlusion occurs at the perfusion port. This will result in loss of signal quality, demonstrated as reduced amplitude and increased duration of the pressure signal which is described as signal damping.

The compliance $\delta V/\delta P$ of the catheter depends on the length, diameter, wall thickness and the elasticity of the material.

To test the system compliance including catheter, occlusion of the perfusion port should result in a pressure rise of at least 300 mmHg in less than one second [5]. This is done by rapidly blocking each of the perfusion ports of the catheter in turn, with the edge of a hard rubber eraser, whilst the perfusion flow is switched on. Figure 2.1 illustrates a compliance test with occlusion of one perfusion port, where the rise rate is 1536 cmH$_2$O per second. The lower the compliance (i.e. the stiffer the catheter wall and the shorter the catheter) the better the reproduction of rapid pressure changes within the oesophagus. Figure 2.2 illustrates a compliance test showing poor response with a rise rate of only 42 cmH$_2$O per second.

Perfusion systems

The first infusion systems used electrical pumps (syringe drivers); a major part of the compliance of the whole system was due to the pump (gear train). The infusion rate needs to be high enough to maintain an unbroken column of fluid from the measuring point to the transducer membrane and to measure rapid pressure changes, yet low enough not to alter the baseline significantly.

$$\text{Perfusion rate} = \text{Deformability} \times \frac{P}{t} \frac{\text{(maximal infusion pressure)}}{\text{(time of contraction)}}$$

Baseline rise is caused by the viscous effect of the fluid and is related to the length and diameter of the catheter according to Poisseuille's equation.

$$\text{Recording fidelity} \propto \frac{\text{duration}}{\text{amplitude}} \times \frac{\text{infusion rate}}{\text{compliance}}$$
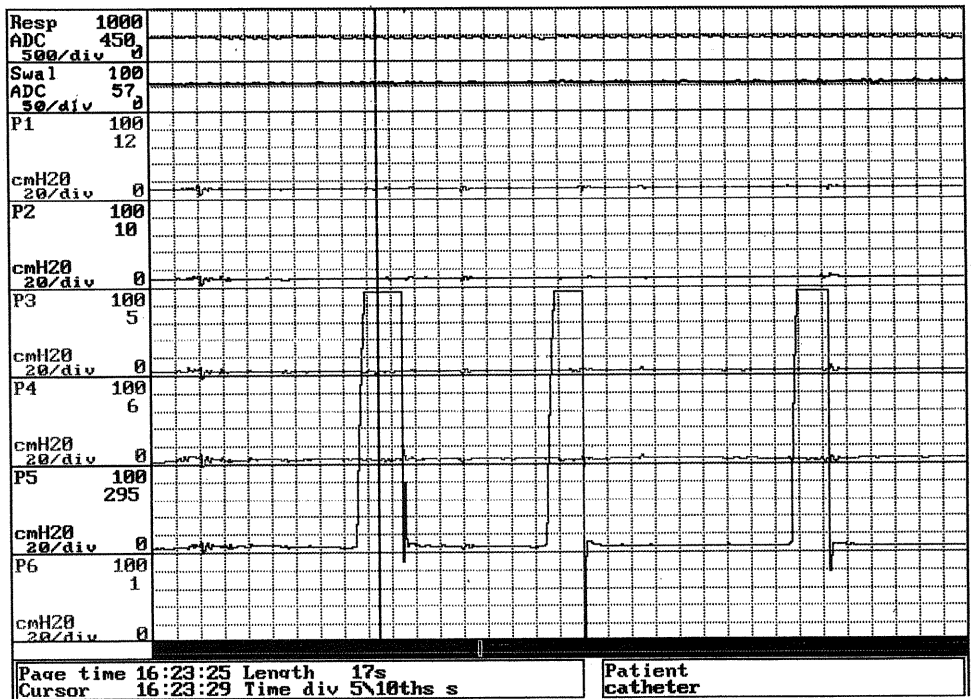
Fig. 2.1 Compliance test showing the rapid change in pressure that occurs when the perfusion port (P5) is occluded.

Trace Information. Lectromed oesophageal motility system (Figs 2.1–2.7).
Top trace—respiration thermistor; second trace—swallow microphone. Other traces as labelled in left-hand boxes. In each box, the top figure is full scale, e.g. 50 cmH$_2$O, but each trace continues at same scaling into next channels when over-range; next figure is pressure value at position of cursor, shown by vertical black line. Length—time per page; Time div—time between faint vertical lines. Distances at top margin—cm to nares. Wet—wet 5 ml water bolus swallow; Dry—dry swallow; Breath—deep breath. These markers are manually entered and hence are several seconds after the event.

Pressure loss is proportional to catheter length and reciprocal of the fourth power of the internal diameter, plus internal surface finish and changes in geometry of fluid pathway (e.g. at connections).

Poiseuille–Hagen equation: Flow (vol/s) $= \dfrac{\pi P r^4}{8 l \eta}$

l = length (metres); P = pressure in Pa; η = kg/m; ηH$_2$O = 10.087 millipoise at 20°C; r = inner radius (metres).

Early perfusion systems were poor at low flow rate, yet high rates induced peristalsis in the oesophagus due to the amount of fluid used.
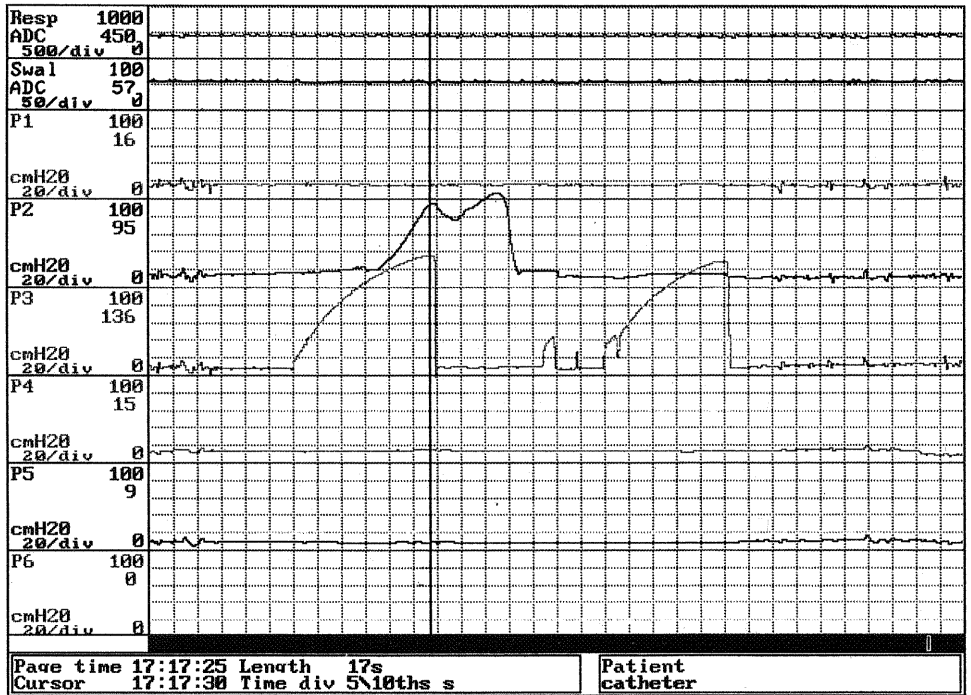
Fig. 2.2 A compliance test showing poor response in P3.

In 1975 Koelz *et al.* [6] introduced a new system using a needle valve directly connected to the transducer, followed by Arndorfer *et al.* in 1977 [7] with a capillary infusion system.

The fluid reservoir is maintained at 1000 mmHg (19.33 p.s.i.) ideally using helium with its low solubility in water. Using stainless capillary tubes between the fluid reservoir of de-gassed water and the transducer, the pressure is reduced at the transducer level to zero due to high resistance to flow, the flow rate at the catheter orifice being approximately 0.6 ml/min, which is adequate to prevent sealing of the orifice.

Solid state catheters

These are discussed in Chapter 5.1.

Measurement principles

Pressure variations in the oesophagus arise from three sources—a primary source in the oesophagus itself, the secondary and tertiary sources being variations due to respiration and cardiac activity.

For oesophageal measurements a recording frequency of at least 2 Hz is required.

Measurement of sphincteric areas are indirect recordings, expressing the relationship between circumference and muscle tension in the area.

The relationship between wall tension T and intraluminal pressure P is given by:

Laplace's Law $P = \dfrac{T \times t}{r}$

where t = thickness of the circular muscle layer; r = inner radius. The introduction of the catheter increases the inner radius, distending the muscle, hence increasing wall muscle tension.

The size of the probe in the oesophagus has little influence on oesophageal pressures until it reaches a size where it acts as a rigid bolus, preventing the circular muscles from reaching their minimum circumference.

Signal quality

The accuracy of the signal reproduction is dependent upon every component part of the system. The amplifiers must be suitable for the range of the biological signal that is to be recorded [5]. The required equipment settings will be supplied by the manufacturers. The system must be capable of accurately reproducing signals with pressure values between −10 mmHg and up to a minimum of 400 mmHg [8–10] with a linear response over this range. For computer-based recording systems, the sampling frequency, which is the number of samples made each second of recording time, described with the unit Hertz (Hz), should be high enough to accurately reproduce the rapid pressure changes with time. The minimum sampling frequency required would typically be between 8 and 16 Hz. For pen-recording systems the frequency response of the pen galvanometers and the linearity must be suitable for the signal.

Sources of inaccuracy

1 Errors can be introduced if the complete system is not checked in order to be certain that all channels are producing the same response. The overall system response for each perfusion port in the catheter can be checked to ensure that they are all similar, by inserting the catheter into a fluid-filled flexible chamber (e.g. an empty IV infusion bag) and gently squeezing it or hitting it rapidly (Fig. 2.3).

2 The flow rates through each of the perfusion capillaries should be routinely checked (by filling syringes connected to each channel for approximately 10 min)

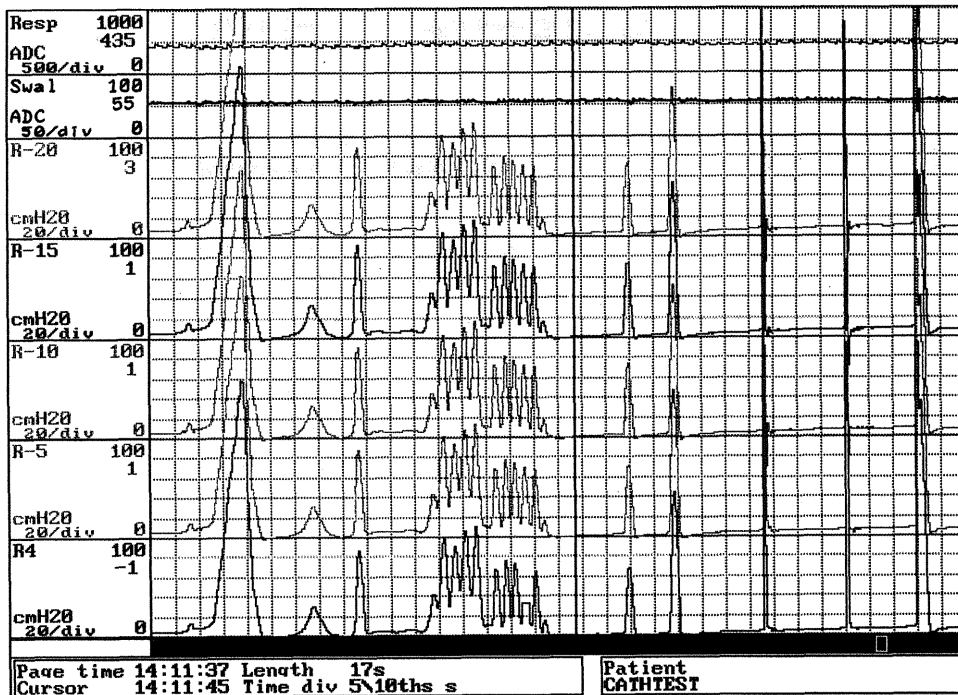**Fig. 2.3** Overall system response for each perfusion port in the catheter on gently squeezing it (top half) or hitting it rapidly as shown in the last three waves.

Fig. 2.4 Elevated baseline due to partial blocking of a perfusion port by food debris returned to normal after flushing in R-5. Also R3 flushed with no change in baseline, once lumen has been refilled by the perfusion pump.

in order to ensure that the flow rates are not becoming reduced due to blockages. One method of freeing a partial blockage is to apply a low vacuum to the reservoir whilst injecting (backflushing) water through the transducer connection using a small bore (e.g. 1 ml) syringe to achieve a high pressure.

3 The response of the system can become heavily damped, the response resembling that shown in Fig. 2.2 if the reservoir water (sterile water for irrigation is used) is not previously degassed using a low vacuum pump or even simply a venturi-type water-jet vacuum pump. Any dissolved gas within the reservoir is at 1000 mmHg above atmospheric pressure, yet when it reaches the transducers it is at atmospheric pressure and any dissolved gas will produce minute gas bubbles which will damp any transmitted pressures from the catheter. The use of helium as the pressurizing medium is preferential, owing to its inertness and low solubility in water. The use
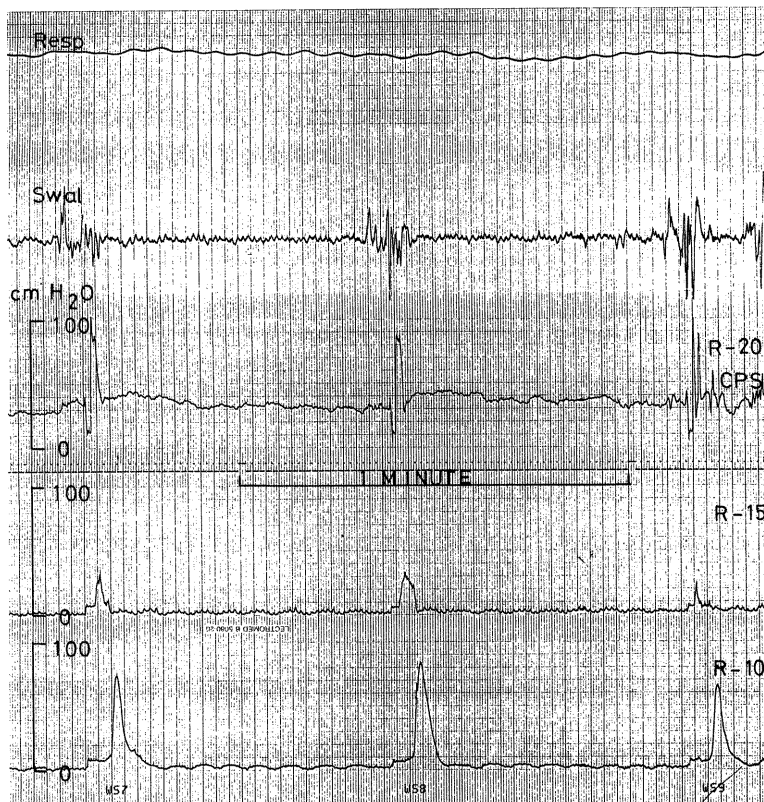
Fig. 2.5 The use of a swallow sensor in detecting double swallows where WS7 and WS8 are good single 5 ml bolus water swallows, WS9 appears to be a normal swallow, yet is clearly a double swallow via the microphone swallow sensor, and on close inspection the double swallow can also be observed in the trace within the crico-pharyngeal sphincter, and amplitudes within the oesophageal body are reduced.
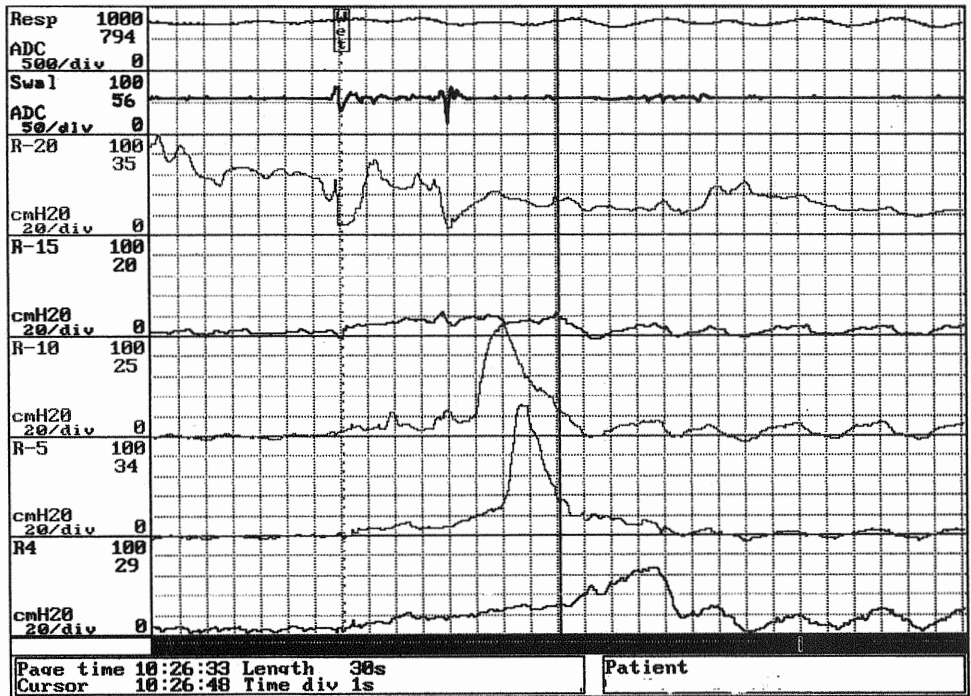
Fig. 2.6 The uppermost port (R-20) is within the crico-pharyngeal sphincter (CPS), whilst the distal port (R4) is at the recommended 3 cm above the lower oesophageal sphincter (LOS) for wet swallows; a double swallow can be seen in the CPS, the upper oesophageal wave is almost ablated and the morphology of the distal wave is abnormal.

of a plastic float on top of the reservoir also helps prevent absorption of the gas. These points are of particular importance in extended studies, or when several studies follow another using the same reservoir.

4 Partial blocking of a perfusion port by food debris (and also saliva containing air bubbles), particularly after insertion in patients with delayed oesophageal or gastric emptying, can cause an elevated baseline in the affected channel (Fig. 2.4). The incidence of this can be reduced by pre-filling the channels with water and sealing the tops with luer-lock caps. The baseline can be returned to normal by flushing the affected channel with 2–5 ml of degassed sterile water via a syringe.

5 The use of a swallow sensor in detecting double swallows, etc. is illustrated in Fig. 2.5, where WS7 and WS8 are good single 5 ml bolus water swallows, WS9 appears to be a normal swallow, yet is clearly a double swallow via the microphone swallow sensor, and on closer inspection can also be observed in the trace within the crico-pharyngeal sphincter, and amplitudes within the oesophageal body are reduced.

6 If there are sufficient perfusion ports or the oesophagus is short, the uppermost port may be within the crico-pharyngeal sphincter, whilst the distal port is at the recommended 3 cm above the LOS for wet swallows and double swallows can usually be detected, e.g. Fig. 2.6, where the upper oesophageal wave is almost ablated and the morphology of the distal wave is abnormal.

7 The maximum range of the transducer and recording system should be sufficient to capture the complete contraction. Figure 2.7a shows what appears to be a single peak contraction but is over-range in the two most distal channels at greater than 300 cmH$_2$O, the peak amplitude; peristalsis (if using the peaks) and the propagation rate cannot be calculated. Figure 2.7b, using a different recorder with a range up to 500 cmH$_2$O, with the same patient, shows the complete contraction and that some waves are double peaked particularly during this section after multiple swallows.

(a)

Fig. 2.7 (a) What appears to be a single peak contraction but is over-range in the two most distal channels at greater than 300 cmH$_2$O, the peak amplitude; peristalsis (if using the peaks) and the propagation rate cannot be calculated. R-20 is in the crico-pharyngeal sphincter. Part (b) appears on p.14.

(b)
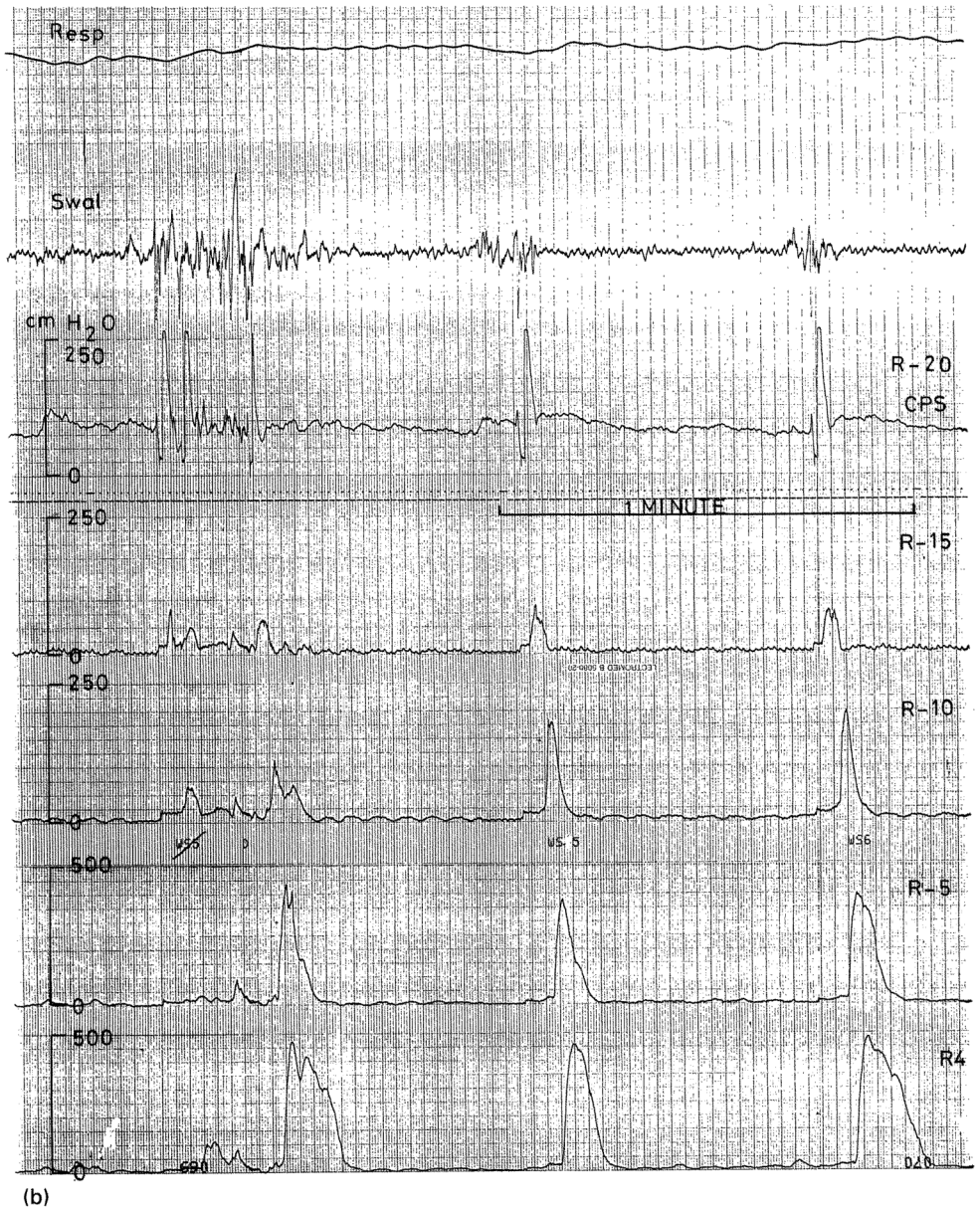
Fig. 2.7 (b) Using a different recorder with a range up to $500\,cmH_2O$, in the same patient, shows the complete contraction and that some waves are double peaked particularly during this section after multiple swallows.

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3 Static manometry

3.1 Equipment and catheters

Josephine D. Barlow

The equipment needed to perform gastro-oesophageal pressure measurements is readily available and relatively inexpensive. The recorded output signal should faithfully reproduce the changes in the biological system that is being investigated. For oesophageal manometric recording both normal and abnormal activity [1–4] must be accurately reproduced.

The basic requirements for pressure measurement are as follows.

1 A catheter with several ports for detecting pressure changes, each port connected to:
2 A transducer which converts the measured pressure to a voltage.
3 An amplification system which amplifies the voltage.
4 A respiration sensor.
5 A swallow detector.
6 Visual display, hard copy printout and analysis of the output signal.

The hard copy, with the analysis and report, should be filed and easily available for review [5]. The most commonly used system was the multichannel chart recorder or polygraph as shown in Fig. 3.1, but this is being replaced by computer-based recording devices as shown in Fig 3.2, which allow visual display with online hard copy output alongside sophisticated, user friendly, easily updatable analysis capabilities [6]. Amplifiers now utilize solid state components which have considerably reduced the overall dimensions without compromising their effective functional capabilities. Compare Figs 3.1 and 3.2.

Catheters

The catheter used must be small enough in diameter to allow easy naso-gastric intubation and be comfortable for the duration of the procedure. The catheter must not be so large as to induce pressure changes within the system being investigated. Manufactured catheters have an outer diameter ranging from 2 to 5 mm. Customized catheters are available with specified parameters such as integral
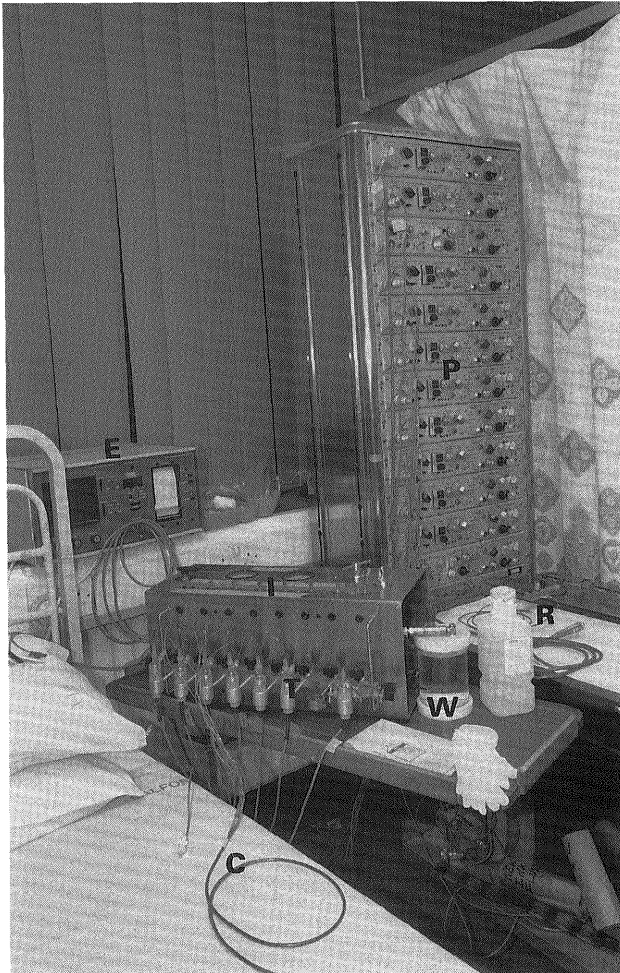
Fig. 3.1 A system for recording oesophageal manometry showing the multilumen catheter (C), each lumen of which is attached to a transducer (T). The transducers are mounted on a low-compliance pneumo-hydraulic infusion pump (I). The water chamber (W) is in view. The output from each transducer is fed into an amplifier on the multichannel chart recorder or polygraph (P). Respiration is monitored with a nasal thermistor (R) and heart activity with a single channel electrocardiograph (E)(optional).

balloons for oesophageal distension during provocation studies as shown in Fig. 3.3D.

The two basic types of catheter are the water perfused type and the solid state type. A variety of catheters for oesophageal manometry are illustrated in Fig. 3.3. Table 3.1 shows the characteristics of the catheters illustrated in Fig. 3.3. Water perfused catheters are robust and relatively cheap and will last several years in constant use.
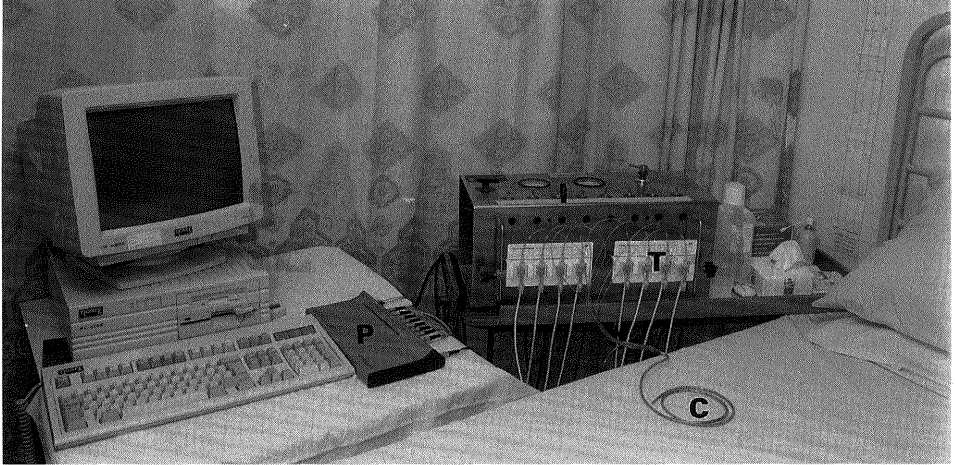
Fig. 3.2 A basic system for recording oesophageal manometry showing the multilumen catheter (C), each lumen of which is attached to a transducer (T). The transducers are attached to a low-compliance pneumo-hydraulic infusion pump (I). Each transducer transmits its signal to a channel in the polygraph (P). The signals are tra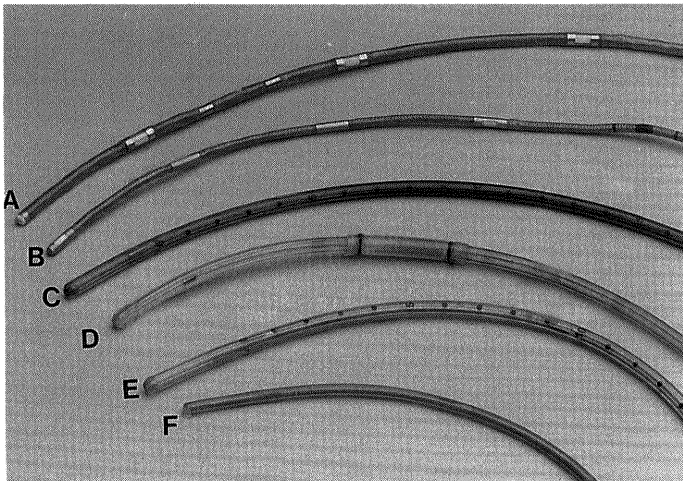nsmitted to the personal computer (PC) via an optical cable. The PC allows visual display, hard copy output and sophisticated analysis of the acquired data.

Fig. 3.3 Commonly used catheters. A: solid state catheter with bipolar ring electrodes either side of each pressure sensor; balloon attachment rings are present. B: solid state catheter with four pressure sensors at 5 cm intervals. C: eight channel, PVC water perfused catheter with perfusion ports at 5 cm intervals and a central lumen. D: six channel, PVC water perfused catheter with perfusion ports at 5 cm intervals and an attached silicon rubber balloon for oesophageal distension studies. E: six channel water perfused catheter with a central lumen and ports at 5 cm intervals. F: four channel water perfused PVC catheter with no central lumen.

Table 3.1 Characteristics of catheters illustrated in Fig. 3.3.

| Catheter	Outer diameter (mm)	Number of lumens or sensors	Radial ports at distal end	Angle between ports	Distance between ports or sensors (cm)	Balloon	Type
A	3	4	0	n/a	5	Yes	Solid state strain gauge
B	2	4	0	n/a	5	No	Solid state strain gauge + bipolar
C	4.5	8	4	90°	5	No	Water perfused
D	4.6	6	0	n/a	5	Yes	Water perfused with balloon
E	4	6	3	120°	5	No	Water perfused
F	3	4	0	n/a	5	No	Water perfused

Water perfused catheters

Multilumen water perfused catheters are made from extruded polyvinylchloride (PVC) or similar materials. A typical 4 mm diameter catheter has lumens within the catheter of approximately 0.8 mm in diameter and has side openings 0.8 mm in diameter. The catheter will ideally have several ports at its distal end for recording different orientations of the pressure profile when traversing the lower oesophageal sphincter (LOS). For example, in a six channel catheter, three ports can be arranged distally and radially orientated 120° to each other and in an eight channel catheter four ports will be arranged distally at 90° to each other with the remaining ports spirally arranged at 5 cm intervals proximal. The outer diameters (OD) are typically between 2 and 4.8 mm. A minimum of four ports radially orientated at 90° at 5 cm intervals, which encompasses 15 cm length, is required to assess peristaltic activity within the oesophageal body. Some catheters also have a larger central lumen which can be used to insert a guidewire for difficult intubations, and infusion or aspiration of fluids during manometry.

Figure 3.4 illustrates an ideal eight lumen catheter plus central lumen, four radial plus four spirally arranged ports at 5 cm intervals, which will allow assessment of a 20 cm length of oesophagus, sufficient to cover most adults at one position and provide a radial profile of the LOS. With this type of catheter the LOS can be assessed using the four radial ports with the next proximal (to detect oesophageal activity) and the next four proximal ports for assessment of the oesophageal body. For paediatric use the diameter of the nares size will determine the maximum outer diameter that can be used and hence will limit the number of recording sites.
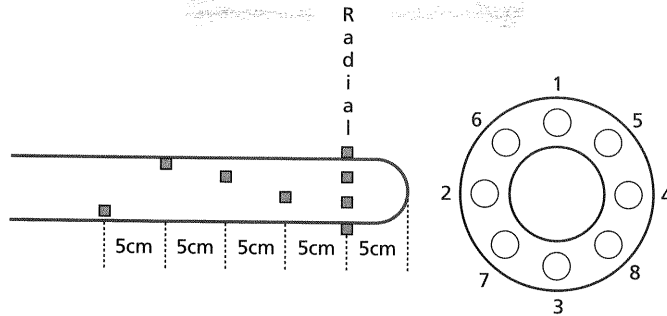
Fig. 3.4 Ideal perfused catheter. Schematic diagram of eight ports plus central lumen catheter.
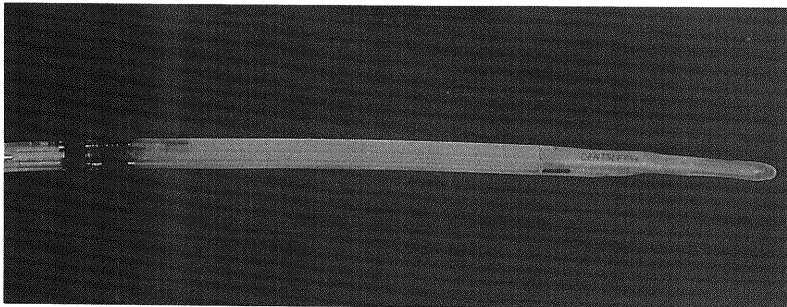
Fig. 3.5 Dent sleeve.

Dent sleeve

An alternative to the radial ports in the distal tip is the Dent sleeve [7](Fig. 3.5). This is a water perfused sleeve which provides a longitudinal pressure sensing system and enables prolonged pressure recording within the LOS. The sleeve detects the maximum pressure occurring at any point over its length and movements of the catheter within the LOS will still allow detection of the maximum pressure. This system will lose the circumferential variation in pressure encountered within the LOS, to give a mean pressure, but is particularly useful in prolonged studies to detect the correlation between transient LOS relaxations and gastro-oesophageal reflux.

Low-compliance pneumo-hydraulic infusion systems

Water perfused catheters require a pneumo-hydraulic infusion pump to generate a constant pressure and hence constant flow rate through each lumen of the catheter [8–11]. In the Arndorfer-type system the water is supplied via a chamber filled

Table 3.2 Examples of infusion rates using a type of low-compliance pneumo-hydraulic infusion pump.

Pounds per square inch (p.s.i.)	Millilitres per channel per minute (ml/ch/min)	Volume (ml) for an 8 channel catheter per hour
5	0.1	54
7.5	0.2	96
10	0.3	144
12.5	0.4	192
15	0.5	240
17.5	0.6	288
20	0.7	336

with sterile distilled water. This is readily available from the hospital pharmacy. The water should ideally first be degassed using a vacuum pump; a plastic float placed on top of the water in the chamber helps to prevent any further gas dissolving into the fluid. Gas bubbles present in the fluid impair transmission of the pressure signal reducing the recording fidelity. Helium in a gas cylinder or compressed via an electrically operated compressor system (with an in-line O_2 and CO_2 absorber) is used to pressurize the water chamber and drive the water into the catheter via capillary tubes and the pressure transducers. Air bubbles must be flushed out of the system as they will impair transmission of the pressure through the water column in the catheter lumens. A pressure of 1000 mmHg (19.33 p.s.i.) will generate a flow rate of 0.6 ml/min through each lumen. This flow rate will provide high fidelity recording of the pressure variations occurring within the oesophagus. Table 3.2 shows the relationship between pressure and flow rates.

Transducers for water perfused catheters

Each lumen of the catheter is connected to an external transducer as shown in Figs 3.1 and 3.2. The pressure is transmitted via the fluid column along the catheter lumens to the pressure transducer. The pressure increase is converted to an electrical signal via the strain gauge within the transducer. This signal can be amplified, displayed and also recorded for later analysis.

Solid state catheters

Solid-state catheters have miniature strain gauge transducers built into the catheter typically at 5 cm intervals and in a four channel catheter these would be radially arranged at 90° (see Figs 3.3A and B) but can also be radially oriented at the same

level. These transducers eliminate the need for water perfusion as the pressure changes directly influence the strain gauge so generating the appropriate output signal [12–14]. Latest developments have reduced dimensions allowing a greater number of transducers to be incorporated without increasing the outer diameter; a catheter with eight sensors and central channel similar to the perfused catheter shown in Fig. 3.4 can now be manufactured. Solid state catheters are considerably more expensive (approximately £5000 for the eight sensor with central lumen) and less robust than water perfused catheters and their functional life span is dependent upon their care in both use and cleaning. One advantage of solid state systems is their ease of mobility for performing studies in different centres with one set of equipment and also for ambulatory recording (see Chapter 5).

Respiration sensors

Two basic types of respiration sensors are used (Fig. 3.6).

1   An elasticated band fastened round the chest, incorporating a stretch/strain transducer. These have the disadvantage of being difficult to adjust if there is little chest expansion or with shallow breathing and can also stick to clothing and are affected by body movement.

2   A single or twin thermistor fastened near the nares to detect the inspiratory/expiratory temperature changes.
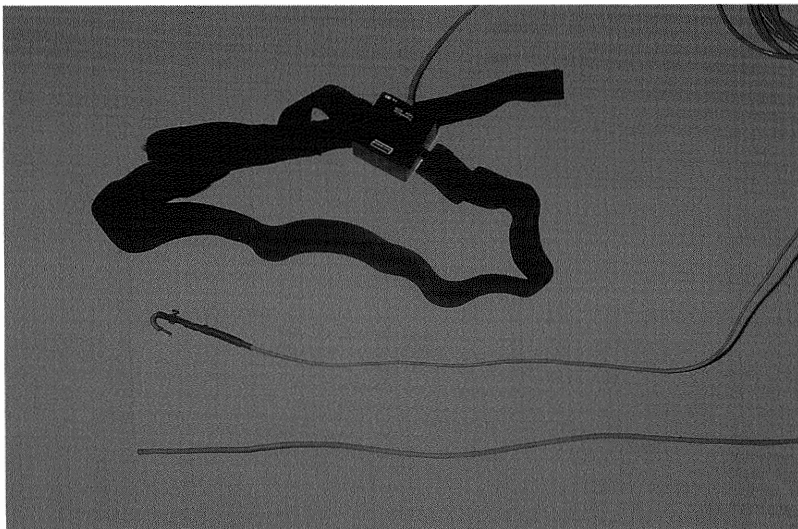

Fig. 3.6 Respiration sensors. Top—chest band. Mid—twin thermistor nasal clip. Bottom—single nasal thermistor.

Utilizing a respiratory sensor ensures that the end-expiratory point can easily be observed, making simple the discrimination of the catheter position as being abdominal or thoracic. This can be particularly useful for identification of the pressure inversion point and in patients with a hiatus hernia, as well as for detecting changes in respiration such as deep breaths and sighs.

Swallow detectors

There are three main types of swallow detector (Fig. 3.7).
1 The most basic is an elasticated strain gauge fastened around the neck, but this can be uncomfortable and difficult to position.
2 A miniature microphone embedded in plastic, such as those used for Korotkoff sounds in cardiac monitoring; this is ideal when firmly fastened with tape over the throat.
3 The most accurate is a pair of electromyogram (EMG) electrodes stuck either side of the hyoid, but the exact position to pick up the swallow response is usually a process of repeated trial and error. Once correctly positioned this type is free from artefact and is ideal for long-term or even ambulatory monitoring. The disadvantages are the difficulty in correct positioning and being unable to attach in bearded patients and poor signal in obese patients and those with large skin folds.
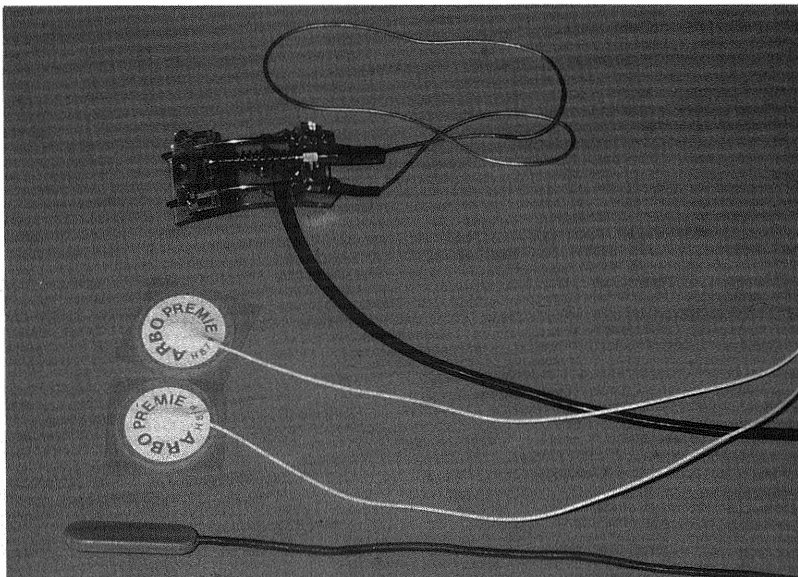
Fig. 3.7 Swallow detectors. Top—neck band. Mid—infant electrodes for hyoid EEG. Bottom—Korotkoff sounds type microphone.
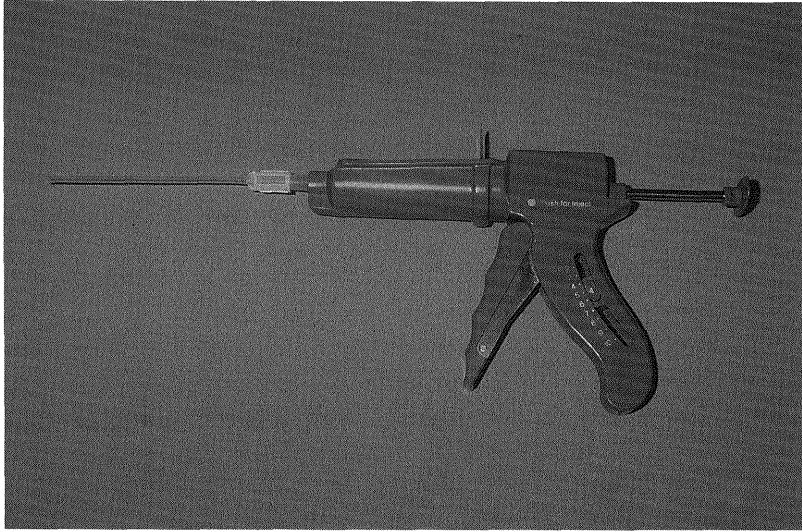
Fig. 3.8 Metered syringe gun for wet swallows.

Metered syringe

The use of a metered syringe gun, which can be set to dispense 5 ml aliquots, ensures a consistent bolus size for wet swallows (Fig. 3.8). Alternatively, a disposable syringe in commonly used.

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3.2   Calibration and intubation

Josephine D. Barlow

Calibration

The transducers are calibrated with atmospheric pressure as the zero level and a pressure of a minimum 50 mmHg or 50 cmH$_2$O or 5 kPa as the high pressure level. With a water perfused system, calibration is performed by having a water column equivalent to 50 mmHg (74 cmH$_2$O) or 50 cmH$_2$O which is applied to each transducer in turn to check the accuracy of the transducer output, see Fig. 3.9a, or by elevating the catheter, Fig. 3.9b. For solid state catheters the transducers are calibrated within a sealed tube and the internal pressure is increased to the desired level using an air-based system such as a sphygmomanometer, but since the silicone in these absorb water, it is advised to soak the catheter for at least 1 hour before calibration. Similarly some solid state catheters should be calibrated at 37°C. Figure 3.10 shows the calibration tubing used in this type of system. The calibrated zero, relative to the patient's position, is not affected by height differences because in this system the equivalent column of air would not generate a measurable pressure difference as occurs with the water-based system.

Cleaning and disinfection

Throughout the procedure staff should wear protective clothing in the form of aprons, eye protection and gloves. Following extubation the contaminated catheter should be washed in water containing a mild detergent which is also flushed through each lumen to remove organic debris and then disinfected by then immersing in, and each channel flushed through and filled with a sterilizing solution such as glutaraldehyde, to destroy micro-organisms that could be transmitted between patients. The use of a cleaning manifold which allows all nine lumens to be flushed

(a)

(b)
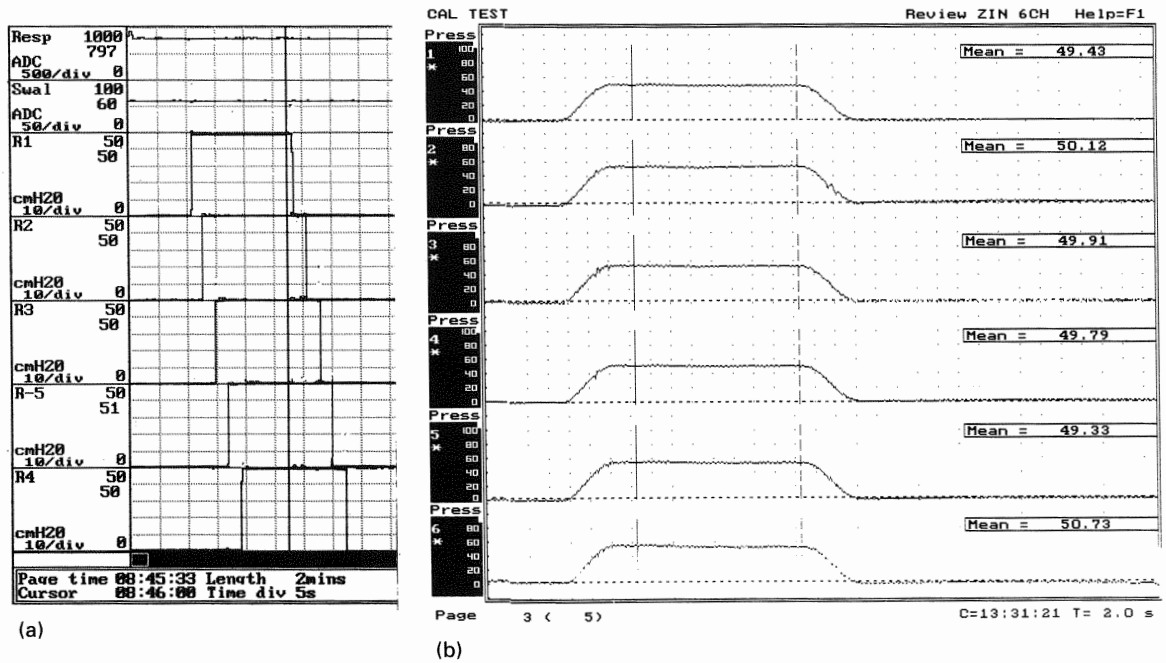
Fig. 3.9 (a) Example of sequential calibration check on each transducer using a water column. (b) Example of calibration signal recorded from each channel of a six channel water perfused catheter. The zero level is recorded by positioning the catheter at mid-axillary level of the supine patient, and the high pressure level by elevating the catheter to a height of 50 mmHg above the zero level.

Fig. 3.10 The system for oesophageal manometry using solid state catheter (C) and a personal computer (PC). The calibration tube is shown (CT). The interface box (B) links the catheter to the PC for data acquisition. The PC enables data display, analysis and hard copy printout.

and filled simultaneously is useful (Fig. 3.11a,b). Immersion times should be for the recommended period according to the current infection control department guidelines; this is typically a minimum of 20 minutes. Toxic substances such as activated glutaraldehyde should be used within a fume cabinet (with a special aldehyde absorption filter), to ensure minimum air pollution levels within the working environment as shown in Fig. 3.12. Current Hospital Health and Safety Guidelines (i.e. British Society of Gastroenterology Endoscopy Disinfection Guidelines) must be adhered to for protection of patients and staff. The catheter must be rinsed thoroughly and each lumen flushed with sterile water to remove all traces of glutaraldehyde. The catheter should be dried using medical grade compressed air and stored dry. If stored more than 6 hours after disinfection, the disinfection procedure must be repeated before reuse.
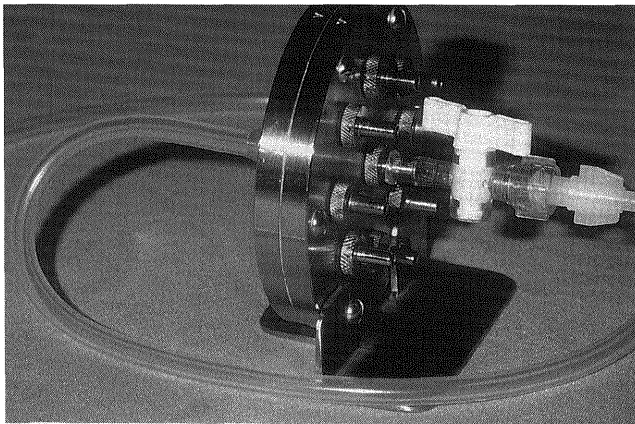
(a)
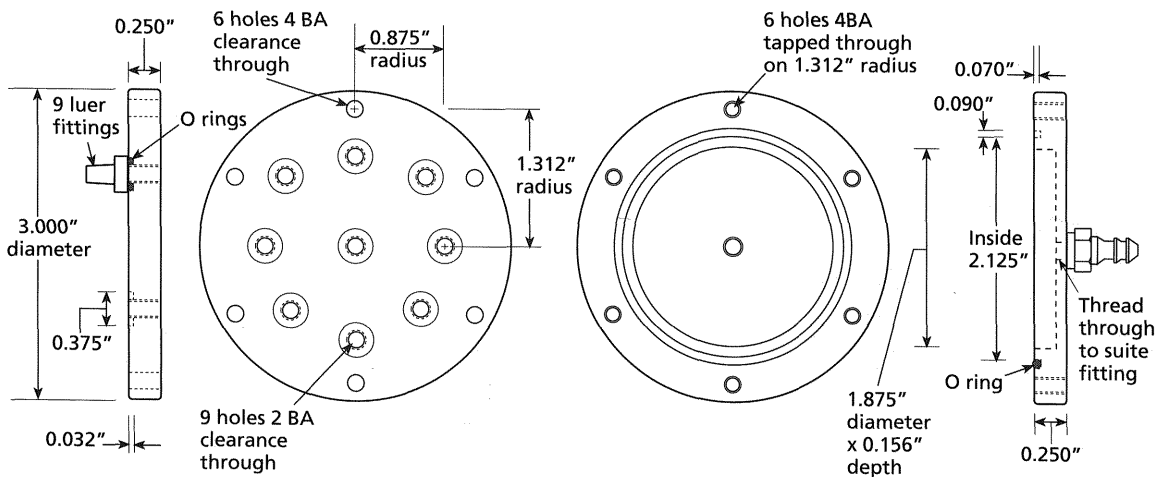
(b)

Fig. 3.11 (a) 'Hull' cleaning nine channel manifold. (b) Technical drawing of 'Hull' cleaning manifold.

Intubation

The ability of the technical staff to intubate patients should be ratified by the Health Authority/Trust, Head of Department and Clinical Consultant in charge as they have the ultimate responsibility for the patients.

Patient awareness and intubation

The patient's anxieties should be minimized by discussion with the investigator regarding their symptoms and the clinical relevance of the procedure to their condition. The patient should be fully informed about the procedure and written consent should be obtained prior to intubation. The operator should be fully aware of the patient's clinical history relevant to the procedure and all other significant medical problems such as respiratory or cardiac problems.

Diet restriction prior to procedure

Most centres require the patient to be fasted prior to the procedure to reduce the risk of aspiration during intubation. This may generate problems in certain patients, for example, diabetics in whom blood sugar levels must remain stable and fasting for a prolonged period may result in hypoglycaemia and fainting during the procedure. Fasting is usually for 4 hours with water allowed up to 2 hours before. Patients with conditions (e.g. achalasia) who are liable to have large volumes of retained oesophageal contents may require oesophageal washout to reduce the risk of inhalation of oesophageal contents, and reduce the volume of fluid in the oesophagus, but the large bore washout tube must not be allowed to pass through the lower oesophageal sphincter (LOS) as this can cause temporary dilatation affecting measurement. This is not routinely performed in the gastro-intestinal physiology department and would only be undertaken on recommendation by the referring doctor.

Medication restriction prior to procedure

Drugs affecting oesophageal motility such as prokinetic agents (which also include some migraine treatments) or Ca^{2+} antagonists should be stopped for 48 hours prior to the test [1]. Drugs for any other medical problems such as cardiac or thyroid dysfunction may be continued as normal, but allowance should be made for the effects of nitrites on the LOS. If an ambulatory pH test is also to be performed then acid suppressant therapy should be suspended prior to the test (see Chapter 4.2) [2,3,4].

Fig. 3.12 The fume cabinet is used for disinfection of the catheters and to house the glutaraldehyde containers. The filter is contained on top of the cabinet which both filters and recirculates the air.

Complications

Complications are vomiting, fainting, broncospasm or respiratory arrest. Investigators should therefore know their hospital's resuscitation procedure and where medical cover can be located instantly.

Intubation procedure

The patient may remove any dentures if they feel more comfortable without them. The catheter lumens should be pre-filled with sterile water and the lumens capped to retain this fluid; this helps prevent saliva and food debris from filling the lumens. The use of a local anaesthetic in the nose and throat to reduce discomfort during passage of the manometry catheter is optional. The first few centimetres of the catheter can be lubricated in a water-soluble gel to reduce friction during intubation. The patient should be seated during intubation, the catheter should be passed horizontally through the nares and into the oro-pharynx across the upper region of the hard palate (Fig. 3.13a,b). The investigator can detect swallows through the catheter as it enters the pharynx (about 15 cm from the nose; it can be useful if the catheter is marked at this level) and the patient experiences the tip of the catheter. At this point the patient should be asked to tilt the head forward towards their chest (see 'chin tuck' below) and to swallow (if difficult it can help to take sips of

water from a cup using a 'bendy type straw'). This will allow the catheter to progress easily through the pharynx and upper oesophageal sphincter. The catheter should be inserted sufficiently, so that at least three or more pressure measuring ports covering at least 10 cm are in the stomach. This can easily be ascertained by the presence of well-defined respiratory increases in pressure on inspiration and the absence of contractile activity when the patient is asked to swallow. Once the catheter is in position the patient should be asked to lie supine with one pillow under the head with the head straight [5] (and replace their dentures if removed). The catheter is connected to the transducers and infusion commenced; a period of at least 10 minutes should be allowed for stabilization of the patient's state and the recording system. This will allow any activity induced by the intubation procedure and the presence of the catheter to settle. The patient should be asked to limit their swallowing as the irritation caused by the catheter in the pharynx is heightened by repeated swallowing and the recording will take longer and will be more difficult to interpret.

(a)

(b)
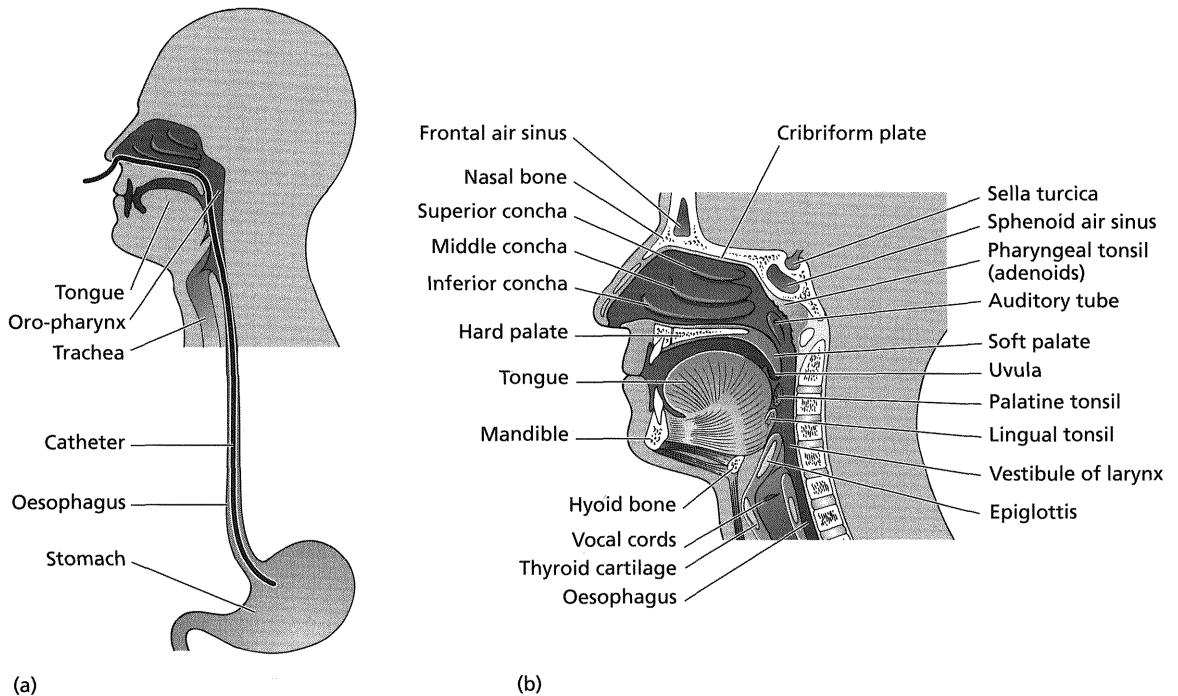
Fig. 3.13 (a) Diagram illustrating the anatomy of the oesophagus and the path taken by the manometry catheter via naso-gastric intubation. (b) Sagittal section through the face and neck. The nasal septum has been removed, exposing the lateral wall of the nasal cavity. Note the position of the conchae (turbinates). From reference [6].

Effect of head position on the dynamics of the upper oesophageal sphincter and pharynx

The 'chin tuck', or flexion of the head, is a standard technique to facilitate a safe swallow. As described by Logemann [7], this manoeuvre physically narrows the inlet to the airway by bringing the tongue base over the laryngeal vestibule, thus protecting the airway. In cases where there is a delayed initiation of the swallow and premature leakage of the bolus, this manoeuvre also widens the valleculae so that the bolus is held in the valleculae rather than spinning directly into the larynx. Conversely, if the head is extended, it mechanically widens the laryngeal vestibule and narrows the valleculae [5].

Monitoring of vital signs

Vital signs should be monitored during the procedure as naso-gastric intubation and anxiety can result in patients having vaso-vagal or fainting attacks. A three-lead electrocardiograph is useful in monitoring cardiac abnormalities in patients with chest pain or known angina. A nasal thermistor can be used to assess respiration. Pulse oximetry can be useful and will allow early determination of patient distress and so allow intervention and pre-empt any untoward event from occurring.

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3.3   Lower oesophageal sphincter: procedure and analysis

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Introduction

Lower oesophageal sphincter (LOS) tone can be measured using computerized systems or chart recorders as previously discussed. The method of measurement can greatly affect the recorded values and when comparing results this must be allowed for.

Three main techniques can be utilized:
1   Station pull-through (SPT).
2   Rapid pull-through (RPT).
3   Static Dent sleeve or sphinctometer.

For routine clinical use the SPT was considered by a working party from the British Society of Gastroenterology Clinical Measurement Associates to be the most informative and most easily standardized technique.

Equipment and procedure

Equipment

1   Water perfused system with inert gas or solid-state transducers.
2   Polygraph and/or computer.
3   Respiration sensor is useful to detect the pressure/respiratory inversion point (PIP, RIP).
4   Swallow sensor preferable to detect and differentiate between primary, secondary and tertiary contractions within the oesophagus above.
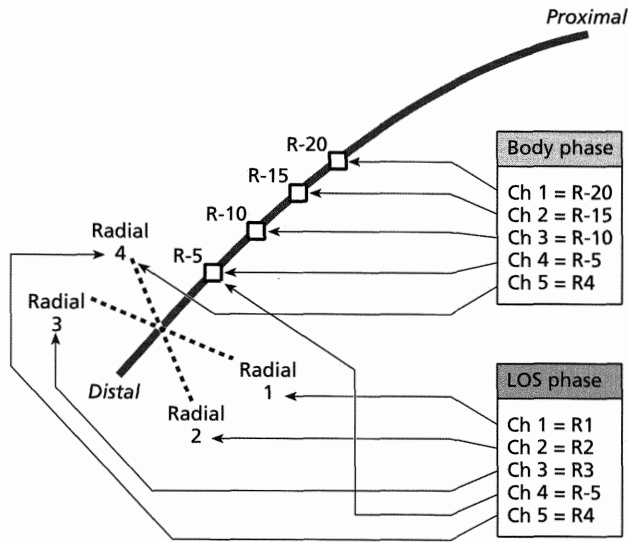
The recording sampling frequency should be a minimum of 8 Hz for the LOS.

High frequency filtering may be required if excessive cardiac interference is observed.

Because the LOS exhibits significant radial asymmetry (Fig. 3.14) [1] the use of a catheter with three or four radially orientated ports at the same distance from the nares, with at least one above, is desirable. The ideal eight channel plus central lumen catheter illustrated earlier in this chapter is recommended (Fig. 3.4, p. 20).

The central lumen can be useful in those patients with a tortuous oesophagus, strictures or suspected achalasia with very tight or narrow LOS. By introducing a 0.035" 'J' tip guide wire through the central channel, when the catheter is approaching the restriction, the guide wire can be advanced (ideally under

Fig. 3.14 Radial asymmetry of the LOS in 18 normal subjects. SPT: slow pull-through; RPT: rapid pull-through. With all methods pressures leftwards were significantly greater than rightwards (From [1]).

fluoroscopic guidance) until it enters the stomach. The catheter is then slowly advanced over the guide wire until the port 5 cm above the radial array is within the stomach. The guide wire is then slowly withdrawn and a plug put back over the channel cap, preventing venting or fluid drainage. A guide wire can also be useful for patients with a wide dilated oesophagus, where the catheter can become curled into a 'U' shape with further insertion causing the catheter tip to approach the pharynx from below; the true path of the catheter can be discovered by the radio-opaque guide wire as it is inserted. Catheters with the radial ports 5 cm from the distal tip are advised, since the direction and 'curl' of the catheter is held in a uniform manner as it is withdrawn through the proximal part of the sphincter. This extended tip also allows easy re-introduction of the catheter into the stomach for a second LOS pull-through, since part of the tip will still be within the LOS when the radial ports have reached the oesophagus. This is particularly useful in patients with tight LOS junctions where re-introduction can be difficult because, for most catheter materials, the catheter is less stiff due to it having reached body temperature and cannot be advanced as easily as before.

With an eight lumen catheter, using only five lumens at each phase produces sufficient information, but does not infuse excessive volumes of water, yet enables a large scale for each channel on the monitor allowing easy discrimination of minor pressure variations. (The use of different colours for each channel on the monitor and printout also makes for easy interpretation, particularly where traces overlap.)

Fig. 3.15 Connecting order for an optimal five transducer system with an eight port catheter. Changing from LOS phase to oesophageal body phase only requires three lumens R1, 2 and 3 exchanging for R-10, R-15 and R-20.

If the transducers are connected in the order first, one radial port, second, the port 5 cm proximal, then the second, third and fourth radial ports, then after completion of the LOSP (LOS pressure) measurement, in order to assess the oesophageal body, only the second, third and fourth radial ports need to be transposed, in the order: first the port 20cm proximal to the radial array (R-20), then R-15 followed by R-10, since R-5 and one of the radials (R) are already connected. This saves time and also reduces the possibility of introducing air bubbles during re-connection (Fig. 3.15).

Calibration

Calibration of the system is essential, as previously discussed. The maximum range (full scale deflection) for each channel measuring the LOSP should be approximately 50 cmH$_2$O (50 mmHg, 5 kPa) so that maximum detail can be observed during recording.

Procedure

Prior to intubation, the transducers should be zeroed to atmospheric pressure. The zero level of the transducers should be at the level of the LOS with the patient supine, 10 cm above the top of couch (from a series of magnetic resonance imaging (MRI) measurements). Alternatively position the transducer zero at the mid-axillary line. It may be useful to raise artificially the zero level of the transducers by 10 cm in order to prevent the maximum positive respiratory oscillations from over-ranging off the top limit of the chart recorder or screen. This method is useful unless the LOSP is very high or the patient is obese where gastric baseline is elevated. A

similar effect can also be achieved by applying a 'voltage backoff' to the transducer/amplifier output signal.

Patients should be supine, in a comfortable position and with the head elevated on one pillow and facing upwards. Any tight clothing or belts should be slackened, the legs can be crossed but not raised in the bent knee position and patients should not rest their arms over their stomachs as this can increase gastric pressure. After intubation the catheter is connected to the transducers or system and, for infusion systems, perfusion is commenced. A 10 minute settling time is then allowed, during which the respiration and swallow sensors are applied and the patient asked to become accustomed to not swallowing unless unavoidable. If they experience difficulty in complying with this, an oral suction tube can be used to remove saliva or regurgitated fluid.

The recording is commenced and the trace observed whilst asking the patient to take a deep breath in and hold it momentarily; a rise in pressure in all channels will indicate correct positioning and the performance of the respiration sensor. A dry swallow is then requested to confirm the response of the swallow detector. Trace speed/scroll rate around 8cm per minute gives good discrimination during recording.

The catheter is then withdrawn using the station pull-through technique at 0.5 cm stations. The time spent at each station (from when the recording port reaches within 5 cm of the distal margin of the LOS) should be long enough to obtain five consecutive stable end expiratory values [2]. An advantage of first observing the LOS with the port 5 cm proximal (R-5) to the radial array is to gain an initial assessment of its position, length and appearance. The catheter is withdrawn in this manner until the radial array has entered the oesophagus (the end expiratory baseline normally being approximately 0 to −5 cmH$_2$O); this can be confirmed by requesting the patient to swallow and observing the response of the radial array compared with R-5 (Fig. 3.16a,b,c). The catheter is then slowly re-introduced 3–4 seconds after asking the patient to swallow, until port R-5 is again within the stomach. The withdrawal procedure is then repeated a second time. Two pull-throughs should be sufficient unless there are great inconsistencies between individual ports/recorded sites, when further pull-throughs should be performed until consistent values are obtained.

Wet swallows are performed during the second pull-through to assess LOS relaxation, with the radial array at the site of maximum sphincter pressure within the abdominal component (i.e. before the PIP). At least two 5 ml wet swallows are given with the time intervals between the wet swallows being a minimum of 20 seconds after the end of the previous swallow complex in the distal oesophagus.

Analysis

The following measurements are required for LOS analysis (see p. 38).
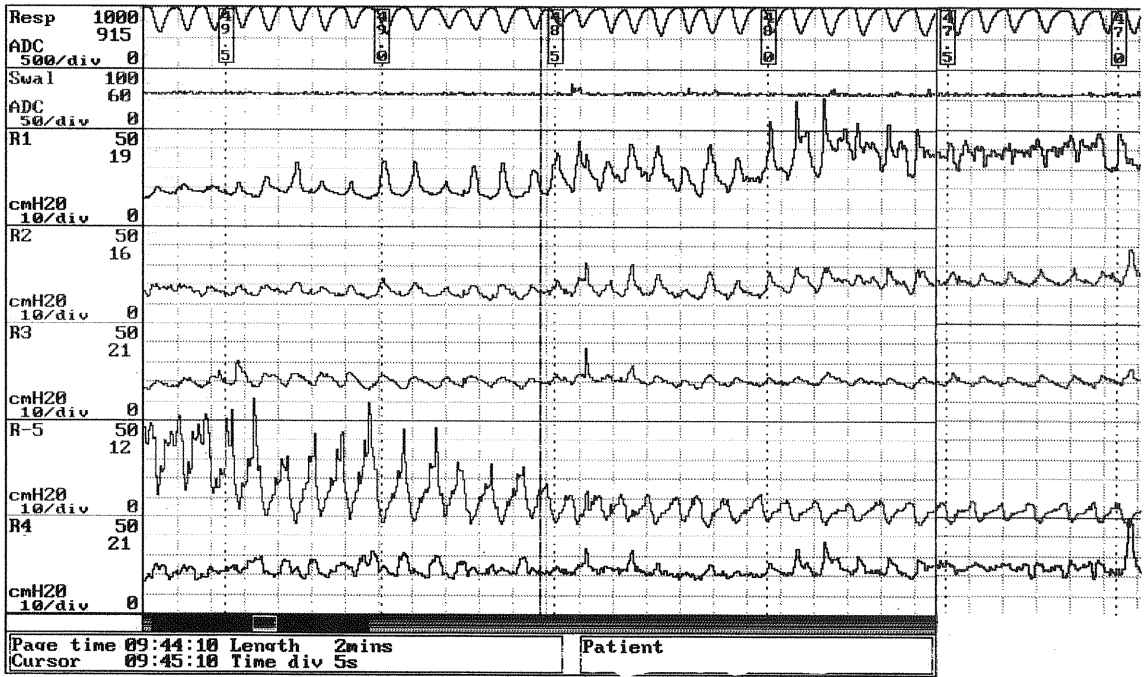
(a)
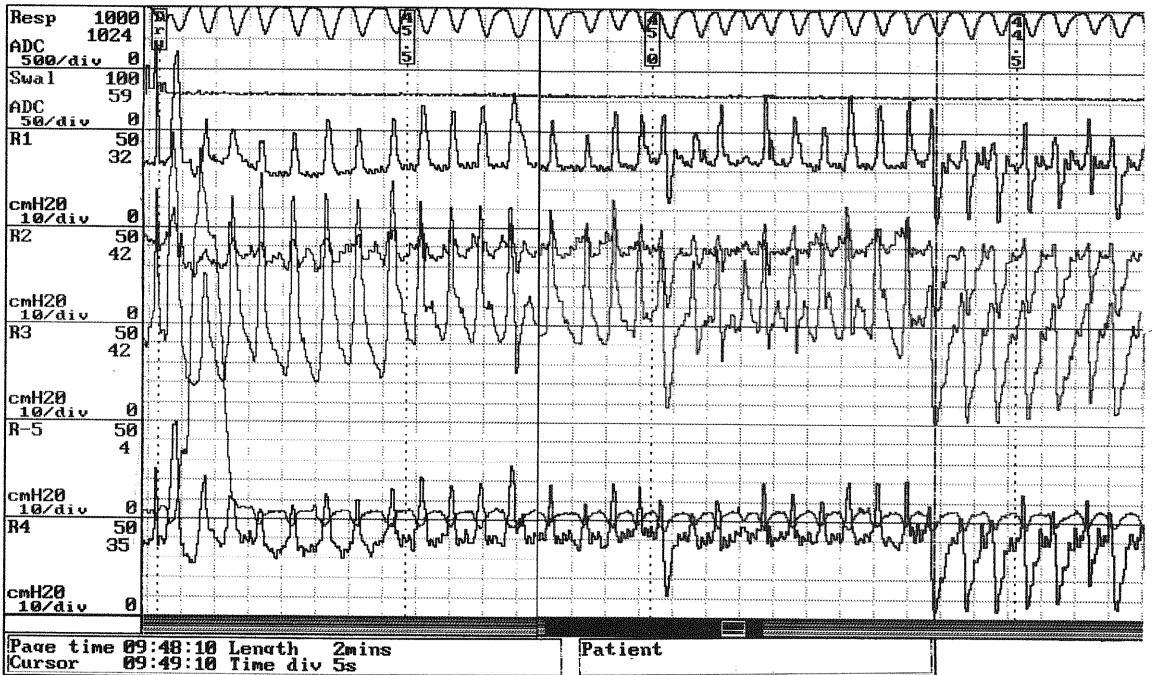
(b)

Fig. 3.16 (a,b) Part of station LOS pull-through, from R-5 just entering oesophagus to all within oesophagus.
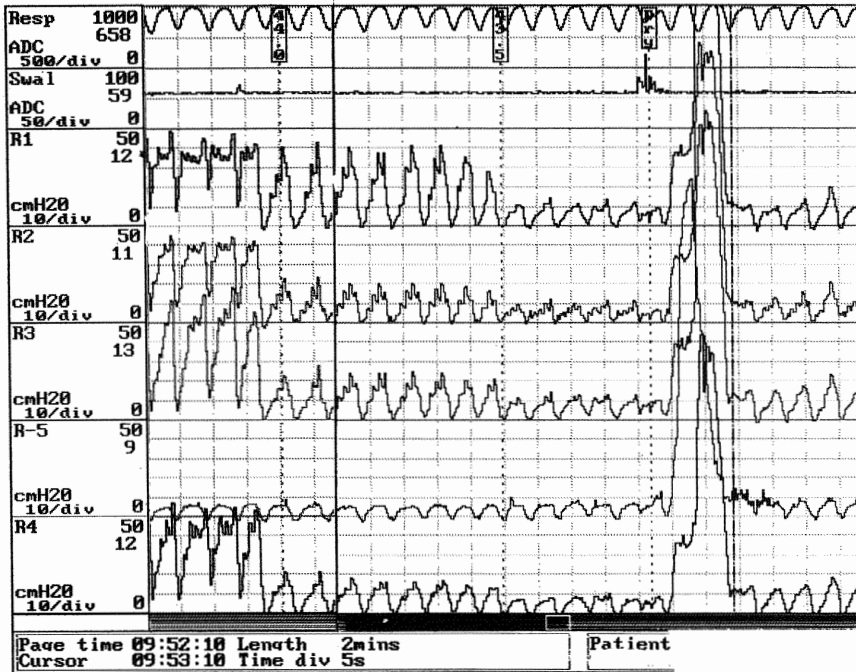
NB. Here, five sequential pages of the trace are combined to make four.

For Fig. 3.16(c) see p. 38.

Trace information—lectromed oesophageal motility system (Figs 3.16–3.27)
Top trace—respiration thermistor; second trace—swallow microphone. Other traces as labelled in left-hand boxes. In each box, top figure is full scale, e.g. 50 cmH$_2$O, but each
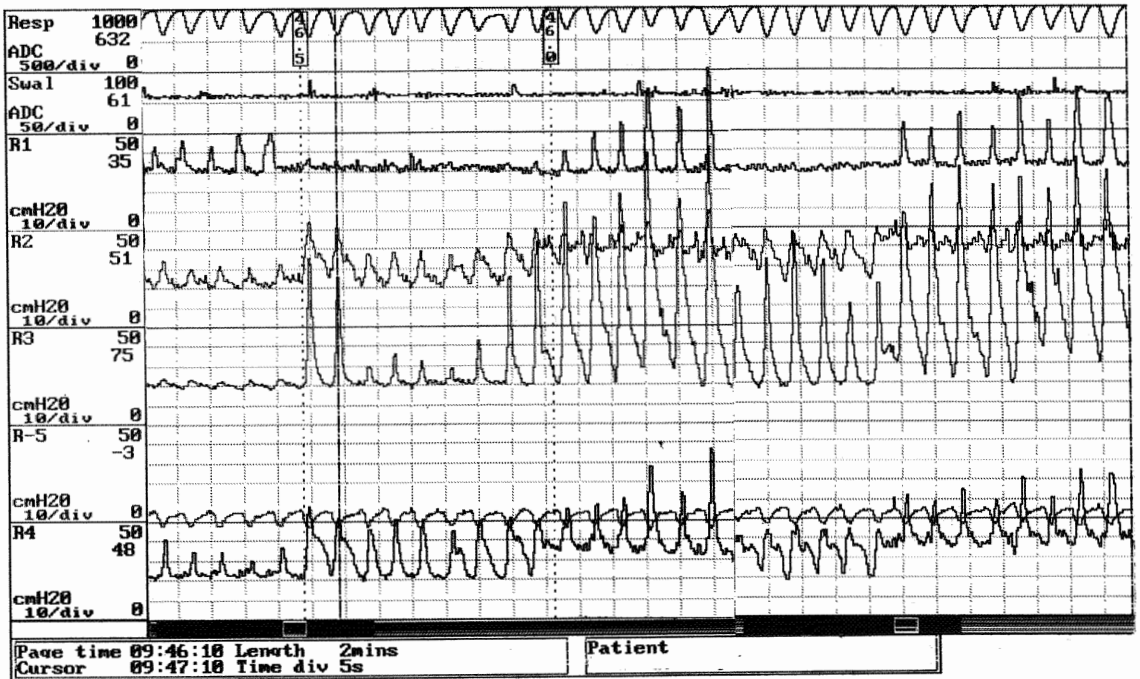
(a)

(b)

Fig. 3.16 (a,b) *Trace information continued.* trace continues at same scaling into next channels when over-range; next figure is pressure value at position of cursor, shown by vertical black line. Length—time per page; time div—time between faint vertical lines. Distances at top margin—cm to nares. Wet—wet 5 ml water bolus swallow. Dry—dry swallow. Breath—Deep breath. These markers are manually entered and hence are several seconds after the event.
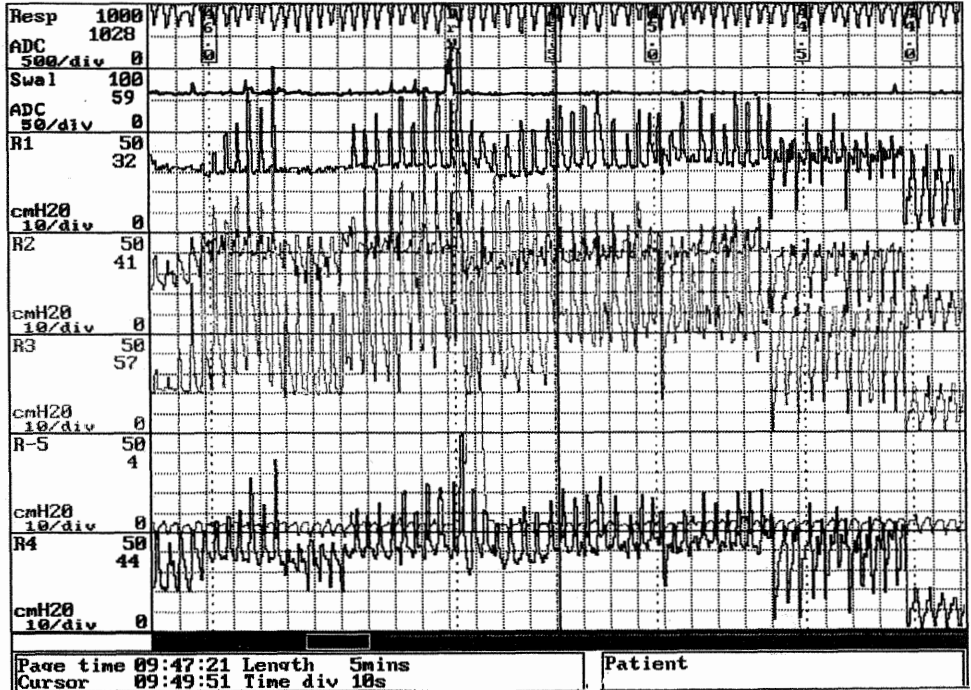
Fig. 3.16 (c) Overall LOS station pull-through compressed onto one page.

Gastric baseline

An average of 10 end expiratory pressure measurements taken within 5 cm from the distal margin of the LOS (Fig. 3.17) signified by either:

1 a step up in baseline pressure;
2 a marked increase in respiratory excursions.

If neither is observed then baseline measurements are taken 5 cm distally to the PIP.

Lower oesophageal sphincter

Distal margin

This is characterized by a 'step-up' in the end expiratory baseline pressure of more than 2 mmHg above gastric baseline [3], e.g. at 48.5 in R1 in Fig. 3.16a.

Sphincter pressure—abdominal component

The site of maximum end expiratory pressure in the abdominal component is chosen [4,5].
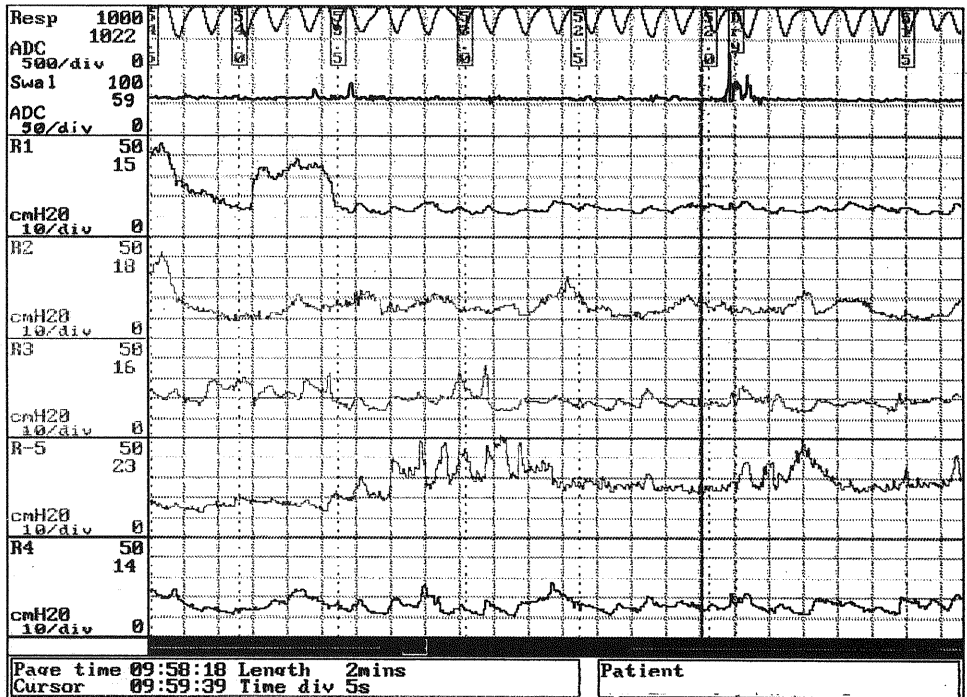
Fig. 3.17 Gastric baseline, measured in R1/2/3 and 4, stable from 53.5 cm to nares.

A mean of five stable end expiratory values is determined. This is repeated for each port/recording site.

Sphincter pressure—thoracic component

This is determined as previously but the site of maximum end expiratory pressure proximal to the PIP is chosen.

Pressure (respiratory) inversion point (PIP, RIP)

Where the end expiratory pressure changes from a negative to positive deflection, e.g. at 44.5 cm to nares in R1 (Fig. 3.16b).

Proximal margin

Characterized by a 'step-down' in end expiratory pressure, e.g. at 43.5 cm in R1 (Fig. 3.16b).

Intra-abdominal component of the LOS

Length of sphincter from the distal margin to PIP.

Intra-thoracic components of the LOS

Length of sphincter from the PIP to the proximal margin. The overall LOS length and intra-abdominal and intra-thoracic components should be reported for each channel.

LOS relaxation

This is measured at the site of maximum intra-abdominal sphincter pressure (Fig. 3.18a,b). Relaxation is expressed numerically for each port/recording site. Overall response is classified as being:

1   complete;
2   incomplete or partial;
3   inconsistent;
4   absent.

Normal relaxation is <5 mmHg above the gastric baseline pressure.
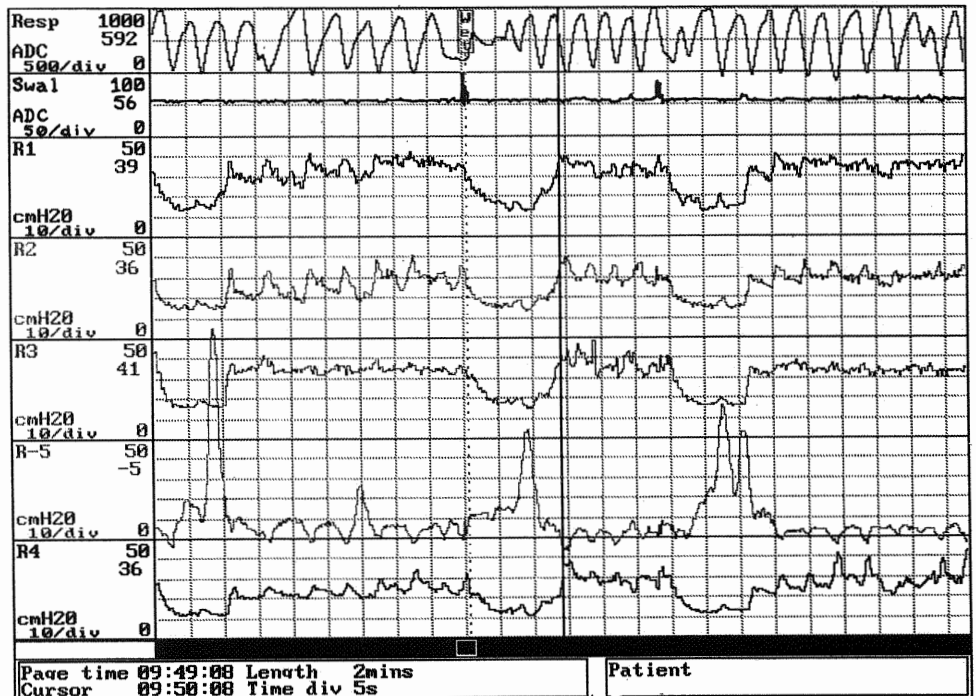
(a)

Fig. 3.18 (a) LOS relaxation on wet swallow.
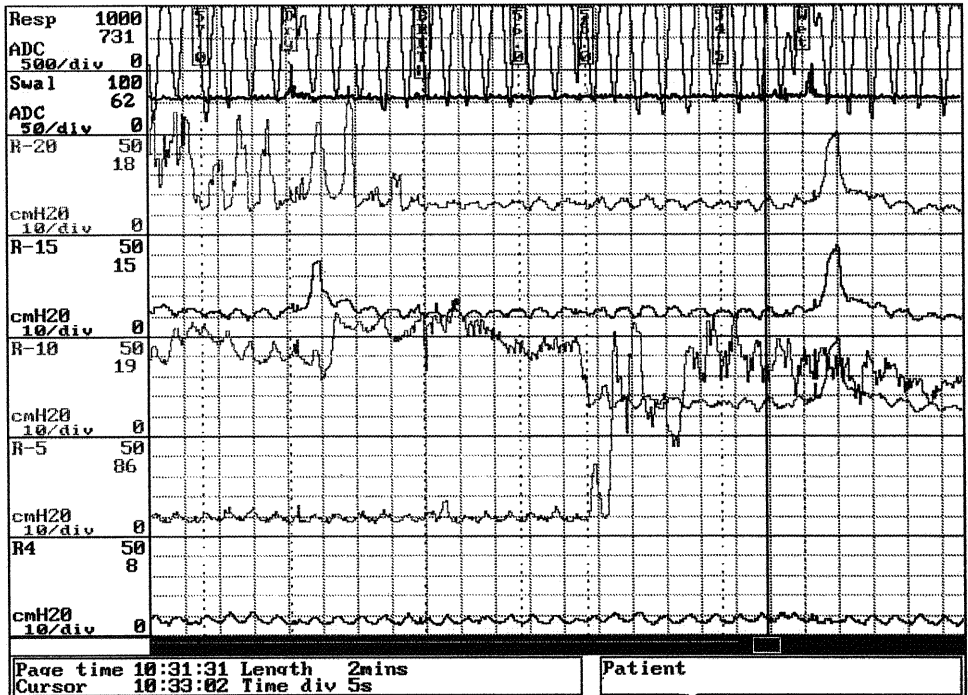
(b)

Fig. 3.18 (b) Virtually absent LOS relaxation on wet swallow in achalasia in R-5. Note raised oesophageal baseline in R-10 above 55 cm to nares where R-10 enters the oesophagus.

Report

LOS pressure

Abdominal component; pressure and length.
Respiratory inversion point; position and pressure.
Thoracic component; pressure and length.

LOS relaxation

Actual residual pressure above gastric baseline.
Relationship to oesophageal wave.
Duration of relaxation.
Asymmetry of relaxation requires commenting on.

Complications influencing measurement

1   *Gastric contractions*. Use of end expiratory values avoids errors caused by large excursions due to respiration and to a limited extent those resulting from large gastric contractions. The migrating motor complex (MMC) affects LOSP and has a duration ranging from 15 to 180 minutes. It consists of three phases:

Phase I—lasting approximately 30 minutes, with only a few contractions in the antrum.

Phase II—lasting approximately 80 minutes, with intermittent contractions of low amplitude.

Phase III—lasting approximately 10 minutes with groups of 2–3 contractions every 1–3 minutes.

All phases produce an effect on LOSP which becomes greatest in Phase III; the increase in LOSP can be as much as 100% (Fig. 3.19) [6,7].

Contractions are usually three per minute and occasionally one per minute (Fig. 3.20a,b).

2   *Large respiratory excursions*. If the transducers are zero balanced in the stomach, it is difficult to know whether this was done during the inspiratory or expiratory phase of the respiratory cycle and also if there was any gastric activity at that time.

3   *Excessive cardiac interference*. End expiratory values become difficult to measure due to cardiac oscillations (Fig. 3.21).

4   *Multiple swallowing*. A stable period of five expiratory excursions between swallow activity can be difficult to obtain, since the record may take up to 2 minutes to stabilize after each swallow.
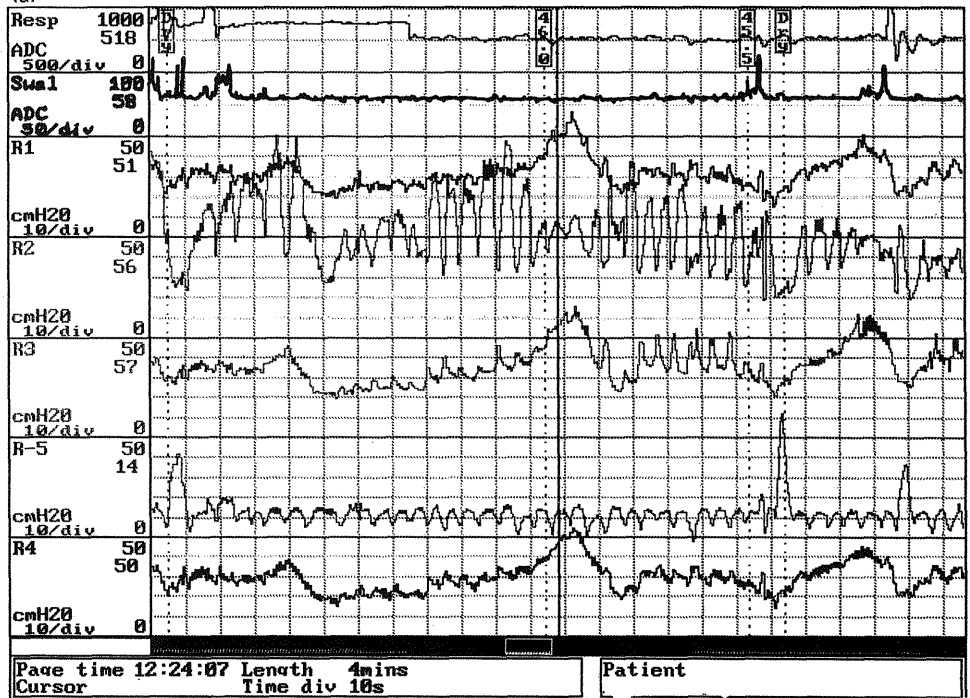
5   *Oesophageal spasm and secondary contractions*. The effects are similar to those in point 4 above. The use of a swallow recorder [8] is useful to differentiate between primary and secondary or tertiary oesophageal contractions.
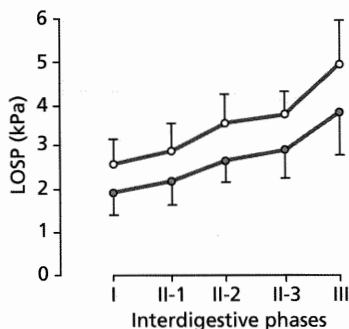
**Fig. 3.19** Effect of migrating motor complex on LOSP (from [7]).
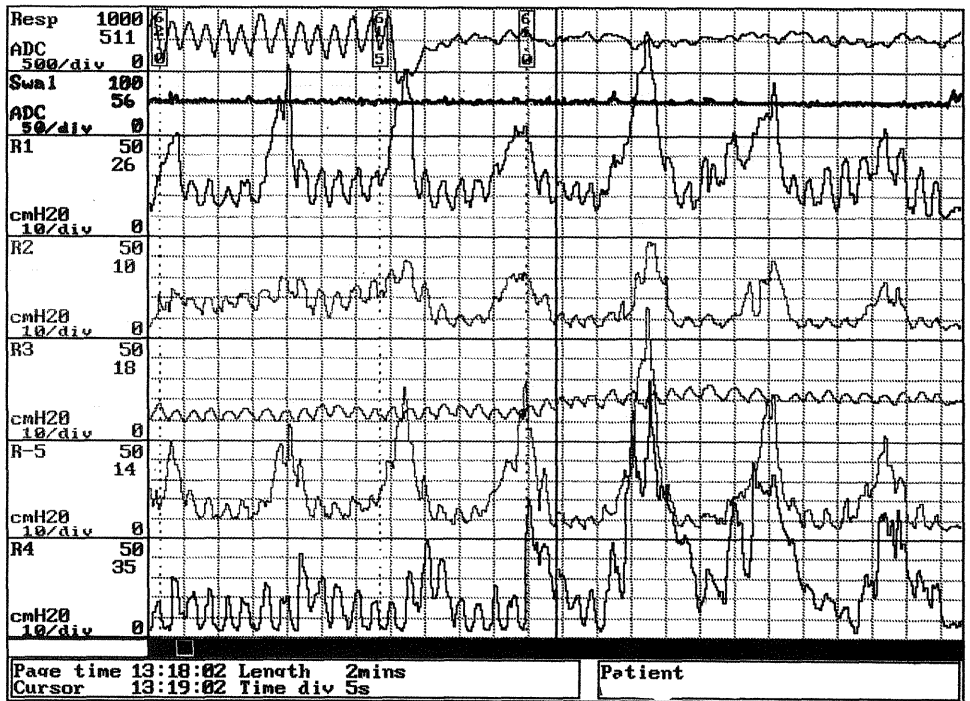
Fig. 3.20 (a) Radial and R-5 ports within stomach illustrating gastric contractions at 3 per minute evident in all ports except R3. (b) Radial ports within LOS, R-5 in lower oesophagus. Gastric contractions 1 per minute; note radial asymmetry of LOS, R2 is in the thoracic zone with respiratory excursions synchronous with R-5 in the oesophagus, whilst other radial ports are still abdominal.
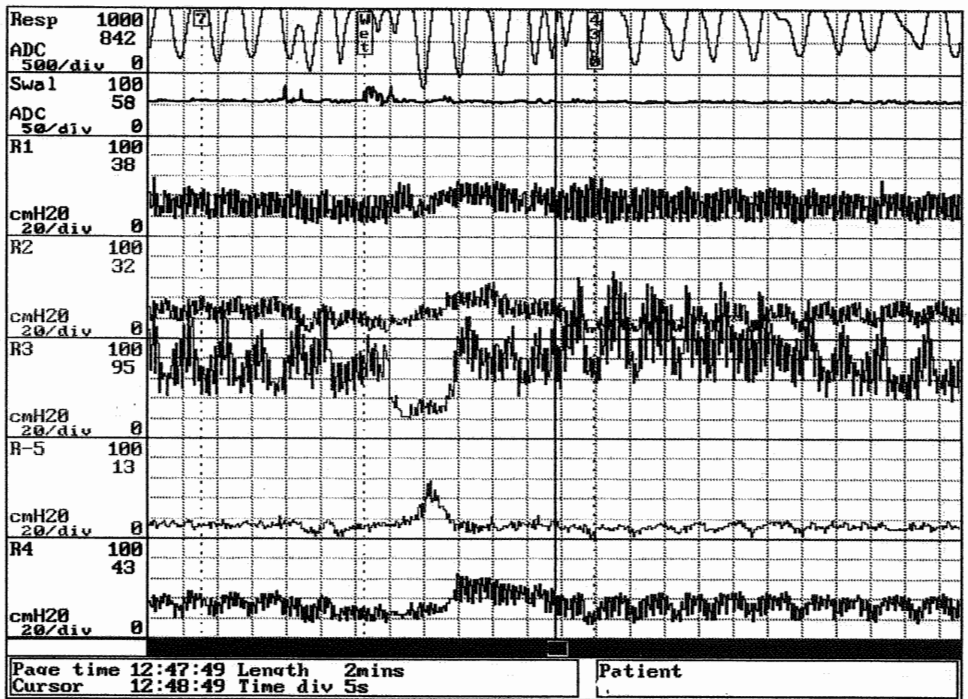
Fig. 3.21 Cardiac oscillations in radial ports within the LOS.

6 *Changes in respiration—deep breaths and sighs.* Deep breaths, etc. can move the catheter position in relation to the LOS and simulate relaxation (Figs 3.22a,b, 3.23, 3.24).

7 *Hydrostatic effect with water-perfused catheters for obese patients.* It is sometimes necessary to increase range to accommodate raised gastric baseline whilst maintaining maximal respiratory excursions within record (compare Figs 3.17 and 3.25).

8 *Asymmetry.* The start, maximal abdominal component and proximal margin are often not at the same distance for each of the four radial ports. The relaxation in response to wet swallows should be repeated for each port at the position of its maximal value if this is the case. The upper margin of the LOS used to calculate the position for the series of wet swallows and for oesophageal pH probe placement should be the most proximal of the radial LOS distances. Figure 3.26 illustrates a simple case where the proximal margin is at the same distance (47.0 cm to nares) in all the radial ports.

9 *Hiatus hernia.* In patients with a hiatus hernia there may be a double PIP. It can also be difficult to assess LOS relaxation since the abdominal component is usually
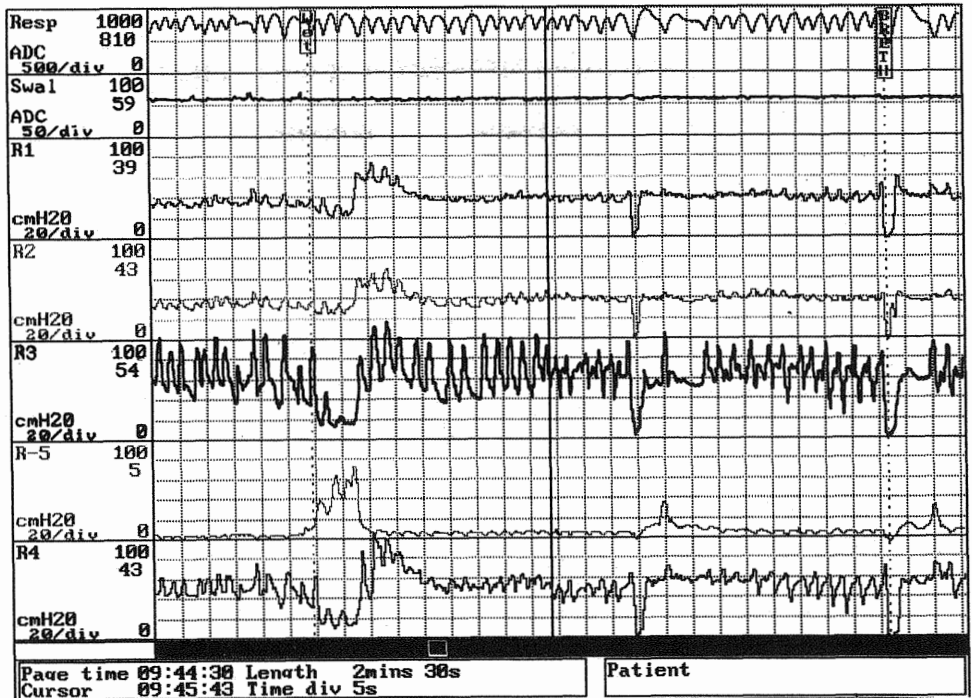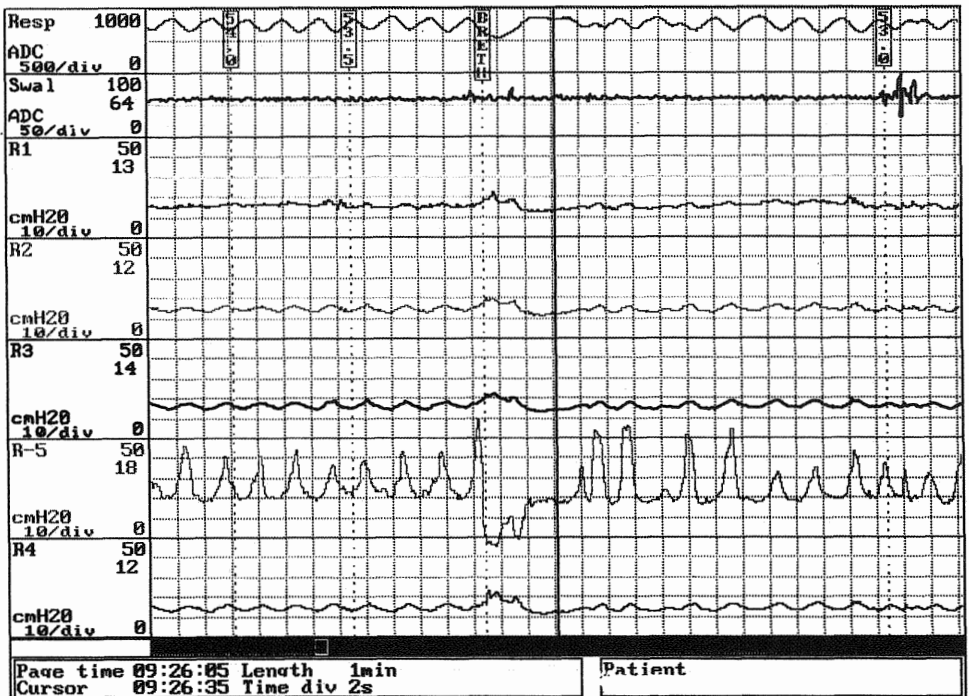
Fig. 3.22 (a) Deep breath whilst radial ports within LOS simulates relaxation, with detectable change in respiration record. In this trace there is a further deep breath to the right of the cursor, approximately 45 seconds before the marked breath. (b) Deep breath showing similar effect to (Fig. 3.22a, R-5 is within the LOS, R1/2/3 and 4 are still gastric and show the increase in gastric pressure on inspiration.
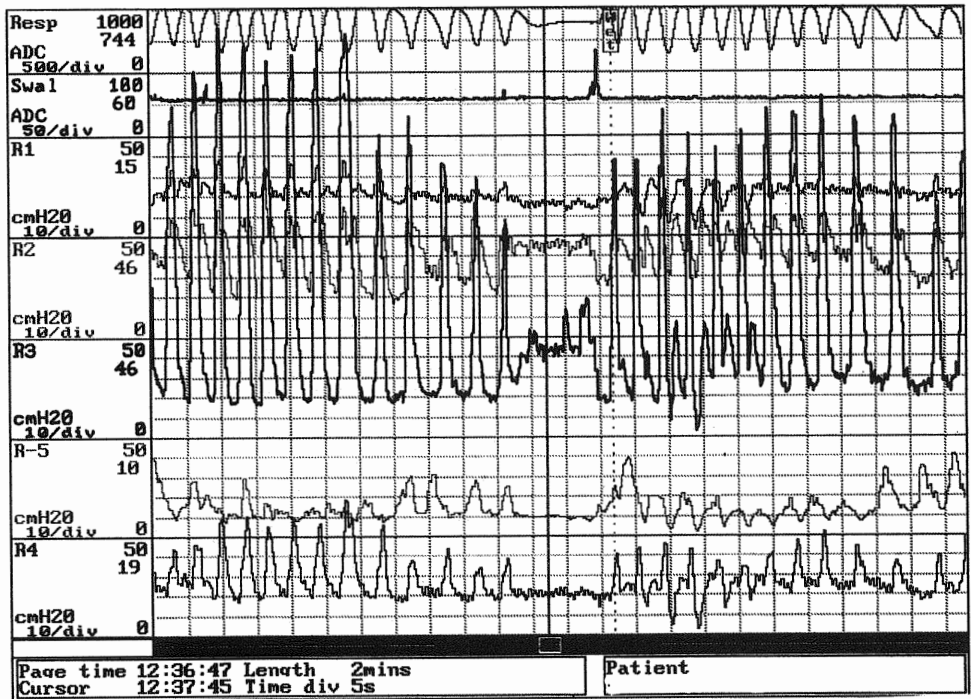
Fig. 3.23 Effect of breath holding prior to wet swallow, R1/2/3 and 4 within LOS, R-5 just within the oesophagus.
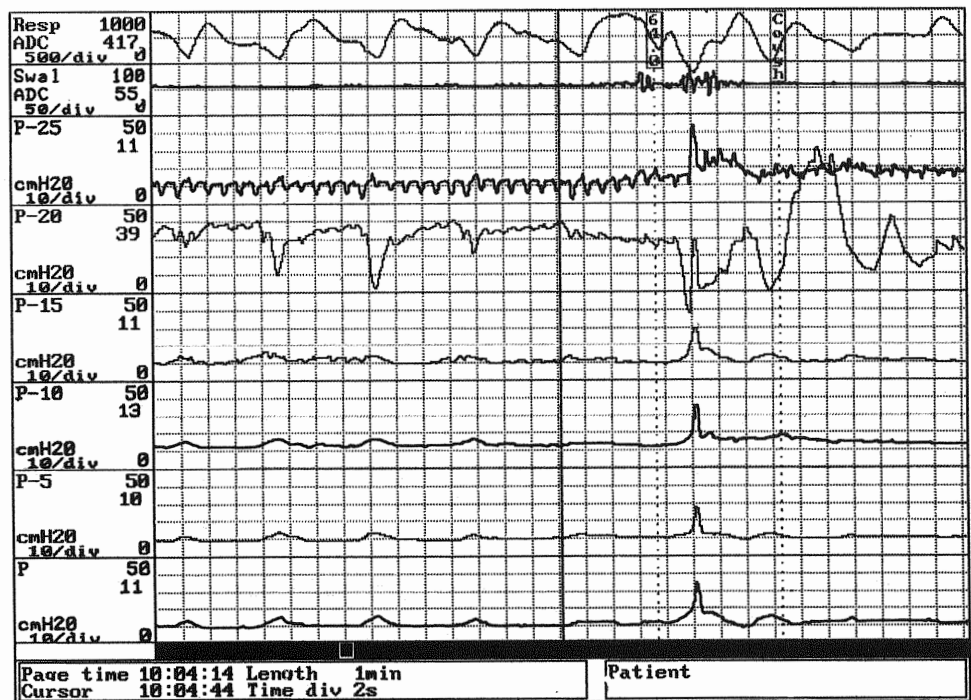

Fig. 3.24 Effect of cough, P-25 in oesophagus, P-20 in LOS, P-15, P-10, P-5 and P all gastric. Cough is 6 seconds before typed marker and shows increase in gastric and oesophageal pressure. The six sensor solid-state catheter has 5 cm spacing between each sensor.
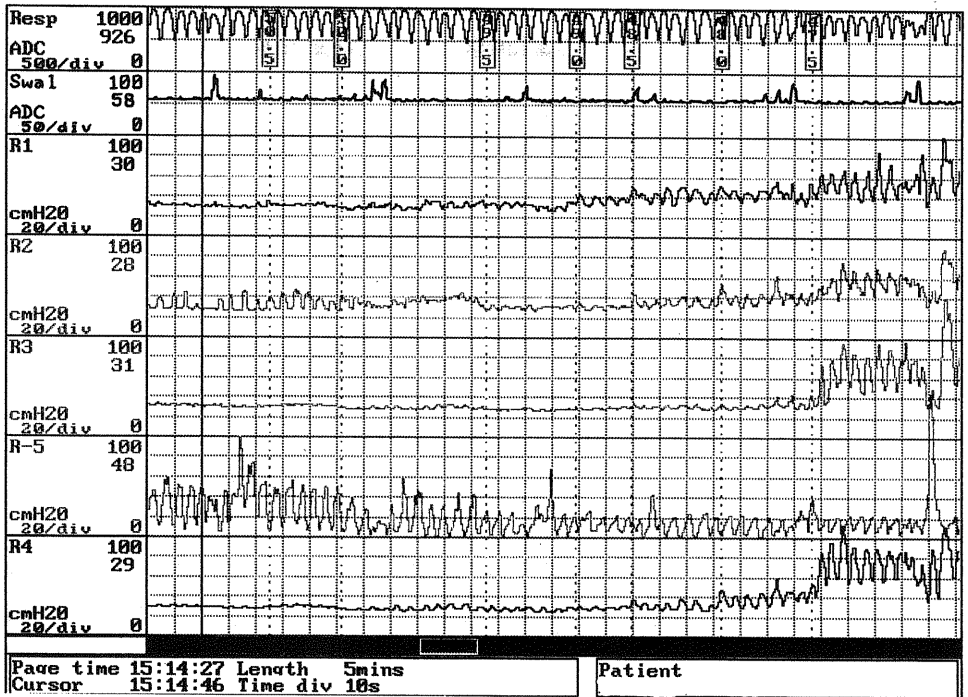
Fig. 3.25 Raised gastric baseline in an obese patient; R1/2/3 and 4 are gastric until 47.5 cm to nares. Note scale is now 0–100 cmH$_2$O not 0–50 cmH$_2$O, compared with Fig. 3.16.
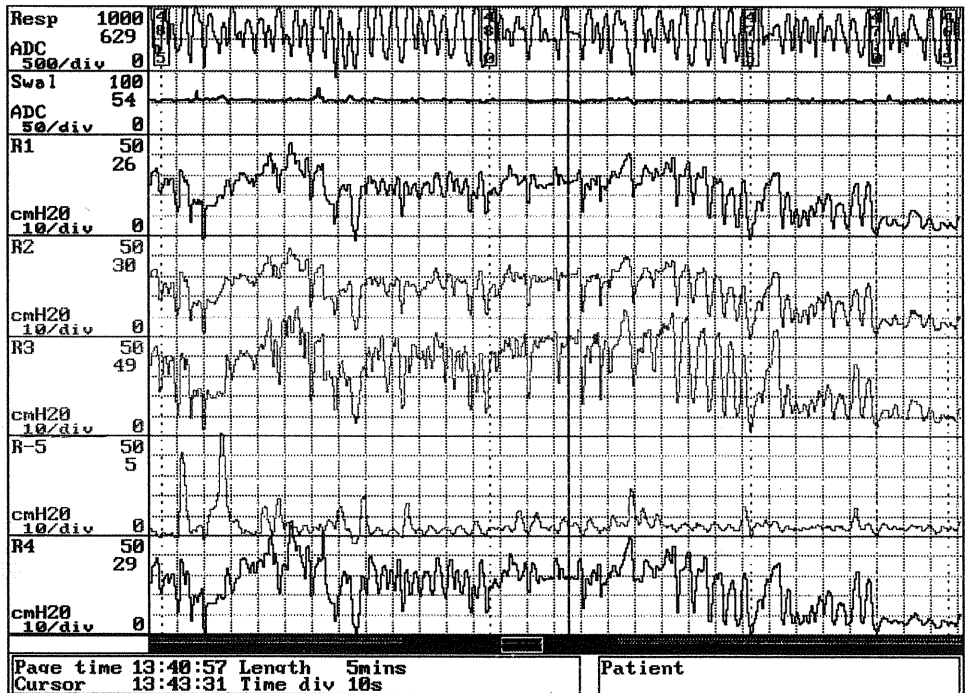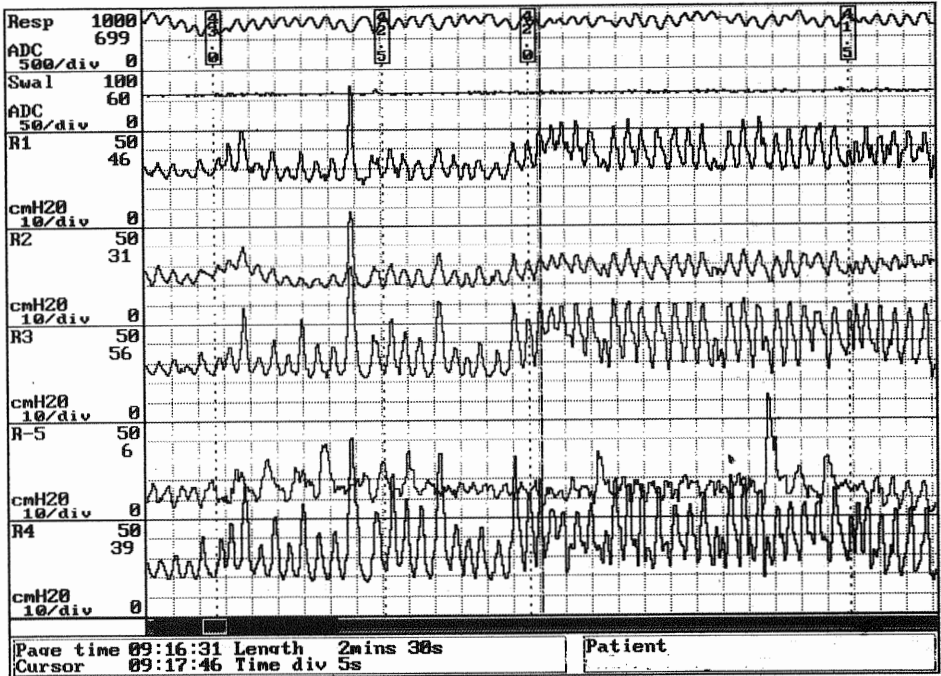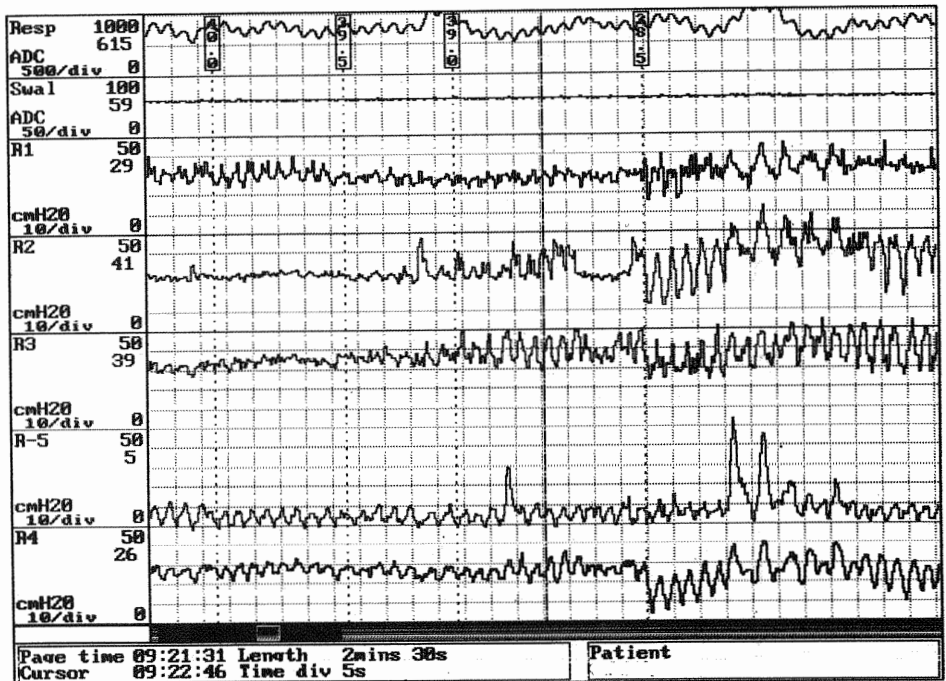

Fig. 3.26 R1/2/3 and 4 in thoracic zone of LOS, R-5 in oesophagus until proximal margin of LOS is reached at 47.0 cm to nares in all radial ports.

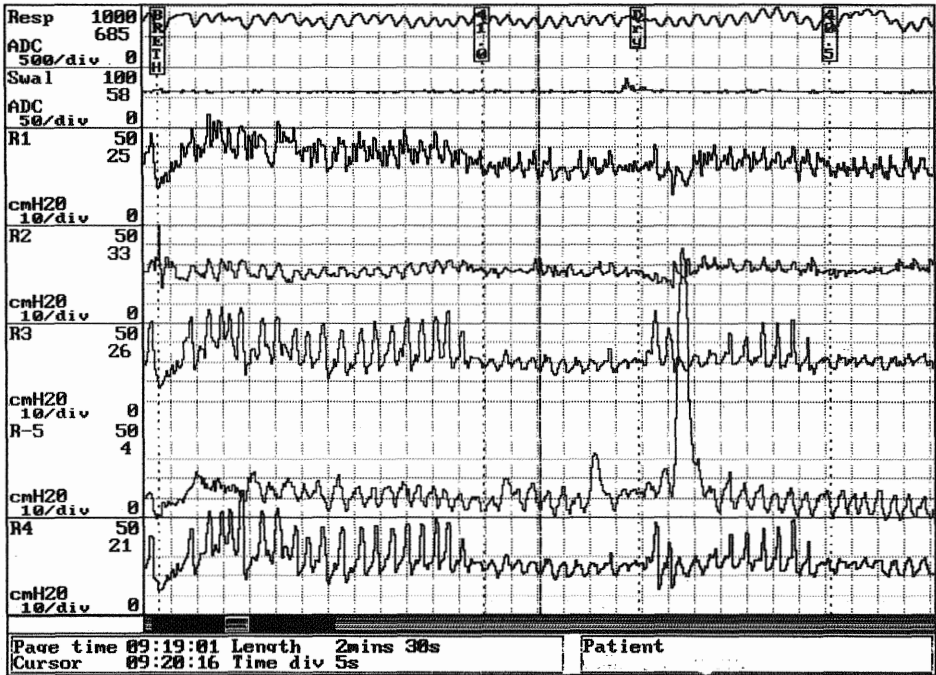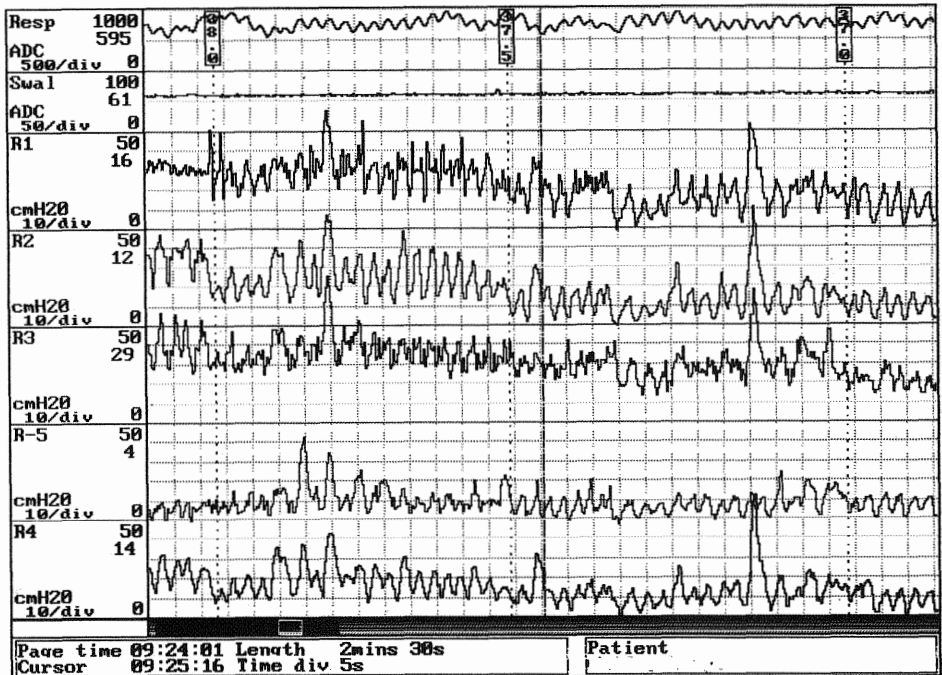(a)

(b)

Fig. 3.27 (a,b) Hiatus hernia seen from 41 to 38.5cm to nares in radial ports. Note reduced respiratory excursions within hernia. Traces continue on facing page.

(a)

(b)

Fig. 3.27 (a,b) *Continued.*

short and poor relaxation can be confused with the lack of response to swallows within the hernia (Fig. 3.27a,b).

10   *Dysphagia aortica*. Vascular compression at the LOS can make LOSP and relaxation measurements difficult [9].

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3.4   The oesophageal body: procedures and analysis

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Oesophageal manometry

Equipment calibration

The recording system should be accurately set up according to the method on pp. 19 and 25 and with reference to the manufacturer's recommended procedure.

Positioning

The patient should be supine and comfortable (see p. 30).

Procedure

In its basal state the oesophageal body is a collapsed, empty tube with a pressure negative in relation to atmospheric pressure and shows only small pressure variations in phase with respiration. Activity is only normally seen on swallowing which occurs at regular intervals to remove secretions from the oro-pharynx. This also clears the oesophagus of gastric refluxate and oesophageal secretions [1–3].

Recording manometric data

A station pull-through in 1 cm steps is the commonest method of manometric assessment of oesophageal body function [4]. Following detailed assessment of the LOS, the catheter is moved outwards in 1 cm steps. Each step is maintained for at least ten respiratory excursions so that the baseline activity can be adequately assessed and any zones of compression (raised oesophageal baseline) due to extrinsic structures, e.g. aorta, bronchus, left atrium, etc. and also oesophageal strictures, webs, etc., observed. Swallow-induced characteristics must be assessed with the catheter positioned such that the distal recording site is 3 cm proximal to the uppermost margin of the LOS. Ten 5 ml water bolus swallows at 20–25°C should be undertaken with the water given via a calibrated syringe with the patient supine (Fig. 3.28) [5–7]. A fixed bolus volume will generate a reproducible degree of pharyngeal and oesophageal body distension and so promote an optimum contractile response. Figure 3.29 illustrates the variation in amplitude between wet and dry swallows [8,9]. Twenty seconds should be allowed after the end of contractile activity in the distal oesophagus between each water bolus to allow recovery and a more reproducible response will be generated. If too short an interval is allowed then inhibition of the propagated response will be induced and inaccurate data recorded. Figure 3.30 illustrates the inhibitory effect of repeated rapid swallowing on peristalsis. If the patient swallows spontaneously between the water bolus swallows, or there are secondary or tertiary contractions, then a similar time period should be allowed before the next bolus is given [10–13]. If the position for wet swallows is such that one of the ports is within a zone of oesophageal compression, peristalsis may be difficult to assess at this level, but this may be noticeable in only one radial direction (Fig. 3.31a,b). If the recording sites do not span the full length of the oesophagus, then the catheter must also be repositioned at a higher level, such that one port is within 5 cm of the crico-pharyngeal sphincter, to investigate the remainder (upper oesophagus) with a further series of ten water bolus swallows. The optimal position is with the most proximal port within the crico-pharyngeal sphincter (Fig. 3.28) (which allows a clear distinction between single and double swallows and also differentiates between secondary contractions) and the next port in the upper oesophagus.
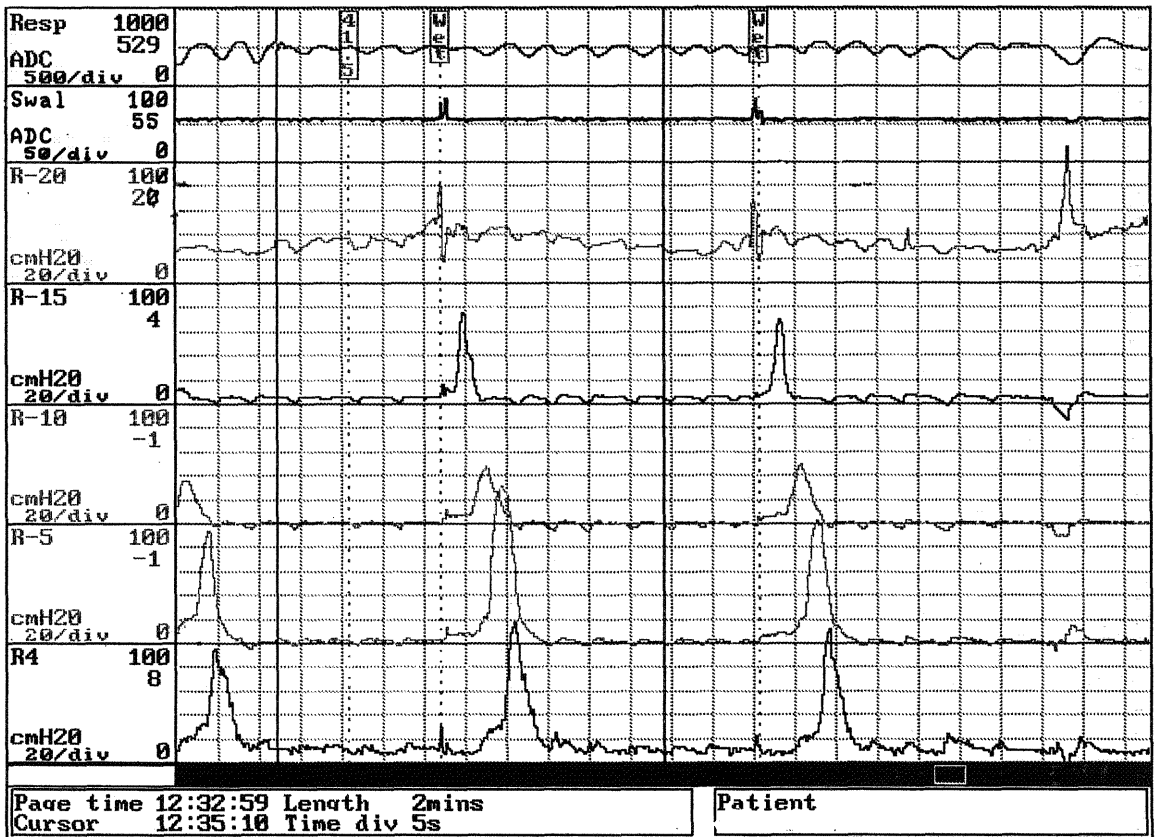
Fig. 3.28 Primary contractions on series of wet swallows, R-20 is in the crico-pharyngeal sphincter (CPS), bottom channel (R4) is 3 cm above the LOS with R-5/-10/-15/-20 at 5 cm intervals above.

Trace information–lectromed oesophageal motility system as for section on LOSP (see p. 36). All traces are shown with the distal port R4 at 3 cm above the LOS unless otherwise described. Cursor position is shown by the heavy vertical black line.

The use of a swallow transducer greatly eases the distinction between single and double swallows and secondary contractions whilst a respiration transducer can detect breath holding, etc.

A crude assessment of UOS position, baseline pressure and relaxation can be achieved by a further pull-through of at least three radial ports through the crico-pharynx (Fig. 3.32). However, accurate assessment of the UOS requires the more sophisticated approach discussed in Chapter 6.
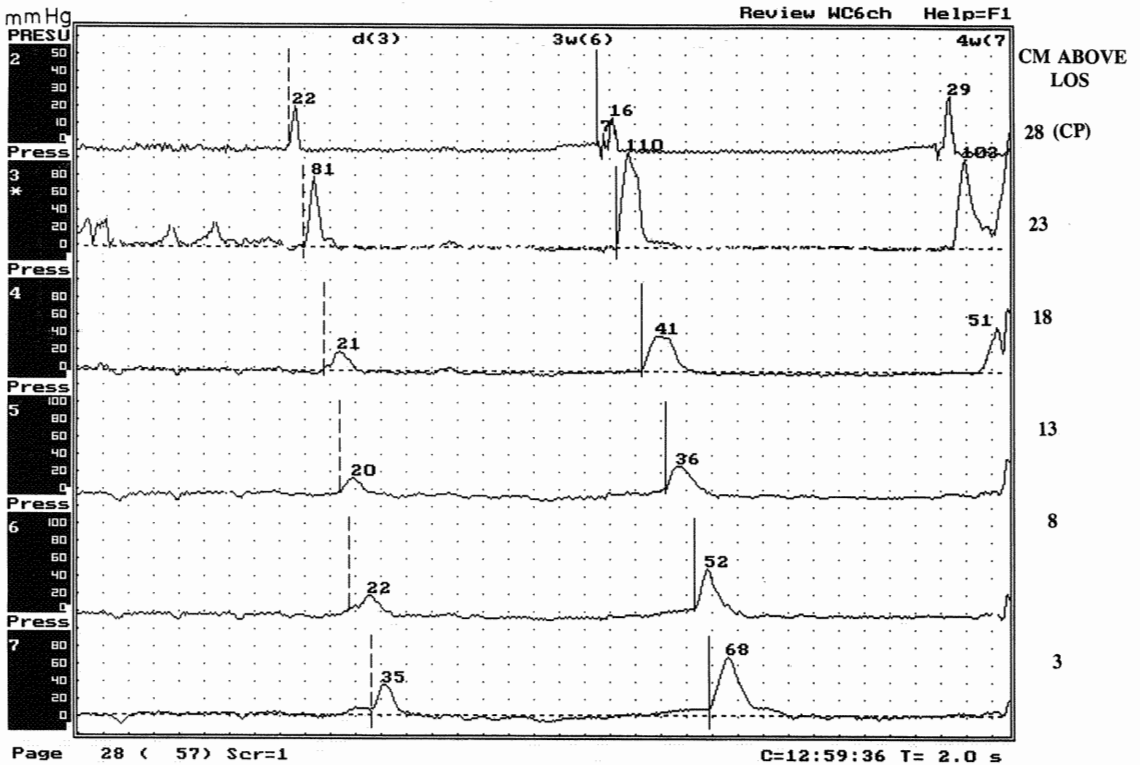
Fig. 3.29 Spontaneous swallows are described as dry swallows, and water bolus swallows are described as wet swallows. The amplitude should be measured from wet swallows which usually induce a higher and more reproducible amplitude compared with dry swallows.

Analysis

Terminology

Oesophageal baseline—taken at the mean respiratory value. A mean of five stable mid-expiratory values is determined prior to the swallow, excluding any periods of oesophageal contractile activity.

*Onset of contraction—*the point of maximum rate of 'up-stroke' extrapolated back to the oesophageal baseline, ignoring the initial 'shoulder' effect if present.

*End of contraction—*the point at which the 'down-stroke' returns to the oesophageal baseline or is extrapolated down to it, allowing for multiple peaks.

*Duration of contraction—*the time interval between the onset and end of contraction as defined above.

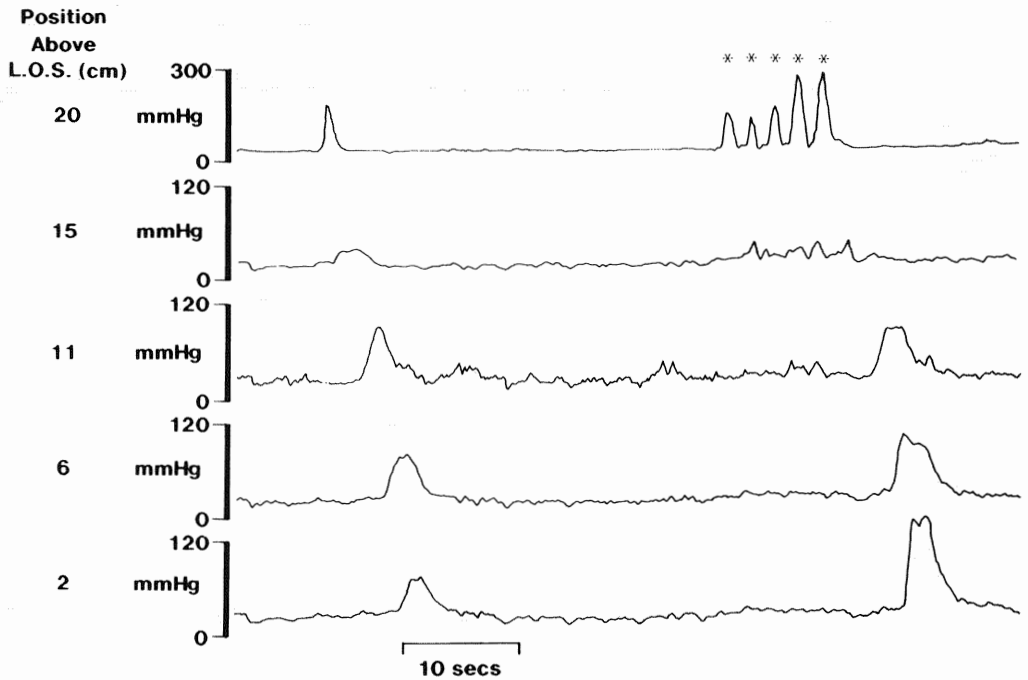**Fig. 3.30** The effect of rapid repetitive swallowing which inhibits oesophageal contractile activity. This is a normal phenomenon and illustrates the need for control of swallow frequency in the assessment of propagation.
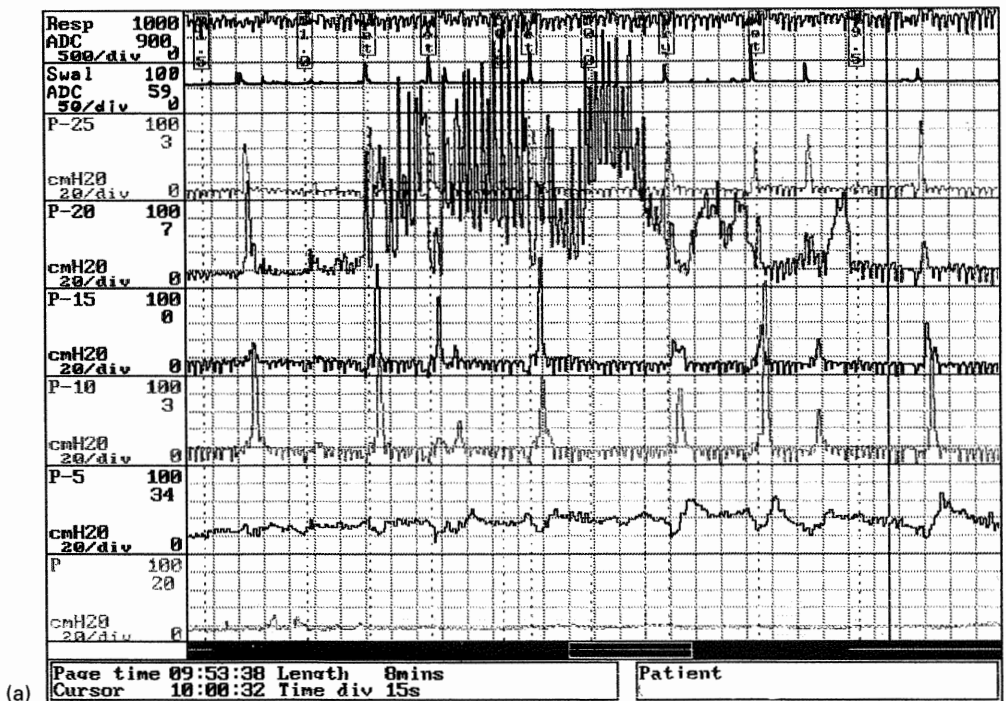

Fig. 3.31 (a) Zone of compression due to extrinsic structure in P-20. Solid state six sensor catheter; P-25 is in the upper oesophagus, P-5 is in the LOS and P in the stomach.

Page time 10:05:39 Length   2mins
Cursor   10:06:39 Time div 5s   Patient
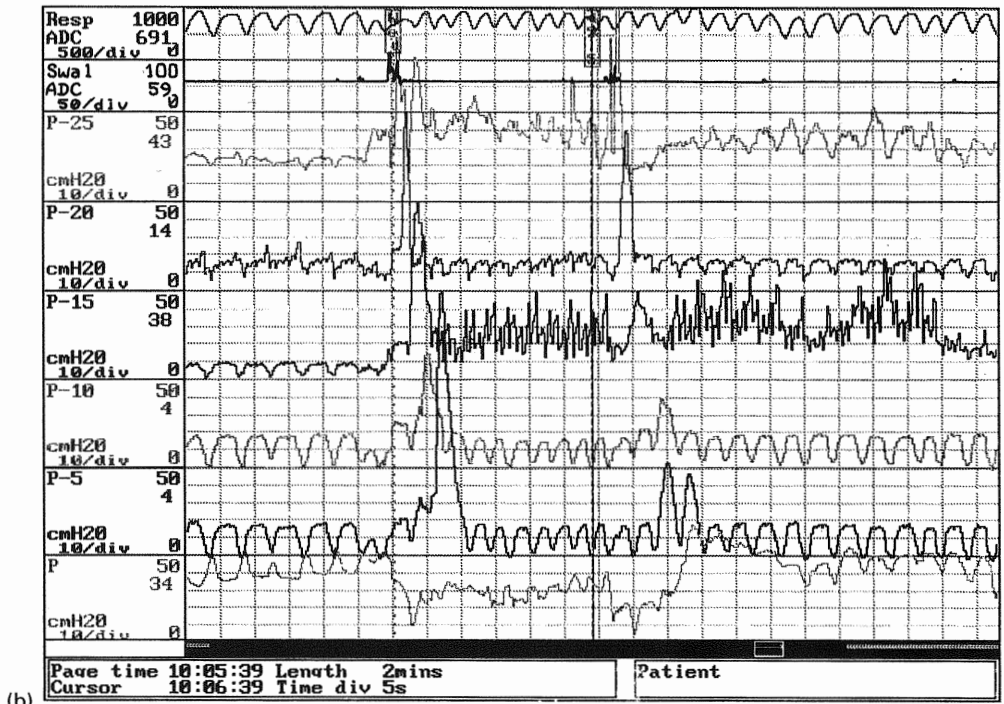
(b)

Fig. 3.31 (b) P-15 is now within the zone of compression, P-25 is in the CPS, P is now in the LOS; cardiac oscillations are less pronounced and the reduced contraction on a dry swallow (centre of trace) can be seen.

Page time 10:08:38 Length   34s
Cursor   10:08:48 Time div 1s   Patient

Fig. 3.32 Crude assessment of the crico-pharyngeal sphincter. P-25 is pharyngeal, P-20 is in the upper oesophageal sphincter (UOS) which relaxes to oesophageal baseline with a wet swallow, bottom channel is 3 cm above the LOS.

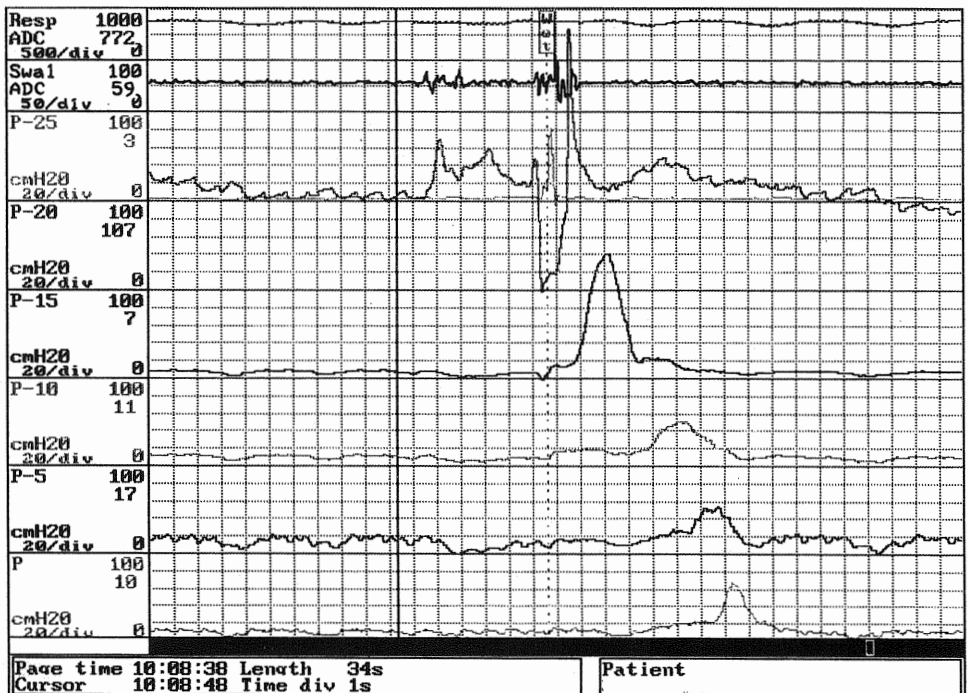*Propagation velocity*—measured from onset to onset or peak to peak of the contraction over a specified oesophageal length, expressed as cm/s.

Amplitude of the contraction—measured from the oesophageal baseline to the maximum amplitude attained, the highest peak for double and triple peaked contractions [1]. Amplitude must be >15 mmHg to be included as a 'contraction'.

Measurements

The essential measurement parameters (Fig. 3.33) are illustrated in Table 3.3.

Amplitude

Measurement of the contraction amplitude at each pressure recording site can be made, although for the investigation of reflux the most significant value will be that in the distal oesophagus where muscle function may be most compromised by the damage from gastric refluxate [2,14,15]. Variation in amplitude over the
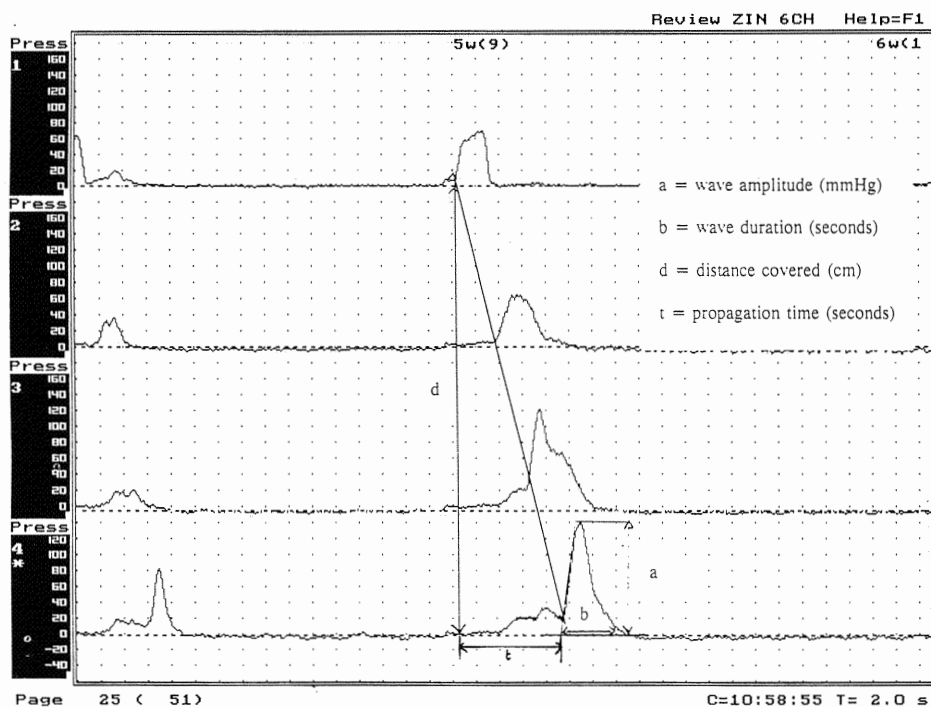
Fig. 3.33 Wave amplitude is measured between the points as defined by line 'a' and repeated for each channel. Propagation velocity 't' is the time taken for the contraction wave to progress between the measurement sites. Wave duration is defined by line 'b'.

Table 3.3 Oesophageal manometry normal values.

Characteristic	Normal range
Mean distal amplitude	30–180 mmHg
Peristalsis	80% of wet swallows should be peristaltic and propagated
Spontaneous activity	None
Propagation velocity	
Proximal oesophagus	1.8–4.2 cm/s
Distal oesophagus	1.70–5.3 cm/s
Wave duration	<7 seconds
Wave morphology	Mono or bi-peaked waveforms

oesophageal body results from the variation in muscle composition with a smaller amplitude being measured in the region of mixed smooth and striated muscle and maximum amplitude in the distal region of smooth muscle [1]. Highest amplitudes are normally found in the cervical oesophagus and they have the shortest duration. The lowest amplitude is found at the level of the aortic arch and at the junction between the striated and smooth muscle segments.

The mean contraction amplitude is calculated from the ten wet swallows [9]. Care must be taken in patients with achalasia in whom, if the LOS is not relaxing, water may accumulate in the oesophagus and the patient may start to regurgitate the fluid.

Duration

The duration of the contraction wave is typically 3–7 seconds, the shortest in the cervical part, and shows a rapid pressure rise and fall phase as illustrated in Fig. 3.28 with no obvious peak plateau phase (Fig. 3.34). Duration is usually longer after wet swallows, but not affected by position. When multi-peaked contraction waves occur the duration of the contraction wave is likely to increase and usually with three or more peaks the duration will extend beyond the 7 second outer limit.

Propagation velocity

The rate at which the contraction progresses down the oesophageal body can be determined by measuring the time taken for the wave to progress across a known
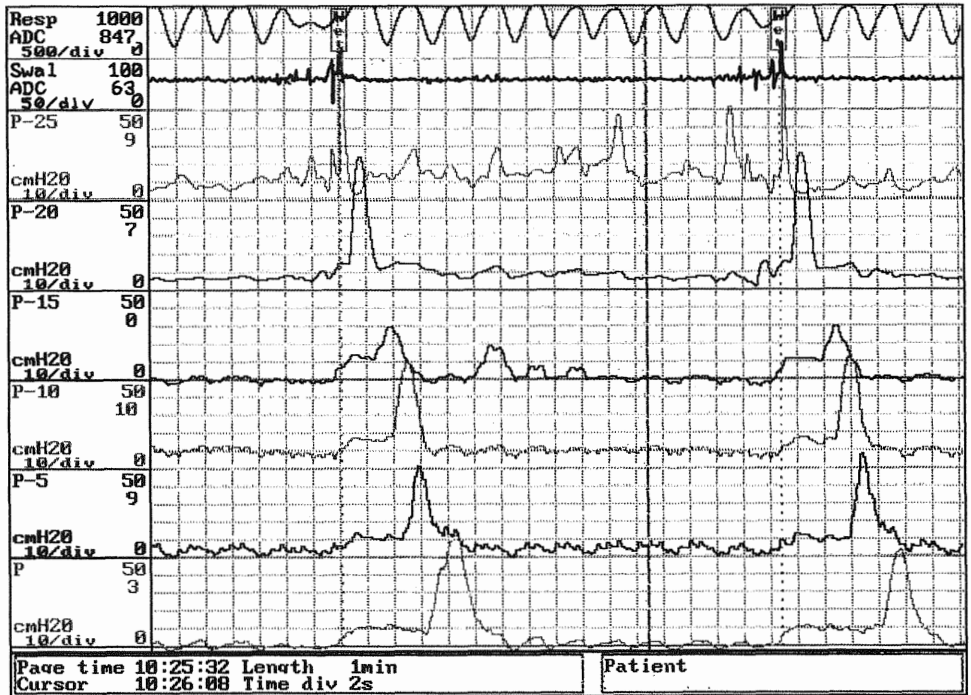
Fig. 3.34 Wet swallows often are preceded by an initial plateau which can be more exaggerated the more distal; this is probably caused by the increase in pressure due to the advancing bolus [16]. P-25 is close to the CPS, P is 3cm above the LOS.

distance. The time is determined from the chart speed and the distance between the recording sites on the catheter.

$$\text{Propagation velocity} = \frac{\text{Distance (cm)}}{\text{Time (seconds)}}$$

The striated muscle portion has a faster rate of propagation than the smooth or mixed muscle regions [1]. Oesophageal wave velocity is fastest in the upper oesophagus and slower in the lower oesophagus in the upright position compared with the supine, and faster throughout with dry swallows.

If there is no time delay (<0.6 seconds) between adjacent channels (5 cm) then the wave is described as simultaneous.

Types of contractions

Terminology—peristalsis

Primary. Co-ordinated swallow induced event where the contraction wave

progresses distally throughout the oesophageal body until it reaches the LOS which relaxes.

Secondary. Contractile activity initiated within the proximal oesophagus, not associated with swallowing where the contraction wave progresses distally throughout the oesophageal body and the LOS relaxes as before.

Primary contractions

Primary contraction in the oesophageal body results from voluntary swallowing which gives rise to pharyngeal contraction, UOS relaxation and a contraction wave that normally moves caudally along the oesophageal body at a velocity between 1.7 and 5.3 cm/s [1,16] until it reaches the LOS which relaxes. The components of the contractile wave are well classified and various parameters can be determined and compared with normal values derived by investigating large numbers of asymptomatic control subjects. Normal values are shown in Table 3.3.

Secondary contractions

Secondary contraction waves (generally propagated) are initiated by oesophageal distension when a bolus is not fully cleared by the primary wave. Secondary activity is intrinsically mediated, beginning within the oesophageal body, and hence pharyngeal activity is absent. Figure 3.35 illustrates a secondary wave occurring between two primary waves.

Tertiary or segmental contraction waves

Tertiary activity is a term also used by radiologists in their assessment of barium X-rays to describe non-propagated oesophageal body activity. Manometrically, tertiary contraction wave may be used to describe contractile activity occurring spontaneously within isolated segments of the oesophageal body (not propagated); aboral propulsion of oesophageal contents will not occur (Fig. 3.37) [17].

Oesophageal contraction wave characteristics

Morphology

The normal contraction wave in the oesophageal body is typically monophasic but occasionally bi-peaked waves may be recorded (see Fig. 3.35). There must be a 10% difference in amplitudes between the two peaks to be classed as biphasic.

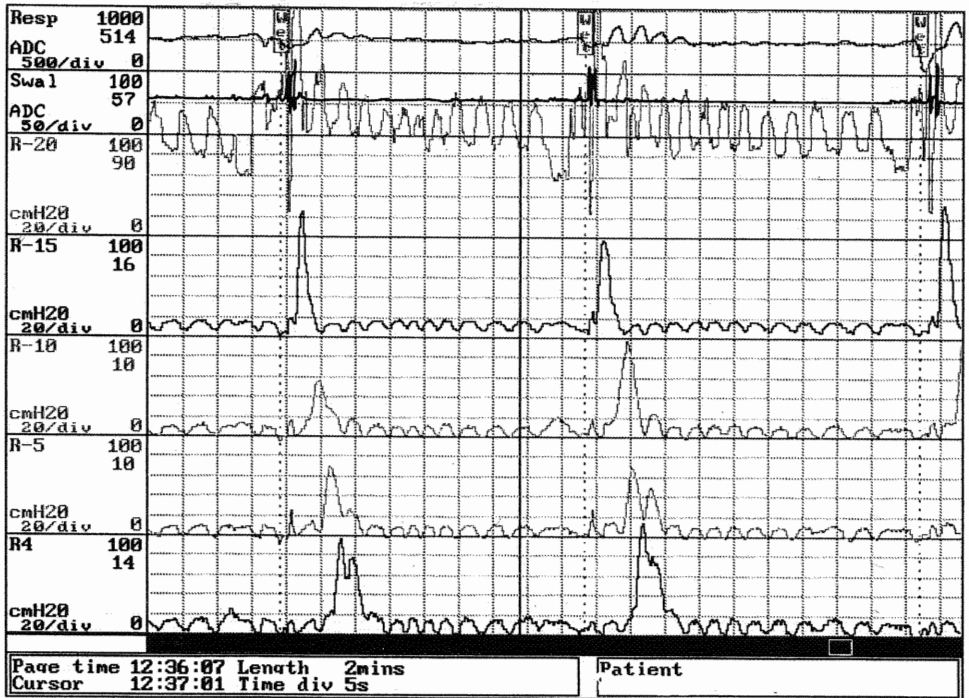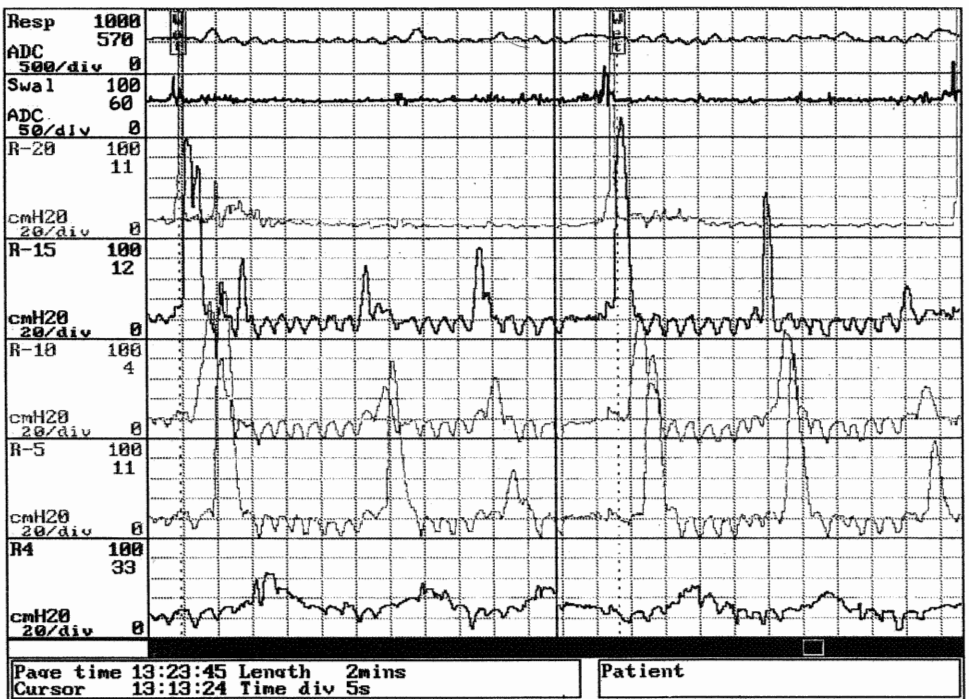**Fig. 3.35** Bifid wave in R4.

Fig. 3.36 Peristaltic secondary contractions between the wet swallows; note no pharyngeal contraction in R-20 or response on swallow sensor. R-20 is pharyngeal, R-15 just below UOS, R-5 is 3 cm above LOS and R4 in LOS.

Fig. 3.37 Tertiary contractions isolated in R-5 at cursor position, and also R-5 and R4 between wet and dry swallows.

Multi-peaked contraction waves with three or more peaks (Fig. 3.38) or repetitive contractions (characterized by multiple independent contractions which return [almost] between each to baseline) are rarely recorded in normal controls and are classed as an abnormal feature [1,17].

Contraction types

Propagated waves

The wave migrates aborally with a time delay between the contraction phase at each successive level of recording in the oesophageal body as shown in Figs 3.28 and 3.33 [18,19]. This is described as peristalsis.

Non-propagated or simultaneous contractions

There is no time delay between the contraction phase at each level of recording in the oesophageal body as shown in Fig. 3.39. This results from loss of the intrinsic inhibitory mechanism that precedes the contraction wave [20,21]. Bolus propulsion is significantly impaired. These are also called aperistaltic contractions.
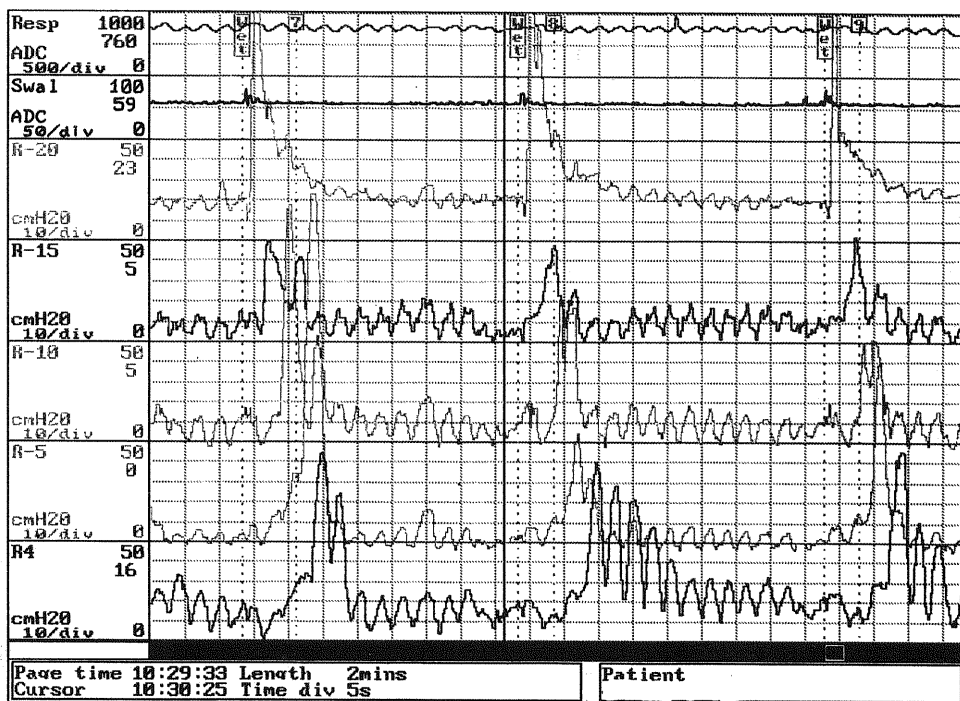
Fig. 3.38 The contraction wave shape or morphology is typically monophasic with a sharp upstroke and downstroke and no plateau phase at maximum pressure. Waves with two contraction peaks are described as bi-peaked or bifid and occur in normal individuals. Waves with more than two peaks are termed multi-peaked and are rarely seen in normals. The wave does not return to the baseline between contraction peaks distinguishing the multi- from repetitive waves in which each individual contraction wave should almost reach baseline. If the repetition frequency is very rapid the response time of the recording equipment may not be fast enough to accurately reproduce the rapidly changing contractile events. R4 is 3 cm above LOS, R-20 near CPS.

Interrupted or incomplete propagation

Occasionally contractions are recorded which may be propagated across some regions but are simultaneous or absent in other regions (Fig. 3.40a,b,c). These are described as having interrupted propagation which may result from partial loss of the intrinsic inhibitory mechanism [20,21].

Absence of contraction

If no contraction is seen in the oesophageal body following pharyngeal contraction and UOS relaxation then the wave is termed amotile, i.e. absent contraction. Figure 3.41 illustrates absent oesophageal body response to pharyngeal activity.
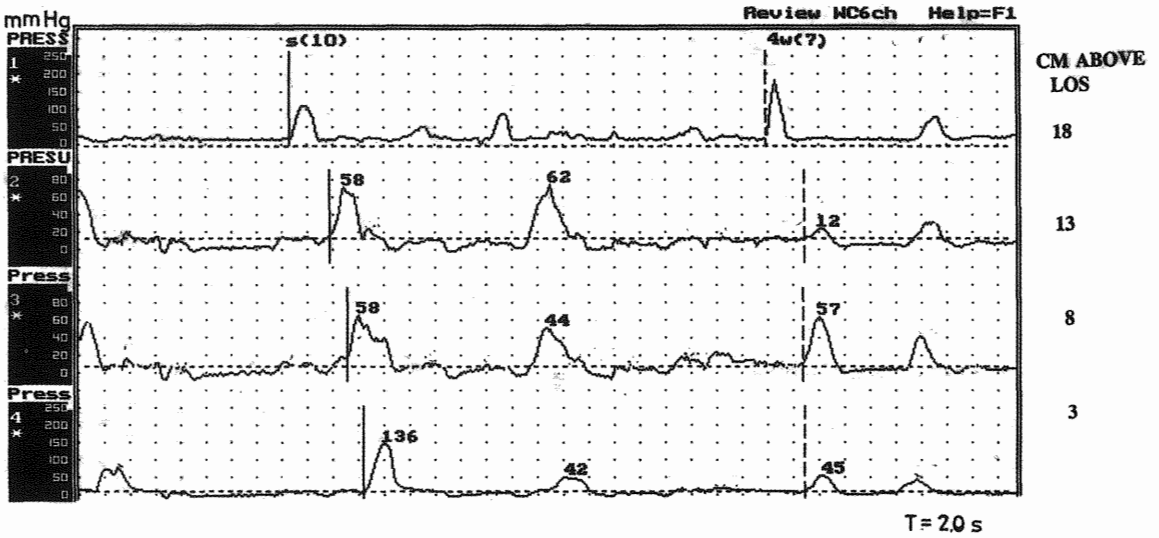
Fig. 3.39 Simultaneous contractile activity in response to wet swallow (4w) is demonstrated in channels 2,3 and 4. Dry swallow (s) is normally propagated.
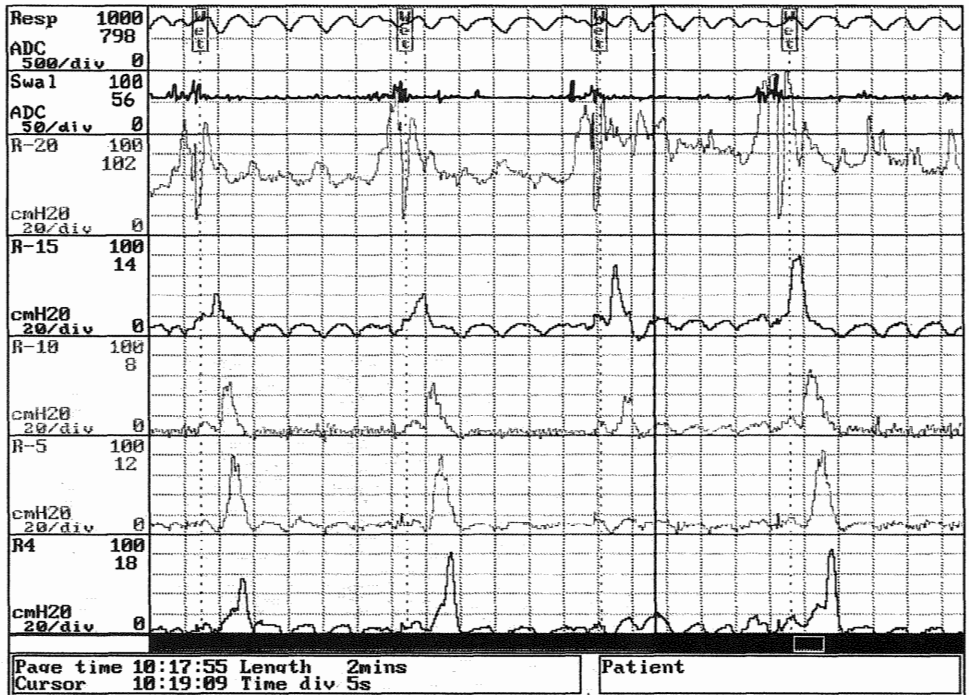
(a)

Fig. 3.40 (a) Non-conducted wave is demonstrated where there is no contraction below R-10 on the third wet swallow but peristalsis is normal up to this level.
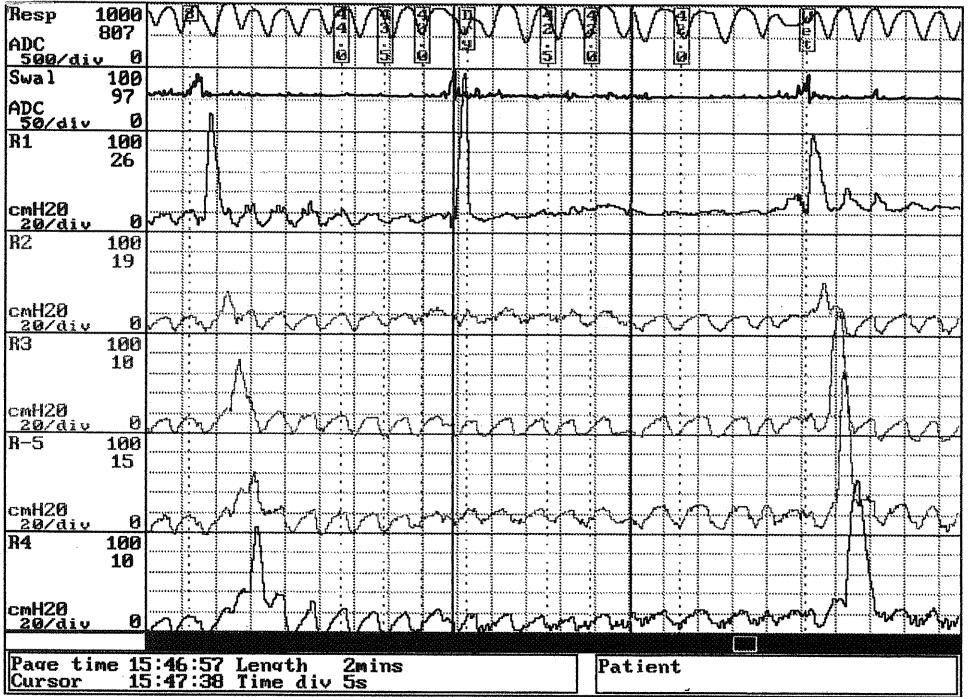
(b)
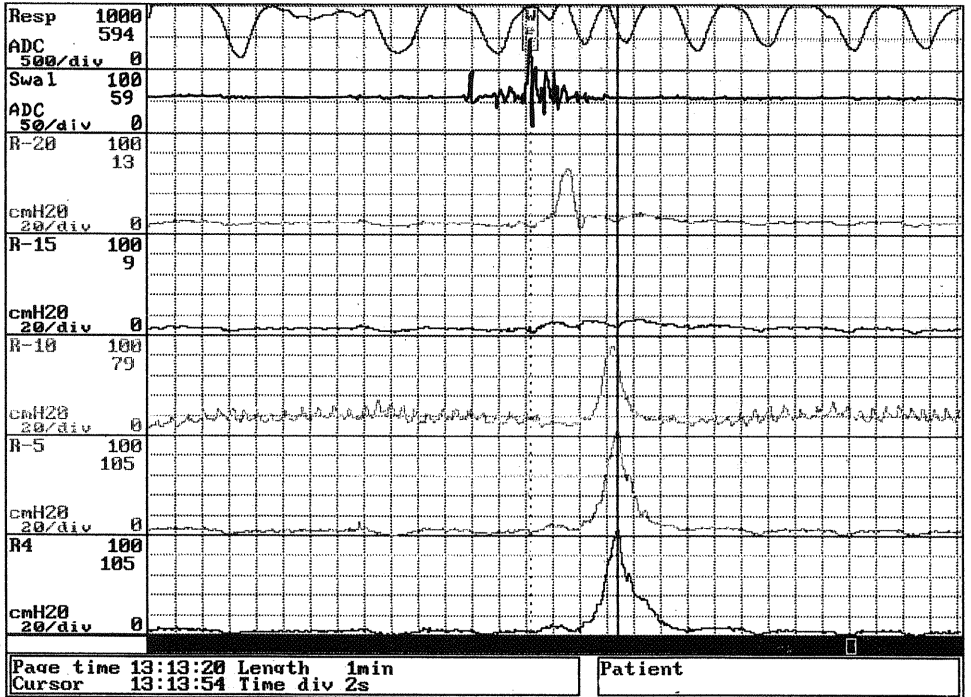
(c)

Fig. 3.40 (b) Non-conducted wave below upper oesophagus on dry swallow. (c) Interrupted propagation in upper/mid oesophagus on wet swallow and simultaneous in mid and distal oesophagus.

Fig. 3.41 Example of an amotile oesophagus. There are no contractions in the oesophagus on wet swallows, but there are pharyngeal contractions (R-20). R-15 is near the CPS.

Manometric classifications

Primary motor disorders of the oesophagus

Achalasia

The most common motor disorder in which oesophageal manometry provides definitive diagnosis is achalasia of the oesophagus. Achalasia results from damage to the intrinsic neural plexus with loss of ganglia and hence loss of the initial inhibitory component of swallow activity [22]. Typical achalasia manifests manometrically as a high pressure LOS which shows incomplete or absent relaxation on swallowing. Baseline oesophageal pressure may also be raised. The swallow activity is simultaneous and usually of low amplitude throughout the oesophageal body as shown in Fig. 3.42a,b. There is little spontaneous activity within the oesophagus, except respiratory oscillations. Occasionally intra-oesophageal pressure may rise as swallowed components accumulate. The pressure will drop following regurgitation of the oesophageal contents or belching.
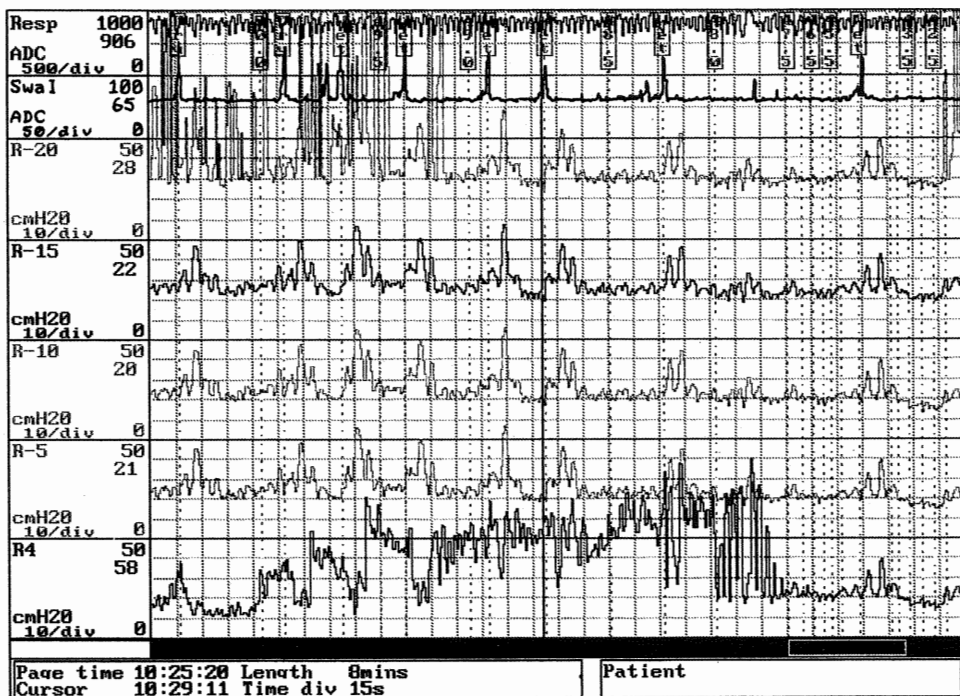
(a)
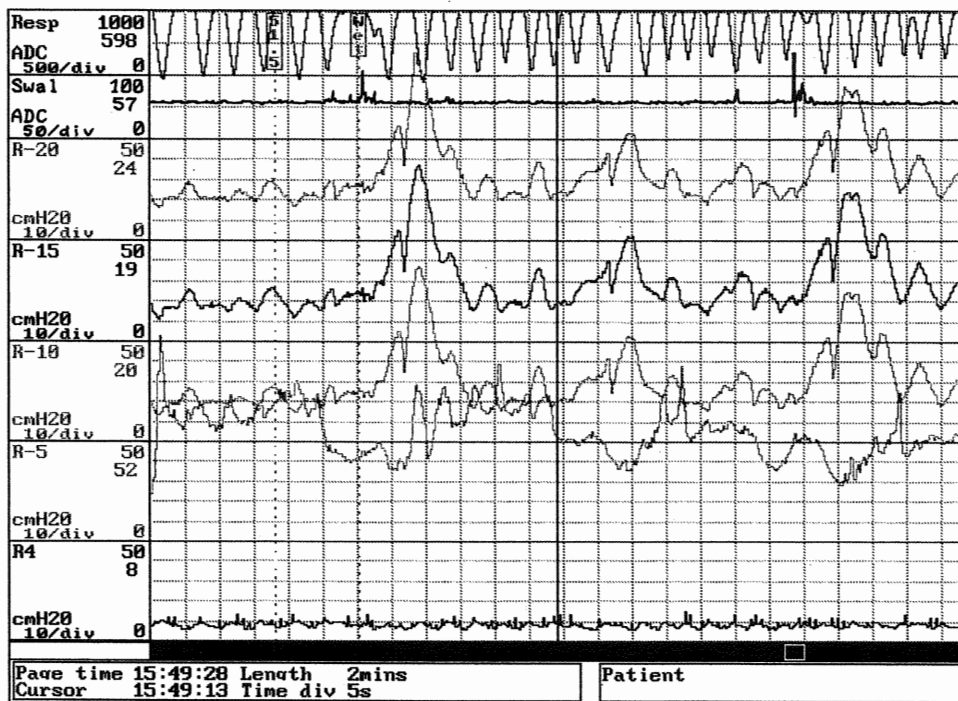
(b)

Fig. 3.42 (a) Achalasia with impaired or absent LOS relaxation; wet swallows (either side of cursor) do not reduce the lower oesophageal sphincter pressure (LOSP) to gastric baseline, the oesophageal contractions are all simultaneous and the oesophageal baseline is elevated. (b) Achalasia with synchronous repetitive contractions on wet swallows. LOSP (R-5) is raised and relaxes poorly. R4 is gastric.

Vigorous achalasia

Two variants to the standard classification of achalasia have been demonstrated and are described as 'vigorous' achalasia [23].

Firstly, high amplitude repetitive contractions are present throughout the oesophageal body. These occur alongside the simultaneous swallow response and classical high amplitude LOS with incomplete or absent relaxation on swallowing. The first variant is shown in Fig. 3.43 and may be a phase in progression of the patient's condition from manometrically determined diffuse oesophageal spasm through to the classic achalasia.

Secondly, cyclical high amplitude contractile activity of prolonged duration occurs simultaneously throughout the oesophageal body as shown in Fig. 3.44. Swallow contractile activity (as noted by the investigator) is superimposed on the cyclical activity. This second variant may be of a different, as yet unidentified, aetiology.
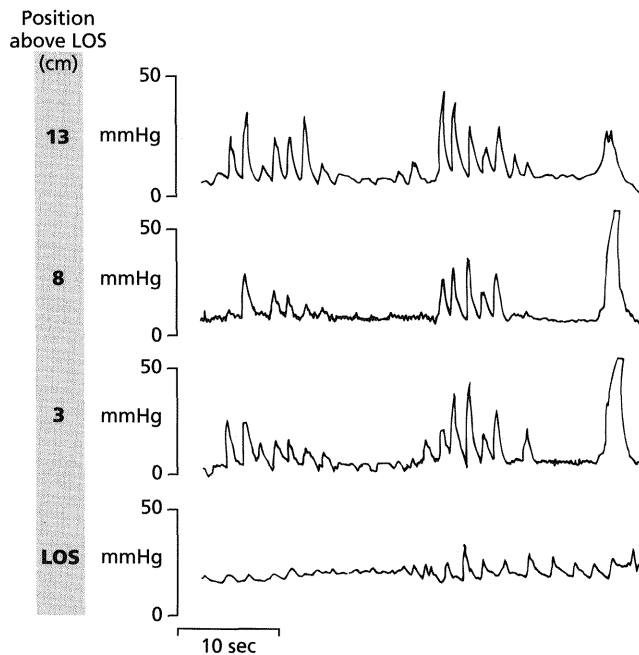
Fig. 3.43 The activity classed as vigorous achalasia in which a high amplitude abnormally relaxing LOS with no propagation of swallow activity is demonstrated but with spontaneous activity and repetitive activity occurring following swallows.
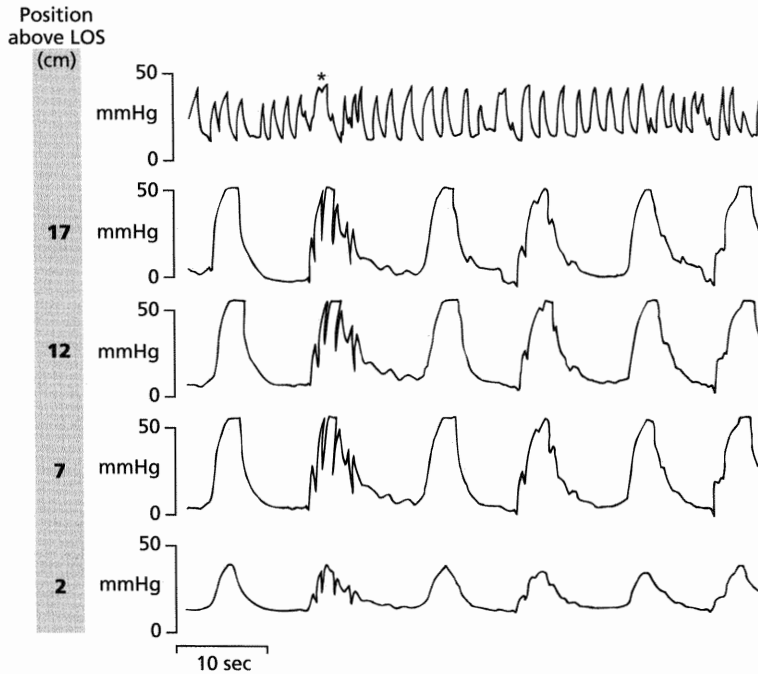
Fig. 3.44 This may also be classed as vigorous achalasia as the typical high amplitude abnormally relaxing LOS occurs but with relatively high amplitude cyclical activity occurring for prolonged periods of time. A voluntary swallow (*) can be seen superimposed over the cyclical activity.

Diffuse oesophageal spasm

The oesophageal body demonstrates a heightened response to swallows with prolonged repetitive contractions following swallow activity and high amplitude spontaneous activity as illustrated in Fig. 3.45. Figure 3.46 illustrates a period of prolonged baseline elevation with high amplitude simultaneous contractions typical of diffuse oesophageal spasm (DOS). The LOS may also show abnormalities with a high resting pressure and abnormal relaxation on swallowing. At least two of the ten water bolus swallows will show abnormal propagation [13,21,24,25].

Nutcracker oesophagus

The amplitude of the contractile response to swallows is significantly high particularly in the distal oesophagus as shown in Fig. 3.47a,b, with amplitudes over 400 mmHg often recorded [26,27]. This may reflect inappropriate contractile muscle function or the loss of an intrinsic or extrinsic feedback mechanism detecting bolus size that acts to modulate muscle contraction [8,20].
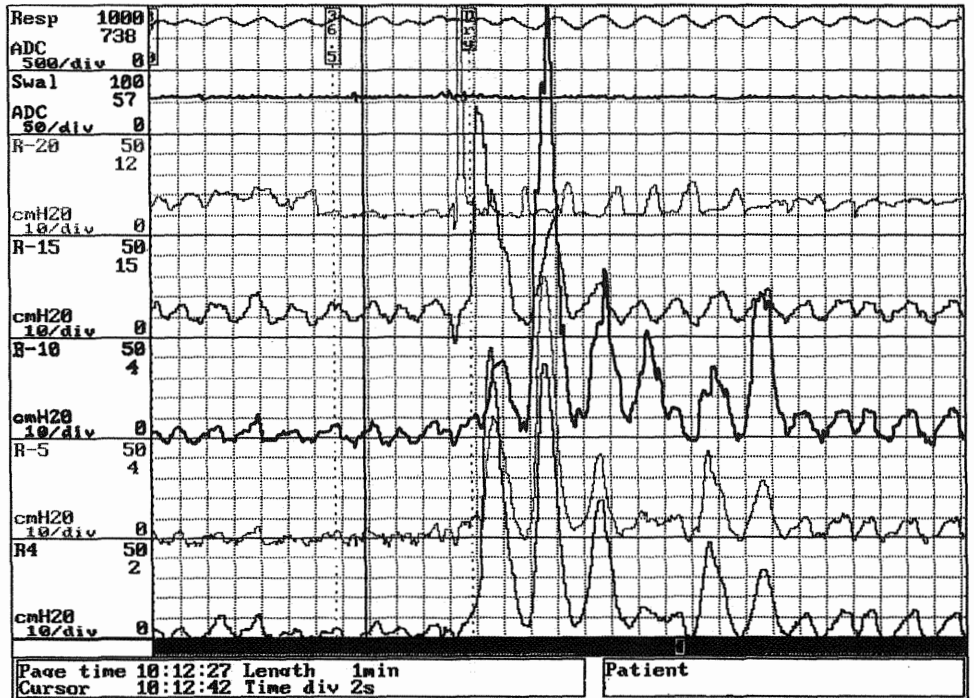
Fig. 3.45 Diffuse oesophageal spasm is characterized by multi-phasic contractions and repetitive waves.
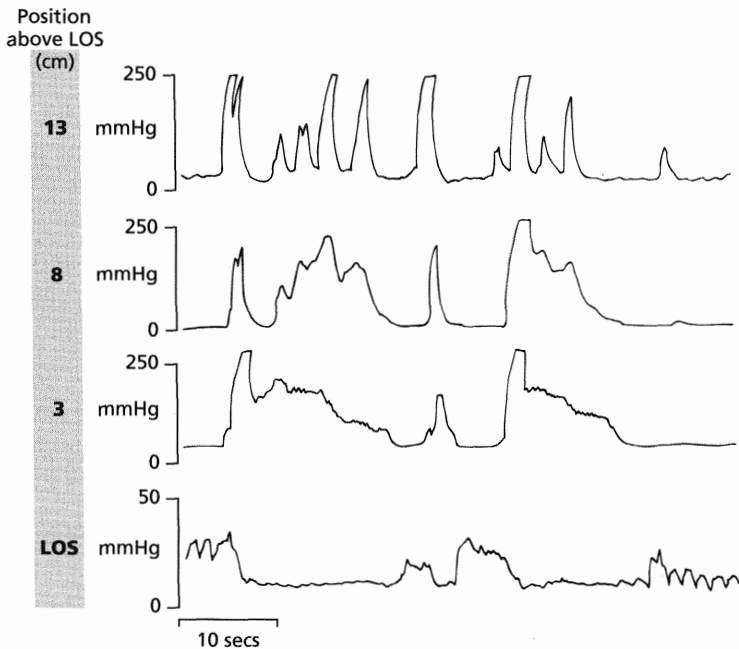
Fig. 3.46 Diffuse oesophageal spasm manifesting with high amplitude simultaneous contractions with prolonged baseline elevation described as spasm. LOS relaxation, shown in the bottom channel, is maintained throughout the episodes of oesophageal spasm.
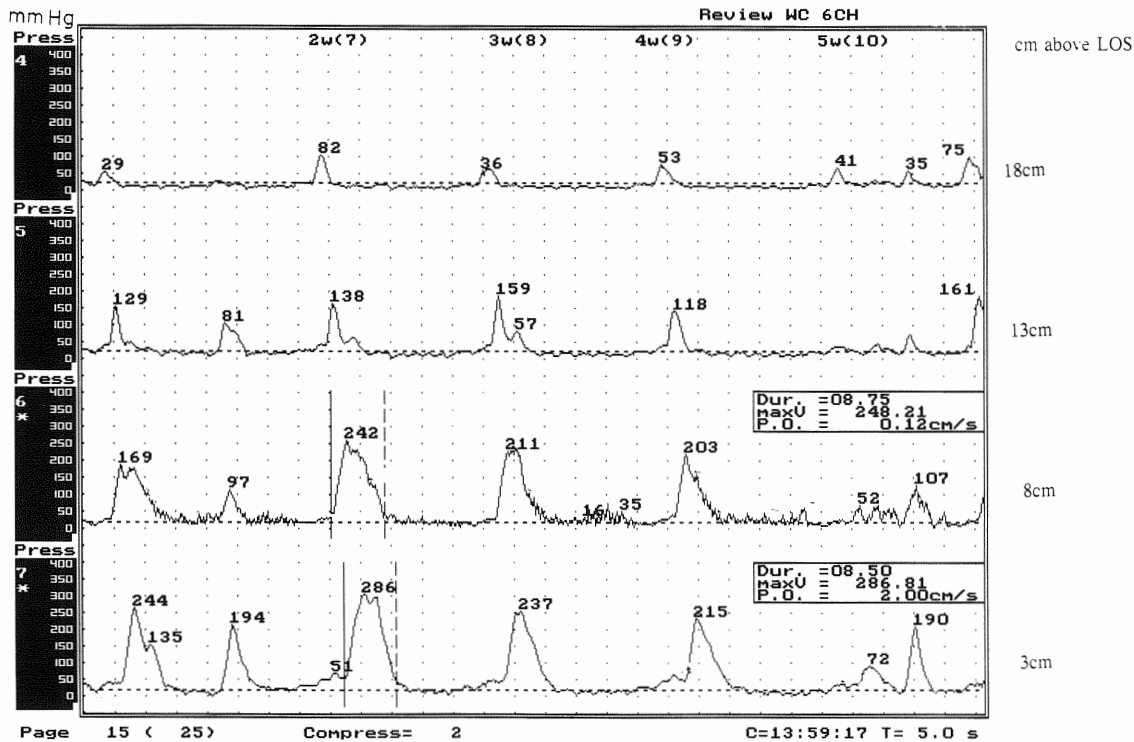
(a)
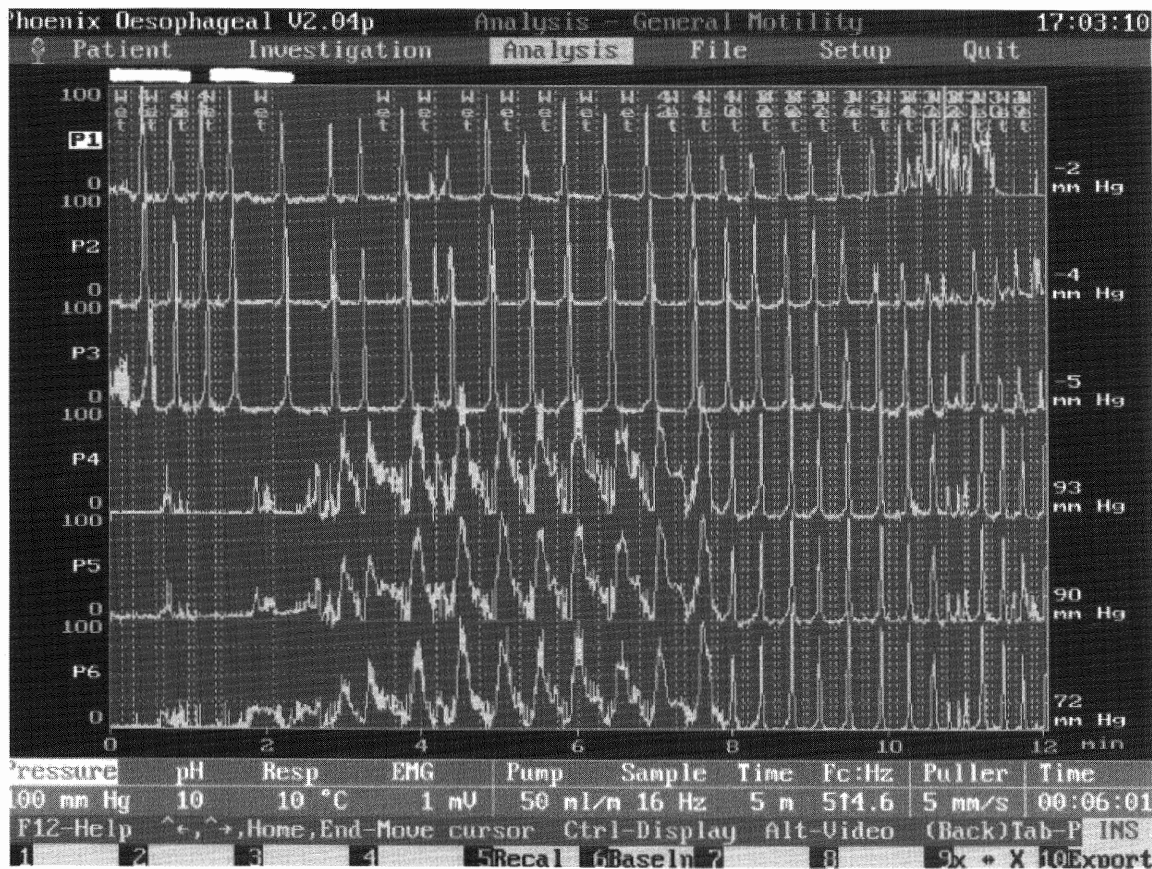
(b)
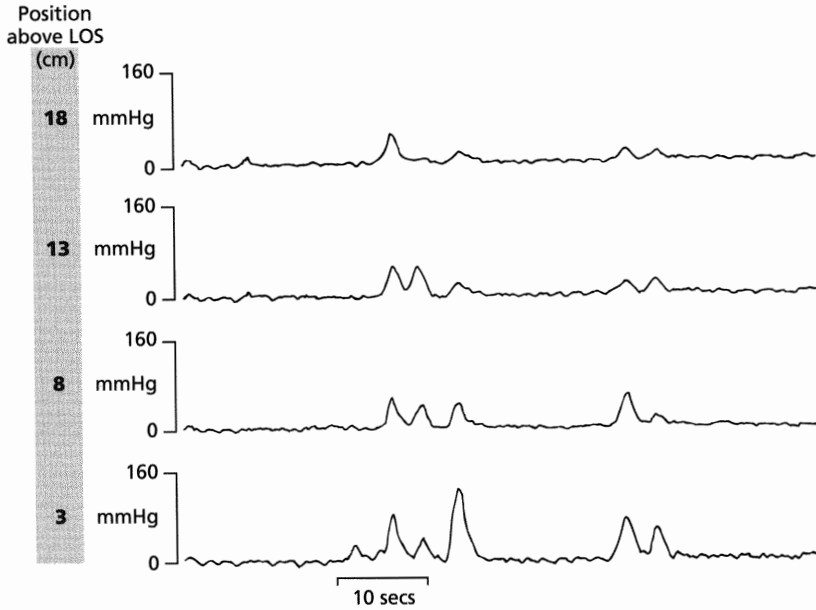
Fig. 3.48 Unusual activity that does not fall into a well-defined classification is classed as a non-specific motility disorder (NSMD). The illustration shows spontaneous non-propagated activity.

Non-specific motility disorders

A manometric recording showing unusual contractile features that do not ascribe to the above manometric classification may be classified as a non-specific motility disorder; an example is shown in Fig. 3.48. The term itself does not describe the manometric features other than that unusual but not defined contractile activity is occurring during the course of the recording. Non-specific motility disorders may be precursors of defined manometric disorders or may represent anomalies within the intrinsic or extrinsic neural pathways of the oesophagus that are yet to be classified [28].

Secondary motility disorders

Systemic sclerosis

The connective tissue disorder systemic sclerosis affects the gastro-intestinal tract.

Fig. 3.47 *Opposite.* (a) An example of Nutcracker oesophagus with the typical high amplitude contractions in the distal oesophagus. (b) Near 'nutcracker'. Peristaltic waves >180 mmHg with high pressure but relaxing LOS. Six channel catheter 4.2 mm outer diameter (OD) with P4/5/6 at tip and P1/2/3 at 5 cm spacing.

Position
above LOS
(cm)
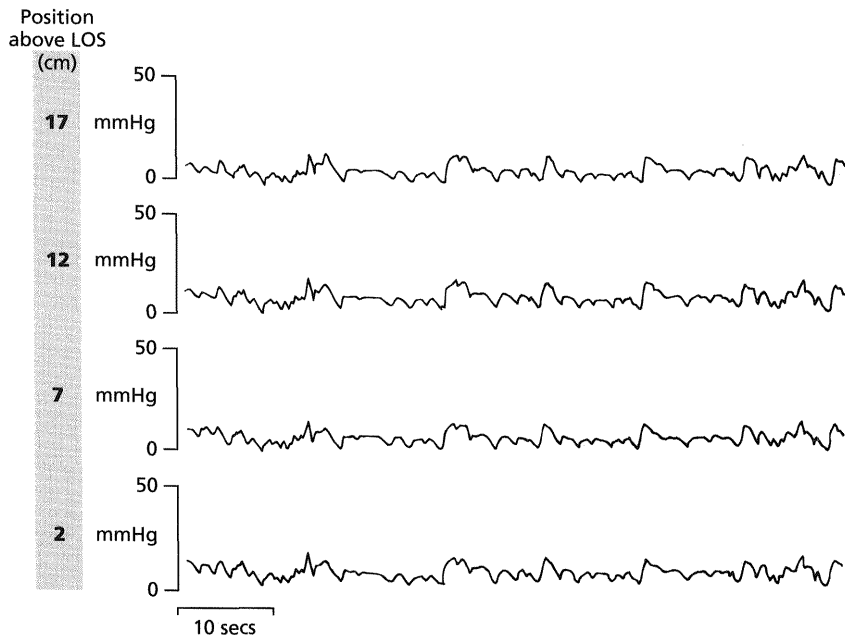
Fig. 3.49 Connective tissue disorders such as scleroderma affect oesophageal function by loss of propagation of the swallow activity and a diminished contraction amplitude as illustrated. The motility pattern is similar to achalasia but the distinguishing factor in scleroderma is the very low LOS pressure.

Within the oesophagus this manifests as loss of contractile activity within the smooth muscle, yet normal contractile activity in the upper region (striated muscle). This results in impaired propulsion of oesophageal contents [17]. The resting pressure of the LOS is significantly diminished giving rise to gastro-oesophageal reflux. The manometric picture shows low amplitude or absent, non-propagated contractions except in the upper oesophagus, as shown in Fig. 3.49, and the LOS pressure will be very low.

Malignant disease affecting the cardia or oesophageal body

The manometric picture can be similar to achalasia with low amplitude, simultaneous swallow contractions. The LOS can also mimic the high pressure which does not relax, or may be of normal resting pressure although the obstructing lesion may prevent passage of the catheter in some cases.

Oesophageal manometry report

The manometry report should include the patient details and a comprehensive breakdown of the measurements including:

1 Propagation characteristics.
2 Propagation velocity (cm/sec).
3 Contraction wave amplitude.
4 Wave morphology.
5 Unusual events observed during the recording period
6 An overall conclusion.

Definitive diagnoses can rarely be based on manometry alone with the exception of diffuse oesophageal spasm, achalasia and oesophageal systemic sclerosis (scleroderma). But the information acquired can be used in conjunction with radiographic and endoscopic studies to provide a clear picture of oesophageal function which may or may not explain the patient's symptoms [17,25,29]. Oesophageal manometry can vary with time and be influenced by both psychological and environmental stress [30]. Provocation procedures such as intra-oesophageal distension can be used to induce symptoms and manometric abnormalities [31] (see Chapter 10, p. 233). Ambulatory oesophageal manometry may be required to record intermittent manometric anomalies [32] (see Chapter 5).

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3.5　Clinical relevance of investigations
John N. Blackwell

Motility disorders of the body of the oesophagus (upper oesophageal disorders are considered elsewhere) present to the clinician with the patient's complaint of dysphagia, food regurgitation (occasionally described as 'vomiting'), chest pain or discomfort, odynophagia or obscure upper abdominal or chest symptoms, sometimes with hoarseness. The clinical relevance of an investigative modality must be considered with regard to symptom presentation, since the ultimate diagnosis is only established after consultation and investigations have been completed. Therefore, manometry must not be considered in isolation, but rather in its relationship to other pertinent investigations. This may be illustrated by the obvious examples of bronchial carcinoma with oesophageal involvement, or carcinoma of the gastric cardia. Both may present with swallowing difficulties or chest discomfort, and both will result in manometric abnormalities. However, serious errors of diagnosis and management will occur if other investigations are not undertaken.

Accordingly, patients presenting with symptoms of possible motility disorders should undergo a series of tests prior to being considered for manometry. These must include routine haematology and biochemistry, chest X-ray, barium radiology, upper gastro-intestinal endoscopy and sometimes abdominal ultrasound. Manometry then follows, usually incorporating a Bernstein test. A pH recording is also usual, utilizing manometry to determine the position of the LOS, to exclude gastro-oesophageal reflux-related dysmotility. Caution must be exercised here, because oesophageal stasis may result in the accumulation of acid food or fluid in conditions such as achalasia.

Consideration must also be given to the relationship between manometry, which measures pressure aspects of function, and both oesophageal scintigraphy to quantitate oesophageal transit and video-fluoroscopy. When the latter technique is appropriately used, there is almost complete (96%) concordance with manometry in assessing oesophageal motility [1]. While most clinicians would be reluctant to abandon the objective measurements made by manometry, in these circumstances, scintigraphy offers little additional information in routine clinical practice.

In essence, the conduct and interpretation of manometry must not be considered in isolation from the clinical context, nor from the findings derived from prior investigations. A primary oeosophageal motility disorder may be considered only after exclusion of gastro-oesophageal reflux disease, mechanical causes, distant malignancies, systemic sclerosis (scleroderma) and other collagenoses, muscle disorders such as myotonia dystrophica, neurological disorders such as multiple sclerosis and motor neurone disease, intestinal pseudo-obstruction and neuropathies especially due to alcohol or diabetes.

Gastro-oesophageal reflux disease

Utilizing manometry to determine the position of the LOS (i.e. distance from the nose) remains the best trusted measurement for the placement of oesophageal pH probes. Even so, this may be problematic in the presence of a significant hiatal hernia, when the lower oesophageal sphincter pressure can be very low.

The measurement of resting LOS pressure (LOSP) [2] is of little diagnostic value in relation to gastro-oesophageal reflux, because there is tremendous overlap with normal, non-refluxers, who can have rather low resting pressures. The LOSP can be seen to rise after pharmacological stimulation, after anti-reflux surgery or after healing of oesophagitis. Such measurements are valuable as research tools but do not help in routine clinical practice where the pH probe reigns diagnostically supreme.

However, manometry is widely used when the severity of the oesophagitis or symptoms leads to consideration of surgical treatment in the hope of better predicting a good outcome. Clearly the previously unsuspected manometric discovery of diffuse oesophageal spasm, or even achalasia, should deter anti-reflux surgery, which otherwise causes worsening dysphagia. None the less, reflux and oesophagitis themselves appear to cause a variety of motility disturbances which may not cause post-operative problems, or may even be improved. Sometimes strong surgical views [3] are expressed, but prudence dictates that caution be exercised where manometry shows that the majority of swallows are not followed by a peristaltic sequence, or where there is major impairment of sphincter relaxation. In the event of post-operative or recurrent symptoms, manometry is an essential part of the objective assessment to aid future management decisions.

Achalasia

Manometry is particularly useful in suspected achalasia [4], once mechanical obstruction has been excluded by other investigations. In the early stages of achalasia, before the oesophagus becomes dilated, 'routine' barium radiology will fail to identify 40% of cases. Here, the manometric abnormalities are virtually pathognomonic. In the occasional late presentation where oesophageal dilation is extreme, it may prove impossible to negotiate the manometric catheter through the LOS.

Following treatment for achalasia, be it Heller's myotomy, pneumatic dilatation, or botulinum toxin injection, manometry has no part to play in routine clinical follow-up. The patient's ability to eat is sufficient guidance to the efficacy of treatment.

There are, however, a few rare conditions. A variety of malignancies occurring elsewhere in the body may cause an achalasia-like picture. The mechanism of this

presumed neuronal toxicity is not clear. In South America, Chagas' disease may mimic achalasia. Amyloid is another rare cause.

There are also the occasional intermediate, or progressive, motility disorders [4]. Patients with non-specific changes, or those of diffuse spasm, may progress to develop more clear achalasia. This has therapeutic implications for the value of follow-up manometry in diffuse spasm when dysphagia worsens. Other patients with apparent achalasia may have partial relaxation of the LOS on swallowing, a normal or low sphincter pressure, or even return of some peristalsis after treatment in early cases where there is no distension of the body of the oesophagus.

Diffuse oesophageal spasm

Difficulty has arisen in the diagnosis and management of this condition because of the intermittent and variable nature of both symptoms and manometry. The manometric criteria are described in an earlier section. Prior investigation is essential to exclude mechanical obstruction, significant gastro-oesophageal reflux or the association with some systemic or other disorder. The manometric diag-nosis of oesophageal spasm may be enhanced by provocative tests (described elsewhere) or by the simple addition of swallowing bread while performing standard manometry [5].

Repeat manometry is not strictly necessary for follow-up, but may be of interest to gain insight into results of treatment, and also because the abnormalities are inconsistent—perhaps less definite on the first occasion. Manometry should always be repeated if dysphagia worsens, to detect the occasional progression to achalasia.

Other motility disturbances [6]

The manometric investigation of patients with a variety of symptoms possibly attributable to the oesophagus, led to the discovery of peristaltic or pressure abnormalities both of the body of the oesophagus and of the LOS. Their clinical importance is often elusive, since there is no clear correlation with particular symptoms, nor any obvious unifying pathogenesis. Patients may exhibit different manometric abnormalities on different occasions. None the less, the grouping of these manometric abnormalities into their various descriptive types has assisted with communication and research. Their clinical relevance should be treated with caution. Other physical disorders or psychological upsets should be considered.

These manometric descriptive groups include the nutcracker oesophagus, otherwise termed symptomatic oesophageal peristalsis, the hypertensive lower oesophageal sphincter, non-specific oesophageal motility disorder and the irritable oesophagus.

The patients remain a management problem. Some may respond to gastric acid suppression, and others to muscle relaxants, such as nitrates or calcium channel blockers. Drugs that reduce pain perception as well as anti-depressants have been successfully utilized.

Non-cardiac chest pain [7]

Recurrent sub-sternal chest pain with apparently normal coronary arteries continues to cause difficulties to the clinician but more especially on-going disability to patients. In the USA there are thought to be 90 000 new cases per year at a cost exceeding $500 million. Controversy continues between those who believe that there 'must be a cardiac cause' (generally the cardiologists), and those who believe that the oesophagus is often responsible. Gastro-oesophageal reflux is a clear cause which should be sought. Reflux and coronary artery disease frequently co-exist and acid suppression has helped many patients with apparently worsening angina. There is also a link between the occurrence of acid reflux and the development of pain with ECG changes. For all the controversy, clear cases of oesophageal dysmotility or gastro-oesophageal reflux are well worth identifying. All the manometric descriptive groups may present with pain, and management should be the same as when dysphagia predominates.

Secondary oesophageal motor disorders

A large number of generalized diseases cause oesophageal dysmotility. This often affects the striated muscle, upper segment of the oesophagus and the pharyngeal swallowing mechanism. These will not be discussed here. Only some of those conditions affecting the distal oesophagus are mentioned.

Systemic sclerosis (scleroderma) and other connective tissue disorders

Oesophageal manometry is abnormal in 50–80% of patients with scleroderma. In the early cases, the manometric demonstration of low amplitude distal oesophageal peristalsis and low LOSP may be diagnostically helpful, as well as indicating the desirability of maximal gastric acid suppression to inhibit oesophagitis and stricture formation. Although not usually diagnostically required, the oesophagus is involved in 20–25% of patients with systemic lupus erythematosus with similar changes to those with scleroderma.

A variety of manometric disturbances are seen in a wide variety of neurological

disorders. Manometry is not usually diagnostically helpful. Clinical attention and effort should normally be paid to supplementing and enhancing nutrition in these patients.

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4 Ambulatory pH monitoring

4.1 Equipment, sensors and recorders

Tracey L. Norris

Introduction

The development of prolonged intra-oesophageal pH monitoring has provided a precise means of directly quantifying the time that the oesophageal mucosa is exposed to refluxed gastric contents. It is a near-physiological test and provides essential measurements of frequency and duration of gastro-oesophageal reflux (GOR) episodes. The ability of the oesophagus to clear refluxate can be assessed and any correlation between oesophageal exposure to gastric contents and the symptoms experienced by the patient can be recorded.

Many patients who present with typical or atypical symptoms of gastro-oesophageal reflux disease have normal radiology, endoscopy and manometry findings. These patients may then be found to have pathological GOR during prolonged oesophageal pH monitoring. This has led to the development of prolonged oesophageal pH monitoring as a 'gold standard' diagnostic investigation for identifying abnormal GOR patterns.

Development of intra-oesophageal pH monitoring

Winklestein in 1935 [1] recognized that oesophagitis could be caused by reflux of acidic gastric contents. Bernstein and Baker in 1958 [2] then found that acid perfusion of the oesophagus induced heartburn in patients with gastro-oesophageal reflux disease (Bernstein test). By installing *in vivo* pH electrodes designed for gastric secretion studies in the oesophageal body, Tuttle and Grossman in 1958 [3] found that heartburn in patients with GOR coincided with a fall in pH to below 4 and were hence probably the first to use an intraluminal pH electrode to diagnose GOR.

The GOR provocation tests—the Bernstein test, Tuttle test [4] and then the 'standard acid reflux test' [5] and acid clearance test—were then developed and popularized during the 1960s and 1970s. However, they were short-term tests and had relatively poor sensitivity and specificity [6,7]. Despite the interest in

continuous or prolonged oesophageal pH monitoring, the clinical implementation was held up by two major factors. The first concerned the use of a reference electrode which is as essential to pH monitoring as the pH electrode itself. The reference electrode was a plastic tube filled with saturated potassium chloride solution which had to be sited next to the pH electrode in the oesophagus, and in constant contact with the mucosa. This made the system stiff, bulky and uncomfortable for the patient. Alternatives were for the patient to keep a finger and glass calomel reference in a beaker of saturated potassium chloride or to sit with the glass electrode in the mouth. These were very restrictive methods and did not work well.

As no studies had been performed on healthy, asymptomatic controls, a second and more significant inhibiting factor to the clinical implementation arose. Long duration reflux episodes and poor clearance in symptomatic patients were misinterpreted as being caused by acid gastric mucus 'sticking' to the pH electrode [8]. It was Miller and colleagues [9,10] in 1964 who first described continuous pH monitoring for 12–24 hours in control subjects and patients with symptomatic GOR. Then Spencer in 1969 [11] heralded the era of prolonged pH monitoring and confirmed that control subjects had no nocturnal GOR whereas symptomatic patients had supine GOR and longer episodes during the day. Spencer also defined a reflux episode as a fall in pH to below pH 4.

Johnson and DeMeester [12] and colleagues [13] carried out extensive studies on healthy individuals and advanced the utilization of prolonged intra-oesophageal pH monitoring as a clinically useful tool in investigating patients with GOR disease. The problem with the reference electrode was overcome by coating the reference electrode with ECG gel and placing it in direct contact with the skin. The electrode was sited on the arm and carefully bound so as to avoid evaporation of the ECG gel. This was far more comfortable for the patient such that they could tolerate being monitored for a complete circadian cycle, i.e. 24 hours. The patient was connected to a paper strip-chart recorder which was used to record pH. This meant that the patient was required to be hospitalized for the test. The recorder was either placed at the bed-side or was mounted on a trolley for 'ambulatory' studies [14]. The patients were therefore sedentary and severely limited in their activities; also, being hospitalized meant additional costs.

In the early 1980s, it was hospital costs and the fact that patients undergoing pH monitoring in hospital were filling much needed hospital beds that encouraged the development of a 'home' monitoring system, or an ambulatory outpatient monitoring system. About the same time, technological breakthroughs in electronics meant that electrical equipment such as pH recorders and computers could be miniaturized. The development of small, portable, light-weight recorders (Figs 4.1, 4.2 and 4.3) afforded more comfort to the patient and allowed true ambulatory studies to be performed in their own homes or at their work place.
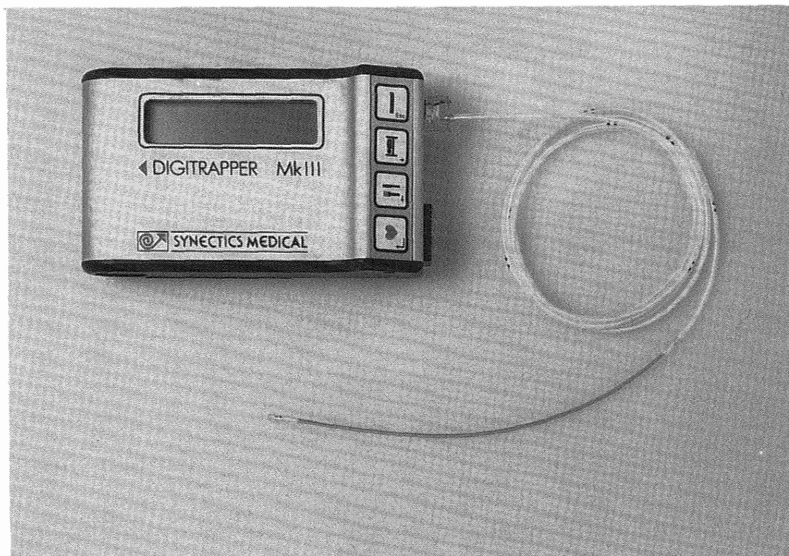
Fig. 4.1 Digitrapper mk III pH recorder with dual sensor antimony pH electrode (Synectics Medical).

Fig. 4.2 Flexilog 2000 pH recorder (Oakfield Instruments).

Fig. 4.3 Orion pH recorder (Medical Measurement Systems).

Equipment

pH electrodes

Glass electrodes

The first pH electrodes were glass electrodes and they are still popular today (Fig. 4.4). The glass electrode pH system contains two basic elements: (1) a reference electrode; and (2) a pH sensitive element, i.e. the glass electrode.

1 *Reference electrode*. The reference electrode has an open junction to the analyte that serves to provide a stable reference potential, ideally without any liquid junction effects. The Ag/AgCl or calomel system is often used.

2 *Glass electrode*. The electrode is composed of a thin glass membrane, one side of which is exposed to the analyte, the other side is in contact with a filling solution of constant composition (saturated solution of KCl). The diffusion potential across the glass membrane is proportional to the pH difference between the analyte and the filling solution. Electrical contact with the filling solution is via a silver wire coated in AgCl. Measurement of the potential difference between this wire and the reference electrode is the method of pH determination.

Due to the electrically insulating properties of glass, the electrode had to be made large or with a thin pH sensitive membrane to keep its impedance within tolerable limits [15]. Specialized electronics are required to cope with the small
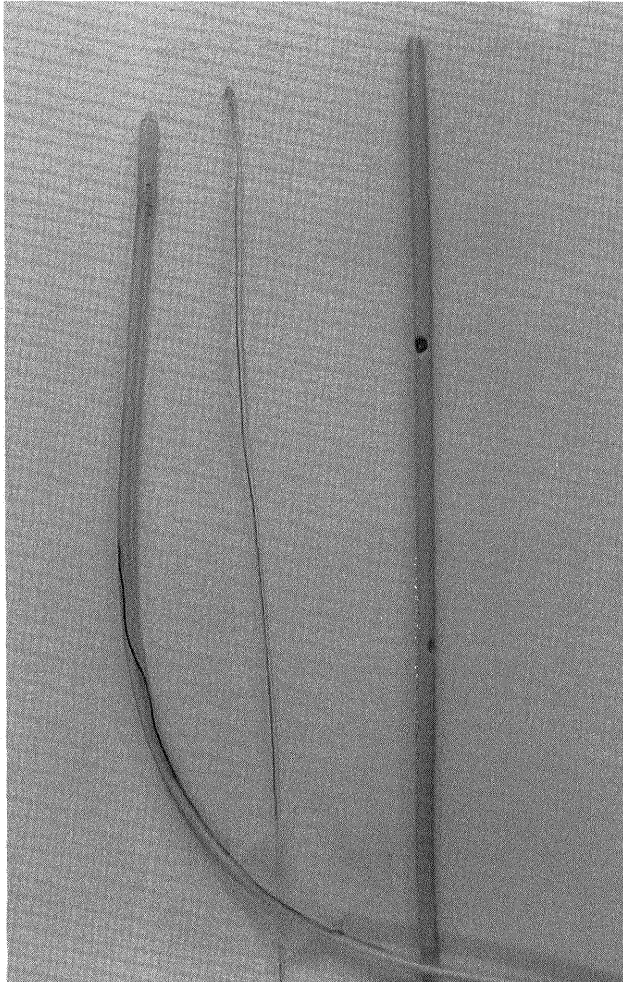
Fig. 4.4 pH electrodes. Left, glass; centre, antimony; right, ISFET.

mV signals. Field effect transistors (FET) are generally used for the critical input stage of the instrument. Noise and electromagnetic interference (EMI) problems are associated with the high impedance of the glass electrode. Care is taken to shield the cable between the glass electrode and the instrumentation. The cables must also be kept as short as possible.

Glass electrodes originally had a rather inflexible cable with the fragile, bulbous glass electrode at the tip. This was unpleasant to pass through the nostril. Today's miniaturized electrodes have a finer, flexible cable with a smooth electrode at the tip, e.g. 1.5–3.0 mm diameter (Table 4.1). Glass electrodes are also expensive but will usually last up to twenty 24-hour recordings provided care is taken with handling and they are not allowed to dry out between recordings. They are available with an external electrode, for example as described above, but usually have a

Table 4.1 pH sensor specifications (subject to change without notification).

|	Manufacturer							
	Synectics Medical	Ingold	Ingold Paediatric	Sentron	Remote Control Systems	Queenston	Konigsberg	Medical Instruments Corporation
Sensor type	Monocrystal Antimony	Glass	Glass	ISFET	Radio-telemetry capsule	Antimony	Antimony	Antimony
Reference electrode	External	Internal	External	External	Internal	External	External	Internal
Operating range (pH)	1–8	1–10	1–10	1–10	1–9	1–14		0.5–8.5
Temperature range (°C)	0–50	0–50	0–50	15–45	0–55	15–40		
Accuracy (pH over 24 h)	<0.1	<0.1	<0.1	+/–0.15		<0.5	+/–0.1	
Response time (s)	<3	1–2	1–2	<3	3	2		
No. of 24-h recordings	7–10	<10–20	10–20	50–75	30	25–50		5
Diameter (mm)	1.5–2.1	3.0	1.5	1.3–2.7	7.3 × 24	1.5–3.0	4.0	2.0
Impedance	<1 MOhm	12 MOhm	12 MOhm	'Low'		1 MOhm	<500 Ohm	
No. of sensors	1–3	1	1	1–6	1	1,2	1–3	1
Sensitivity	55.3 mV/pH	54.5 mV/pH	54.5 mV/pH	52.0 mV/pH	3.0–4.5 KHz/pH	57.0 mV/pH		50.0 mV/pH

built-in internal reference. Glass electrodes are recommended for both prolonged oesophageal and gastric pH monitoring [16]. Technical details are given in Table 4.1.

A variation on the cable glass electrode was very popular in the 1980s. This was the combination glass radiotelemetry capsule or 'pH radio pill' (Fig. 4.5). This consists of a transducer, a mercury battery and low power transmitter sealed in a non-toxic glass capsule measuring 24 mm × 7.4 mm. Housed in a cylindrical electronic insert is a transistor oscillator; its frequency is controlled by the voltage developed across its pH-sensitive ion-selective electrode. The potential difference between the pH electrode and the Ag/AgCl reference electrode situated in the reference cap is the method of pH determination as described with the cable glass pH electrode above. Thirty 24-hour recordings can be obtained from each replaceable cap and mercury battery.

The advantage of the radiotelemetry pH capsule is that no external reference electrode is required. The capsule is swallowed and is tethered by a nylon thread to the cheek. Sometimes the thread may pull on the corner of the mouth and interfere with swallowing. The patient also has to wear a bulky aerial belt around the chest to pick up the signal from the capsule and if this slips during the monitoring period there may be signal loss. Interference from external sources can also be a problem. Despite these problems Branicki *et al.* [17] and Ward *et al.* [18] claimed the results obtained and patient acceptability are similar to cable glass electrodes. Even though still commercially available, the popularity of the radiotelemetry capsule has diminished.

Antimony electrodes

Antimony (Sb) electrodes are of the metal/metal oxide type and were first used in
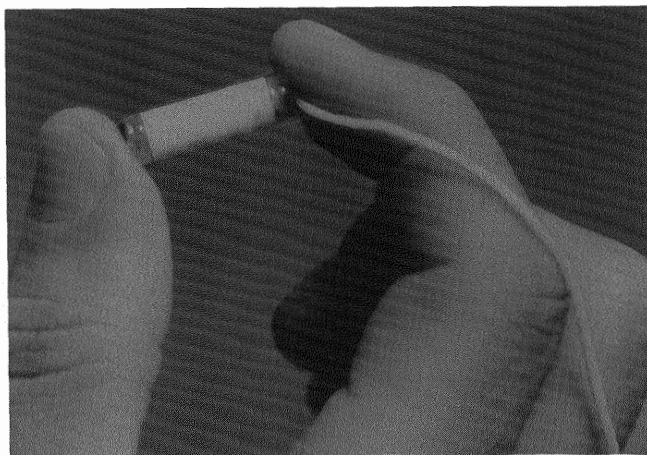

**Fig. 4.5** Radiotelemetry capsule with tether (Remote Control Systems).

medical pH determinations *in vivo* in 1927 by Buytendijk. They are a popular alternative to glass electrodes. They can be miniaturized to 1.5 mm diameter, are more flexible, durable, have low impedance and are cheaper (Figs 4.4 and 4.6). There are two forms of the electrode—polycrystalline and monocrystalline.

An antimony sensor is made from cutting a small cylindrical segment out of a large pure single antimony crystal and electrically connecting it to a signal lead with conductive epoxy resin and gluing this into PVC tubing [15]. Unlike the glass electrodes, the potential of an antimony electrode is its corrosion potential. During usage, the surface of the electrode is oxidized by the measuring solution and antimony dissolution is one of the main potential determining reactions. As the electrode potential is also sensitive to changes in the oxygen partial pressure of the solution, oxygen reduction most probably constitutes the other potential determining reaction. The potential of the corroding antimony [15] is determined by the anodic metal dissolution reaction and the cathodic oxygen reduction. Anodic metal dissolution reaction:

$$2Sb + 3H_2O \rightleftharpoons Sb_2O_3 + 6H^+ + 6e^-$$
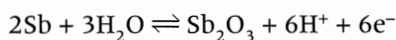
Cathodic oxygen reduction reaction:

$$O_2 + 4H^+ + 4e^- \rightleftharpoons 2H_2O$$
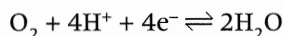
The corrosion attacks, and subsequent metal dissolution, mean that antimony electrodes have a short life of around seven 24-hour oesophageal pH studies.

Polycrystalline antimony has a large number of grains of various shapes and sizes so corrosion is not uniform across the surface. The constantly on-going corrosion changes the surface continuously through pitting or by laying down of corrosion products and this leads to changes in the potential. For this reason, polycrystalline antimony electrodes are said to have poor stability and reproducibility of the electrode potential [15] and are sensitive to complex forming ligands [19] in the measuring solution. They are therefore thought to be inferior electrodes to
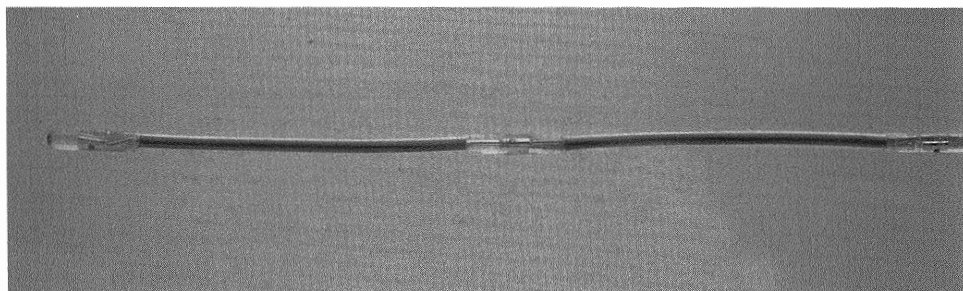
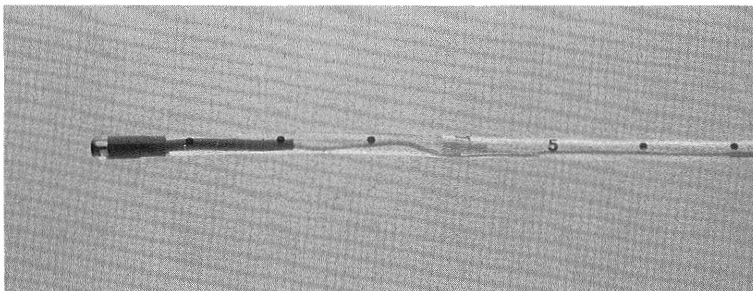**Fig. 4.6** Monocrystalline antimony pH electrode with three sensors (Synectics Medical).

monocrystalline antimony electrodes. Monocrystalline antimony electrodes are made from pure antimony that has been crystallographically orientated by X-ray diffraction. This means that only one plane surface at a time is exposed to the measuring solution and this uniform plane of high atomic density leads to a low corrosion rate and a more stable electrode [15]. Because of the low impedance of antimony, the reference electrode can be far from the pH sensor without noise interference. An Ag/AgCl reference can be used. Antimony electrodes with external reference electrodes can be stored 'dry'.

Antimony electrodes are also available as disposable, i.e. single use, electrodes with a built-in internal reference electrode (Fig. 4.7). These arrive in sealed foil packets. 'Semi-disposable' antimony electrodes with internal reference are available. These require quite a lengthy soak in buffer (check with manufacturer) before each use and they can be used up to five times. Some studies have shown that monocrystalline antimony electrodes are suitable for either intra-oesophageal or intra-gastric pH monitoring [20,21]. However, Geus *et al.* in 1994 [16] studied the basic operating characteristics of the two types of electrodes, i.e. response time, sensitivity, hysteresis and drift in an *in vitro* study. This showed that mono- and polycrystalline antimony electrodes are acceptable for prolonged intra-oesophageal but not intra-gastric pH monitoring. Although the characteristics of the two antimony and the glass electrodes were similar during the pH range 2.5–7.0, a marked drift was observed for both antimony electrodes when the pH was below 2.5. Glass electrodes are, therefore, more reliable for intra-gastric pH studies.

Antimony electrodes are available with 1–4 pH sensors (Fig. 4.6) and and because of their small size can be incorporated into solid state combined manometry and pH catheters, though the life of this type of catheter is dictated by that of the antimony sensors.

ISFET pH electrode

The ion-sensitive field effect transistor (ISFET) is a modification of the normal

Fig. 4.7 Disposable polycrystalline antimony pH electrode with internal reference (Zinectics).

field effect transistor (FET) as described in the glass electrode system (see above). However, an ion-sensitive (IS) membrane, e.g. aluminium oxide, is deposited directly on top of the metal gate normally used as input. This achieves a low output impedance by putting the pre-amplifying element directly under the insulating membrane. The filling solution has also been eliminated, so a small $(1.5 \times 0.6 \times 0.3\,mm)$ solid state device is achieved (Figs 4.4 and 4.8). The ISFET requires a constant current power supply so that it will produce a voltage that is linearly proportional to the pH of the surrounding fluid over the range of pH values found in the gastro-intestinal tract [22]. Connecting cables with excessive shielding are not required so several of these small electrodes can be sited in a single small calibre catheter; for example, a five sensor assembly has a diameter of only 2.7 mm. This type of multisensor electrode can be used in the study of reflux dynamics [23]. ISFETs are also ideal for incorporating into multifunction catheters to use in ambulatory combined manometry and pH monitoring. They are currently used in conjunction with an external Ag/AgCl reference electrode. Duroux *et al.* [22] compared ISFET and glass electrodes under *in vitro* and *in vivo* conditions and found them both to have a linear response over the pH range 1.3–8.0 and that they have a very similar response time and drift over 24 hours. SFET electrodes are much smaller, durable and cheaper than glass electrodes.

If multisensor (more than two sensors) gastric pH monitoring is required, glass electrode assemblies may be too large to pass transnasally. If they are passed orally they are very uncomfortable and can only be tolerated for a few hours. ISFETs are much smaller than glass electrodes and are therefore ideal for this type of work. If they could be produced commercially in large numbers, then the multisensor ISFET ph catheter could be 'disposable'. The ISFET has to be soaked in buffer pH 7 for at least 4 hours prior to its use in order to overcome an initial non-linear drift [22,23]. However, one current commercial supplier suggests that only a 15 minute soak in buffer pH 7 is necessary.

Another example of a small inexpensive pH electrode is the 'plastic' pH sensor. Unfortunately, these only cover a selected pH range depending on the membrane composition and other ions that are present in the monitored environment at any
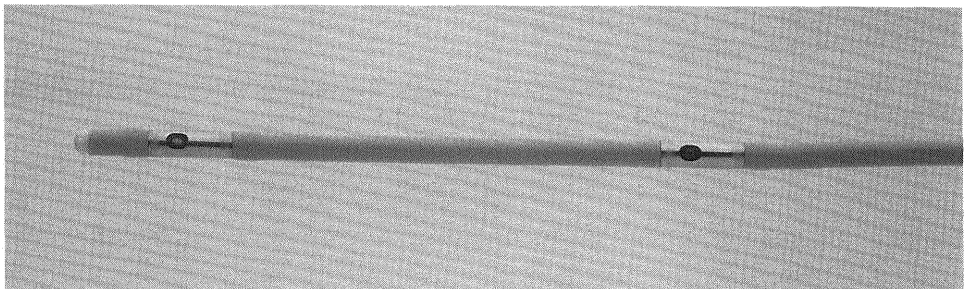
Fig. 4.8 ISFET pH electrode (Sentron).

one time. A collection of pH sensor specifications from different manufacturers is given in Table 4.1. These specifications are subject to change.

Recording systems

The first compact portable recorders were magnetic tape recorders. The tracings were replayed onto a chart recorder which could take up to an hour. The traces were analysed manually and problems with the recorder included interference from outside sources, and mechanical problems such as tape jamming. Solid state recorders are now available with none of the problems associated with mechanical moving parts (Table 4.2 and Figs 4.1–4.3). They can be as small as a cigarette packet and can weigh as little as 150 g. Most are provided with a carrying pouch and belt and are usually worn around the waist. They can have up to eight event markers for the patient to activate for symptoms (e.g. heartburn or chest pain) or when the patient is eating or recumbent. Most centres find that asking the patient to use just one marker and keeping a detailed diary of symptoms and activities is far less confusing for the patient.

**Table 4.2** pH recorder specifications.

|	Manufacturer				
	Synectics Medical	Oakfield Instruments	Medical Instruments Corporation	Medical Measurement Systems	Albyn Medical
Model name	Digitrapper Mk III	Flexilog 2010	Gastrograph Mk III	Orion	Nymph
Weight (g)	300	397	150	310	350
Sample rate	Every 4, 8 or 16 secs	1 or 6 per sec	4 per sec	Up to 8 per sec	Every 1–20 secs
Memory size	96 kB	96 h @ 6 sec sample rate	96 kB	256 kB	1–4 MB
No. of event buttons	1–4	1	6	5	8
Power supply	9 V alkaline battery	9 V alkaline battery	1.5 V AA × 2 batteries	1.5 V AA × 2 batteries	1.5 V AA × 2 batteries
Display	32 character LCD	16 character LCD	LCD	32 character LCD	32 character LCD

LCD, liquid crystal display.

Solid state recorders have a large memory capacity, e.g. up to 4mB, which means that pH can be monitored at multiple sites throughout the oesophageal body. The recording capacity depends on the sampling frequency which is usually variable. The recommended minimum sample frequency is 0.15 Hz. Stored data can be downloaded onto and analysed by a computer within a few seconds. The data can be presented graphically or numerically (Figs 4.9 and 4.10). The software analyses are constantly being upgraded and it is advisable to register with the program supplier whose software is being used in order to be informed of any new programs/updates as they are developed.

Technical considerations when using pH electrodes

There are several technical factors that may affect the absolute pH accuracy of the recording system which may be overlooked or ignored.
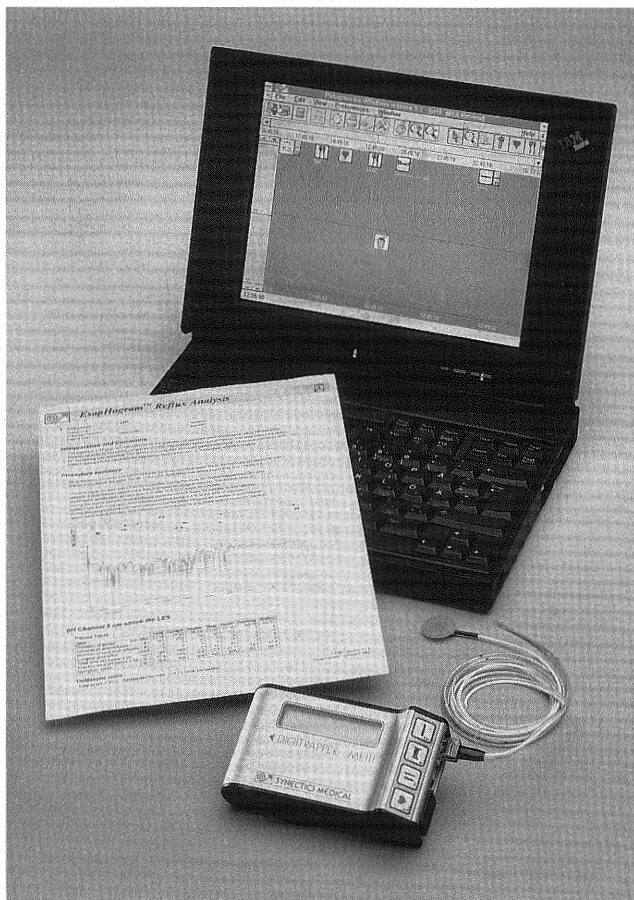
Fig. 4.9 EsopHogram reflux analysis (Synectics Medical).
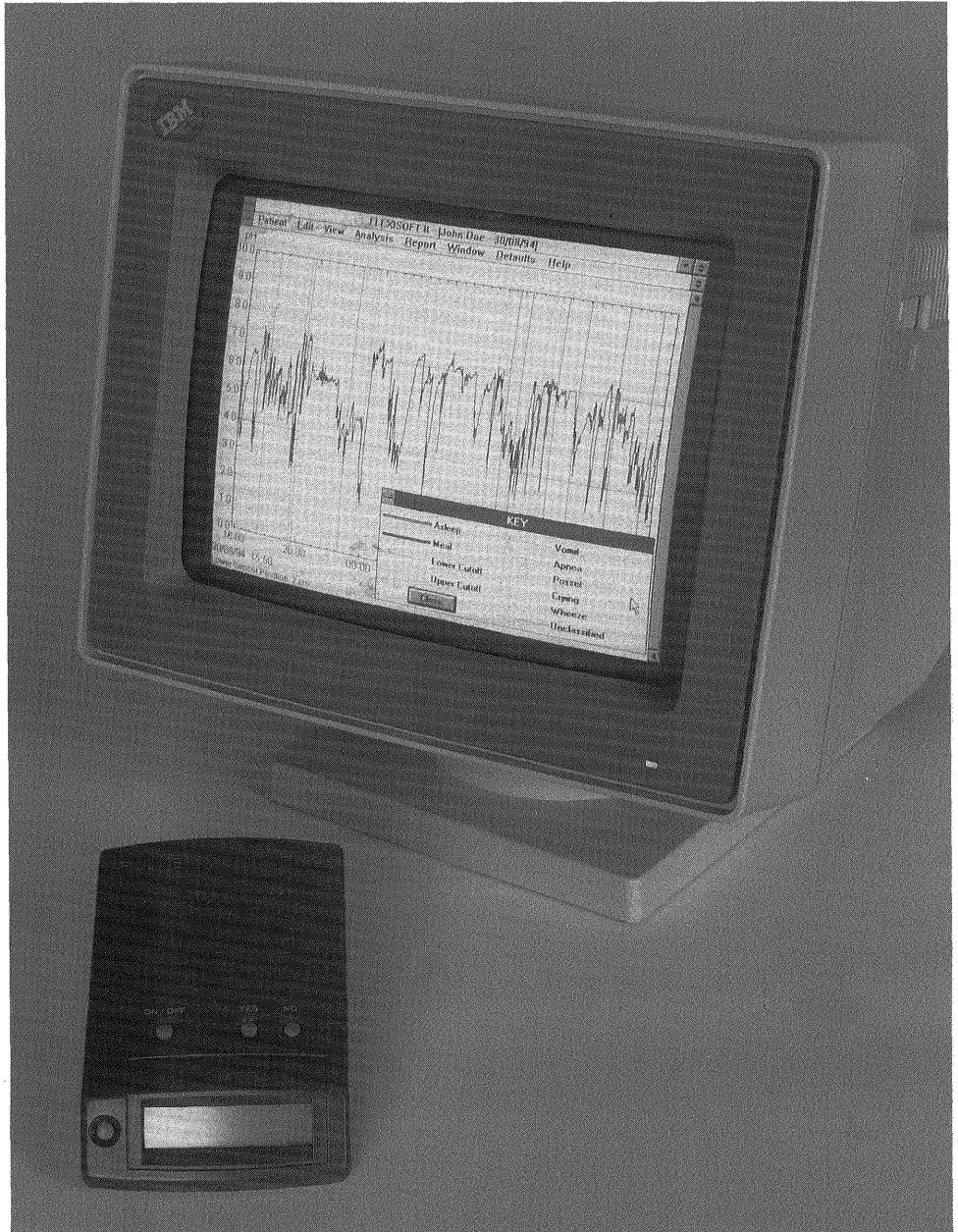
Fig. 4.10 Flexisoft pH analysis (Oakfield Instruments).

Type of electrode used

The first concerns are the type of electrode used. Because of the different mechanism of pH determination between antimony and glass electrodes, there is a large difference in their mV range, i.e. the antimony electrode range is –617 to 0 mV, the

mV range of a glass electrode is −167 to +450 mV. The recorder needs to be adjusted accordingly. Some recorders have an internal option switch for glass or antimony, some recorders require the option to be input directly or it may be necessary to input the information into the system constants of the pH program you are using. Some newer recorders can 'automatically recognize' the electrode type during calibration.

Composition of calibration buffers

Only phosphate-free buffers such as TRIS (trishydroxymethyl-aminomethane) should be used when calibrating antimony electrodes. This is because complexes are formed with the antimony which affect the response of the antimony especially between pH 4 and 7 [19]. Other ligands known to form complexes with antimony are tartrate, citrate and oxalate so buffers containing these should also be avoided. Other electrode types require the use of high Cl ion buffer composition.

Reference electrode and gel

The reference electrode used in pH monitoring is an Ag/AgCl electrode. This is either integrated into the pH catheter or applied externally to the skin. With the external electrode, the potential difference is determined by the chloride ion concentration of the electrode gel surrounding the electrode. For accuracy, the chloride ion concentration of the buffers should ideally be equal to that of the electrode gel and that in the gel should be equal to the chloride ion concentration in the extracellular fluid in order to minimize the liquid junction potential over the skin. It is therefore advised to use only the electrode gel recommended by the manufacturer.

Placement of reference electrode

The external reference is usually positioned on the upper chest just beneath the clavicle as there is very little body movement here and it will not interfere with clothing. This is also close to the oesophagus. In children the reference may be placed on the back to prevent them from removing it inadvertently. An abrasive ECG cream is rubbed into the area with a tissue (the area may need to be shaved first in some men). An alcohol wipe is used to clean away the preparatory cream and then the area is blotted dry with another tissue. Cut an approx. 7.5 cm square of adhesive tape. Press the back of the electrode into the middle of the square of the tape so that it adheres to it. Apply the recommended electrode gel to the centre well of the electrode, just enough to fill it. Place the taped electrode over the prepared skin and press down the tape all around the electrode firmly to seal it. Alternatively,

there are commercially available double-sided adhesive tapes. The electrode should be allowed to stabilize for at least 20 min [24].

Temperature affects both pH and reference electrodes and should be taken into account. The internal pH electrode is at body temperature (37°C); external reference electrode gel, however, is at skin temperature of around 30°C. The temperature at which the calibration is carried out also has to be considered and correction factors for both glass and antimony electrodes have been calculated. The following equation for antimony takes these factors into consideration:

pH real = pH shown − (1.9(Tsb − Tcal) + 0.6 (Tgel − Tcal)/53

where pH real = true pH; pH shown = pH seen on the meter; Tsb = temperature of the antimony probe; Tcal = temperature at which calibration is performed and Tgel = temperature of the electrode gel.

The '53' is derived from the sensitivity of the antimony (−53 mV/per pH) [24] and it is slightly sub-Nernstian. Nernst equation is as follows:

$$E = E_0 + 2\frac{RT}{F} \cdot \ln a_H^+$$

where R is the gas constant, T is the absolute temperature, F is Faraday's constant and aH^+ is the hydrogen ion activity.

Correction factors and calibration

When using some antimony electrodes (Synectics Medical) it is possible to calculate the overall single correction constant when taking the following factors into consideration:

1 The temperature dependence of :
    (a) The monocrystalline antimony electrode (1.9 mV/°C);
    (b) the reference electrode (0.6 mV/°C);
    (c) the buffers.
2 The voltage offsets due to:
    (a) the difference in chloride ion concentration between the buffer and the reference electrode gel (Hellige)(26 mV);
    (b) the difference in the chloride ion concentration between the reference electrode gel and the skin (−6 mV);
    (c) the junction potentials between the buffer and the extracellular fluid (+5 to −19 mV).

Calibration of electrodes

There are generally four ways to calibrate a pH monitoring system. The buffer can
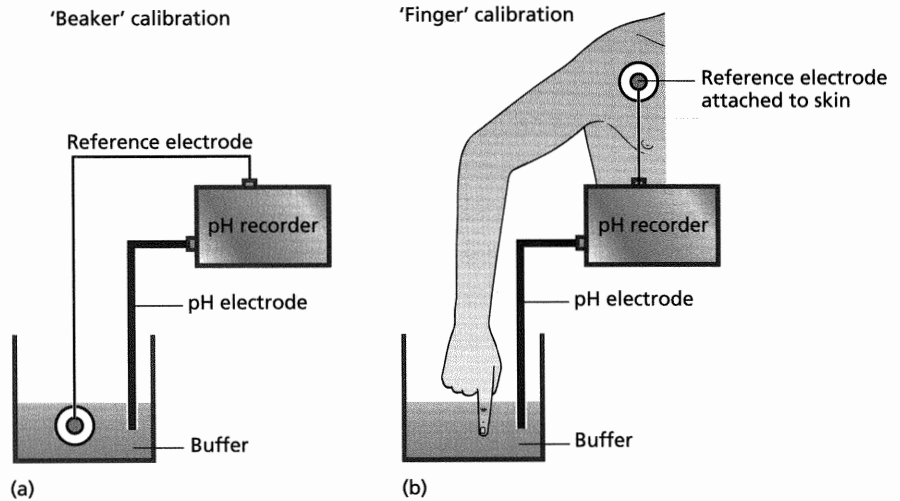
Fig. 4.11 (a) Beaker calibration and (b) finger calibration.

be at room (25°C) or body temperature (37°C). The pH and reference can both be inserted together in the buffer (beaker calibration; Fig. 4.11a) or the patient can have the reference attached to the chest as described above and can close the circuit by inserting his finger in the buffer (finger calibration; Fig. 4.11b).

Calibration method 1: beaker calibration at room temperature

For pH catheters with external reference, an antimony pH electrode for example, both the antimony and reference electrodes are connected to the recorder and are immersed in the room temperature (25°C) buffers. After calibration the gelled reference electrode is attached to the patient's skin at 25–30°C and the pH electrode is positioned in the oesophagus at 37°C. The calibrating and monitoring temperatures are not identical; both the antimony electrode and reference electrode are calibrated at a lower temperature than their monitoring temperature. For this reason, correction factors need to be applied (Table 4.4, Method 1).

Calibration method 2: beaker calibration at body temperature

The table of correction factors now differs since the temperature of the antimony electrode, for example, during the calibration is the same as its monitoring environment. The reference electrode, however, is calibrated at a higher temperature that its monitoring temperatue (Table 4.4, Method 2). Warming of buffer pH 1 does not change the pH markedly but buffer pH 7 is more temperature dependent. At 25°C the pH 7 buffer has an actual pH of 7.01 and at body temperature its pH may be decreased to as low as pH 6.7 depending on the composition of the buffer.

Table 4.3 Correction factors for pH calibration.

	'Beaker' calibration		'Finger' calibration	
	(1) 25°C	(2) 37°C	(3) 25°C	(4) 37°C
1 Antimony electrode is calibrated at 25°C but is monitoring at 37°C	+0.6	—	+0.6	—
2 Reference electrode is calibrated at 25°C but is monitoring at 30°C	+0.1	—	—	—
3 Reference electrode is calibrated at 37°C but monitoring at 30°C	—	−0.1	—	—
4 Difference in Cl⁻ concentration between buffers and electrode gel	−0.5	−0.5	—	—
5 Difference in Cl⁻ concentration between gel and extracellular fluid	+0.1	+0.1	—	—
6 Error due to junction potential between finger and buffer	—	—	−0.1 ± 0.3	−0.1 ± 0.3
7 Buffer pH 1 has a pH closer to 1.1 than 1.0 (for pH 1 level only)	−0.1	−0.1	−0.1	−0.1
8 Buffer pH 7 has a true pH of 6.7 at 37°C (for pH 7 level only)	—	+0.3	—	−0.3
Total correction factor:				
For pH 2	+0.2	−0.6	+0.4 ± 0.3	−0.2 ± 0.3
For pH 7	+0.3	−0.2	+0.5 ± 0.3	+0.2 ± 0.3

Calibration method 3: finger calibration at room temperature

The reference electrode is applied to the skin. One of the patient's forefingers is cleaned with abrasive ECG gel in much the same way as the skin preparation for the chest reference electrode. The reference and pH electrode are connected to the recorder, then the forefinger and the active electrode are placed in the buffer together. The patient's finger acts as an access point to the extracellular fluid [24].

The correction factor for the electrode being calibrated at 25°C but monitoring pH at 37°C applies. However, because the reference electrode is attached with its gel to the patient it will be monitoring at the same temperature so corrections for reference electrode temperature and differences in chloride ion concentrations between buffer–gel–extracellular fluid are not necessary. Unfortunately, however, a new junction potential is introduced between the finger and the buffer. Measurements of the junction over the finger indicate that this potential varies considerably so it can be a source of error [24] (Table 4.4, Method 3).

Calibration method 4: finger calibration at body temperature

This method is identical to method 3 except that the buffers have been warmed to 37°C. The correction factors are shown in Table 4.4, Method 4. Because the uncertainty of the junction potential at the finger is a source of error, it is generally recommended that a 'beaker calibration' be performed before and at the end of the recording [24]. The beaker calibration also has the advantage that the calibration can be performed prior to the patient's arrival. After a finger calibration both buffers have to be discarded as they are immediately contaminated.

The only calibration option for pH electrodes with built-in references is the 'beaker calibration'. Examples of correction factors for pH electrodes other than the semi-disposable monocrystalline are given in Table 4.4. These correction factors only apply if reference electrodes/gels/buffers, etc. recommended by Synectics Medical are used. Other manufacturers may have their own correction factors.

Table 4.4 Recommended correction factors for a 'beaker' calibration at room temperature (Synectics Medical).

	Correction factor	
	pH 1	pH 7
Disposable antimony with internal reference	+0.4	+0.9
Glass electrode	−0.35	0.0
ISFET electrode	0.0	0.0

Practical suggestions for preparation of pH measurements

1 On receipt of a new pH recording system always note down the serial number. Keep the delivery note and all related paper work together in a labelled folder. Write the Unit name and address on the back of the recorder in case of loss. If the recorder needs to be returned to the manufacturer for updating or repair someone else's recorder will not be sent by mistake.

2 If reusable, give pH electrodes a reference number written on a small 'flag' of tape and attach to the plug end of the catheter. Keep a record of the date/patient name/type of recording, i.e. oesophageal or gastric pH, on the back of the individual electrode's packet. It will become apparent when it is coming to the end of its life. It is also easy to spot if there is a problem with individual or batches of electrodes.

3 When calibrating, never change from a low pH buffer to a high pH buffer when checking electrodes or calibrating without thoroughly rinsing the electrodes/ fingers in distilled water and drying them in between. It is very easy to 'contaminate' a high pH buffer with H^+ ions from the low pH buffer.

4 Do not put any used beaker buffer back into the original source bottle, because this will cause contamination. Store buffers at recommended temperatures (usually 4°C) but allow them to come to calibration temperature before calibration.

5 Mark out a ruler in cm, 70 cm long, along the edge of the bench with a permanent marker. It is then easy to measure out the desired length of a pH probe for monitoring by simply holding it straight and horizontally along the ruled line and wrap a narrow strip of tape around the catheter at the desired length. This provides a 'marker'. The distance markers originally on the pH electrode do not last and sometimes they are marked incorrectly. Using the bench rule is reliable and very quick.

6 Insert the pH electrode further than required, i.e. until there is a gastric pH reading (pH 1–2). Withdraw the catheter until the marker tape appears at the nostril. The electrode is then lying correctly and not curled. If an acid reading is not obtained the catheter may be curled in the oesophagus. This is usually felt as a resistance and the catheter feels 'springy'. If in doubt, the probe position can be checked radiologically.

7 Clean electrode gel from the centre of the Ag/AgCl reference electrode using a warm soapy solution of hibiscrub and a soft toothbrush and then dry.

8 Remember that the belts and pouches housing the pH recorder are often worn next to the skin. They can be surface cleaned with an alcowipe but can also be washed in the washing machine (if not leather) at 40°C.

9 When using a catheter with an internal reference electrode it will usually have to be soaked in buffer pH 7 for a minimum period in order to stabilize. For example, the ISFET electrode requires to be soaked for 15 min prior to the calibration.

10 A millivolt meter with appropriate sockets for the pH electrode will serve as a probe checking device using calibration buffers.

11 Immediately prior to calibration, 'buff' the antimony sensor gently with a small piece of pan scourer to remove any oxidation/corrosion products.

An in-depth knowledge of the equipment, how to use it safely and correctly is essential if meaningful results are to be obtained. The operator must understand all potential sources of error and be able to recognize instantly when there is a fault and how to rectify it. An erroneous 24-hour pH recording due to operator incompetence can result in misinterpretation and misdiagnosis.

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4.2   Procedures for prolonged pH monitoring

Anne Pryde

Introduction

Prolonged intra-oesophageal pH monitoring was first demonstrated in the 1960s [1,2] and it was later shown that postprandial gastro-oesophageal reflux (GOR) occurs in normal individuals [3]. Researchers throughout the 1970s and 1980s produced evidence of different patterns of reflux in relation to posture and eating habits [4–7] and with improvements in both recording equipment and electrodes [8,9] it became obvious that to detect abnormal GOR a 24-hour recording period was necessary [10,11]. The technique of prolonged ambulatory pH monitoring is now described as a 'gold standard' for diagnosing GOR [12]. Therefore, the need for standardization of the technique has long been apparent. Considering these points the Clinical Measurement Associates (CMA), after consulting major gastro-intestinal units throughout the UK, suggest the following

Table 4.5 Indications for ambulatory pH monitoring.

Reflux symptoms which fail to respond to medical treatment
   Normal oesaphageal mucosa on endoscopy
Atypical symptoms
   Dysphagia
   Non-cardiac chest pain (where cardiac tests are negative)
   Respiratory symptoms, e.g. asthma, aspiration pneumonia, chronic cough
   ENT symptoms, e.g. laryngitis, hoarseness, globus sensation
Post-treatment for achalasia
Pre- and post-anti-reflux surgery

recommendations and guidelines for the basic clinical technique of ambulatory oesophageal pH monitoring.

The exposure of the oesophageal mucosa to refluxed gastric acid causing symptoms and damage resulting in gastro-oesophageal reflux disease (GORD) is very common [13]. When the symptoms are typical of GORD then treatment may be started without further investigation [14]; however, if symptoms are persistent or atypical then ambulatory pH monitoring is useful in the investigation of GORD (Table 4.5).

Ambulatory pH monitoring technique

Prior to performing the procedure the patient and equipment must be prepared.

Patient preparation

The patient should be informed to attend for the investigation having fasted for a minimum period of 4 hours, to stop certain medications (Table 4.6) and that they will be returning to home or work with the recording equipment fitted. On attendance the patient should receive a full explanation of the test including how the test will be performed and why they have been referred for the investigation. The patient should be interviewed to obtain a detailed history of their symptoms and at this point any questions or anxieties they might have could be discussed. Written consent should be obtained and a contact number should be given to the patient to reassure them that although they are going home help is available if needed. Any contact number should be the hospital switchboard, who can then contact the appropriate person, as it is not recommended that medical/technical staff give personal telephone numbers to patients.

Table 4.6 Medication to be discontinued before investigation.

Medication	Discontinue prior to study
Antacids/alginates	24–48 hours (depending on local policies)
Histamine receptor antagonists	48 hours
Prokinetic agents	48 hours
Proton-pump inhibitors	5 (minimum) to 7 days

Advice should be taken from referring cardiologists on stopping anti-anginal therapy in patients with non-cardiac chest pain.

Equipment preparation

Recorders are fitted with new batteries, electrodes of choice and must be calibrated [15]. Some pH electrodes have an in-built reference but many require external reference electrodes. It is essential that all pH electrodes are calibrated correctly. Pre-test calibration has been described earlier and it is also recommended to repeat the calibration procedure at the end of the recording period where possible to check for any drift in pH. The sample frequency of the recorder should be set (recommended minimum—one sample /6 s (0.15 Hz). The real time display should be checked for accuracy and the recording period set to the appropriate value (usually 24 hours).

Intubation

The ability of non-medical staff to intubate patients should be clarified by the Health Authority or Trust and head of department or clinician in charge as they have ultimate responsibility for the patients. Prior to intubation the patient's nose and pharynx may be sprayed with a proprietary local anaesthetic (e.g. xylocaine or benzocaine). The investigator should always wear gloves, for their own safety and that of the patient. The recording surface of the external electrode (if required) is smeared with the appropriate electrode gel and placed on an even area of the chest, which must be cleaned by scrubbing with an abrasive paste and an alcohol swab. Areas where there is excessive body hair must be avoided or shaved. Preparing the chest in this way is essential to ensure good adherence of the electrode to the skin, otherwise poor contact will produce a faulty electrical circuit resulting in artefact and an uninterpretable study.

pH electrode positioning

The electrode is marked, with a strip of tape, at the appropriate length (Fig. 4.12a),

to position the pH sensor correctly. The recommended position of the pH sensor used to detect GOR is 5 cm above the manometrically defined proximal border of the lower oesophageal sphincter (LOS) [10].

Where manometry is not available, some pH sensor manufacturers provide a pH electrode that has a built-in solid state pressure transducer or a perfused lumen that can be connected to an isolated pressure transducer. By withdrawing the pressure sensing device from the stomach through the diaphragm and into the oesophageal body, a rudimentary LOS pressure profile can be obtained enabling accurate positioning of the pH sensor.

The pH sensor is positioned with the patient seated, preferably on a couch (Fig. 4.12b), in case of difficulty during the intubation where it may be necessary to reposition the patient supine (in cases of fainting). A little lubricating gel on the tip of the electrode will help passage through the nose. The electrode is inserted through the nose and when the patient feels it in the back of the throat, with the aid of sipping water through a straw and their chin on their chest, the electrode is advanced to the appropriate level (Fig. 4.12c). The electrode is secured to the nose and the side of the face taking care not to obscure the mouth (Fig. 4.12d).

It is important to be aware of the complications that could arise when intubating patients, i.e. vomiting, fainting, broncospasm or respiratory arrest, therefore investigators should know their own hospital's resuscitation procedure and where medical cover can be immediately located. All non-medical personnel should be trained in the recognition and first aid of respiratory or cardiac arrest.

Notes on electrode position. The recommended pH sensor position is 5 cm above the proximal border of the manometrically determined LOS [10]. Electrodes positioned more distal than 5 cm from the proximal border of the LOS should not cause false reflux measurements as it has been shown that electrodes so placed are unlikely to migrate into the stomach with changing body position [16]; however, it has been shown that the further the pH probe is from the LOS the lower the values of acid exposure that are recorded [17].

Alternative methods of pH probe placement are:

1 Radiology. The probe may be positioned fluoroscopically 5 cm above the diaphragm with reasonable confidence so that it is 5 cm above the gastro-oesophageal junction. However, in patients with hiatus hernia this method has been shown to be unreliable [18].

2 Gastric withdrawal using the balloon technique has been found to be reliable [19]. This does however necessitate two intubations.

3 The point of pH change on withdrawal of the electrode from the stomach has been used but has been shown to be unreliable [20] in comparison with the manometrically determined LOS.

4 Endoscopically. The gastro-oesophageal junction assessed at endoscopy with
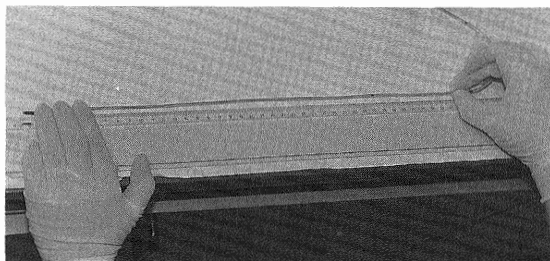
(a)

(b)
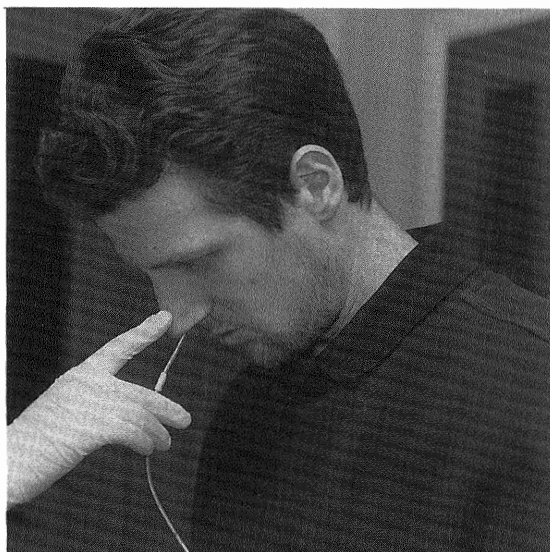
(c)
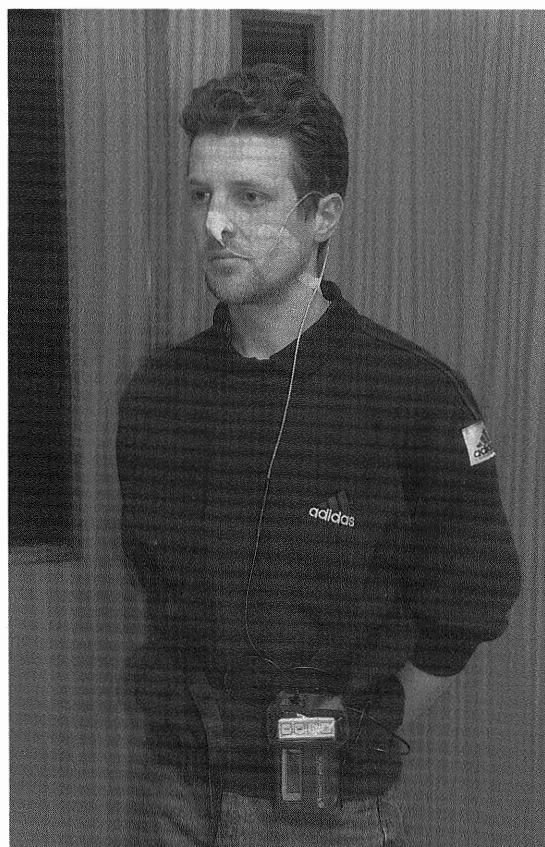
(d)

Fig. 4.12 (a) Distance markings to appropriate length on the pH electrode (40–50 cm). (b) Patient in sitting position ready for intubation.
(c) Intubation with the patient's chin on chest.
(d) pH probe fixed in position; the patient is ready to go home.

adjustment made for the nasopharynx may be used but can be grossly inaccurate [20].

Station or rapid pull-through manometry, either with standard or LOS finder techniques, is the most accurate technique for determination of the LOS position and subsequent pH probe placement. Other techniques will give rise to errors in measurement of GOR.

Multisite measurements

When two or more pH sensors are used to record from different sites in the oesophagus or gastric lumen, the reference sensor is always positioned at the distal oesophageal site (5 cm above LOS) and the other or others may be positioned above or below at intervals set by the inter-electrode distance (usually 5, 10, 15 or 20 cm). These studies are particularly useful in more detailed examinations of acid and alkaline levels around the gastro-oesophageal junction (Table 4.7) and for determining the proximal spread of gastric juice into the oro-pharynx and above. The major problem with this technique is that there are no guidelines published yet for normal values at these sites so assessment of recordings remains subjective.

Patient instructions

The purpose of a diagnostic assessment for GOR is to determine the pattern of reflux normally experienced by the patient, therefore the patient should be encouraged to carry out their normal daily routine and not to deviate from their usual eating, drinking, smoking and sleeping habits unless the test is part of a clinical study requiring restrictions. Acidic food and drink can result in brief falls in intra-oesophageal pH [21] but non-acidic food may also influence the pH by

Table 4.7 Suggested indications for combined distal and proximal oesophageal pH measurements.

Adult	Paediatrics
Regurgitation	Vomiting
Hoarseness	Cyanosis/apnoea
Wheeze/asthma	Near-miss cot death
Palatal tooth wear	Chest infection
Acid suppression treatment failures (on therapy)	
Suspected duodeno-gastric or bile reflux	

buffering [22]. Smoking and alcohol intake, tight or restricted clothing have all been shown to affect total oesophageal acid exposure [23,24]. Therefore, the recommendations regarding instruction to patients are as follows:

1 *Food and drink*:
   (a) unrestricted (unless as part of a controlled trial);
   (b) acidic food restriction (optional).

2 *Sleep and posture*: the importance of recording both periods of lying down and sleeping whether or not they occur at the same time.

3 *Activities*:
   (a) unrestricted (encouraged to follow a normal routine);
   (b) smoking is unrestricted but recorded;
   (c) alcohol is unrestricted but recorded.

4 *Medication*: patients are instructed to remain off their medication for GOR until the pH study is completed.

During the 24-hour test period the patient is asked to keep a written diary (Fig. 4.13a) and to use the event marker buttons on the recorder (Fig. 4.13b). The diary is explained to the patient and they are requested to record:

1 Meals—time of eating/drinking and the content.

2 Sleep—time of sleeping or lying down.

3 Symptoms—time of symptom occurrence and the duration.

4 Other—helpful information, e.g. belching; acid in the mouth; time of cigarettes.

Duration of the study

Many researchers have investigated the value of shorter periods of pH monitoring, looking at acid reflux 3 hours after a meal [21,25,26] or recording periods including the evening meal and night-time [27,28], finding sensitivities around 80% and specificities of 96%, producing good correlation with the results of 24-hour studies. However, for diagnostic purposes it is recommended that 20–24 hours should be the period of choice [9,29,30] because this increases the ability to assess correlation between symptoms and reflux episodes providing more information on the patient's usual reflux pattern. At the end of the recording period the patient returns, the pH probe is removed and the data from the logger transferred to the computer and stored on disk. The software packages available can automatically provide a detailed analysis of pre-set parameters printing both a summary of variables and also a graphical representation of the 24-hour study.

Safety

The safety aspects of the procedure must take into account the patient, the investigator and the equipment.

NAME: _____   DATE: _____

D.o.B. _____ _____ NO. _____   START TIME: _____

PROBE AT: _____ HOME/WARD _____   FINISHING TIME: _____

PLEASE INDICATE THE TIME YOU DO ANY OF THE FOLLOWING

WHAT YOU EAT+TIME	WHAT YOU DRINK+TIME	TIME GO TO BED	TIME GET UP	TIME FEEL PAIN	TIME ACID IN MOUTH	TIME BURP

(a)

(b)

Fig. 4.13 (a) Example of a patient diary. (b) Event marker buttons on datalogger.

The patient

The patient's safety must be paramount. All modern pH monitoring equipment is battery operated, which is required by law, and safeguards against electrical shock. Therefore, the consideration of patient safety is in the intubation phase of

the procedure. As long as the previously mentioned precautions are followed (i.e. patient sitting on a couch, care not to intubate the trachea, location of resuscitation equipment and the whereabouts of medical help) then the patient should be safe from mishap.

The investigator

The investigator should wear gloves during intubation and extubation. This has a two-way effect on safety.

The equipment

The safety of the equipment is another essential. The datalogger should be handled carefully ensuring that batteries are never left in the logger when it is not in use. Care must also be taken with electrodes making sure that they are properly cleaned between investigations.

Cleaning and disinfection of pH probes. The recommended method of cleaning and disinfection of pH probes is:
1   Wipe clean with a tissue.
2   Rinse in water.
3   Wash with detergent (Dettox is not recommended).
4   Soak in glutaraldehyde for 20 min.
5   Rinse in sterile water.
6   Wipe with an alcohol swab.
7   Store in pH 7.0 buffer or recommended solution or dry until its next use according to manufacturer's instructions.

Summary of procedure

1   The patient is informed to attend, off medication and fasted for 4 hours.
2   The history is taken, the investigation explained and consent obtained.
3   The pH probe is calibrated, marked at the appropriate level and the patient intubated.
4   The pH probe is fixed in position, the patient is given instructions and a diary.
5   The patient is allowed home and given a contact number.
6   The patient returns, the pH probe is removed and the data transferred to a computer.
7   An analysis of the recording is printed out.
8   The battery is removed from the datalogger and the pH probe is cleaned.

Conclusion

The benefits of ambulatory pH monitoring are that the actual time the oesophagus is exposed to acid gastric juice can be quantitated. This can be divided into a daytime/ upright period and a nightime/supine period. It allows the ability of the oesophagus to clear refluxed acid to be assessed by calculating the clearance time. Any direct association between the patient's symptoms and reflux events can also be assessed by calculating a symptom reflux association/index. The symptom index is extremely useful as it gives an indication to that sector of the population who have a high correlation between symptoms and reflux events despite having normal oesophageal acid exposure [31–33]. There are limitations to the technique in that pH monitoring only detects the presence of acid gastro-oesophageal reflux and gives no indication of the actual volume of acid refluxed. The test can neither detect the extent of mucosal damage nor determine why there is an increase in oesophageal acid exposure. However, despite these limitations ambulatory oesophageal pH monitoring, when performed in conjunction with endoscopy and manometry, is a useful tool in the diagnosis of atypical patients suspected of having acid gastro-oesophageal reflux and especially helpful in relating the patient's symptoms to the occurrence of reflux events.

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4.3   Analysis and interpretation of results

David F. Evans

Introduction

There has been much research in the development of the methods by which the data recorded by intra-luminal oesophageal pH sensors are displayed, analysed and interpreted. A number of objectives have been defined:

1   To quantify the amount of gastric juice refluxing into the oesophagus during the recording period.

2   To determine whether the refluxate is primarily acid or alkaline.

3   To categorize the reflux in terms of circadian pattern (upright, supine, post-prandial).

4   To correlate gastro-oesophageal reflux (GOR) with symptoms.

5   To discriminate between normal (physiological) and pathological (symptomatic) GOR.

In order to satisfy these objectives most modern recording systems incorporate digital data collection and storage devices to capture the pH information generated by the intra-luminal pH electrodes. This data is subsequently analysed by computer software packages to provide all the necessary data to enable the clinician to make management decisions relating to the patient's oesophageal pH profile.

Display

The simplest but most inaccurate means by which a pH recording can be assessed is by direct visual scanning by an experienced observer. Although a hard copy of the pH recording is essential for many reasons, in terms of an objective and critical analysis, a simple visual scan of the pH time plot can only ever be accurate at the

two extremes of GOR, that is, where there is zero reflux or when acid is present for the major part of the recording. Even then, without manually counting the episodes and ruler measuring the duration of episodes, this technique is of little use. With that in mind, it remains important for the analyst to have sight of the pH plot, in order to confirm the validity of the automated analysis that accompanies every recording. The reason for this is that there are many operational and tech-nical problems that can cause artefacts and these can have a major effect on the calculations. These problems can easily be assessed by a trained eye such that they may then be eliminated from the analysis.

Causes of artefacts relevant to analysis of data

Electrode drift

Any electrode drift, whether caused by problems or malfunction of the active or reference electrode, may result in an offset of the original calibration values and a corresponding change in the reference baseline pH. This could therefore also drastically alter the final analysed reflux parameter calculated by the computer software. For example, a shift of one pH unit upwards (i.e. a baseline shift from pH 7 to 8) would cause a gross underestimation of acid exposure time and possibly reflux frequency. A similar shift downwards (i.e. from 7 to 6) would cause a similar increase in the reflux estimation.

To compensate for this problem, without having to repeat the investigation, it is possible to artificially shift the pH analysis threshold as long as the magnitude of the drift can be estimated by examining the record. For example, if there has been a shift of one pH unit downwards for any particular part of the recording then resetting the pH analysis threshold to pH 3 (rather than 4) for that part of the recording would automatically correct the acid exposure analysis and episode detection algorithms for that period. For this reason, it is therefore essential to visually examine each recording to check stability.

The most accurate way of estimating electrode drift is to undertake a post-procedure calibration. Some systems have a facility to perform this and where possible this is therefore recommended to avoid having to repeat investigations unnecessarily.

Displacement of pH electrode

Displacement of the active electrode will cause analytical inaccuracies in the form of either over or underestimation of GOR. Should the active electrode be displaced distally, it is possible that acid exposure time may be overestimated as the tip of the electrode becomes repositioned near to or across the cardia into the acid environ-

ment of the stomach. Displacement proximally may cause an underestimation of GOR in that it migrates only short distances into the oesophageal body.

Care taken to affix the electrode to the patient's face and a careful check of the electrode position at the end of the investigation should overcome these problems in all but a few cases.

Displacement of external reference electrodes

Displacement of the skin surface reference electrode, for example in hot weather where sweating is common or during physical activity, can cause serious analytical problems. This normally takes the form of an unpredictable, rapidly changing pH on examination of the recording. This is made easier where a two channel recording is taken as the signal artefacts will be identical in both channels (see section on multichannel recording, p. 105). Figure 4.14 shows an example of a trace where displacement of the reference electrode has caused such a problem.

To compensate for such problems it is essential to have a facility in the analysis software for exclusion of one or more parts of the recording. This often takes the form of movable markers or an 'ignore' facility where a time window can be specified around the offending section where the electrode has become displaced. This problem, when present, again emphasizes the importance of a brief visual examination of the recordings prior to automated analysis.
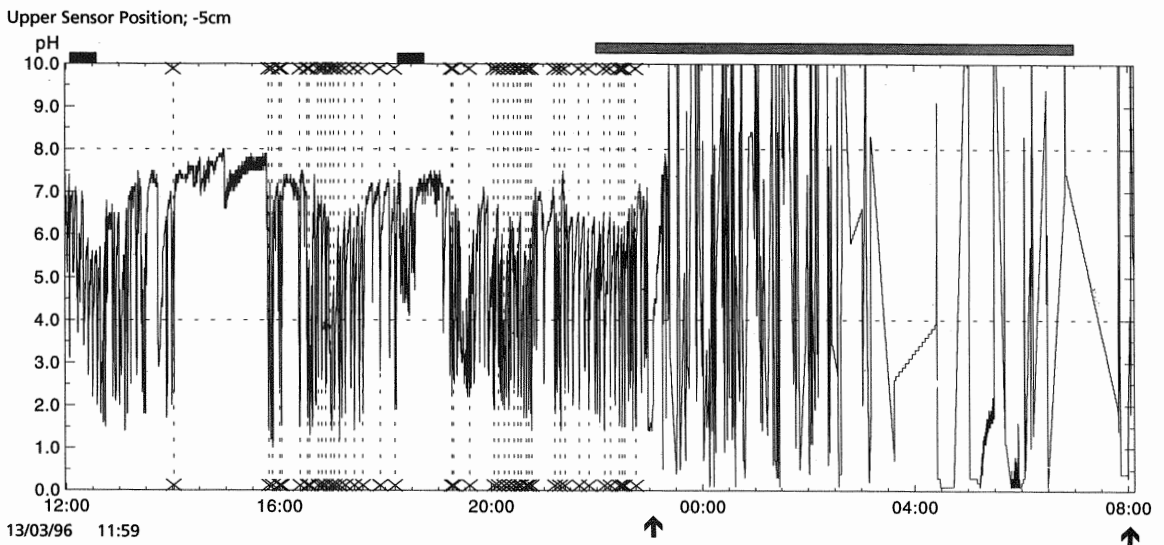
Fig. 4.14 Example of a 24-hour pH trace where reference electrode displacement has caused an unanalysable section of the trace (between arrows).

Rejection of recordings

Occasionally, where a recording is judged to contain more than an acceptable level of drift or when a large period has to be excluded due to electrode displacement, it will be necessary to repeat the 24-hour pH examination. This is best assessed by having rigid criteria for a user's own particular laboratory.

As a guide, it is suggested that recordings be rejected if the pH electrode is estimated to have drifted more than 0.5 pH unit either way and it is impossible to compensate for this by adjusting the pH threshold. Equally, if more than 20–25% of the day or night period is lost due to electrode displacement, this may also be judged a criterion for exclusion and repeat examination where possible.

Basic analysis

In order to attempt to standardize levels of GOR universally, a number of basic measurement and analytical standards have been adopted by most clinicians. Figure 4.15a–c shows examples of 24-hour pH plots of mild, moderate and severe GOR in symptomatic patients. Although the distribution and quantity of GOR are visibly different, there remains a requirement to objectively analyse the recording. The following describes the majority consensus.

Electrode position

In the case of a single pH detector, the universally accepted position of the pH electrode is 5 cm above the proximal margin of the lower oesophageal sphincter [1,2]. This position is determined accurately by pull-through manometry and is the only recommended method for probe positioning. Any deviation from this siting may affect the quantity of GOR detected and standardized analytical criteria will become invalid.

Definition of acid reflux episode

pH threshold

Reflux of acidic gastric juice into the oesophagus, as detected by an intra-oesophageal pH electrode positioned in the distal oesophagus, is said to occur when the recorded

Fig. 4.15 *Opposite.* (a–c) Examples of 24-hour pH traces illustrating mild, moderate and severe gastro-oesophageal reflux (GOR). The horizontal bars indicate sleep (long bar) and meals (short bars). The vertical lines indicate symptoms.
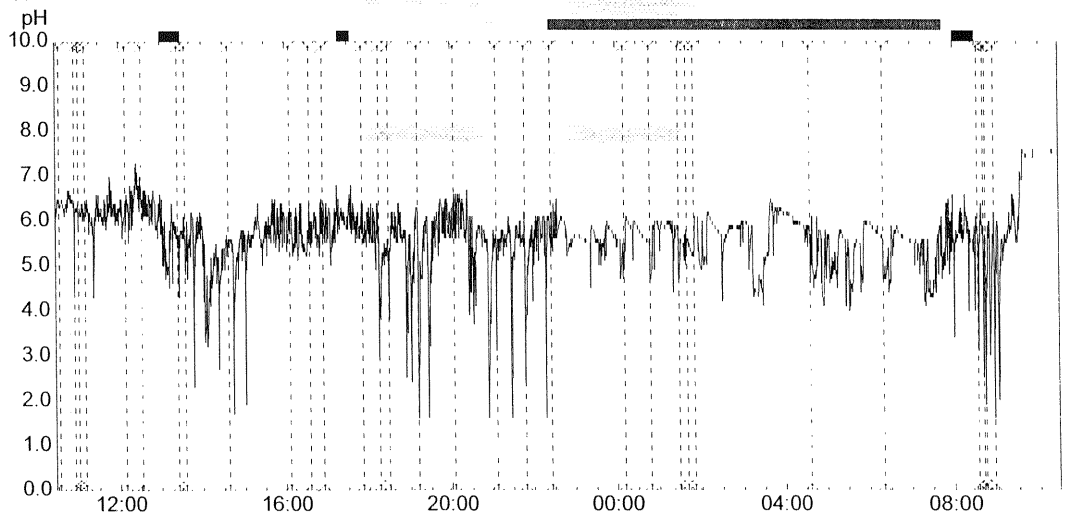
Upper Sensor Position; -5cm

(a) 02/08/96   10:28

(b) 09/08/96   18:35
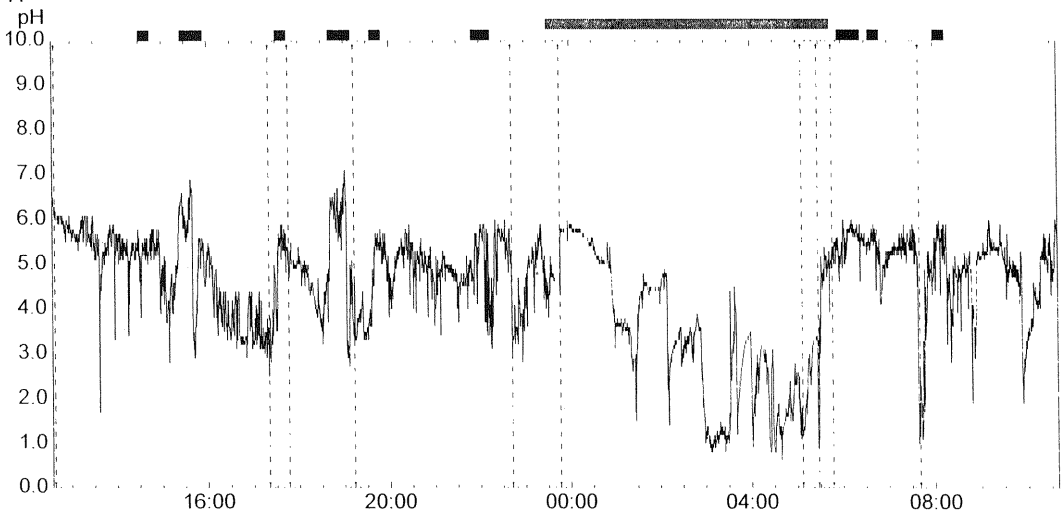
pH falls from a stable near-neutral baseline (pH 6–7) to an acidic value. The threshold pH for reflux is now universally accepted as pH 4 [3] but other thresholds have been advocated (pH 3, 5 or others) [4,5] but with fewer normal values for comparison.

The pH 4 threshold is derived from the fact that H^+ concentration at pH 4 is 10^{-4}M and this is regarded as the limit of tissue damage. Also, practically, most symptoms arise when the pH in the oesophagus is pH 4 or lower although in some patients with a so-called 'sensitive' oesophagus, symptoms may be experienced at pH's >4.

Onset, duration and end of a reflux episode

An idealized episode of GOR is depicted in Fig. 4.16 and the following represents the consensus view of determination of the analytical parameters that define reflux measured by intra-oesophageal pH.

Onset of episode
1   A reflux episode is said to begin when a fall in pH below the preset threshold (usually pH 4) is recorded.
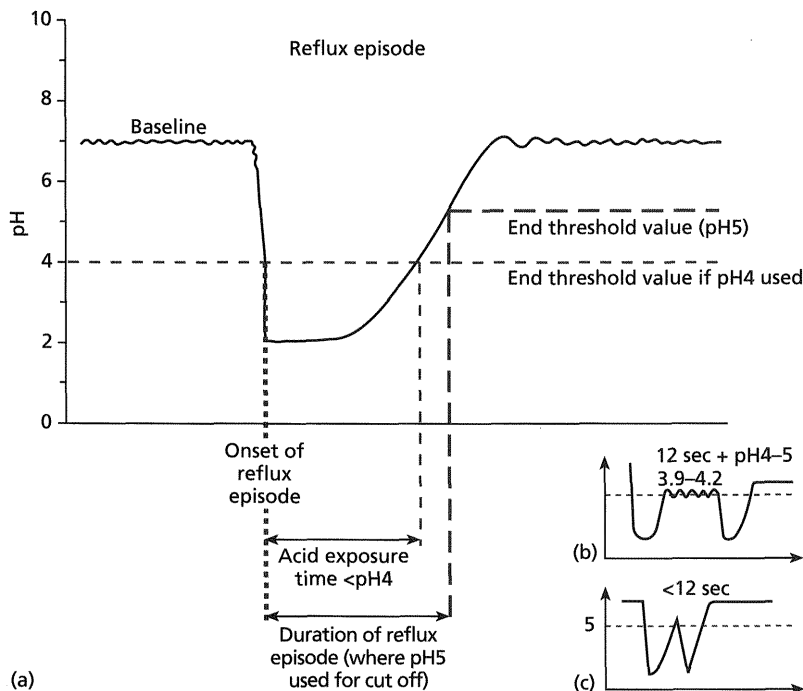
Fig. 4.16 Idealized reflux episode showing the analytical thresholds of onset, duration and termination of the episode.

2 A 'true' episode is usually associated with a sharp fall and this has been defined as a rate of change of pH from baseline to threshold in less than 15–20 seconds [3]. Slower changes would continue to score towards acid exposure time (AET) but may not count in the total frequency score.

Duration of episode

1 The duration of the pH fall must be for a minimum period of time in order to avoid over estimation of reflux episodes by rapidly changing values caused by electrode artefacts (i.e. displaced reference electrode, cable or connection problems). This minimum recording period is recommended as being 12 seconds per episode, i.e. two samples at 6 seconds per sample.

2 Having satisfied the criteria for the onset, the total duration of any episode is determined by the length of time that the pH remains below the threshold which is defined as the end of an episode.

End of episode

1 The end of an episode may be simply the point at which the pH value returns above the onset threshold (usually pH 4).

2 In cases where there is concern regarding episodes where the pH oscillates around the pH 4 threshold (that is, for example, rising to 4.1 then dipping to 3.9 repeatedly, etc.) (inset Fig. 4.16), an alternative approach is to set the end of the episode to pH 5 or higher. The consensus view of this level is a rise to pH >5 sustained for 15 seconds or three samples (i.e. 18 seconds at a sample rate of 0.15 Hz). This ensures that the reflux episode is truly returning to near-baseline values (i.e. pH 5–7). Most commercially available analytical packages allow the user to manipulate the criteria for setting the thresholds for GOR and users should be careful to check that the default settings are in agreement with their own standards (i.e. those by which their normal values have been derived).

Analysis standards

Table 4.8 summarizes the commonly used parameters calculated from pH traces to objectively describe GOR. Normal values are derived from one of the most recent series of data collected from 50 healthy volunteers [6].

Acid exposure time (AET), % time

Definition. This is defined as the time period expressed as a percentage of the total analysed time when the distal oesophageal pH is at or below the threshold set by the user. It is also effectively the area under the pH threshold curve. The AET may differ from the total duration divided by the total time period if the reflux endpoint

Table 4.8 Major analytical parameters used in 24-hour pH recording. Normal values are derived from 50 normal volunteers [6]. Each parameter can be analysed for total recording time and separated into daytime (upright) and nightime (supine) GOR.

Parameter	Unit	Normal value Median (95th centile)
% time <pH 4	% AET	1.2 (4.5)
% upright <pH 4	% AET	1.6 (8.4)
% supine <pH 4	% AET	0.1 (3.5)
Frequency	Episodes/h	16 (47)
Longest episode	Minutes	4.0 (19.8)
No. episodes >5 min	Number	0.0 (3.5)

GOR, gastro-oesophageal reflux.

is greater than pH 4. In this case the total duration will be longer, depending on the limit of the cut-off threshold.

Interpretation. The AET describes the fraction of the recorded period when acid is in contact with the distal oesophageal mucosa. It therefore records the severity of acid mucosal contact time and, by epoch selection, the specific time period when acid exposure is at its highest. AET does not describe the manner in which the oesophageal mucosa is exposed to acid. There may be one single reflux episode of long duration responsible for the total AET or there may be numerous shorter episodes which together add up to the total.

In spite of these limitations, the % AET remains the most widely used single GOR variable in common usage that is quoted to represent the severity of GOR in prolonged pH monitoring.

Frequency of GOR

Definition. The frequency of reflux is the number of times the pH falls below and returns above the pre-set pH threshold. In theory, a minimum of 0 and a maximum of 2880 could occur in 24 hours assuming a minimum of 30 seconds per episode. In practice only total numbers exceeding 47 are regarded as significant of pathology (see Table 4.8).

Reflux episodes can be expressed as a total number or as a rate per hour, but the actual definition is tied to the way in which an episode is defined (see previous section). The pH drop and return to baseline criteria are critical in determination of the final numbers calculated for any given patient. Of all parameters calculated, the frequency of reflux is probably the one value that

can be influenced in a major way by the choice of definition. Fortunately, the frequency of GOR is one of the parameters of lesser importance in terms of a severity index.

Interpretation. The frequency of reflux gives useful information regarding the number of discrete reflux episodes occurring during a 24-hour recording. It gives a rule of thumb guide as to the severity of GOR but as an isolated parameter it is not particularly helpful without any information regarding acid exposure or clearance times (duration). However, used together with a symptom marker, the frequency of reflux gives essential data regarding correlation of symptoms with acid exposure and is therefore an essential part of any calculation of GOR.

The difficulties in the accurate definition of the parameter make this the most difficult of all of the calculated values to standardize universally from centre to centre and from manufacturer to manufacturer.

Longest episode and reflux episodes >5 min

Definition. The longest episode is the calculated reflux episode that achieves the longest measured duration and is used as a guideline as to the maximum acid clearance time in any particular recording.

All reflux episodes greater than 5 minutes duration are regarded as pathological in their own right and the total numbers longer than 5 minutes duration give an indication of overall reflux severity.

Interpretation. These parameters of reflux duration are used in some scoring systems in the overall determination of GOR status. In general terms, the longest reflux episode (especially when supine) gives information to the clinician regarding oesophageal acid clearance and the total number of episodes >5 min indicates the severity of the problem in any individual patient.

Symptom index

Definition. The symptom index is defined as a positive correlation between a symptom as indicated by a marker incorporated within the recorder and a reflux episode recorded by the pH sensor. The symptom must be recorded either during, or within, 2 minutes of the calculated episode end. The proportion of reflux episodes that correspond to an indicated symptom event can be expressed as an index using the following formula [7]:

$$\text{Symptom index (SI)} \% = \frac{\text{No. of symptoms with pH} <4}{\text{Total no. of symptoms}} \times 100$$

Interpretation. The symptom index gives objective information regarding the relationship between symptoms and the presence of gastric juice in the oesophagus and is therefore one of the important diagnostic criteria of prolonged oesophageal pH measurement. The greater the percentage correlation, the higher the probability of GOR being the cause of symptoms. Although symptoms and reflux have never been shown to correlate perfectly, the evidence of some degree of agreement between patient symptoms and acid exposure to the distal oesophagus is compelling evidence of cause.

In general, a correlation of 50% or more has been suggested as being clinically significant [8] although some workers have suggested that a symptom index as little as 25% will ensure the correct diagnosis and avoid false negative results [9]. That is, if the symptom marker is pressed within a set time period during or after a reflux episode, a positive correlation is said to exist.

Some form of symptom or event marker, whether single or multiple, is therefore an essential part of any recording device used for oesophageal pH measurement. In particular, the correlation of symptoms with GOR is an important marker of cause, especially where symptoms are atypical (respiratory, cardiac-like and oropharyngeal) or when total GOR does not exceed the pathological thresholds but when symptoms are clearly caused by acid reflux (the 'sensitive' or 'irritable' oesophagus).

Epoch analysis

Prolonged ambulatory oesophageal pH monitoring was developed to detect pathological GOR in order to discriminate between physiological and pathological reflux. the 20–24-hour period was designed to detect reflux in as near a normal setting as possible. The analysis of the component parts of the total time period is specifically aimed at increasing the diagnostic yield and to increase the usefulness of the investigation.

The principle behind the division of the total period is that GOR is experienced to a greater degree by some patients during digestive periods after meals or at night when supine. Much research has been undertaken to increase the sensitivity and specificity of prolonged pH measurement and the following represents the consensus view of the majority of the profession.

Division of analysis periods

The total recording time is 20–24 hours in order to include the major periods when GOR may be present in a normal circadian cycle. pH measurement must include a sufficient time period of the three major representative epochs known to be important in analysis: nocturnal, interdigestive and post-prandial.

The nocturnal period is approximately 8 hours in duration and the daytime period will be divided into mealtimes and the interval periods immediately after food and between meals. It is accepted therefore that the total recording period will contain at least two meals and the whole of the night. For patients who have unusual life styles, such as shift workers, due account must be taken of the differences in circadian activity patterns.

The total recording time will certainly need to be at least 18–20 hours to cover the requirements of epoch analysis. Obviously, 24 hours is the optimum period, but constraints on patients' and operators' time give rise to a reduced recording period in some instances and the calculation of GOR can be standardized by calculation of % times or divided into unit time (e.g. frequency *per hour*).

Effects of meals

Physiologically, the major influence on gastric acid secretion, and therefore the potential for pathological reflux, is food intake. The act of eating and the presence of food in the stomach activates the digestive processes with a rise in gastric acid secretion and pepsin to initiate digestion. The influence of food on GOR is therefore important and cannot be ignored in the investigation of reflux disease. Users should be aware of misinterpretation of long acidic episodes that may be caused by delayed oesophageal transit (as in scleroderma and achalasia). These may give rise to a false diagnosis of 'true' GOR.

The daytime period can be divided into prandial, post-prandial and inter-prandial periods. Differences in eating habits, food components and the variable habits of 'snacking' between meals make standardization of food intake during pH measurements difficult, except possibly where drug trials are being undertaken where food can be more closely controlled. Some measurement protocols advocate the exclusion of certain 'acidic' foods and drinks to attempt to reduce the errors caused by: (i) artefact of 'simulated' GOR as acid material transits the oesophagus; and (ii) increases in actual GOR caused by the gastric stimulus of similar food components.

Analysis of daytime data, where meals are taken, may make a major difference to total GOR. Four analytical approaches may be adopted to accommodate these possible differences.

1 Total inclusion—all data are analysed together, regardless of meals taken.

2 Total exclusion—meal and post-meal periods are excluded (1–2 hours post-prandial). There is a danger here of reducing the effective recording period to an unacceptable level.

3 Meal analysis—post-prandial period is analysed separately and displayed as a separate analysed data set.

4 Partial exclusion—post-prandial period is analysed and compared with inter-prandial period.

In general, although shorter total recording periods than 24 hours have been widely researched [10,11], a diagnostic study should be as near 24 hours as possible to take into account the effect of meals and supine periods. Most modern recording systems have a fixed minimum 24-hour recording time incorporated with a facility to prematurely end the recording if required.

The principles of epoch analysis described here reflect the normal circadian patterns of activity for adult subjects. For infants and children, a different wake/sleep/meal pattern exists, usually dependent on age; paediatric data are generally therefore handled differently from adult studies. This is described more fully in the paediatric section (see p. 130).

Normal values

A crucial factor in ambulatory oesophageal pH measurement is the discrimination of pathological from physiological GOR. It was DeMeester and Johnson's early work [1,2] that set the initial upper limits of normality of GOR for prolonged pH monitoring. Fifteen normal subjects were studied in a hospital setting and upper limits of normality set for each of the GOR parameters previously described. In addition, a scoring system was also derived from these data (see below). Subsequently, normal data have been derived from many other studies investigating truly ambulatory subjects and the DeMeester group have upgraded their data to address the issues of ambulation, subject numbers and statistical correctness [6].

Since the early 1980s, it has been accepted that prolonged oesophageal pH monitoring should be performed where practical in an ambulatory, outpatient setting. Two studies demonstrated that ambulatory pH was superior to in-hospital monitoring in the discrimination of physiological and pathological GOR [12,13] and therefore normal values must also be measured in a similar fashion.

Considerations in obtaining control data

How many subjects is enough? This is the first question to be addressed when attempting to describe a 'normal subject'. Statistically, the answer is the greatest number available from a randomly sampled selection of an age- and sex-matched group of asymptomatic controls. Practically, the answer is usually determined by availability, resources and time available for study.

What is a 'normal' subject? Again, this is a difficult question to address. In theoretical terms, an eligible control subject is one who has no symptoms of GOR at any time. As GOR is very common, the selection may be more difficult than at first thought. Other important criteria might be the absence of oesophagitis (in

theory every control subject should undergo oesophagoscopy) and avoidance of reflux inducing foods and other substances (alcohol, smoking, exercise, obesity, etc.).

Statistical handling of normal data

GOR data are extremely variable in both the normal asymptomatic population and in patients with GOR disease (GORD). This is because the extremes of GORD (0 minimum—theoretically 100% AET, although practically usually not greater than 50%) are not best described by the mean value. Group data must therefore be handled in statistical terms as non-parametric, i.e. non-Gaussian distribution. In practice this requires the use of medians, centiles and ranges to describe group data and non-parametric statistical tests to analyse grouped data. It has therefore now become standard practice to describe normal values and test data in this way.

Scoring systems

From its inception, the analysis of the data from prolonged measurements of oesophageal pH provoked much discussion and controversy among its enthusiasts. Which of the many analysable parameters is the most important? Is frequency more important than duration? Is the longest episode of most relevance to pathology severity? Is nocturnal reflux more important than post-prandial?

DeMeester score

In order to address this problem, attempts were made to combine data and present the result, in comparison with normal values, as a score or index: one parameter was desirable that represented the total amount of data collected. The first, and probably remaining the widest, used was the Johnson and DeMeester score [1]. Shortened to DeMeester, but clearly a combined effort, this was the original scoring system which takes into account frequency, duration, longest episode, episodes greater than 5 minute's duration and even the daytime/night-time reflux ratio. This original work calculated a single score by combining the values stated and calculating the upper limits of normality from 15 healthy volunteers studied in non-ambulatory conditions. Table 4.9 illustrates the criteria used in the derivation of the original Johnson/DeMeester scoring system with the upper limits of normality and final upper limit of normality score calculated. The score was derived by calculating a number which represented a value for each parameter and using the standard deviation as a weighting factor to derive a component score for each parameter measured. This meant that parameters which were infrequent in normal subjects, i.e. nocturnal GOR, were more highly weighted than parameters occurring

Table 4.9 Derivation and values of the original Johnson/DeMeester scoring system.

24-h Component	Mean ± sD	Normal value	Score
% time < pH 4 total	1.5 ± 1.4	<4.2	3.0
% time < pH 4 upright	2.3 ± 2.0	<6.3	2.98
% time < pH 4 supine	0.3 ± 0.5	<1.2	3.06
No. of reflux episodes < pH 4	20.6 ± 14.8	<50	2.99
No. of episodes > 5 min	0.6 ± 1.3	3 or less	2.93
Longest episode (min)	3.9 ± 2.7	<9.2	3.0
Total score			17.96

more often, i.e. total number of episodes. The component score for each parameter is summated to form a composite score. The final score is abnormal if exceeding that achieved by the control group. In the original DeMeester paper this was 17.96. Any score above this was regarded as pathological.

This system was regarded as the standard for a number of years although some doubts were cast upon it due to the subject selection and number, mode of measurement and the fact that means and sDs were used when the data collected was clearly non-Gaussian distributed. Consequently, in 1992 a modified DeMeester score was publicized [6]. The revised DeMeester score is taken from 50 controls using median and interquartile values and is shown in Table 4.8.

Other scoring systems

Various other scoring systems and graphical representations have been developed over the years and many are available as optional facilities in commercial software systems. Two widely used software packages (Gastrosoft and Flexisoft) offer these alternative calculated packages, which are listed in Table 4.10. Examples are the cumulative acid exposure graphs and composite scoring graphs shown in Figs 4.17 and 4.18.

Multichannel measurements

Multiple pH recordings are being utilized more widely to give additional information relating to GORD and its complications. Interpretation of these additional channels is marred by the paucity of normal data in the literature.

GOR higher than 5 cm

GOR occurring higher in the oesophagus than 5 cm indicates the possibility of

Table 4.10 Additional derived parameters and scoring systems for pH analysis.

DeMeester score [1]
Frequency–duration index [14]
Kaye score (post-prandial) [15]
Cumulative pH plots [16]
Reflux index
Meal reflux index
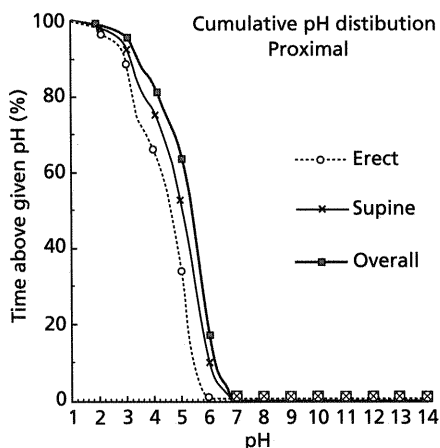
Fig. 4.17 Cumulative % exposure graph.
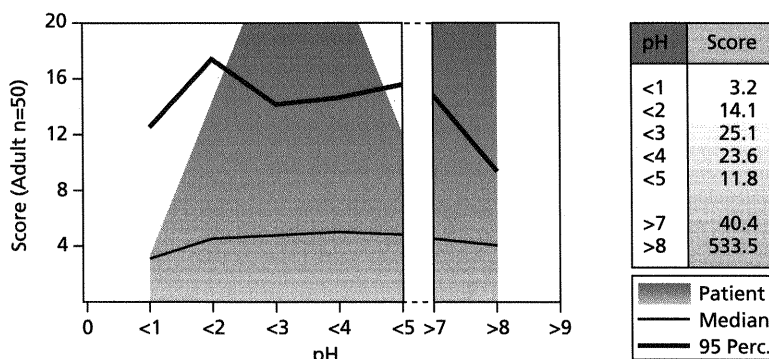
Fig. 4.18 Composite scoring graph.

regurgitation of gastric juice into the mouth giving rise to complications including aspiration into the airways and tooth wear. Dual-channel pH studies, where the second channel is sited higher than 5 cm, are therefore useful in examination of the proximal spread of GOR. Data may be analysed in a similar way to that in the distal oesophagus but with the possible partial neutralization of refluxate as it

migrates proximally, perhaps thresholds higher than pH 4 should be considered. Bartlett [13] suggested that values of pH 5, 5.5 and 6 might be useful although little in the way of normal data are available.

Gastric pH

Gastric pH may be measured simultaneously with oesophageal pH to give useful information relating to alkaline or duodeno-gastric reflux (see below) or as a marker of efficacy of anti-secretory agents. For the former, the gastric pH sensor detects alkaline changes in the gastric reservoir to act as a confirmation of proximal movement of alkaline agents. In terms of acid suppression, the gastric pH channel monitors the percentage time at any pH threshold (the most commonly used being pH 4) in the stomach to give an objective assessment of acid inhibition. Figure 4.19 is an illustration of a two-channel pH trace with the second channel sited in the

Upper Sensor Position: -5cm

Lower Sensor Position: +10cm
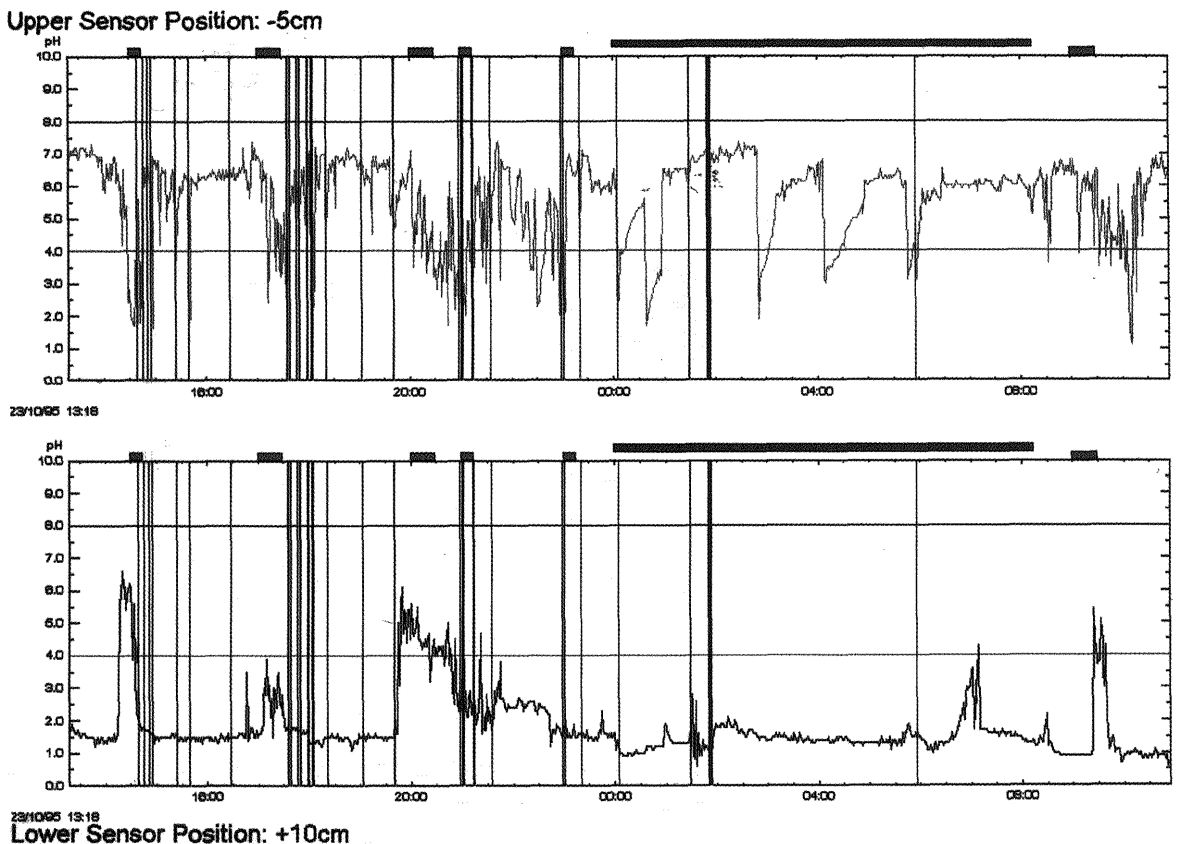
Fig. 4.19 Two-channel pH trace showing gastro-oesophageal reflux (GOR) and gastric pH. Sensor position is in relation to proximal border of LOS.

gastric body, 10 cm below the LOS. The patient exhibits severe GOR which is symptomatic and the gastric pH remains highly acidic, apart from short periods where a meal buffers the pH to a higher level. Software is available to calculate cumulative percentage graphs and figures to illustrate the data. pH values can be used to calculate H^+ ion concentration.

Reporting

pH traces can be generated with automated analysis and these can be used for reporting purposes. It may be preferable to generate a condensed report with a summary and this can be achieved with a suitable database such as Microsoft

---

Dr   *15 August 1996*
Consultant Physician

London Independent Hospital
1 Beaumont Square,
Stepney Green,
London, E1 4NL

Patient: /robil 80466   **Date of Birth:** 18-Apr-66
        Island Gardens
        London   **Hospital no:**
        E14 3EW

ADULT 24-HOUR AMBULATORY pH STUDY

Indication: 8y history of GOR, worsening   **Study status:** Diagnostic study

Date of test: 09-Aug-96   **Medication:** Off medication

	Abnormal values in bold	Upper Normal limits
Total % time <pH4	**16.7%**	4%
Erect % time <pH4	**22%**	6%
Supine % time <pH4	**5.9%**	2%
Total no. reflux episodes	46	50
Erect no. reflux episodes	44	
Supine no. reflux episodes	2	
Longest reflux episode (Erect/Supine)	**64/35** min	10 min
No. > 5 minutes	**27**	< 3
Symptom Index	**82%**	50%
Episodes/symptoms	9/11	

SUMMARY Severe day & night reflux with good symptom correlation. Would be a suitable surgical candidate in view of the poor response to medical therapy.

Fig. 4.20 Example of pH report using a Microsoft Windows database.

Access (Microsoft Inc). Figure 4.20 is an example of a pH report using such a system. The report allows for 'expert' interpretation of the analysis and is often helpful to clinicians who may have a limited understanding of the raw data.

Alkaline GOR

Alkaline reflux is defined as the reflux of non-acidic, corrosive agents into the oesophagus. Practically, alkaline reflux is likely to be composed of a mixture of acidic and non-acidic substances, the non-acidic being predominantly from the duodenum (duodeno-gastric reflux (DGR)) and possibly arising from the biliary tract (bile and pancreatic secretions). The difficulty in detection of alkaline reflux by pH is the definition of thresholds where alkaline reflux can be discriminated from the normal pH environment. For example, it has been shown that saliva can have pH values as high as pH 7.8 and many ingested food stuffs may have a pH greater than 7. In addition, a mixture of alkaline and acid refluxate may have a combined pH within the normal range (i.e. pH 4–7). Therefore a single measurement of pH in the oesophagus may miss the presence of any corrosive refluxate. For example, a ratio as high as 10:1 of bile to acid is required to raise the pH of the resultant mixture to greater than pH 8 [17].

Definition

The definition of alkaline reflux as measured by oesophageal pH monitoring is the presence of alkaline juice in the distal oesophagus to levels above pH 7 [18]. This criterion, however, does not adequately detect DGR in all cases and refinements of the technique to achieve a higher diagnostic yield include multiple sensors placed in the gastric antrum, body and fundus [19]. Other researchers have attempted to correlate pH levels with DGR aspirated and detected with chemical methods with only partial success [17,20].

Rationale for detection of alkaline GOR by pH measurement

By current criteria, elevation of oesophageal pH above 7, reinforced by similar alkaline changes in gastric pH at one, or preferably two or three, gastric sites, is the best means of detection of alkaline reflux arising from the duodenum and biliary system into the oesophagus. New techniques are becoming available including the 'Bilitec', a spectrophotometric device which detects oesophageal bilirubin. This may be promising in the investigation of DGR but so far is only at the research stage [21].

Summary

Analysis of GOR data by dedicated software provides objective assessment of 24-hour pH recordings in patients with reflux symptoms. The discrimination of pathological from physiological reflux and a positive correlation of symptoms with acid exposure to the distal oesophagus allows the clinician to make a diagnosis and to determine the optimum course of management with confidence from the data obtained from the pH recordings.

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4.4   pH measurement in infants and children

Yvan Vandenplas and Kris Van de Maele

Introduction: why monitor the pH in the oesophagus?

Modern electronic technology has profoundly changed the practice of medicine, principally through its ability to monitor, record and analyse large volumes of data. The introduction of computers has provided physicians with powerful tools to identify elusive and intermittent disorders, such as gastro-oesophageal reflux (GOR) disease, that previously defied diagnosis. Two major but totally different indications for oesophageal pH monitoring exist: (i) in clinical and laboratory research; and (ii) as a routine clinical procedure in the diagnosis of GOR disease in children that present with atypical manifestations (Table 4.11), and the evaluation of GOR treatment [1,2].

Hardware and software: paediatric needs

Device

Although pH equipment is discussed extensively in Chapter 4.1, we would like to focus on a few relevant details for paediatric use. The greatest advantage of pH monitoring is probably related to the possibility of realizing a 'true ambulatory recording', even in young children, enabling the detection of GOR in physiological conditions. Devices no larger than a credit card, although of course a little thicker, are commercially available.

Table 4.11 Symptoms of GOR disease.

Oesophageal manifestations
Specific symptoms
  Regurgitation
  Nausea
  Vomiting
Symptoms possibly related to reflux oesophagitis
  Symptoms related to anaemia (iron deficiency anaemia)
  Haematemesis, melaena
  Dysphagia (as a symptom of oesophagitis and/or due to stricture formation)
  Weight loss and/or failure to thrive
  Epigastric or retrosternal pain
  'Non-cardia angina-like' chest pain
  Pyrosis or heartburn, pharyngeal burning
  Belching, post-prandial fullness
  Irritable oesophagus
  General irritability in infants ('colic')

Unusual presentations
GOR related to chronic respiratory disease (bronchitis, asthma, laryngitis, pharyngitis, etc.)
  * Cystic fibrosis
  * Sandifer Sutcliffe syndrome
  * Rumination
  * Apnoea, apparent life-threatening event, sudden infant death
  syndrome

Purchase costs, system abilities, costs in use, number of measurements and durability of the material are all factors to consider before purchasing equipment. Of importance for paediatric use, is a time-indication on the display (be it the number of data recorded, the real time, the duration of the investigation) and the protection of the event marker(s) to avoid erroneous use by the child [2]. A system should refuse to work if not calibrated properly.

Electrode

Since glass electrodes appear to be slightly more precise than antimony electrodes [3], glass electrodes with an internal reference electrode are in general recommended. However, these electrodes have a rather large diameter (3.0–4.5 mm). The passage of such an electrode through the nostrils of young babies is a real problem, although the fact that the passage is mechanically possible certainly does not mean that it is well tolerated. From a recent experience with combined pressure–pH recordings, it became clear that the larger the diameter of the electrode(s), the more the patient

had to swallow (unpublished). A large sized electrode might have a normalizing effect on pH monitoring data, since the more the patient swallows, the more primary peristalsis is induced, and the better the oesophageal clearance. Because of their smaller diameter, antimony (2.1 mm) or glass micro-electrodes (1.2 mm) are preferable in infants. Antimony electrodes also exist with a diameter of about 1.5 mm for use in premature babies; these electrodes are too flexible for older babies. Antimony electrodes with multiple recording sites exist.

However, most antimony and all glass micro-electrodes need an external cutaneous reference electrode, which is a possible cause of erroneous measurement resulting from transmucosal potential differences. The cutaneous electrode and the contact gel used for the calibration need to be identical to those used for the recording, since all these factors will influence the pH measured [3,4]. If the environmental temperature is high or the patient sweats a lot, the contact gel might dry, resulting in a less accurate conduction of the electric potential.

Recently, antimony electrodes with a diameter of about 2.0 mm with an internal reference electrode have been developed (Zynetics, M.I.C.[1]), providing comparable results (unpublished data, Table 4.12), suggesting that this new type of electrode might become the electrode of choice in the future; it is accurate, thin, flexible and easy to place in the oesophagus, and there is no longer need for a cutaneous reference electrode. Whatever the type of electrode chosen, each centre should preferentially use only one type of electrode since each type of electrode has its own characteristics (Table 4.13).

Table 4.12 Advantages and disadvantages of pH monitoring to diagnose GOR disease.

	Advantages	Disadvantages
Technique	Physiological conditions Normal ranges Good reproducibility Long duration (24 hours)	Physiological conditions Social discomfort (electrode)
Diagnosis	Quantification number of pH changes Quantification duration pH changes Time-relation symptom-pH change	Measures pH change, not GOR Alkaline GOR (?) No neutral GOR
Complications	Area under pH 4: related to oesophagitis	No direct information tissue damage
Treatment	Contributes to choice of treatment Evaluation of treatment	No acid secretion of H_2-blocker

[1] Zynetics, Synectics: Stockholm, Sweden. M.I.C.: Solothurn, Switzerland.

Table 4.13 Comparison between data recorded with an antimony electrode with internal reference electrode and a glass micro-electrode with external reference electrode in 20 patients with two Gastrograph Mark II devices. No significant difference between the different parameters studied was found.

	Antimony	Glass
Reflux index	3.94 ± 3.68	3.61 ± 3.25
Number of episodes	15.15 ± 11.09	17.45 ± 10.41
Mean pH/24 h	5.46 ± 0.39	5.33 ± 0.25

The location of the electrode

There is abundant evidence in the literature that the location of the electrode is of critical importance regarding the number and duration of the reflux episodes recorded. It seems logical that the closer the electrode is located to the LOS, the more acid reflux episodes are detected [4,5]. Several methods have been proposed to determine the location of the electrode: fluoroscopy, calculation of the oesophageal length according to Strobel's formula, manometry and endoscopy. Ideally, the electrode should be sited in reference to the manometrically determined LOS. However, this has at least two inconveniences: (i) manometry in infants and children is time-consuming, rather invasive or at least unpleasant (in most clinical situations the pressure of the LOS will not change patient management); and (ii) this method would have the inconvenience that the electrode is located at a fixed distance to the LOS while the length of the oesophagus increases from less than 10 cm in a newborn to over 25 cm in an adult. Moreover, manometry cannot be performed in all centres. Therefore, the ESPGAN-Working Group on GOR recommended the use of fluoroscopy to locate the electrode [2]. The radiation involved is minimal and the method can be applied in each centre. As the tip of the electrode moves with and during respiration, the tip should be positioned in such a way that it overlies the third vertebral body above the diaphragm throughout the respiration cycle. Dislocation by a curled electrode is also prevented with fluoroscopy.

Patient preparation

No special patient preparation is required for pH monitoring. However, it is preferable not to introduce the electrode during the immediate post-prandial period to avoid nausea and vomiting. To facilitate insertion, a gel can be placed on the electrode (but not on the pH sensitive point) and/or a local anaesthesia of the mucosa of the nostrils can be advised, although in general we do not do this.

H_2-blockers should be stopped at least 3–4 days before a diagnostic pH monitoring, on condition the investigation is not performed to evaluate the acid-buffering effect of the drug. Prokinetics should be stopped at least 48 hours before the pH monitoring [4]. The continuation or not of drugs such as prokinetics will also depend on the aim of the pH study.

Patient-related influencing factors: recording conditions

'Patient-related factors' that possibly influence pH monitoring results constitute one of the most controversial topics [2,4]. The answer to the fundamental question of whether these factors should be minimized and standardized or not, is difficult and necessarily ambiguous. If the pH monitoring is performed as part of a diagnostic work-up in a patient, it is interesting to study the patient during normal daily life, enhanced by as unrestricted recording conditions as possible. But, on the contrary, if the pH monitoring is performed as part of a (clinical) research project, recording conditions should be as standardized as possible. The standardization of recording conditions inevitably causes a loss of patient-specific information. Feeding, position and physical activity are examples of patient-related factors greatly influencing pH monitoring data.

Duration of the recording

The duration of the recording should be 'as near as possible to 24 hours', and at least 18 hours, including a day and a night period [2,6,7]. If the pH monitoring is performed for diagnostic purpose, there is no indication for short-duration pH tests (such as Tuttle and Bernstein tests, 3 hour post-prandial recording, etc.). There is now substantial evidence that oesophageal acid exposure is highest during the day in the majority of patients, probably because of provocation of GOR by food ingestion and physical activity. Controls also have more reflux upright than supine or more reflux awake than asleep [8]. The relation between oesophagitis and nocturnal reflux is far from clear [9–11].

The first reports on the clinical use of pH monitoring concerned oesophageal tests of short duration. Tuttle and Grossman developed the 'standard acid reflux test' [12]. This test was modified by Skinner and Booth [13] and Kantrowitz *et al.* [14], demonstrating that pH tests can contribute to define abnormal GOR. The Tuttle test was reported to have a sensitivity of 70% [15]. After great initial enthusiasm for this test, criticism became more and more common. The test is unphysiological in requiring intra-gastric instillation of acid and various artificial manoeuvres to raise intra-gastric pressure. In the early 1980s it was reported that the false-positive rate might be as high as 4–20%, and the false-negative rate as high as 40% [16–18].

Bernstein and Baker demonstrated in 1958 that heartburn could be provoked by infusing diluted hydrochloric acid into the oesophagus in susceptible individuals [19]. This test was shown to be 100% positive in reflux patients [20]. A modified Bernstein test was used to illustrate the relation between GOR and apnoea and stridor, and between non-specific chest pain and GOR [21,22].

Provocative testing can be used in particular conditions, to demonstrate the relation between GOR and specific symptoms (bradycardia in relation to the oesophageal presence of acid). However, provocative testing has always the inconvenience that the conditions are unphysiological. The latter might be the cause of some discrepancies in the literature. Ramet *et al.* showed a prolongation of the R–R interval in infants during provocative testing with acid instillation in the oesophagus [23], while others [24,25] could not reproduce these findings in 24-hour recordings under physiological conditions.

Feeding

Feeding during pH monitoring has been and still is an area of controversy. On the one hand it seems logical to forbid the intake of acid foods and drinks. However, many 'paediatric' foods and beverages have a pH of <5.0 (cola drinks, fruit juice, tea, soup, etc.), resulting in a quite restricted diet. A too-restricted diet might alter the patient's normal daily habits in such a way that the investigation is no longer performed in physiological conditions. Electrodes are temperature sensitive, and therefore very hot beverages (coffee, tea, etc.) or chilled food (ice cream, etc.) should be forbidden [2].

In infants, it has been suggested to replace one or several feedings during pH monitoring by apple juice [26]. This would certainly partially solve the problem of gastric anacidity after a milk feeding, but besides a pH of about 4.0 apple juice has also a very rapid gastric emptying. Our policy is to let the diet free with avoidance of very hot and chilled beverages and food. Parents and children are asked not to exaggerate 'acid' ingestion. Although the ingestion of the latter might simulate a reflux episode, the duration of ingestion is limited to a few minutes and most of the time is irrelevant to the total 24-hour data. To minimize this negative influence on the data, it is always possible to eliminate these false reflux episodes from the data with the help of a precise diary. All the above is true for diagnostic investigations. However, for research, the opposite might be valid: all factors possibly influencing the pH data should be controlled and standardized as much as possible.

The influence of a particular food on the incidence of acid GOR episodes detected by pH monitoring might be opposite to its influence on the incidence of reflux episodes: a fat meal is known to provoke GOR, because of its delayed gastric emptying. The duration of post-prandial gastric anacidity after a fat meal is prolonged, resulting (probably) in less acid reflux episodes detected by pH monitoring [27]. Some drugs

influencing gastric emptying (e.g. prokinetic agents) have a comparable effect on pH monitoring data: these drugs enhance gastric emptying, shorten the period of post-prandial gastric anacidity and prolong the periods during which acid GOR can be detected.

Position

Different patterns of GOR (upright, supine, combined) do exist in older children, similar to the reports in adults [28]. Quite contradictory opinions exist nowadays about the optimal position for infants. Orenstein *et al.* suggested that prone is the preferred position, since crying time is decreased if compared with the supine position [29–31]. Different papers provide evidence that prone-antitrendelenburg 30° is rather effective in the treatment of GOR, although this position is difficult to apply correctly (infants have to be tied up in their bed). Meanwhile, the literature on sudden unexpected death in infants shows that infant mortality decreases if they sleep in the supine position. Accordingly, the therapeutic recommendations for GOR disease in infants have been adapted [32,33].

Data analysis

Interpretation and parameters

A correct interpretation starts by a visual appreciation of the whole pH tracing, which is certainly subjective and difficult to standardize. Nevertheless, it is of utmost importance 'to have a look' at the tracing (Fig. 4.21). Of all 'classic' parameters, the acid exposure time (reflux index) is the most relevant. The other 'classic' parameters are closely related to the acid exposure time, which is logical since they are based on the same boundary levels: the number of reflux episodes with pH <4.0, the number of episodes lasting more than 5 minutes, the duration of the longest episode. There is a good correlation between all four parameters [34]. Single oesophageal pH monitoring cannot detect alkaline reflux [35].

The parameters should also be (automatically) calculated for different periods of interest: sleep, wakefulness, feeding, post-prandial, fasting, body position. An exact time-relation between atypical manifestations (cough) and 'changes' in pH (not necessarily a drop in pH below 4.0) should be searched for. It should not be forgotten that the response time of an electrode (the time needed to reach 95% of the exact pH) is about 5 seconds.

The 'area below pH 4.0' is a parameter considering the acidity of the reflux episodes [36] which has been shown to correlate better with the presence of reflux oesophagitis than the reflux index.
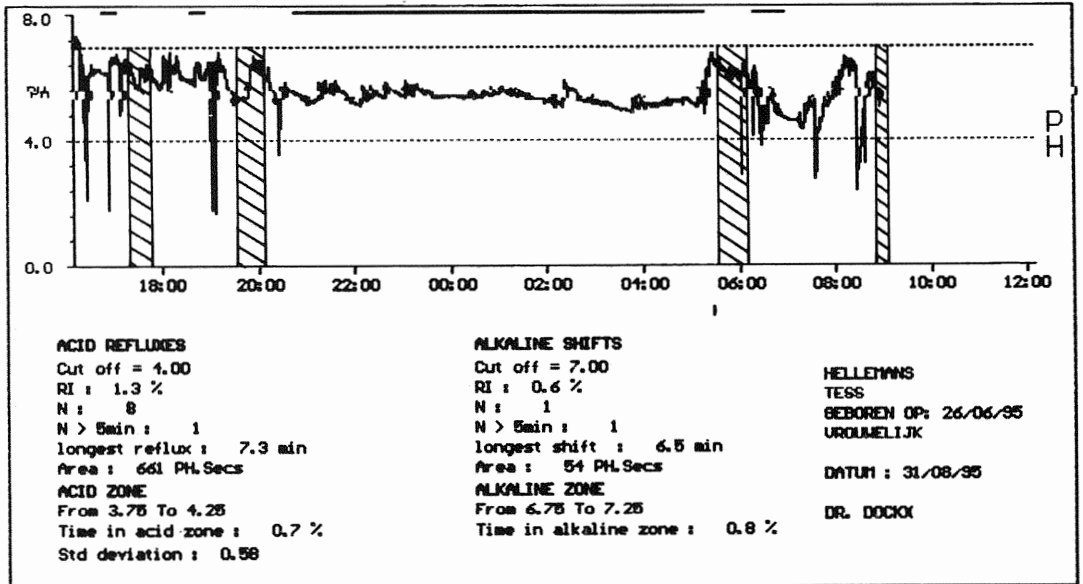
Fig. 4.21 24-hour pH tracing included meals (hatched area) and sleep period (line at the top of trace).

A major interfering factor for a correct interpretation of pH monitoring data is the 'yes' or 'no' interpretation of the data by computer software: a pH of 4.01 will be regarded as normal whereas a pH of 3.99 will be considered as giving evidence of the presence of acid in the oesophagus. Minimal changes of oesophageal pH will give rise to totally different interpretation, although there is no difference in its clinical meaning (Table 4.14). Therefore we developed the 'oscillatory index', a parameter measuring the time the pH oscillates around pH 4.0 [37].

Normal ranges

Although pH monitoring has recently been repeatedly reported as the 'gold standard' of all reflux investigations, its limitations have to be remembered: it only measures the pH in the oesophagus, and not GOR. As there is no GOR investigation which always provides a clear-cut discrimination between normal and abnormal, there is no reason why pH monitoring results should do so. Various complex reflux scoring systems (Jolley, DeMeester, Branicki, Kaye, Boix-Ochoa scoring systems) have been developed, most of which, together with the parameters most usually measured or calculated, have been developed for assessing reflux oesophagitis in adults. In marked contrast to these complex scoring systems is the simple recommendation

Table 4.14 Dependability of oesophageal pH monitoring data on the software program (37 recordings).

Parameter (mean ±, SD)	Program		
	1	2	3
Reflux index (% <4.0)	4.85 ± 3.84	4.86 ± 3.90	5.02 ± 4.15
No. of episodes/24 h	87.38 ± 149.14 (a)	16.05 ± 10.38 (b,c)	19.05 ± 9.85 (a,b,c)
No. of episodes >5 min/24 h	2.32 ± 2.42 (b)	2.27 ± 2.25 (c)	2.92 ± 2.78 (b,c)
Duration of longest episode (min)	18.54 ± 18.07	17.45 ± 16.84	15.33 ± 11.17

Program 1: MIC-program for Gastrograph Mark II: four measurements per second; the program calculates 360 medians per 24 hours.
Program 2: MIC-program for Gastrograph Mark II: four measurements per second; the program calculates 43 200 medians per 24 hours.
Program 3: Program for Gastrograph Mark II, developed by another company.
(a): $P < 0.001$; (b) and (c): $P < 0.05$.

by some investigators that total acid exposure time (reflux index) should be regarded as the most important, if not the only, variable in clinical practice [34].

Normal ranges proposed by one group can be used by another group only if the investigations are performed and interpreted in a comparable way. This means that the materials and methodology have to be identical. Since GOR is a naturally occurring phenomenon, there will inevitably be an overlap between 'normal' and 'abnormal' data. However, for some individuals and for some clinical situations it is more important to relate 'events' (coughing, wheezing, apnoea, etc.) to 'pH changes' than to know if global results are within normal range or not. It should be borne in mind that 'normal ranges' for a group are not always applicable to an individual (Table 4.15).

Standard oesophageal manometry and combined pressure–pH recording: applications in paediatrics

Oesophageal pH monitoring is often considered as an investigation technique studying oesophageal motility, although it does not measure 'motility' because it does not measure GOR. Oesophageal pH monitoring measures the pH in the oesophagus. The fact that this information only indirectly related to GOR and to oesophageal motility is far too often overlooked. For a practical patient-related diagnostic approach, pH monitoring in most situations is sufficient. However, if one is interested in the understanding of the pathophysiological mechanisms causing GOR and/or clearing the reflux out of the oesophagus, combined pressure and pH recording could be a more appropriate technique.

Table 4.15 Normal ranges for GOR in infants aged 0–15 months according to age ($n = 285$).

Age	n	Reflux index	Reflux episodes Duration of longest (seconds)	No./24 h	No. lasting >5 min
5–15 days	92	1.20(0.91)	230(115)	7.73(6.51)	0.64(0.51)
24–37 days	28	1.71(1.39)	404(327)	8.24(7.78)	0.88(1.44)
7–8 weeks	44	2.52(2.25)	369(225)	13.5(12.7)	1.57(2.23)
3.5–4.5 months	52	4.18(2.60)	706(467)	20.0(16.1)	3.24(2.41)
5.5–6.5 months	30	3.27(3.00)	540(416)	20.0(12.6)	2.14(2.32)
7.5–8.5 months	24	3.93(3.72)	610(511)	17.9(10.5)	3.08(2.25)
14–16 months	15	2.65(1.90)	520(428)	19.4(14.7)	2.21(1.22)

All values are mean (SD).

Patient preparation

The patient should fast for at least 3–5 hours before the study, depending on the age. If the child is able to communicate, it is important to reassure the child at the beginning of the study and explain what will happen. The child should understand that the passage of the catheter through the throat is uncomfortable, but after the first few swallows it will feel better. Children less than 5 years old should be wakened early in the morning, at least 5–6 hours before the study, so that they nap spontaneously during the test. Sedation should not be employed, because the sedative may interfere with swallowing and influence pressures.

Conclusion

The miniaturization of devices and electrodes has made pH monitoring a routine diagnostic procedure, even in the youngest children. Patient-related factors influence pH monitoring results; feeding and physical activity are factors of great importance in children.

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4.5   Clinical relevance of investigations

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The advent of ambulatory intra-oesophageal pH monitoring has provided a new

tool with potential to aid both research into gastro-oesophageal reflux (GOR) and the clinical management of patients. Its use in clinical practice requires that a reasonable consensus emerges among clinicians about the optimum approach to investigation and assessment of patients with suspected reflux disease, and this in turn requires agreement about the interpretation of clinical features and the diagnostic value of other investigations available. These matters are reviewed first so as to set the context in which recommendations about the use of pH monitoring can be made.

What do patients with gastro-oesophageal reflux disease (GORD) present with?

Patients who describe the classic symptoms of retrosternal heartburn, waterbrash and acid regurgitation represent the archetype of GORD and for these individuals the clinical history is usually sufficient for a reliable diagnosis to be made. These symptoms, when predominant within a patient's symptom complex, may be regarded as specific though insensitive indicators of GORD [1]. The relative rarity of the 'classic' symptom pattern has been described in the older literature [2] and was also convincingly illustrated by Wienbeck and Berges [3], in a study of 45 patients with oesophagitis. They found 29 of these patients to have symptoms of upper abdominal pain, nausea or vomiting which were at least as prominent as any of the 'thoracic' symptoms of heartburn, regurgitation, waterbrash or dysphagia. Thus while there was little doubt about the upper gastro-intestinal nature of symptoms in all the patients, a confident diagnosis of reflux disease was possible in fewer than half. These observations confirm that investigation is necessary in most patients with suspected reflux disease if a well-founded diagnosis is to be made.

   Although most patients with GORD present with symptoms which are obviously upper gastro-intestinal, the so-called atypical presentations are also clinically important. Otolaryngologists are well aware that hoarseness (related to posterior laryngitis) and a proportion of cases of globus pharyngitis are caused by gastro-oesophageal reflux. Respiratory physicians recognize GORD as an uncommon cause of chronic unexplained cough, and of asthma [4]. Cardiologists are well aware that GORD may give rise to a pain clinically indistinguishable from that of myocardial ischaemia. The fact that exertion may promote gastro-oesophageal reflux compounds this diagnostic difficulty when a patient identifies exertion as a precipitant of symptoms. Finally, a small proportion of patients present with oesophageal complications of reflux disease but seem to have little or nothing in the way of primary oesophageal symptoms. Dysphagia due to a benign stricture may be described in patients who seem never to have suffered heartburn. Occasionally, patients are encountered who have developed anaemia from

oesophagitis associated with chronic blood loss, yet give no history of significant upper gastro-intestinal disturbance.

Some type of investigation is therefore necessary to establish a firm diagnosis of GORD in the majority of patients encountered in gastro-enterological practice. Before appraising the available investigations, it is important to consider when immediate investigation might be unnecessary.

Which patients require investigation?

When clinical features invite a presumptive diagnosis of GORD, empirical therapy is often appropriate. Indeed, very many patients have already treated themselves with over-the-counter (OTC) medications, and seek medical attention only because of the duration of symptoms, or because of unease about their underlying cause. Investigation of symptoms suggesting GORD is essential if the symptom complex includes dysphagia, repeated vomiting or features of anaemia, and is highly desirable in patients over the age of 45 years if the symptom complex includes upper abdominal discomfort justifying a label of dyspepsia. Patients without these features can be subjected to an empirical trial of therapy, provided that there is a clear commitment to assess the success or failure of that therapy some weeks after it is initiated.

Contrast radiology has long been accepted to be of limited value in the assessment of GORD [5], though it is of some value in excluding the presence of pathology such as chronic peptic ulcer or malignancy. Upper gastro-intestinal endoscopy is the most appropriate initial investigation for patients with upper gastro-intestinal symptoms, and the appearances of reflux oesophagitis detected on endoscopy are highly specific. However, it is important to recognize that a substantial proportion of patients with GORD—perhaps as many as 50%—do not have oesophagitis [6]. In these individuals, endoscopic appearances of the upper gastro-intestinal tract are entirely normal.

In whom should pH monitoring be performed?

There are four main groups of patients in whom intra-oesophageal pH monitoring is helpful. They fall into two main subdivisions: those with classic reflux symptoms and those with less typical presentations.

Firstly, patients with clinical features suggesting GORD who have responded inadequately to conventional anti-reflux therapy always represent something of a problem of clinical management. Should medication be intensified, or could the diagnosis be mistaken? These decisions must always be taken on an individual basis, but when doubt has arisen about a clinical diagnosis of GORD, intra-oesophageal pH monitoring is the best means of attempting resolution of the

uncertainty. If the diagnosis is confirmed, changes in the therapeutic regimen may then be made with much more confidence.

A related patient group are individuals shown to have oesophagitis at endoscopy, but who remain symptomatic despite adequate therapy. Intra-oesophageal pH monitoring may show that the total acid exposure time is abnormal despite medication, and may also show that the symptom–reflux event correlation remains high, thus confirming the fact that the patient's continuing symptoms are indeed reflux related [7]. The value and interpretation of intra-oesophageal pH monitoring studies undertaken on medication are perhaps less firmly established than purely diagnostic tests, but there seems little doubt that such investigation is sometimes useful. Of course, it is important to remember that some troublesome symptoms in GORD relate to the reflux of fluid volume, and may occur whether the refluxate is acid or neutral. Only the former will be recorded by conventional electrodes.

Intra-oesophageal pH monitoring is extremely valuable to confirm the diagnosis of GORD in patients with normal oesophageal appearances at endoscopy. The diagnosis of GORD should be established beyond question when the use of medication on a long-term basis is contemplated, or if surgery is considered. When no endoscopic abnormality has been identified, confirmation of the diagnosis can be achieved only by pH monitoring.

Patients with atypical symptoms of GORD represent the final group in whom intra-oesophageal pH monitoring is helpful in diagnosis. Nevertheless, it should be noted that most clinicians believe that patients with pain suggesting myocardial ischaemia should always undergo cardiological assessment initially. Subsequent oesophageal assessment is undertaken on a patient who may then properly be described as having non-cardiac chest pain.

In almost all patients undergoing pH monitoring for diagnostic purposes, it is important to record both the total acid exposure time (and other quantitative indicators of acid reflux) and also to record the coincidence or otherwise of symptoms such as pain, heartburn or regurgitation and acid reflux events.

Apart from the purely diagnostic use of oesophageal pH monitoring, many surgeons take the view that pre- and post-operative pH monitoring studies are desirable in patients undergoing anti-reflux surgery to provide some objective 'quality control' of the success of the operation. Many patients are very willing to undergo post-operative assessments of this sort but obviously there is a clear obligation to ensure that the patients are fully informed about the purpose and context of these tests when their cooperation is requested. Trimble *et al.* in 1995 [8] suggested a protocol for the clinical use of oesophageal pH monitoring (Fig. 4.22). Each patient's situation must be considered in the context of their age, sex, duration and type of symptoms, response to previous therapies and possible future treatment.
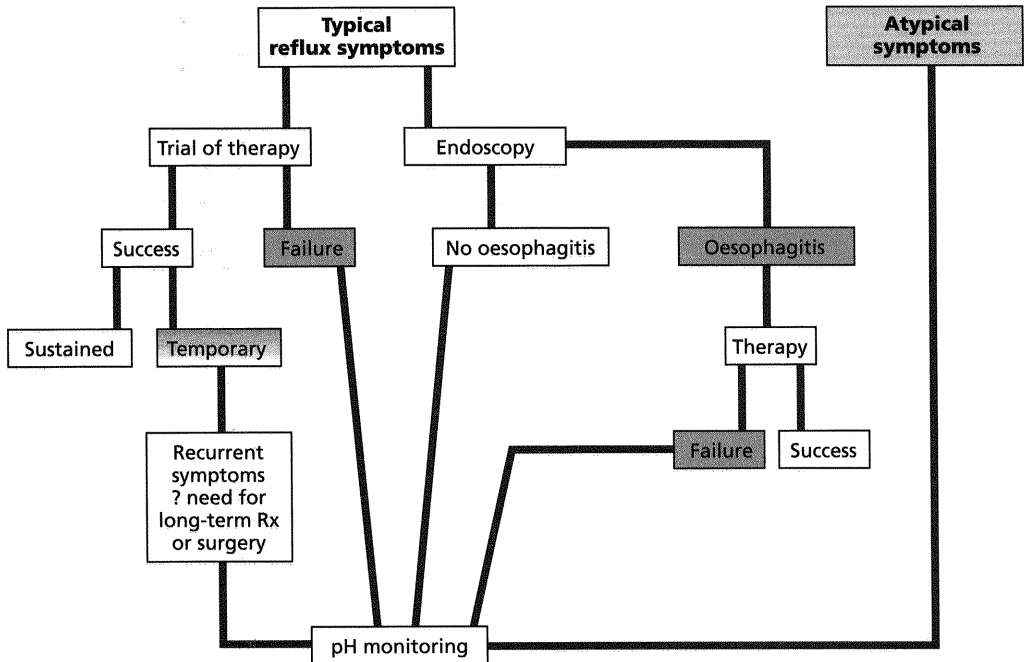
Fig. 4.22 Suggested clinical application of oesophageal pH monitoring (from reference [8]).

Clinical interpretation of oesophageal pH monitoring

Bontempo *et al.* [9] have shown that despite considerable intra-subject variability of the magnitude of reflux on repeat testing, the distinction between normal and abnormal reflux is consistent and reliable. Greater variability may be encountered when the smaller antimony electrodes are used because they may lie between collapsed folds in the oesophagus where acid may pool, especially when the patient is recumbent [10]. The slightly larger (though more expensive) glass electrodes may thus have some advantage.

Several groups of investigators have identified a distinct group of patients who give a history consistent with GORD, show a good coincidence of symptoms with acid reflux events and yet have an oesophageal acid exposure time well within normal limits. A report by Shi *et al.* in 1995 [11] identified 12.5% of 771 consecutive patients as fulfilling this pattern and proposed that these patients have an oesophageal hypersensitivity to acid. In other laboratories, patients with these features are perhaps encountered a little less frequently, but their existence is also recognized. Some of these patients have been shown to have lowered sensory thresholds to balloon distention in the oesophagus [12] and altered visceral sensation may be part of the explanation for their perception of symptoms in the absence of

excessive acid reflux. These patients thus have symptomatic, though not excessive, gastro-oesophageal reflux and usually show both prompt clearance of refluxed acid from the oesophagus and an entirely normal oesophageal pH profile [11]. Interestingly, they usually give positive results to acid perfusion tests [13,14].

The measurement of symptom index (SI) [15–17] or symptom specificity index (SSI) [18] has been proposed as a means of measuring the strength of temporal associations between the occurrence of symptoms and the timing of reflux events. Caution is necessary when interpreting the extremes of the SI or SSI. If only a single episode of pain is reported by a patient within a 24-hour period, and this correlates with a reflux event, the calculated symptom index is 100% but common sense dictates that this may be less significant than a symptom index of 90% derived from a patient reporting 10 episodes of pain, nine of which coincide with acid reflux. Likewise, it is difficult to calculate a meaningful symptom–reflux correlation in a patient who reports near-continuous pain.

Despite the greater mathematical sophistication of the SSI, it remains true that an SI ≥ 50% is a simple and practical basis to make a first estimate of the correlation between symptoms and reflux, thus identifying patients who warrant a diagnosis of GORD regardless of the magnitude of oesophageal exposure. Further, this measurement can confirm that an abnormal degree of reflux recorded by pH monitoring is indeed responsible for the patient's symptoms. Such confirmation may be especially valuable when the clinical presentation is atypical.

One of the difficulties encountered in clinical practice is defining the upper limit of normal for distal oesophageal exposure to acid. Reported values vary considerably and this understandably raises some doubt about the reliability of the tests. Why does this substantial variation occur? Reviewing the literature, it is evident that different authors have used different populations to establish their normal controls. Some completely exclude volunteers who report any symptoms of reflux yet others would argue that infrequent reflux is not by definition pathological. Where should we draw the cut-off line in the spectrum of 'normals'? Should a control population being used to establish normal values be subjected to endoscopy to ensure that none have unrecognized oesophagitis [19,20]? Should the normal range relate to the age of the subject, since total acid exposure time is known to increase with age [21,22]? Should subjects undergoing oesophageal pH monitoring be allowed to follow their normal pattern in respect of diet, exercise, sleeping, smoking, etc. or should there be standardized conditions for performing the test as it seems inevitable that the magnitude of reflux both in healthy controls and in patients will be influenced by these variables? Does the presence of the tube itself interfere with patients' activities such that it is almost impossible to capture a true representation of the subject's normal daily habits?

Different investigators have come to different decisions on these questions, partly explaining the variation in recorded 'normal' values. On present evidence

and depending on technique, a value of between 4.5 and 7% for the upper limit of normal for distal oesophageal exposure to acid is reported. Standardized conditions are usually applied in respect of stopping acid suppression therapy, forbidding the use of antacids during the study and placement of the probe 5 cm above the upper margin of the manometrically determined lower oesophageal sphincter.

Standard probes are reasonably accurate for measurement of pH levels between 1 and 8. Above this, alkaline reflux cannot be determined reliably although specialized equipment is being developed for this purpose [23]. It is important to remember that saliva has a pH of around 8, and that if this pH is recorded at a single point in the oesophagus, there is no means of knowing whether it reflects an episode of duodeno-gastro-oesophageal reflux, or whether it is merely recording the pH of swallowed saliva.

Like most other test, the results of pH monitoring must be interpreted in the context of other clinical findings, both from the clinical history and other investigations. Provided interpretation is undertaken in this context, ambulatory pH monitoring is an immensely valuable aid in the diagnosis and assessment of GORD.

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5 Combined measurement of pH and manometry

5.1 Equipment and catheters

Richard H. Lowndes

Introduction

Ambulatory pH studies currently form one of the principal ways of investigating potentially reflux-related upper gastro-intestinal (GI) disorders. Whilst this technique can provide data of great diagnostic value, a proportion of patients still elude a satisfactory explanation of their symptoms. Oesophageal dysmotility can play an important role in the aetiology of upper GI symptoms such as non-cardiac chest pain [1], and it is possible that the response of the oesophagus to reflux may be responsible for symptoms [2,3]. It is likely, therefore, that the simultaneous monitoring of both oesophageal pH and motility will be of greater diagnostic value than either parameter in isolation [4–8].

In recent years, the progress in digital electronics and microprocessor technology has brought multichannel pressure measurement combined with pH monitoring within the grasp of the GI laboratory [9,10]. At the time of writing, digital recording and storage devices (dataloggers) with memory capacities of 2 Mb and 4 Mb are commonplace, with devices of 8 Mb and even 16 Mb soon to be available. Using sophisticated data compression and retrieval techniques, many dataloggers can record up to fourteen channels of pressure and pH, and even an ECG channel and EMG swallow detector, for periods of 24 hours or longer.

Combined ambulatory pH/motility recorders (dataloggers)

The clinical measurement specialist has a wide range of dataloggers to choose from, most of which are designed to run for 24 hours or more from standard alkaline batteries, and with an overall size similar to a paperback book and a weight of around 500–600 g, the dataloggers themselves cause minimal inconvenience to the patient.

Datalogger design

All more or less conform to a similar design and method of operation, and Fig. 5.1 illustrates in simplified form the various block components of such a datalogger, and provides some indication of the level of complexity achieved in these devices. The heart of such dataloggers is the microprocessor which, just as in a desktop PC, handles all of the functions via a pre-programmed set of instructions installed by the manufacturer into the EPROM. Some of the parameters in the instruction set are user-definable and can be accessed either via the display on the datalogger itself, or via a PC whilst the datalogger is plugged in via its communication port. The pre-amplifiers condition the signals from the connected sensors, and the type of pre-amplifier fitted will determine the type of sensor that can be used. The microprocessor will often contain a built-in analogue-to-digital (A–D) converter, which ascribes a digital value to the voltage output from each of the pre-amplifiers in turn. This digital value is then further processed and passed to memory for storage. Other designs will use independent A–D converters; the overall result is much the same. The calibration and offset circuitry automatically performs the task of balancing the pressure sensors against their respective offset voltages, and supervises the calibration procedures for all sensors and pre-amplifiers. The clock provides the timing signals for all the microprocessor operations and also provides real-time markers for the recorded data.

Connectors, display and data storage

The random access memory is the storage area of the datalogger. The use of data compression techniques allows more data than would at first appear to be possible
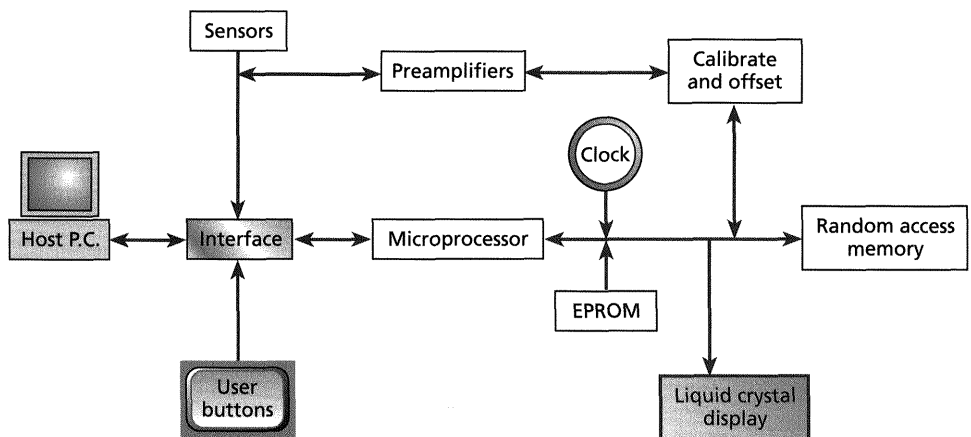
Fig. 5.1 Simplified representation of the main components of a typical digital datalogger.

to be stored in memory. A recent alternative data storage medium is the use of removable 'Flash or PCMCIA' cards such as have become popular in laptop computers. These allow almost unlimited data storage (up to 40 Mb) and can be changed mid-study to allow even greater data capacity when required.

The actual amount of data that can be stored for any one study will depend on the number of channels used and the sampling rate. The sampling rate chosen will determine the fidelity of the recording—the higher the sampling rate, the better the resolution. Modern dataloggers are capable of sampling rates from 1/128 Hz to 128 Hz; recording times of several days can be achieved with the former, a few hours with the latter. For combined ambulatory pH and motility recordings priority must be given to the motility channels, and a sampling rate of 4 Hz should be considered to be the absolute minimum rate for the accurate reproduction of oesophageal pressure waves. A slower sampling rate may result in inaccuracies of both frequency and amplitude of the recorded waveforms (Fig. 5.2). Subsequent expansion of the downloaded data will not compensate for slow sampling rates.

Most systems incorporate an LCD display on which real-time and recording parameters may be continuously displayed. Control buttons on the recorder are the means by which the investigator can alter certain parameters such as number

Original signal

Sampled at 1Hz

Sampled at 2Hz

Sampled at 4Hz

1 sec
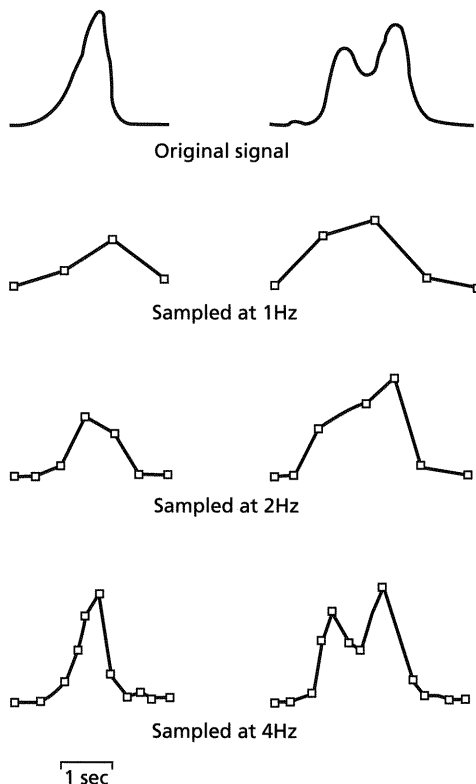
Fig. 5.2 Low sampling rates can lead to inaccuracies of both frequency and amplitude of recorded waveforms.

of channels to use, etc. (some models can also do this via the host PC). These are often also the means by which the patient can mark the recording with relevant events such as symptoms, eating and drinking, lying down, etc.

Careful design of external connectors which are used to attach the recording catheters to the datalogger are also very important. Small, tidy and reasonably concealed connections minimize the chances of accidental disconnection during a study. Care must be taken when performing studies involving two or more sensors of the same type. If these can be connected without due regard to their relative positions in the oesophagus, errors will result in incorrect interpretation of the recorded data.

Catheters

The investigator has a choice at the outset, when purchasing a combined ambulatory pH/motility system, of whether to opt for separate catheters and to combine them in whatever configuration suits the particular investigation, or to purchase specialized catheters containing both pressure and pH sensors together in the same housing.

The use of separate catheters offers the greater versatility of investigation; the relative positions of the pH and pressure sensors can be tailored, each time, to the particular needs of the patient and investigation such that the data obtained can be of maximum value for the diagnosis of the patient's condition. Once the particular combination of pH and pressure channels has been decided, the two (or three) catheters can be fastened together using, for example, a self-adhesive wound dressing material such as Op-site (Fig. 5.3). The combined catheters are then passed as one, taking care not to introduce any slack in one or other catheter. Separate catheters also allow the investigator to maximize usage of equipment; if the pH catheter fails to calibrate, it is a simple matter to replace it rather than having to send the whole combined assembly away for repair.

Combined catheters offer ease of use, calibration, cleaning and sterilization. They maintain the same configuration for all tests performed and should therefore minimize any variations that could otherwise be attributed to sensor orientation, interaction, etc. The convenience of such catheters does, unfortunately, come at a price. The cost of a two-channel pH, three-channel pressure combined catheter can be double that of the same combination obtained using separate pH and pressure catheters.

Pressure catheters

Virtually all catheters currently available for combined ambulatory pH/motility investigations are so-called 'solid state' catheters. This is a somewhat misleading
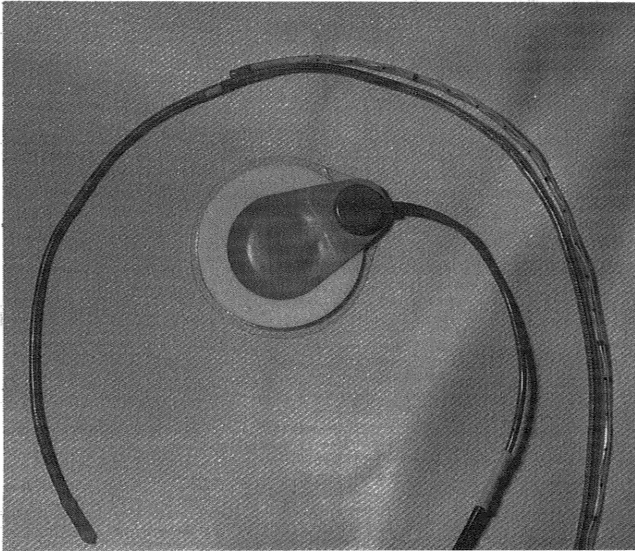
Fig. 5.3 Separate pH (antimony) and pressure (Gaeltec) catheters joined together for a combined study. The skin reference electrode (R-00-S ECG electrode) is also shown.

term, since only catheters of relatively recent design (e.g. Sentron) are truly solid state in the sense that they employ silicon semi-conductor technology to effect the actual pressure measurement. These sensors are designed such that the silicon 'chip' responds directly to applied pressure, albeit beneath a protective layer of silicone rubber. Some signal conditioning will also take place on the chip before applying the signal to the datalogger input.

Other 'solid-state' catheters (e.g. Gaeltec, Konigsberg) employ miniaturized strain gauge transducers which are photo-etched onto thin metal diaphragms; each individual sensor is embedded in a protective layer of silicone rubber. Each strain gauge forms one or more arms of a Wheatstone bridge circuit; any movement of the diaphragm will result in a voltage output proportional to the amount of movement [11]. These types of sensor are therefore displacement transducers and are extremely sensitive to any directly applied pressure—they should not be tested by tapping with a finger, because very expensive damage can easily result!

All types are available in a variety of configurations; two sensors 5 cm apart is the absolute minimum requirement for detection of peristalsis. Three sensors spaced at 5 cm intervals is probably the most common arrangement; additional sensors may be desirable but will be limited by the number of pH sensors incorporated and the total number of channels and memory available on the datalogger. Individual pressure sensors are usually uni-directional, and therefore not suitable for long-term monitoring of lower oesophageal sphincter (LOS) pressure. However, there are two catheters now available which have been designed to overcome this problem. The first is an oil-filled 6 cm sleeve surrounding one sensor (sphinctometer)[12] such that it becomes omni-directional with regard to LOS pressure; in effect this is
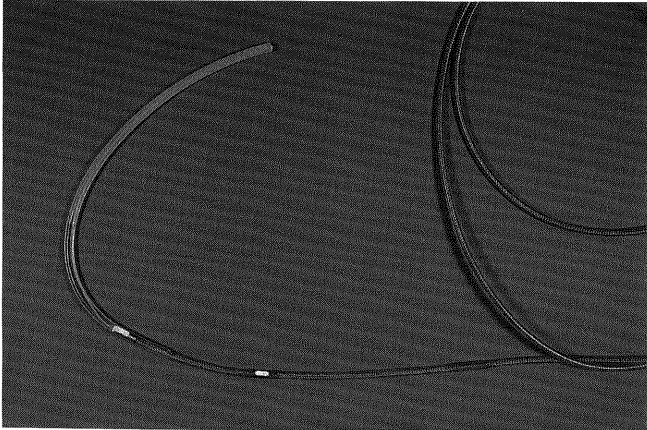
Fig. 5.4 Strain gauge microtransducer pressure catheter incorporating a 'sphinctometer' positioned around the tip transducer. The oil-filled silicone tube senses pressure changes over a 6 cm length.
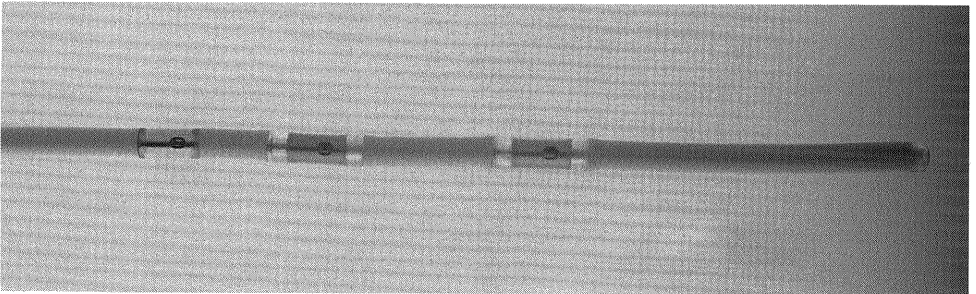
Fig. 5.5 Solid state pressure catheter (Sentron) showing two circumferential sensors 5 cm and 8 cm from tip, and a conventional uni-directional sensor 10 cm from tip. (Courtesy of Synectics Medical Ltd.)

the solid state equivalent of the Dent sleeve used with a perfused system (Fig. 5.4). The second option is a design that senses pressure circumferentially [13] (Fig. 5.5), although with this configuration there remains the possibility that the sensor becomes displaced as the oesophagus shortens and lengthens during swallows and after food. It must also be remembered that as the number of sensors increase, so does the diameter of the catheter. Depending on make and type, a two pH, three pressure catheter may be up to 5 mm in diameter and this is usually sited transnasally and has to be tolerated for up to 24 hours.

pH catheters

pH catheters for ambulatory studies are discussed in detail in Chapter 4.1. Those used in combined pH/pressure catheters are usually of the antimony type, ideally with an internal reference electrode. Placement of pH sensors within the catheter

is, to some extent, dependent on what manufacturers make available, though most are willing to make up catheters to specific requirements. Standard pH analysis software is calculated on the assumption that one sensor is located 5 cm above the proximal border of the LOS; the placement of further sensors within the oesophagus will depend on the investigator, and the information required from the test [14,15].

Glass pH catheters are not at present suited to combined catheter designs owing to difficulties in construction. Although antimony catheters are both an economical and practical alternative to glass types for detecting acid reflux [16], there have been doubts about their accuracy and performance in the long term [17,18]; this is of some importance if they are to be permanently housed in a £3000 catheter. A new type of pH probe is showing promise in the GI field—the ion-sensitive field effect transistor (ISFET) pH electrode. These sensors are essentially a type of transistor in which the gain controlling gate is replaced by an ion-sensitive membrane. The sensor transistor can itself be part of a silicon integrated circuit containing signal conditioning and amplifying electronics. Early reports suggest that they have similar characteristics to glass electrodes [19].

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5.2   Procedures and analysis

Angela Anggiansah

Preparation and procedure

Preparing the combined pressure and pH recorder

The main procedure before the patient arrives is the preparation of the recorder and calibration of the pressure and pH sensors. This has to be performed before every test. It is essential to install new batteries in the recorder immediately before each study to conserve useful recording time, as currently, with these types of recorders, battery power is usually only sufficient for a limited time and any wasted standby period should be avoided to retain battery power. Any previous recording should be also be cleared from the recorder's memory before calibrating the sensors.

Pressure sensor calibration

For ambulatory pressure monitoring, suitable sensors are the intraluminal miniature pressure microtransducers. There are two types commonly available: the metal

diaphragm strain gauge transducer (Gaeltec, Isle of Skye, UK and Konigsberg USA) and the piezoresistive silicon chip transducer (Braun Melsungen AG, Germany; Cordis/Centron, The Netherlands; Keller AG, Switzerland) [1]. For those systems which use a sphinctometer (Gaeltec Ltd) to monitor lower oesophageal sphincter function, it is advisable to delay calibration until the sphinctometer has been immersed in water for 4 hours at room temperature. This is because an initial increase in recorded pressure (baseline drift) is the unavoidable consequence of the change in volume which occurs due to water absorption by silicone rubber when immersed in water. An *in vitro* study has shown that the extent of baseline drift of the sphinctometer falls after an average of 4 hours immersed in either water or normal saline. Calibration of the sphinctometer after immersion in water will retard the baseline drift *in vivo* but unfortunately some drift may continue after intubation. The sphinctometer cannot therefore give totally reliable absolute measurements of the lower oesophageal sphincter pressure and prior static manometry should be used for this reason.

Calibration

Calibration of microtransducers is somewhat different from that of perfused tube catheters although similar principles apply. Calibration can be performed using either positive or negative calibration (Fig. 5.6), but positive calibration is more
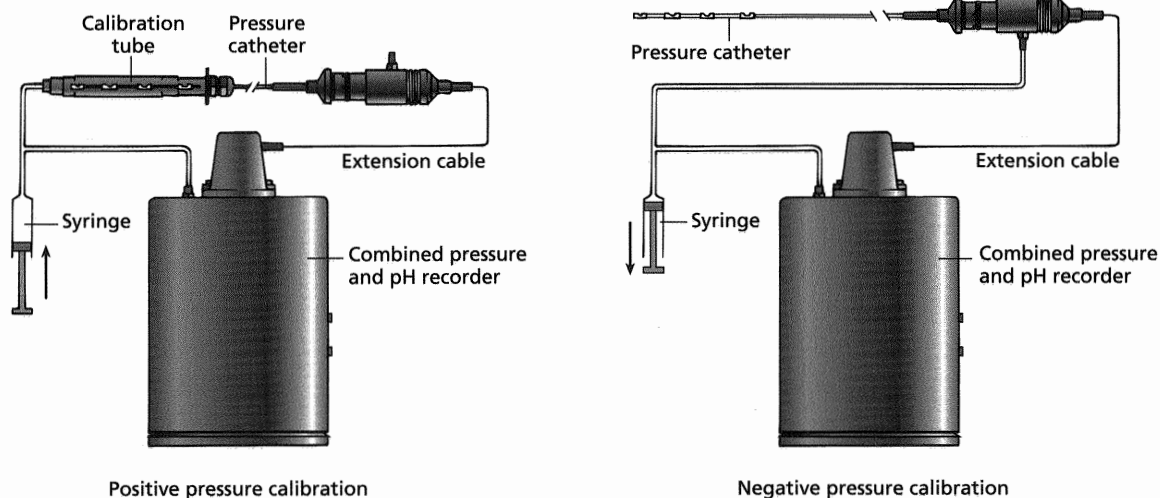
Fig. 5.6 Positive and negative pressure calibrations. Air is introduced into (positive) or withdrawn (negative) from the syringe, via a three-way tap to the pressure sensors and reference transducers, steadily increasing or decreasing the pressure until a predefined value is attained.

commonly used. An internal reference pressure transducer in the recorder provides any necessary correction during calibration and ensures that recorded pressure values are accurate. For positive calibration, the pressure catheter is placed inside a calibration tube and connected to a three-way tap which allows the pressure sensors to be opened to atmospheric pressure to establish 'zero' pressure before air is introduced from a syringe. The syringe is pressed steadily until a predefined pressure is achieved and displayed by the recorder. For negative calibration, the procedure is the same, but instead of applying pressure, air is withdrawn from the inside of the catheter to a predefined vacuum, on the principle that when air is withdrawn from the inside of the catheter the same pressure differential develops across the transducer diaphragm as is generated when a pressure is applied to the outside of the catheter.

An advantage of positive calibration is that although it is a delicate procedure (the pressure catheter has to be positioned inside the calibration tube through a small opening and care must be taken not to damage the outer cover of the pressure catheter), it is easy to verify the accuracy of the applied pressure by using a sphygmomanometer connected via a three-way tap to the calibration tube and the reference pressure. Negative calibration is easier to perform but has the disadvantage that it can be inaccurate if the pressure catheter is kinked, and consequently fails to transmit the calibration pressure to the pressure sensors. Negative calibration can be verified by use of a vacuum gauge, but this is not so readily available as a sphygmomanometer. Whichever calibration technique is used, it is important that the pressure sensors are checked by being immersed vertically into a cylinder of water of known depth to verify that they are all reading correctly before use.

pH calibration

pH calibration is identical to that described in Chapter 4.1; details of calibration procedures may be found on p. 94.

Preparation of the patient

Patients referred for assessment are informed about the test by letter, with a detailed explanation of the discomfort and implications of the investigations. Combined ambulatory pH and pressure studies are usually performed on an outpatient basis. Patients are requested to refrain from taking antacids for 24 hours, H_2 antagonists for 48 hours and proton-pump inhibitors for 7 days prior to the test. Provided the referring doctor agrees, patients are also asked to stop taking motility-altering drugs such as nitrates, calcium-channel-blocking agents, anticholinergics, prokinetics and sedatives for 48 hours before the study. In order to reduce the risk of vomiting on

intubation, subjects are advised to have nothing to eat or drink for 4 hours before their test.

As patients referred for combined pH and pressure studies may have atypical symptoms, including angina-like chest pain, it is essential to have a full history taken with particular reference to specific symptoms, duration of complaint and drug therapy. A full explanation of the investigation to be performed is given and written consent is obtained.

Before intubation, a small amount of electrode gel is placed in the well of the external pH reference electrode (if using a unipolar pH sensor) and it is secured to the subject's chest by a double-sided adhesive ring. The combined pressure and pH-sensing catheter is introduced transnasally under local anaesthesia. The recorder normally functions as a portable stand-alone unit, but at the start of the test the recording is monitored on the host computer to display and confirm that all pressure and pH channels are functioning. After correct positioning of the pressure and pH sensors (usually determined by station pull-through manometry), the system is tested by giving 10 wet swallows (5 ml boluses) at 30 second intervals to ensure that the recorder is in working order before ambulatory pressure and pH recording starts. In our studies a five sensor pressure catheter is utilized which incorporates a pharyngeal sensor to detect initiation of swallows, three oesophageal body sensors and a sphinctometer. A two-channel pH sensor is attached to the pressure catheter such that the tip sensor lies 10 cm below the gastro-oesophageal junction and the proximal sensor 5 cm above the proximal border of the lower oesophageal sphincter (LOS) (Fig. 5.7).

Patients are instructed to carry on their usual daily activities during the test, but to avoid taking specified food and drinks according to the study regime (see Chapter 3, 4). The type or quantity of the food is not restricted, but subjects are asked to finish their meal within 30 minutes if possible to avoid long periods where swallowing is a part of food ingestion. In addition to normal meals, the subjects are allowed to take water, but asked to record this and food intake in a diary. Event markers incorporated on the recorder allow the patient to record symptom events, changes in position from upright to supine or vice versa, eating and other events such as belching, sneezing or coughing. Unfortunately, patients tend to be confused by multiple event markers, therefore it is essential for the patient to also complete an activity diary during the study. All the activities and symptoms have to correlate with the exact time on the recorder and the patient should only press the event button when a symptom occurs.

At the completion of the recording on the following day, the position of the catheters should be rechecked and the catheters removed and washed. The pH probe is recalibrated and both the pH and pressure catheters (excluding the reference electrode) are disinfected (see Chapter 4). The data are downloaded onto the computer for automatic analysis.
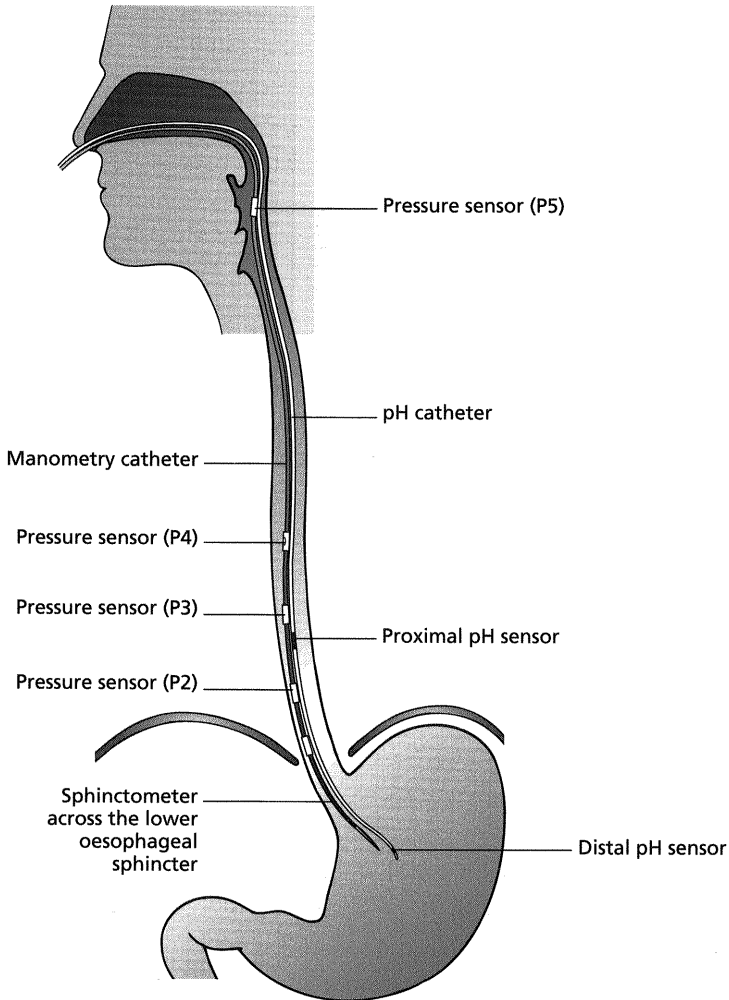
Fig. 5.7 Positioning of the combined pH and pressure catheters. The pressure catheter consists of five pressure sensors. Pressure sensor P5 is in the pharynx to detect voluntary swallow, P4, P3 and P2 are in the lower body of the oesophagus to record motor activities and the sphinctometer is in the LOS to monitor LOS function. The separate dual-channel pH catheter is bonded to the pressure catheter so that the proximal pH sensor is at 5 cm above the LOS and the distal pH is 15 cm below the proximal pH sensor.

Data analysis

Analysis of pH data

pH data are analysed for the presence of gastro-oesophageal reflux (GOR) according to the standard criteria described in Chapter 4. Where pH and pressure are combined it may be desirable to perform some form of interactive analysis to examine any

causal relationship between GOR and LOS or oesophageal motility abnormalities. At present most users rely on visual subjective assessment as there have been few studies utilizing automated techniques with interaction between the pressure and pH channels. In future, as computer-aided analysis becomes more sophisticated, it will become easier to examine the relationship between GOR and dysmotility interactively.

Studies to date to establish normal values for GOR have positioned the tip of the catheter (pH sensor) 5 cm above the LOS. However, a combined pressure and pH study may have a sphinctometer in the LOS and also an attached dual-channel pH catheter passing through the LOS. The data remain inconclusive on the possibility of a catheter positioned across the LOS promoting GOR in supine healthy controls [2]. This led Kuo and Castell [3] to study a group of supine healthy controls in the immediate post-prandial state, when the likelihood of the occurrence of GOR is greatest. They concluded that a 3.8 mm diameter catheter through the LOS did not promote GOR in healthy controls. Their finding was supported by Emde *et al.* [4] and Anggiansah *et al.* [5]. The latter study was performed in a group of reflux patients with a catheter of 5 mm combined width across the LOS.

Analysis of pressure data

The quantity of data collected during 24-hour oesophageal pressure recording is too large to analyse manually; to overcome the data storage problems some workers [6,7] use data compression methods during recording. Automatic analysis has been used to analyse the vast amount of pressure data objectively and consistently.

The automated analysis is evaluated in three distinct stages: (i) to detect contraction waves at all channels; (ii) to reject the non-active oesophageal contractions and to relate the active oesophageal contraction waves at different channels into a relevant contraction sequence; (iii) to define the characteristics of contraction waves and the patterns of contraction.

1 Wave identification

A contraction wave is recognized when a sufficient increase in oesophageal pressure (predefined threshold pressure) occurs compared with the baseline pressure. A baseline pressure relative to atmospheric pressure is calculated for the period between contractions. Each pressure wave is said to commence when the predefined threshold pressure (minimum 15 mmHg or up to 20 mmHg above the baseline pressure) (Fig. 5.8) is exceeded and to end when it falls below a threshold value (typically 10–15 mmHg above the baseline pressure). If there are additional rises and falls of a similar magnitude occurring while the pressure remains above the threshold, the number of such peaks is registered as a multipeaked contraction.
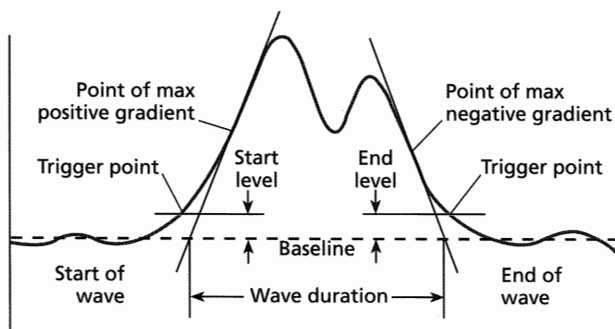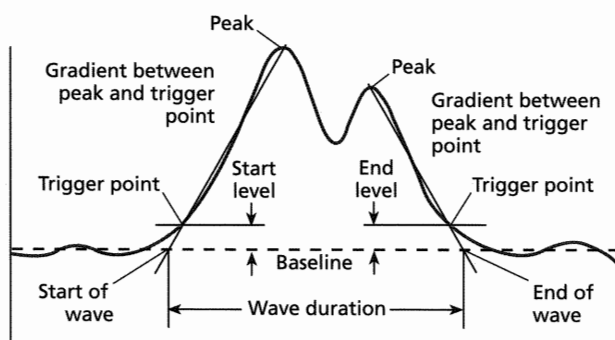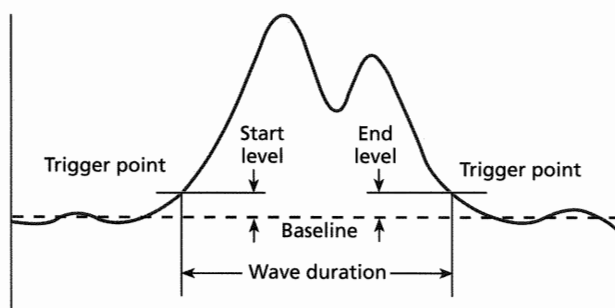
Fig. 5.8 Wave detection. Each pressure wave is detected as it rises above a specific threshold pressure (15 mmHg) and ends when it falls below a specific threshold pressure (15 mmHg). Additional rises (15 mmHg) and falls of a similar magnitude occur while the pressure remains above the threshold; the number of such peaks is registered as one of the wave characteristics. The duration of a wave is evaluated by the three possible methods as shown here.

2 Non-active oesophageal pressure elimination

For waves to be included in the analysis, a minimum of 15 mmHg onset threshold and a minimum duration of 1 second are chosen to eliminate oesophageal wall movements not associated with swallowing or distension, such as respiration, cardiac activity or coughing.

3   Wave characterization and patterns of contraction

Wave characterization. The features of contraction wave generally chosen for study are: duration and maximum amplitude of the wave, area under the wave and peristaltic velocity.

The duration of a wave in seconds has several possible definitions: the interval between the points of intersection of extrapolation of either the maximum gradients or the average gradients at the onset and end threshold and the baseline, or the time interval between the onset and end of the contraction wave (Fig. 5.8).

The amplitude of the wave in mmHg is determined by finding the highest pressure and subtracting the baseline pressure.

The area under the wave in mmHg* sec is calculated by integrating the pressure value between the points of intersection of the wave and the baseline as defined in the wave duration.

The peristaltic velocity is expressed in cm/sec for the transit of an individual wave between two adjacent sensors, and has been calculated by many methods. Investigators have used the onset of the contraction [8,9], the point of maximum slope of a contraction [10] or the peak of the contraction [11,12] as a reference point for the velocity measurements. Although it is more physiological to use the onset of the contraction as the reference point, Bremner *et al.* [13] validated a commercially available software program (Multigram 5.00, Gastrosoft, Irving, Texas) and showed that measurements by computer analysis using the peak of contraction were more reliable than those using the onset of contraction.

Classification of the patterns of contraction. The time interval between contractions at two adjacent channels (usually 5 cm apart) is used as a base for the patterns of contraction and it is a matter of choice whether the interval is taken between the peaks of contraction or the onsets. There are no universally agreed standard time intervals between contractions at two adjacent channels to be used when defining contraction patterns, therefore those described below are presented as a guide only.

1   Peristaltic activity is defined as a time interval of between 0.25 and 7 seconds between contractions in two adjacent levels, 5 cm apart.

2   Simultaneous activity is defined as a time interval of less than 0.25 seconds between the peaks of contractions at adjacent levels, 5 cm apart.

3   An isolated contraction is defined as a contraction detected at a single site when no appropriate matching contractions can be found at the other levels.

4 Reverse peristaltic activity is defined as occurring when the time interval between the peaks of the contractions in two adjacent levels is between −0.25 and −1 second, 5 cm apart.

5   Mixed activity has a mixture of simultaneous and peristaltic contractions, including reverse peristaltic contraction.

Twenty-one possible subtypes of patterns of contraction were defined for three pressure channel recording (Fig. 5.9) and grouped into four main types (where P4, P3 and P2 represent pressures recorded at the upper, middle and lower pressure sensors at 5 cm intervals positioned at the body of the oesophagus). They are:
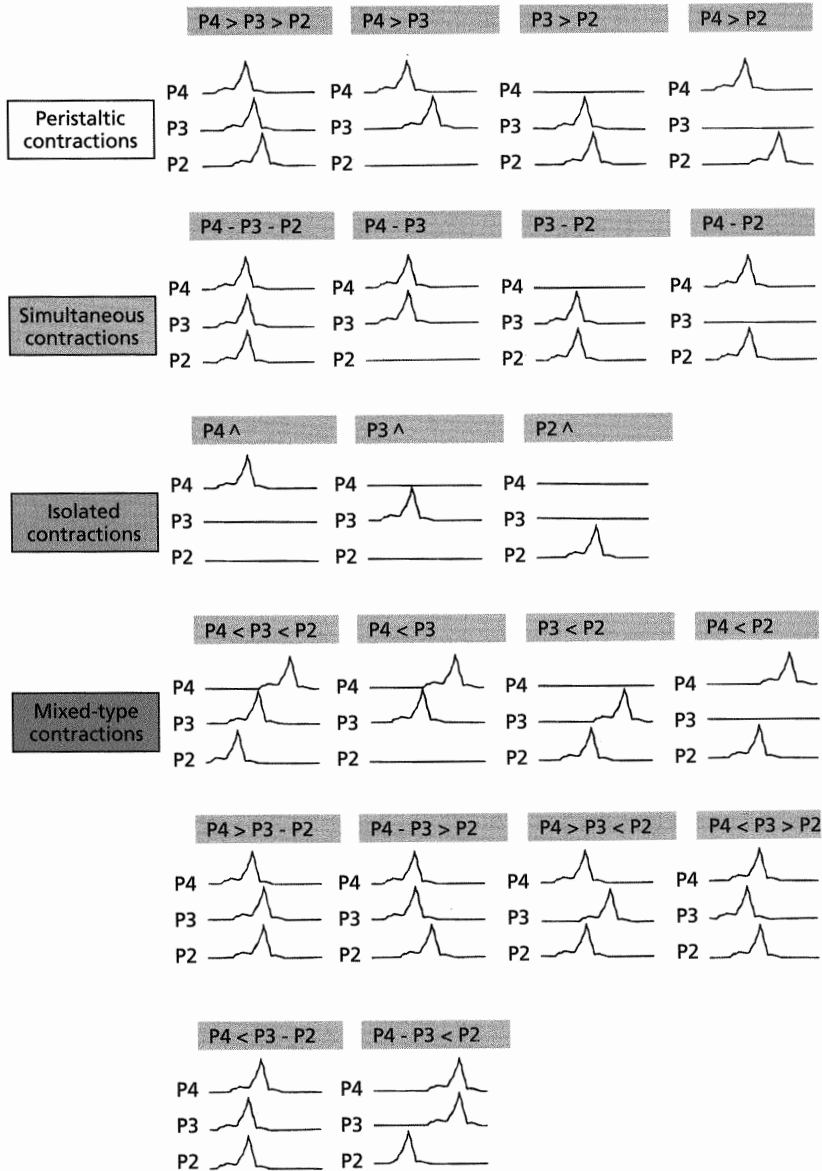
Fig. 5.9 Twenty-one subtypes of patterns of contraction derived from three channel pressure recording. Oesophageal pressures are recorded at upper (P4), middle (P3) and lower (P2) pressure channels in the body of the oesophagus.

Type 1: P4 > P3 > P2; P4 > P3; P3 > P2; P4 > P2, where > means peristaltic contraction (e.g. P4 > P3, where > means P3 follows P4).

Type 2: P4–P3–P2; P4–P3; P3–P2; P4–P2, where – means simultaneous contraction (e.g. P4–P3, where P4 and P3 occur simultaneously).

Type 3: P4ˆ; P3ˆ; P2ˆ, where ˆ means isolated contraction (e.g. P4ˆ means P4 occurs on its own).

Type 4: P4 < P3 < P2; P4 < P3; P3 < P2; P4 < P2; P4 > P3–P2; P4–P3 > P2; P4 > P3 < P2; P4 < P3 > P2; P4 < P3–P2; P4–P3 < P2, where < means reverse peristaltic contraction.

The distribution of the four types of patterns of contraction in normal controls is: 56.4% ± 10.6% (sd) *Type 1* (peristaltic contraction); 11.6% ± 4.7% (sd) *Type 2* simultaneous contraction); 25.2% ± 8.4% (sd) *Type 3* (isolated contraction); and 6.8% ± 3.4% (sd) *Type 4* (mixed-type contraction).

An overall summary of the pressure wave characteristics (amplitude, duration, area under the wave and velocity) during supine periods, including sleeping, eating, drinking, post-prandial and fasting, is presented in Table 5.1. Figures 5.10–5.16 illustrate the value of combined pressure and pH studies in establishing normal physiological variables related to oesophageal motility patterns with and without GOR present. The response to normal events such as belching, coughing and hiccups demonstrates the importance of establishing 'normal' motor events in response to physiological stimuli and recognizing the incidence of such events in a normal, asymptomatic population.

Summary table

Automatic analysis provides a summary table of detailed information on the contraction patterns and the characteristics of the pressure wave identified during the long-term pressure recording. Ambulatory oesophageal pressure data contain a greater variety of motility patterns than do data from static manometry. Isolated and simultaneous contractions occur throughout the day in normal controls. It

Table 5.1 Parameters of the normal characteristics of the pressure wave at the lower body of the oesophagus during supine eating, drinking, post-prandial and fasting periods are represented by mean ± sd.

	Supine	Eating	Drinking	Post-prandial	Fasting
Amplitude (mmHg)	54.6 ± 11.6	67.4 ± 14.8	56.6 ± 10.1	50.0 ± 11.4	49.5 ± 10.8
Duration (sec)	3.3 ± 0.42	3.0 ± 0.62	2.5 ± 0.3	2.6 ± 0.3	2.7 ± 0.4
AUC (mmHg*sec)	114.8 ± 39.7	116.6 ± 40.3	84.9 ± 21.8	81 ± 21.6	82.6 ± 21.5
Velocity (cm/sec)	4.9 ± 1.1	3.3 ± 0.62	4.6 ± 0.9	5.2 ± 1.1	4.8 ± 0.9

AUC, area under curve.
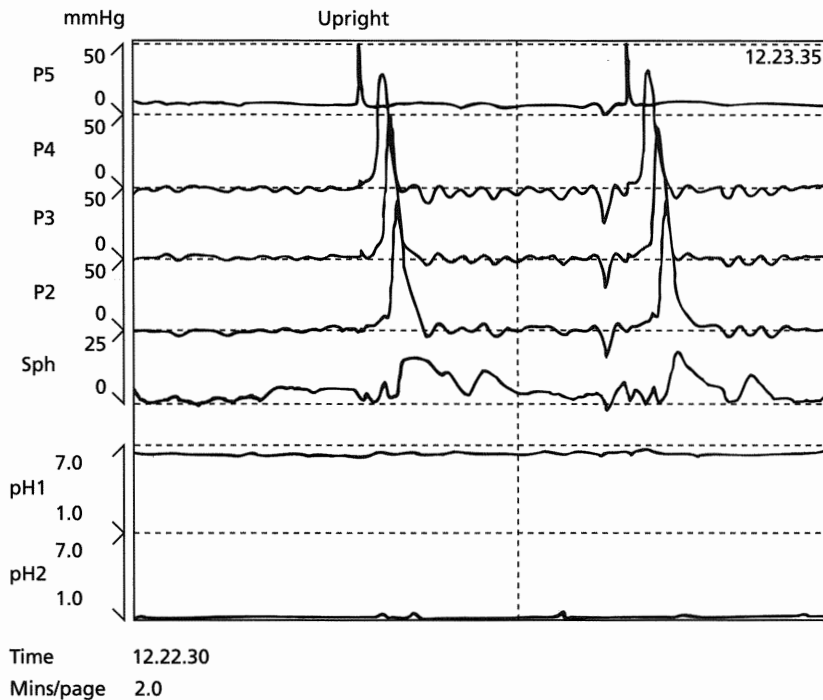
Fig. 5.10 Tracing showing when gastro-oesophageal reflux (GOR) was absent.
A 2-minute sample when no GOR is present during the 24-hour pH and pressure
recording. Pressure sensor P5 is in the pharynx, pressure sensors P4, P3 and P2 are in the
lower body of the oesophagus and the sphinctometer (Sph) is in the LOS. The pH sensor
1 is situated 5 cm above the LOS and pH sensor 2 is 15 cm below the proximal pH sensor.
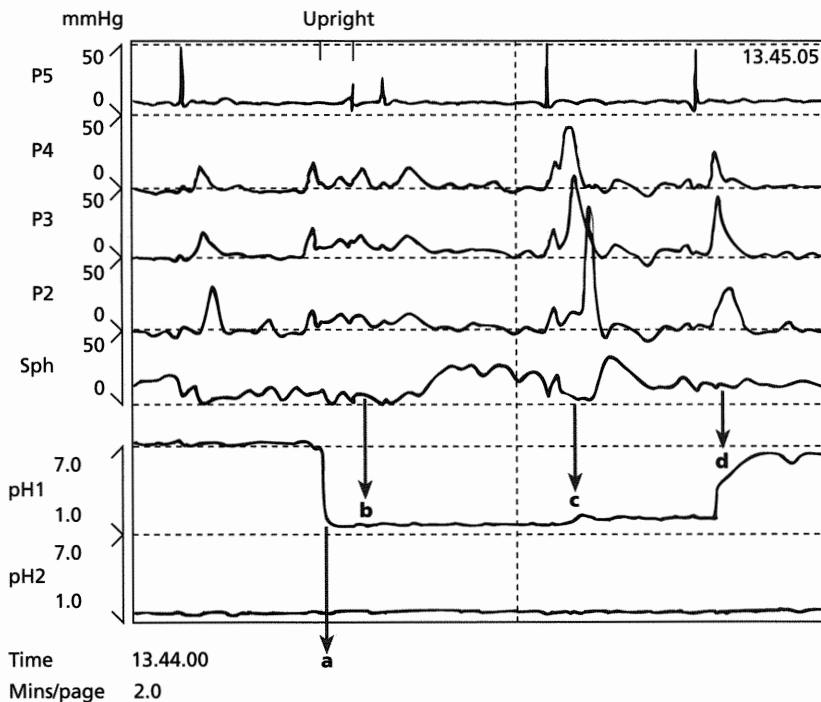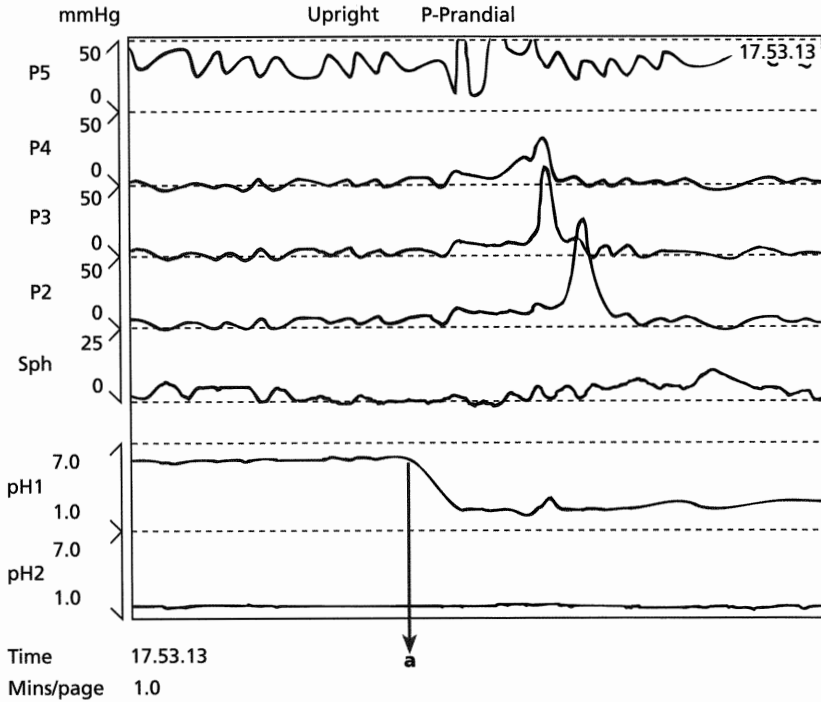
Fig. 5.12 A recording of spontaneous gastro-oesophageal reflux. Acid reflux occurs through the lower oesophageal sphincter with a low basal pressure and not associated with any preceding activity (a).

is essential that motility data are analysed in total, supine and upright periods with the latter analysed separately in meal and inter-prandial periods because the pressure data differs significantly from one period to another. Parameters of the normal wave characteristics from our laboratory are shown in Table 5.1.

Summary

Combined pressure and pH monitoring can be used to establish a causal relationship between patients' symptoms and oesophageal abnormalities, because it is generally agreed that a temporal correlation has to be found. The symptom index [14] has been used in ambulatory pH monitoring to relate symptoms to reflux episodes. If required, the combined pressure and pH study can also be used to calculate the symptom index as has been defined in pH monitoring to identify whether the patient's symptoms are due to gastro-oesophageal acid reflux or oesophageal motility

Fig. 5.11 *Opposite.* Tracing showing when gastro-oesophageal reflux (GOR) was present. A 2-minute sample when GOR is present during a 24-hour pH and pressure recording. A fall in pH is seen in the first minute at pH sensor 1 (a), little change in pH occurs at (b) or at (c) in response to motor activities, but at (d) a marked change in pH takes place.
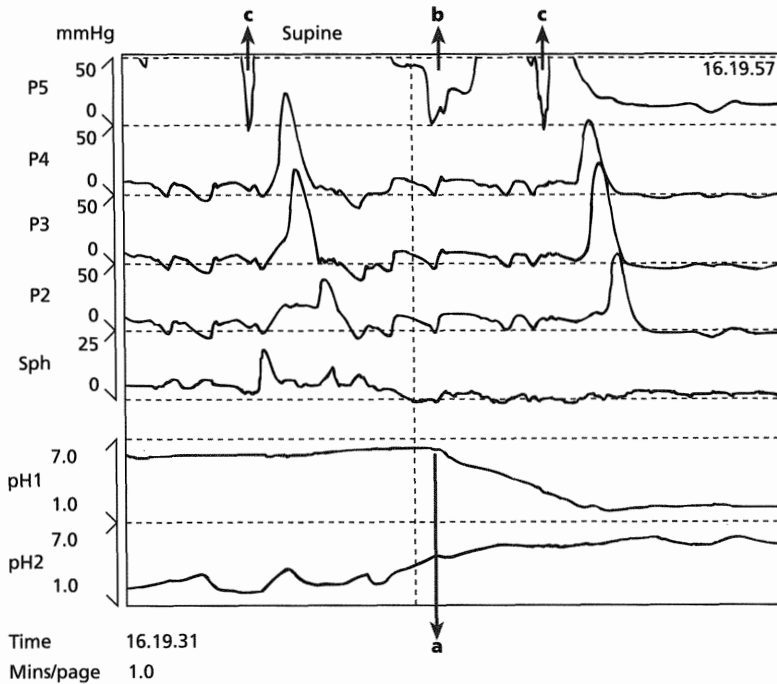
Fig. 5.13 A recording of gastro-oesophageal reflux associated with belching (gas reflux). Gastro-oesophageal reflux associated with belching (a) is recognized by a simultaneous increase in oesophageal pressures in Sph, P2, P3 and P4. The crico-pharyngeus (P5) relaxes to vent the gas as shown in (b). The duration of the crico-pharyngeal relaxation (b) in response to belching is longer in comparison with swallowing.
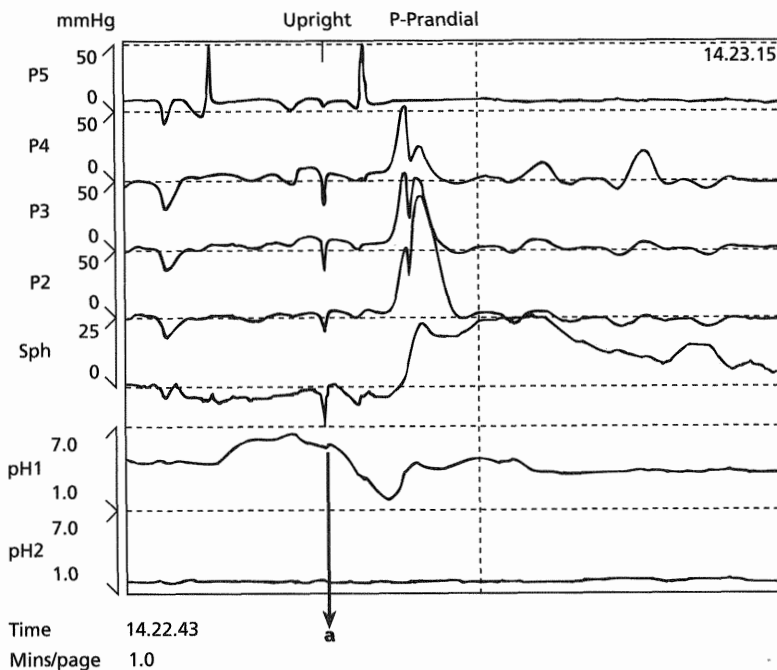
Fig. 5.14 Gastro-oesophageal reflux associated with hiccups as shown at point (a).
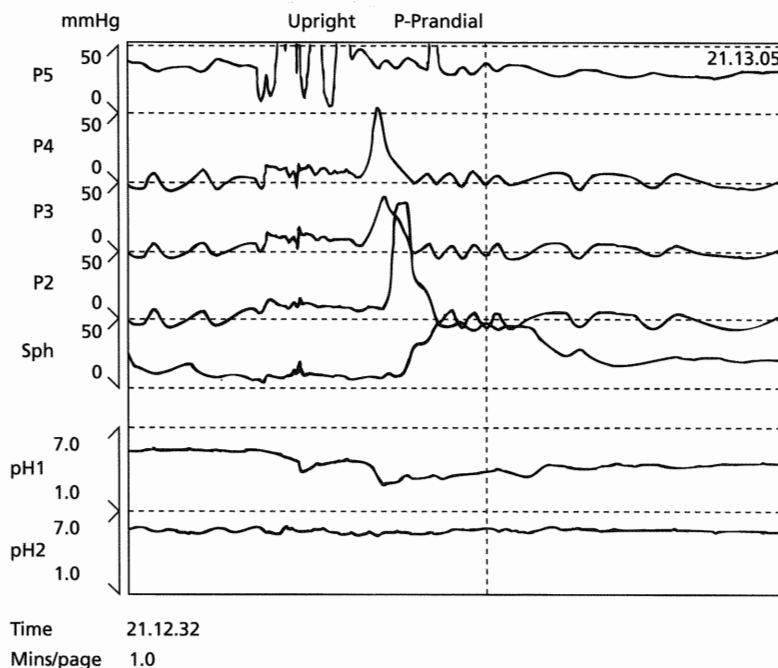
Fig. 5.15 Gastro-oesophageal reflux associated with rapid swallowing. The lower oesophageal sphincter remains relaxed during the rapid swallowing that precipitated gastro-oesophageal reflux. However, the oesophageal body is inhibited from a peristaltic response until the last swallow.
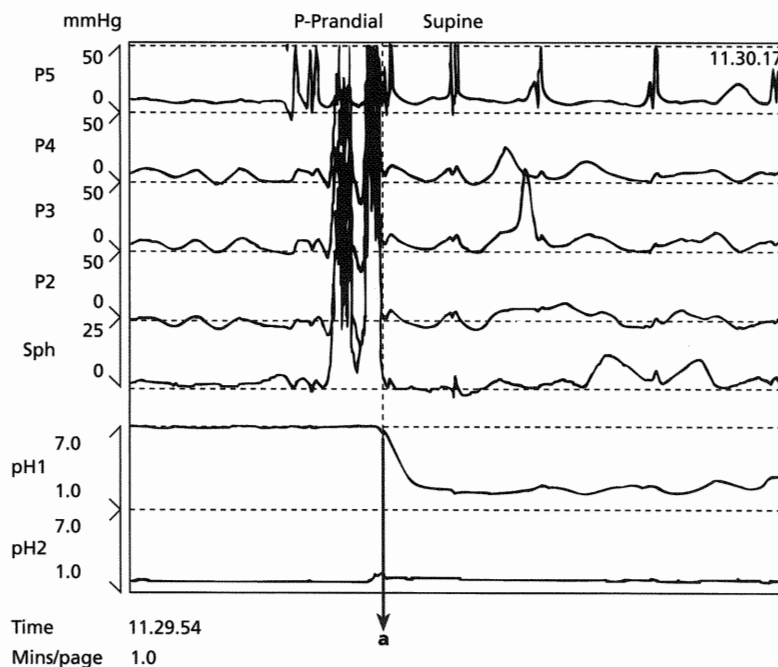
Fig. 5.16 A recording of gastro-oesophageal reflux associated with cough (a).

disorders. Furthermore, it can also be used to study the acid clearance mechanism after a reflux episode [15,16] (Fig. 5.11) and the mechanism of gastro-oesophageal reflux [17,18] (Figs 5.12–5.16).

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5.3

Clinical relevance of investigations
C. Paul Barham and Derek Alderson

Introduction

The last few years have seen rapid advances in computer technology with increasing power and miniaturization. The first recordings of oesophageal pressure events obtained under normal ambulatory conditions used analogue magnetic tape systems but were limited by the large amounts of data from 24 hours of recording. Various strategies were used to overcome these limitations, such as shorter recording periods, fewer measured parameters and recordings from selected time periods (i.e. during symptoms and intermittent baseline recording) [1,2]. Today, fast microprocessors with large amounts of memory allow prolonged digital recordings of several parameters simultaneously, but, as Ward commented in 1986 with reference to 24-hour pH recordings, the technology is available but has it a clinical application [3]?

24-hour pH recordings have become the 'gold standard' in the quantitative and qualitative assessment of gastro-oesophageal reflux disease replacing less objective methods of determining whether reflux is occurring (endoscopy, barium swallows, acid perfusion tests, etc.) [4]. Assessment of oesophageal motor function is also possible by several different tests including video barium swallows and oesophageal scintigraphy, although to date the most widely used method to assess oesophageal motility is the conventional static manometric study. This employs a station pull-through assessment of the position and pressure of the lower oesophageal sphincter (LOS) and an estimation of the motor ability of the oesophageal body by a series of ten swallows of 5 ml of water at 30-second intervals. A huge literature exists using this as the standard method of determining oesophageal motility despite the fact that conclusions are based on ten primary swallows whereas the number during 24-hours of recording is between one and two thousand [5,6]. The standard motility test has also been used to classify several primary oesophageal motor disorders, based mainly on variations in the wave parameters found in normal control subjects [7,8]. Such classifications are also open to question. The standard study takes place in the artificial setting of a physiology laboratory with the patient starved, supine

and immobile. If the investigation is performed for a suspected oesophageal dysmotility as a cause of intermittent symptoms then the chance of typical symptoms occurring during the study may be minimal. Various manoeuvres have been employed to increase the diagnostic yield of the standard motility test such as employing solid swallows [9], using edrophonium [10] or balloon distension [11] to replicate pain and dysmotility but all methods are artificial and may be only poor substitutes for events that occur during normal activities and naturally occurring symptomatic events. The advantage of combined ambulatory pH and motility recording of the oesophagus is the greater chance of demonstrating or excluding the oesophagus as a cause of symptoms provided the patient experiences symptoms during the study [1,2,12].

The clinical uses of combined ambulatory pH and pressure recordings are in the diagnosis of certain primary oesophageal motor abnormalities, the investigation of non-cardiac chest pain and to a lesser degree in the assessment of patients prior to anti-reflux surgery or for precisely establishing the nature of problems following unsuccessful oesophageal surgery.

Oesophageal motor disorders

Four primary oesophageal motor abnormalities are generally recognized on the basis of criteria established from conventional manometry studies: achalasia, diffuse oesophageal spasm, nutcracker oesophagus and non-specific oesophageal motor disorder. The basis for these criteria is the finding that normal control subjects produce nine or ten peristaltic swallows to the ten-wet-swallow test with amplitudes greater than 30 mmHg but less than 180 mmHg [7]. Results outside these criteria are grouped under the following definitions.

In the following examples of these motility disorders, prolonged recordings were made using the catheter assembly depicted in Fig. 5.17.

Achalasia

In achalasia destruction of the ganglion cells in the oesophagus results in an inability to produce coordinated peristaltic contractions down the oesophageal body and a failure of appropriate LOS relaxation. This results in the diagnostic features of established disease of a hypertensive, non-relaxing LOS with simultaneous oesophageal body contractions (Fig. 5.18). Early in the condition, before oesophageal dilatation occurs, the simultaneous contractions can be quite powerful, and, in addition to a partial or totally non-relaxing LOS, may contribute to the dysphagia. In some of these cases a barium study may be normal but, as all attempts to swallow result in simultaneous contraction, the diagnosis of achalasia can readily be made by a conventional manometry study. A few patients persist in getting dysphagia
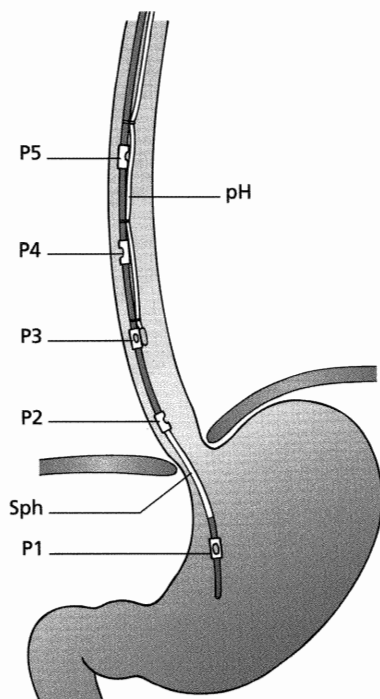
Fig. 5.17 Position of the combined pH/pressure catheter. P1, gastric transducer; Sph, sphinctometer in LOS; P3–P5, oesophageal body pressure transducers. Oesophageal pressure transducers are 5 cm apart. pH probe is positioned 5 cm above the LOS.

after ablation of their LOS (confirmed by radiology and conventional manometry) and in these a 24-hour study may reveal the cause (such as intermittent powerful oesophageal body contractions; Fig. 5.19). In addition, some patients with achalasia do get chest pain and 24-hour manometry may reveal the underlying cause of this pain (Fig. 5.20). 24-hour studies may be necessary in patients who are symptomatic after cardiomyotomy (+/– an anti-reflux procedure) to differentiate between motor and acid reflux problems (Fig. 5.21).

Diffuse oesophageal spasm

Diffuse oesophageal spasm (DOS) is a rare disorder producing intermittent chest pain and dysphagia. It was first described in 1889 [13] and early manometry and radiological studies in the 1950s described its salient features as powerful simultaneous oesophageal body contractions [14–16]. These contractions were usually multi-peaked, of prolonged duration and produced the well-recognized radiological feature usually described as a corkscrew oesophagus (Fig. 5.22). As the contractions were usually simultaneous in nature, the subgroup of patients who demonstrated more than two simultaneous contractions during their conventional manometry study (with the rest being peristaltic) were given the label of DOS [17]. As patients with DOS produce intermittent symptoms, the definition based on a standard
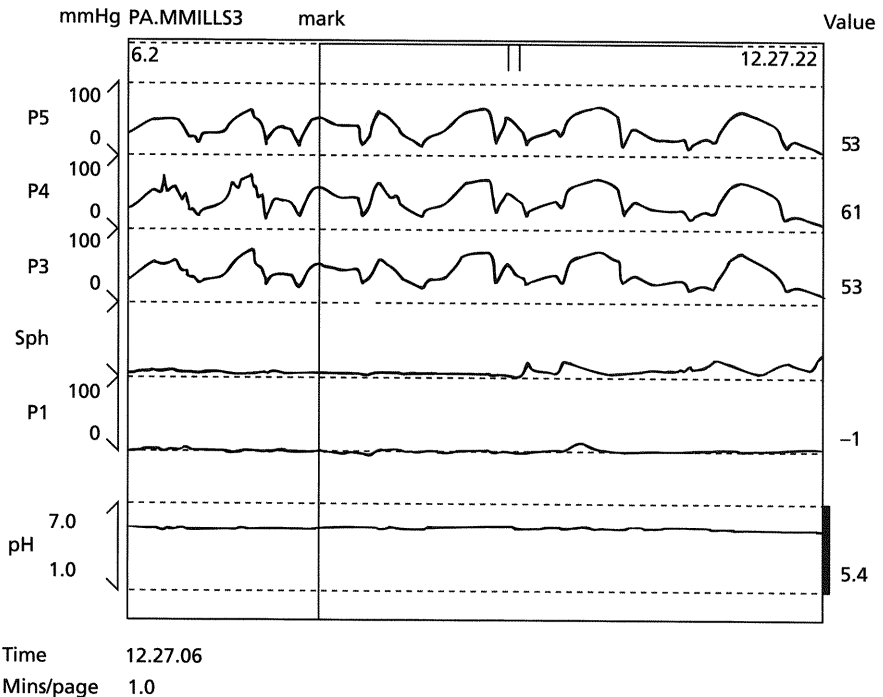
Fig. 5.18 Simultaneous oesophageal body contractions causing dysphagia (note event mark at top of picture) during a meal. The LOS, although not hypertensive, fails to relax during swallows. These appearances are typical of achalasia.

manometry study (often divorced from their symptoms) may be inaccurate. Indeed from our experience of over 600 24-hour pH/manometry studies we found it reasonably common to find patients with three or four simultaneous low amplitude contractions during the conventional study (these patients would have been labelled as having DOS by standard criteria) who failed to have any symptoms or motility abnormality during the 24-hour study. Conversely, patients with symptomatic powerful, prolonged multipeaked simultaneous contractions typical of DOS on the 24-hour study (Fig. 5.23) often have a completely normal conventional manometry study [18]. Another feature of this condition not previously described in detail (because of the limitations of a standard motility assessment) is the nocturnal nature of the contractions. Almost all of our DOS patients had 'spasm' contractions in the early hours of the morning and if severe and prolonged would wake the patient from sleep (Fig. 5.24). It is predominantly this severe primary oesophageal motor abnormality which requires ambulatory 24-hour pH and motility recording for its detection and the conventional manometric definition for its diagnosis should be reconsidered.
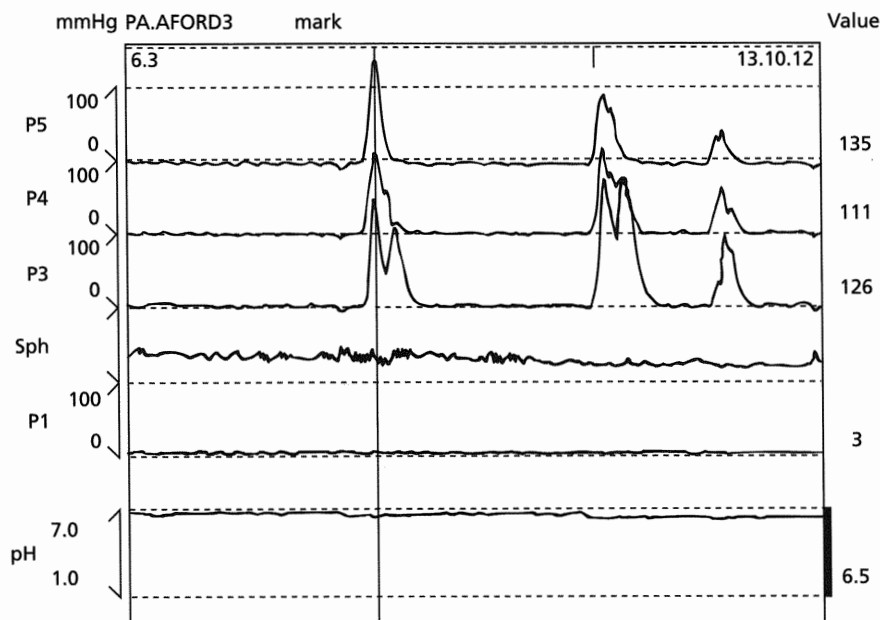
Fig. 5.19 Treated achalasia patient with persistent dysphagia. Negligible LOS pressure (on pull-through assessment) but powerful (>100 mmHg) simultaneous oesophageal body contractions producing dysphagia (note the event mark at the top of the picture).

Other motor abnormalities

Nutcracker or super-squeeze oesophagus, hypertensive LOS, non-specific oesophageal motor disorders and secondary oesophageal abnormalities have all been classified on the basis of variations of the standard motility test again often divorced from the patient's symptoms [8]. It may well be that after more research using prolonged manometry recordings, combined with further studies of oesophageal pathophysiology, some of these definitions will be modified.

Non-cardiac chest pain

Chest pain is an alarming symptom that often results in an emergency hospital admission, especially with increasing public awareness of medical matters. Many of these patients have no objective evidence of cardiac disease and indeed approximately 25% of those undergoing coronary angiography have neither significant cardiac lesions nor coronary artery spasm (during ergonovine provocation) [19,20].
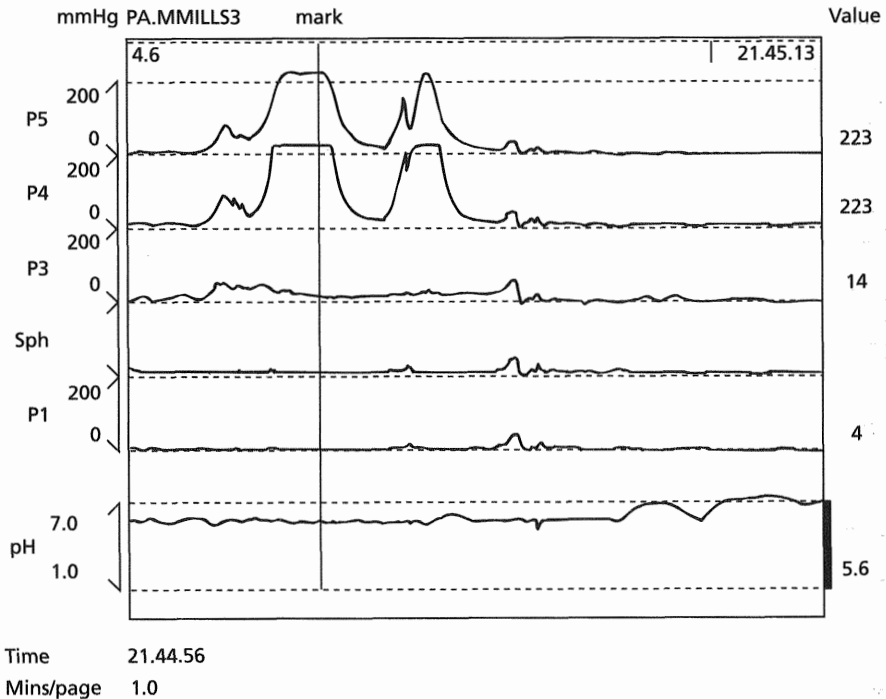
Fig. 5.20 Painful symptomatic contractions (amplitude >200 mmHg) in the proximal oesophagus in a patient with achalasia (note the event mark at the top of the picture).

Of these patients, approximately 50% may have demonstrable oesophageal abnormalities during radiology, endoscopy, conventional manometry or oesophageal provocation [21]. These tests, however, give only indirect evidence of an oesophageal cause of the chest pain as, again, patients are rarely symptomatic during laboratory studies and the oesophagus can only be considered the source of the pain when gastro-oesophageal reflux or severe motor abnormalities are shown to correlate in time with the episodes of chest pain.

The results of 24-hour pH and motility assessments in patients with non-cardiac chest pain have been conflicting [1,2,22,23]. At best, 24-hour recordings have shown the oesophagus to be the likely cause of the chest pain in 35% of the patients, though the diagnostic detection rate is higher than this if the pain is experienced daily or at least several times a week. Gastro-oesophageal reflux is the most likely diagnosis made (25% of studies) but in all papers the majority of typical pain episodes correlated poorly with any objective oesophageal motor abnormality. Our experience confirms these findings. The greatest chance of finding abnormalities occurs when there is a history of frequent pain, nocturnal pain or where dysphagia is a component.

mmHg PA.MPARRY3   mark   Value

| | 10.1 | | | 17.46.56 | |

P5   50
      0   8

P4   50
      0   14

P3   50
      0   25

Sph

P1   50
      0   18

pH   7.0
      1.0   2.2
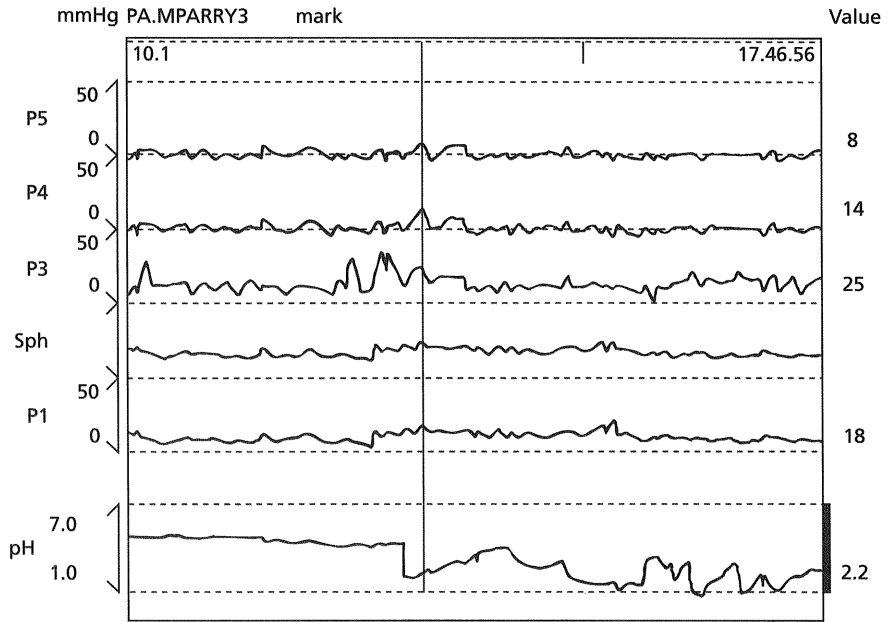
Time   17.46.05
Mins/page   2.0

Fig. 5.21 Acid reflux episode causing symptoms in a patient with treated achalasia (note the event mark).
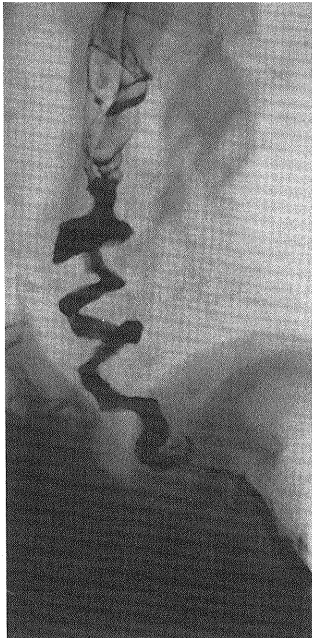
Fig. 5.22 X-ray appearance of corkscrew oesophagus in diffuse oesophageal spasm.
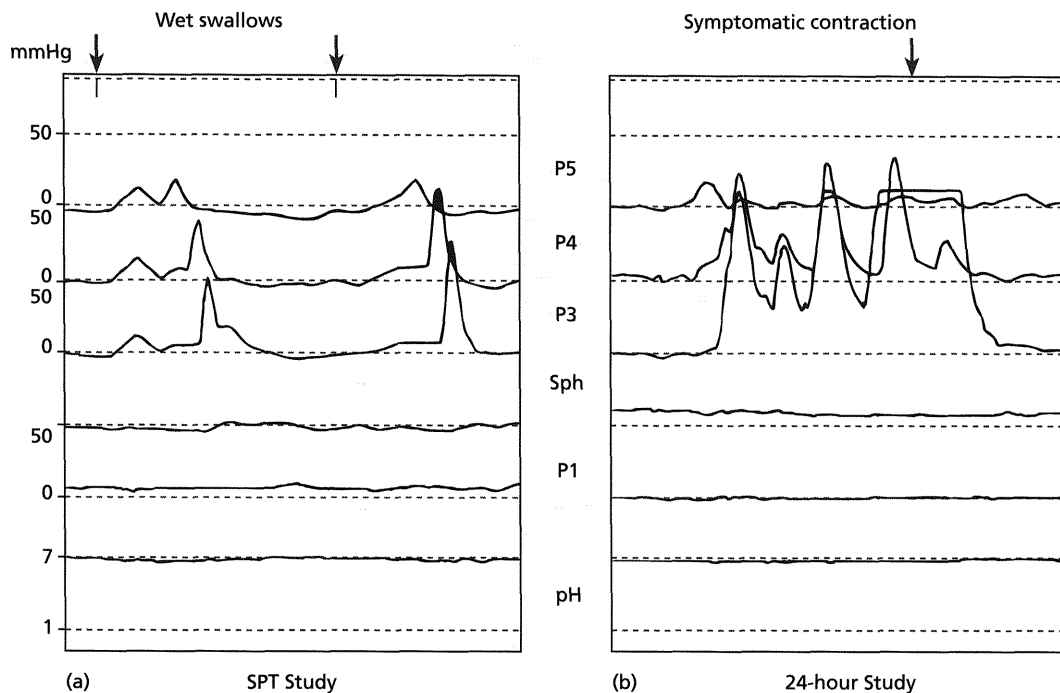
Fig. 5.23 (a) Normal swallows during the conventional laboratory based manometry study. Contraction amplitudes are <100 mmHg. (b) Typical spasm contractions of diffuse oesophageal spasm recorded during the ambulatory study of the same patient. Pressure scale in plate (b) is 0–100 mmHg per channel so peak contraction amplitude of the spasm contraction is >230 mmHg. Time scale is 45 seconds for (a) and (b).

With increasing advances in microprocessor power it is now possible to combine ECG recordings with 24-hour measurements of oesophageal pH and motility and further studies measuring all three modalities at the same time are needed to see if this increases the diagnostic yield in this difficult clinical area.

Gastro-oesophageal reflux disease

In the majority of patients with gastro-oesophageal reflux disease the diagnosis can readily be made by a typical history, the findings of oesophagitis on endoscopy or barium swallow and the improvement of symptoms by acid reducing drugs. In a few patients the diagnosis requires a 24-hour pH study (i.e. typical symptoms but no oesophagitis or only partial response to proton pump inhibitors). Manometry is only required if anti-reflux surgery is being considered, when it is inadvisable to form a distal oesophageal high pressure zone in the presence of a severe primary oesophageal motor disorder or if oesophageal peristalsis is inadequate to propel food through the new 'sphincter'. A standard manometry study demonstrating
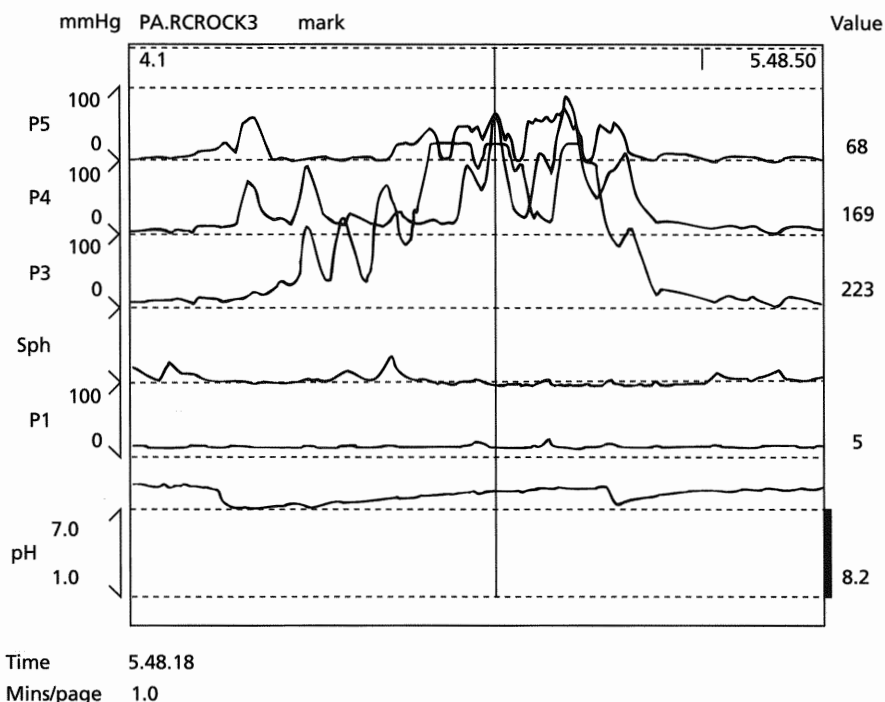
Fig. 5.24 Typical spasm contractions occurring during the night and waking the patient from sleep (note the event mark). Contractions are prolonged (>30 seconds), multipeaked and have excessive amplitudes (>180 mmHg).

good contraction amplitudes usually indicates normal oesophageal motor function. A standard manometry study demonstrating poor oesophageal motility (failed peristalsis or low contraction amplitudes), however, does not always mean that motility is inadequate. It is common for these patients to have normal oesophageal function on a 24-hour study (particularly during eating—personal observation) and it may be for this reason that some researchers have found no relationship between an abnormal standard manometry study and the results of anti-reflux surgery [24]. While the diagnostic accuracy of the conventional manometry study can be improved by the addition of semi-solid or solid food boluses [9,25], a 24-hour study, combining the pH measurement with manometry, provides additional information required to assess suitability for surgery.

Conclusion

Combined ambulatory 24-hour pH and manometry equipment has recently become more widely available for clinical practice but its final role is still under evaluation. It is the method of choice for the diagnosis of diffuse oesophageal spasm and

for the investigation of non-cardiac chest pain which occurs on a daily (or near daily) basis. Its use will allow a better classification of primary oesophageal motor abnormalities. It has a limited but evolving role in the pre- and post-operative assessment of patients with suspected gastro-oesophageal reflux disease and in the assessment of patients with known motor abnormalities who fail to respond to conventional treatments. The addition of ECG may further improve the value of prolonged pH and manometry recording in the oesophagus.

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6 Upper oesophageal sphincter manometry

Janet A. Wilson

Introduction

Technical considerations

Early attempts to define the manometric pattern of the hypopharynx identified specific problems of pressure measurement in this area [1]. In the registration of tonic pressure in the upper oesophageal sphincter (UOS) there is a marked radial asymmetry such that pressures registered in the anteroposterior plane are about three times greater than those registered in the lateral planes. This is in part due to the anterior mass of the larynx which compresses the UOS into an oval slit-like aperture, closed at rest, against the prevertebral fascia. Indeed, the UOS must remain closed at rest otherwise aerophagy would occur with each inspiration, due to the negative intra-thoracic pressure in the tubular oesophagus. The UOS also demonstrates axial asymmetry. In the anterior plane maximum pressures are more proximal than in the posterior plane where the greatest pressures are in the most distal component of the high pressure zone. More recently, several groups have identified radial asymmetry in the hypopharynx [2–4]. The radial asymmetry in the hypopharynx is similar to that in the UOS. Maximum pressures are registered in the posterior plane (Fig. 6.1). The Castell group describes radial asymmetry being present only in the distal 4 cm of the hypopharynx [3]. The results of rapid swallows at the level of maximal posterior pressure response in the distal pharynx showed no evidence of fatigue as a causative factor for this asymmetry. Knowledge of the exact position and orientation of the transducers is necessary to obtain accurate, reproducible pharyngeal manometry.

The well-recognized response of oesophageal musculature to the diameter of the recording catheter is exaggerated in the striated upper third of the oesophagus, in the UOS and in the hypopharynx. Comparison of pressure recordings using a sleeve device with those obtained using a fine bore intraluminal strain gauge assembly showed that the broad Dent sleeve catheter generated much higher recorded pressures than those obtained from the strain gauges [5]. A study of 20 healthy subjects using water-perfused oval catheters of three different external diameters (4.5×3 mm, 8×5 mm and 10×9 mm) showed that pressures obtained were directly proportional to catheter diameter [6]. More reliable pressures appeared
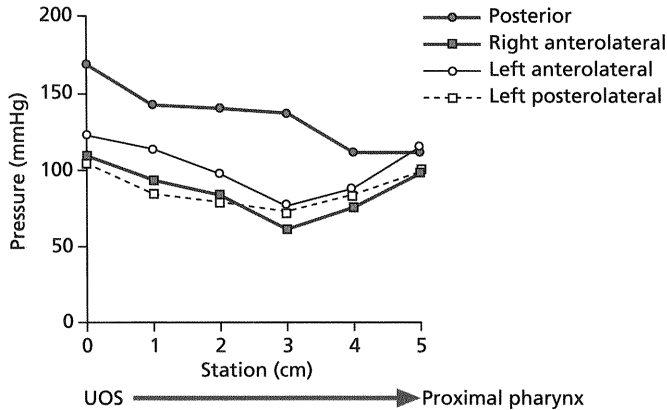
Fig. 6.1 Pharyngeal radial and axial asymmetry (mean of 20 recordings). Note highest pressures in posterior plane. There is an apparent lateral pressure trough about 3 cm above the upper oesophageal sphincter (UOS) which may represent the upper border of the thyropharyngeus. (From reference [4] with permission.)

to be obtained using large and medium diameter catheters, in contrast to the earlier study which showed a greater repeatability using an intraluminal strain gauge assembly [6]. A further biological factor which renders UOS manometry problematic is the rapid sequence of events in the pharyngo-oesophageal segment during deglutition. Dodds *et al.* [1] demonstrated that accurate quantification of pharyngeal motor activity was not possible using a water-filled catheter system, even with high infusion rates. Furthermore, the sensitivity of the hypopharynx to perfused water makes high infusion rates impractical. A subsequent study by the same group indicated that a frequency response flat to 5 Hz was adequate to record accurately 98% of oesophageal peristaltic waves, but that a recording accuracy up to 48 Hz was required for high fidelity recording in the pharynx [7]. These findings clearly confirmed the need for strain gauge probes to register pharyngeal pressure transients. At all sites except the distal pharynx the rates of pressure wave rise somewhat greater than those of wave relaxation. The peristaltic pharyngeal waves exhibited a fundamental frequency of 1–6 Hz and up to 18 harmonics were required for accurate recording of wave amplitude and form.

A final important technical problem to be considered when conducting UOS manometry is that of sphincter on catheter movement [8]. A single sensor placed within the UOS high pressure zone at rest registers pressures outside the sphincter during the major part of deglutition. Isberg's study suggested that at least three sensors placed at different levels, about 10 mm apart, were required if consistent pressure recording within the high pressure zone was to be achieved. It should be remembered, however, that sphincter elevation on swallowing is in fact an act of the protective part of the swallow reflex, which helps minimize laryngeal
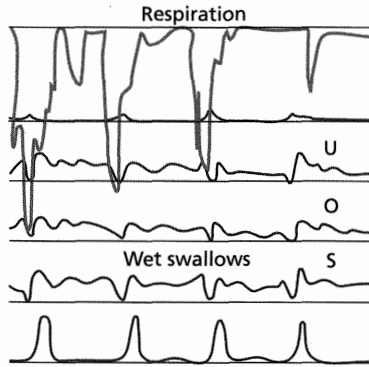
Fig. 6.2 Series of water swallows recorded into pharyngo-oesophageal segment. The subject was very anxious—note the wild pre-swallow inspiratory excursions in the respiratory trace.

penetration of ingested food stuffs. Similarly the inspiratory tonic UOS pressure augmentation provides additional protection against oesophageal air entry during respiration. What appears to the manometric investigator as the troublesome artefact of sphincter elevation is a critical part of the competent swallow which the reader can confirm by attempting to swallow while fixing the larynx and hyoid manually (Fig. 6.2).

Biological variables

Notable differences occur in pharyngo-oesophageal manometry with increasing age. Mean maximum tonic UOS pressure shows a significant decline over the age of 60 years. Conversely several groups confirm the presence of increased pharyngeal contraction amplitudes due in both water and bread swallows with increasing age [9]. The Castell group have postulated that with increasing age the UOS becomes less compliant and therefore a higher hypopharyngeal pressure is required in order to propel the bolus through the less distensible sphincter. There are also subtle differences in motility between the two sexes as one might expect given the importance of anatomical factors in some of the passive pressures in the area and given the marked differences in laryngeal anatomy between males and females which can be readily confirmed by inspecting the cervical contours of men and women, confirming the much more marked thyroid prominence in male subjects. Male subjects show greater UOS axial asymmetry than females, perhaps for this reason.

The biological factors which result in variation in UOS pressure include sleep [10] and stress [11]. Upper oesophageal acid exposure consistently has failed to show a resulting augmentation of UOS tonic pressure. During sleep there is a marked fall in UOS barrier pressure which may become incompetent in subjects with oesophago-pharyngeal reflux and cervical symptoms. Stress, for example, experimentally induced by a dichotic listening test induces an augmentation of

UOS pressure which appears to be of a similar intensity in patients with globus sensation (a feeling of something in the throat) and healthy volunteers [11]. In short, therefore, it is not surprising that some of the measured parameters of UOS manometry show marked intra-subject variation. The most stable measurement on repeat testing at an interval of a few weeks appears to be tonic UOS pressure [5].

It should be borne in mind, however, that while much is made of the so-called 'swallow reflex', the swallow phenomenon is only partly reflex. We are all aware that we have some volitional control over the moment at which we choose to swallow a bolus and conversely we can retain it in the mouth for considerable periods if we so wish. The components of the reflex are modified, not only by age, sex and bolus variables, but the actual muscle functions appear to be under some element of volitional control. Indeed voice therapists exploit this by prolonging the period of laryngeal elevation in patients at risk of aspiration. Pouderoux and Kahrilas [12] have also indicated how different individual components of pharyngeal function may be modified volitionally. Studies to assess the effects of various manoeuvres including change in body posture and the administration of bethanechol and edrophonium have failed to show any significant impact on UOS relaxation or swallow co-ordination. In contrast, the UOS resting pattern shows large intra-subject variations.

Equipment

Recording catheter

The conventional perfused Arndorfer-type catheter is adequate for the registration of tonic UOS pressure, although the site of perfusion is likely to provoke excessive swallowing or throat clearing. Also the device has no compensation for sphincter on catheter movement. The Dent sleeve catheter (Fig. 6.3) has a 6 cm sleeve sensor. The sleeve is positioned so that the sphincter overlies the distal portion in the resting phase; upwards exertion of the UOS during a swallow allows the sphincter to remain in contact with the upper portion of the sleeve. The sphincter irritation is minimized as the perfusate is vented distally. The rate of pressure rise of ($\delta p/\delta t$) of the side holes and the sleeve catheter is 400 mmHg/sec, but the maximum rate of rise of the sleeve sensor itself is only 35 mmHg/sec compared with a maximum fall off in excess of 200 mmHg/0.1 sec. This slow rate of rise following dry swallows can make baseline UOS pressure recording difficult and may even require the use of an oral suction catheter to prevent saliva swallows during the test. The sleeve has theoretical advantages for prolonged registration of UOS pressure where catheter fixation may be a problem. Its broad diameter tends to provoke artefactual pressure increases within the sphincter, however, and most workers now favour some form of strain gauge assembly.
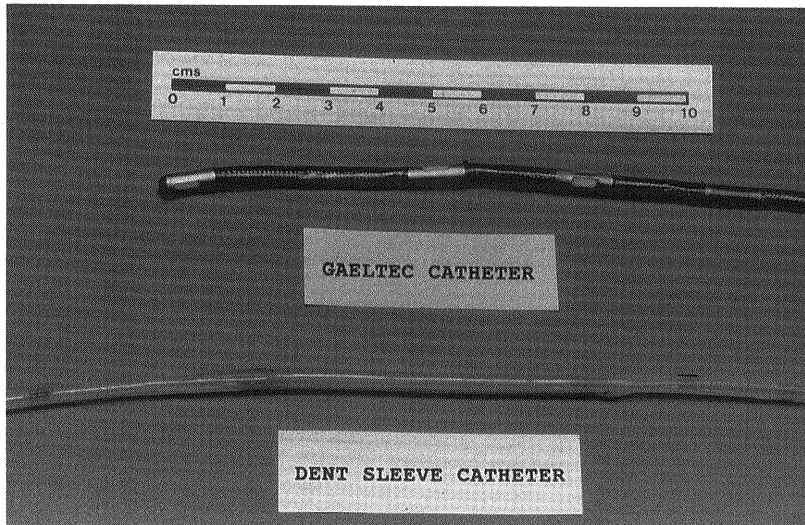
Fig. 6.3 Dent sleeve catheter and a six sensor strain gauge assembly (Gaeltec). The sleeve is 6 cm long, D-shaped in cross-section and the catheter is 7.2×3.2 mm in diameter. The strain gauge assembly has six sensors, three at one level at 120°. The sensors are all at 60° to each other to allow representative radial sampling. The assembly diameter is just 2.8 mm.

In order to provide adequate radial sampling of the pharyngo-oesophageal segment the assembly must comprise either a number of radially orientated sensors, positioned so as to sample from multiple points, or a circumferentially sensitive transducer. Comparison of a multiple strain gauge assembly with a sleeve sensor showed that UOS tonic pressures were lower and more reproducible when obtained with the strain gauge assembly [5]. A comparison of a radially sensitive with a circumferentially sensitive microtransducer [13] used assemblies of 5.5 and 6 mm diameter respectively. In only three of 52 manometric parameters measured were differences between mean values for the two probes statistically significant. Intra-subject variability was substantial using both methods, but significantly less with the circumferentially sensitive probe (coefficient of variation 37%) than with the radially sensitive three sensor assembly (coefficient of variation 53%).

Recorder

Stationary manometry

The majority of manometry laboratories continue to use chart recorders for manometric studies carried out throughout the upper gastro-intestinal tract. Several groups have attempted to digitize the output of manometric chart plotters and to

analyse the resultant data by computer. This type of analysis is particularly suited to the study of pharyngo-oesophageal coordination in view of the many parameters which may be studied for each swallow complex. A further logical development is to perform the original manometric recording on a digitized computer system rather than on an analogue plotter (Fig. 6.4).

A computer based system offers several advantages over a conventional chart recorder or polygraph. Firstly, the accuracy of the recording is more certain as the output voltages from the transducers are read directly and compared with pre-calibrated reference values. Secondly, measurements of manometric parameters may be made by using the same algorithms each time, thus eliminating observer bias. Thirdly, the computer allows measurement of parameters which are not easily determined manually from a conventional chart recording. Finally, a considerable time saving is apparent for both routine and research analysis [14]. A study of simultaneous pressure registration by a four channel analogue chart recorder and a solid state recorder indicated good agreement between the two systems during preliminary bench tests [15]. A simultaneous recording of 13 parameters of upper and lower oesophageal motility was then performed on 34 patients undergoing manometric investigation. The percentage standard deviation of differences for all pressures was an acceptable 2–10%. Greater agreement was obtained with peak than tonic pressures, which probably reflects observer error in the manual calculation of tonic pressure throughout a fluctuating respiratory cycle from an
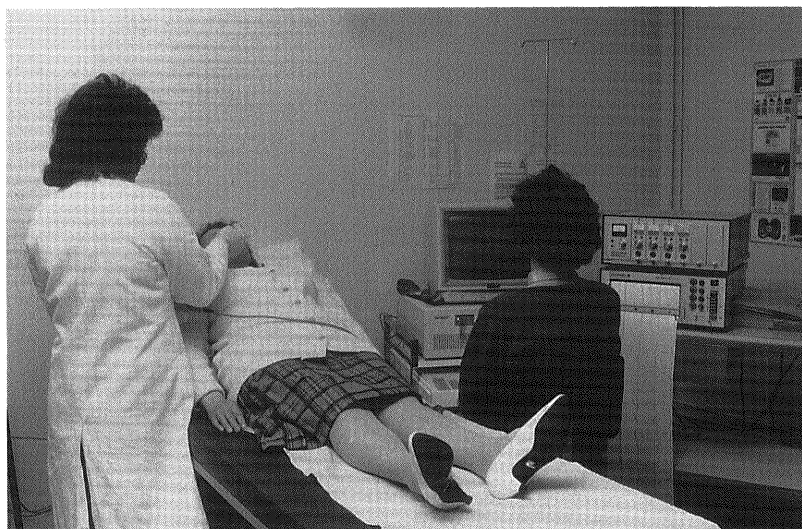
Fig. 6.4 Validation of a computerized waveform analysis system (Gaeltec Ltd) by simultaneous recording on a conventional chart recorder through an A/D converter in the computer mother board.

analogue trace. The increasing availability of very powerful PCs allows very rapid sample speeds and a high degree of temporal resolution for the most recently developed manometric systems. Unfortunately, few systems are as yet available based on Windows software, and manufacturers seem less interested in the development of systems which will allow patient data collation automatically within a database, than in furthering more technical aspects of development. None the less, data transfer to a database held on the same hard disk as the recording software is not an unduly onerous task.

A laboratory equipped with a solid state recording system and a strain gauge transducer assembly is undoubtedly easier to run on a day-to-day basis, although it must be borne in mind that the strain gauge assemblies are both expensive and more fragile than their historical perfused counterparts.

Ambulatory recorders

There have been several preliminary attempts to obtain prolonged ambulatory outpatient manometric data from the pharyngo-oesophageal segment [16]. It appears that during sleep there are two phases of upper sphincter activity. One is characterized by moderate levels of tonic pressure interspersed with dry swallow activity. At other times the resting pressure drifts to very low barrier pressure levels and dry swallow activity is absent. No widely available system for the automated analysis of ambulatory pressures is however yet available and this limits the applicability of the methodology for obvious reasons.

Procedures

Rapid pull-through

The measurement of tonic UOS pressure is usually expressed relative to intra-pharyngeal zero baseline, which more or less equates to atmospheric pressure. Typically the analysis of pharyngo-oesophageal motility takes place after a lower oesophageal sphincter and tubular oesophageal peristaltic study. The strain gauge assembly requires therefore to be withdrawn into the pharynx so that the sensors may be re-zeroed relative to intra-pharyngeal pressure. This being the case it makes sense to carry out a preliminary rapid pull-through of the UOS prior to zeroing the sensors. This gives a rough indication of the anatomical location of the sphincter and allows the gain settings on the chart or computer recorder to be set to the appropriate band width. If rapid pull-through techniques are carried out (1 cm/sec) with reference to the appropriate zero in a more formal manner then the results are very comparable for those obtained from a station pull-through (Fig. 6.5). There is therefore no need to carry out both a rapid and a station pull-
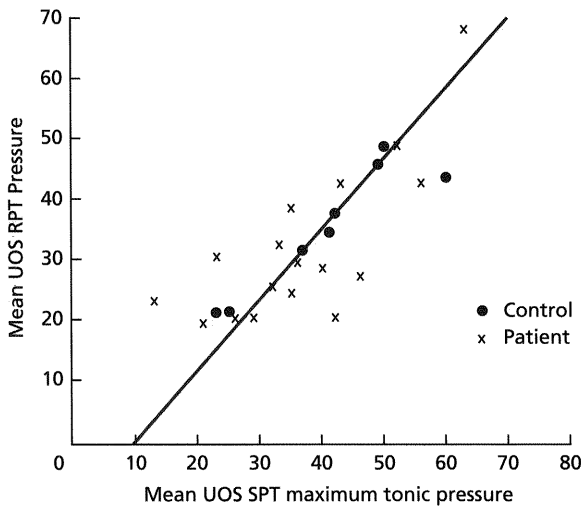
Fig. 6.5 Comparison of mean maximum tonic upper oesophageal sphincter (UOS) pressure recorded during a rapid pull-through (1 cm/sec) and a station pull-through (0.5 cm increments with 20 seconds at each station in eight volunteers and 17 patients). There is a good correlation of the two measures.

through. As most workers wish to carry out a series of swallows at some location within the sphincter, a station pull-through is usually required and there is little additional benefit to carrying out any rapid pull-through other than the preliminary 'scout' view of the UOS for zeroing the sensors.

Station pull-through

Because of the sensitivity of the striated muscle in the region to catheter diameter and catheter movement and also because the pressure can vary quite markedly from 1 cm interval to the next, station pull-through should be at 0.5 cm increments with at least 20 seconds spent at each station to allow acclimatization of the sphincter to the presence of the catheter. For each sensor tonic pressure will be registered at different levels. The maximum of these tonic pressures can be averaged from several radially disposed sensors to give a mean maximum tonic UOS pressure (Fig. 6.6).

Deglutition dynamics

A minimum of three sensors is required to measure dynamic motility: one in the hypopharynx, one in the UOS and one in the upper oesophagus. If only one sensor is to be sited in the UOS, it should be circumferentially sensitive for the reasons cited above. During the station pull-through therefore the anatomic level at which the sensors are placed within the UOS register maximum tonic pressure is noted. When the station pull-through is complete the catheter is repassed so the relevant sensor once again registers maximum tonic UOS pressure. If possible the pharyngeal
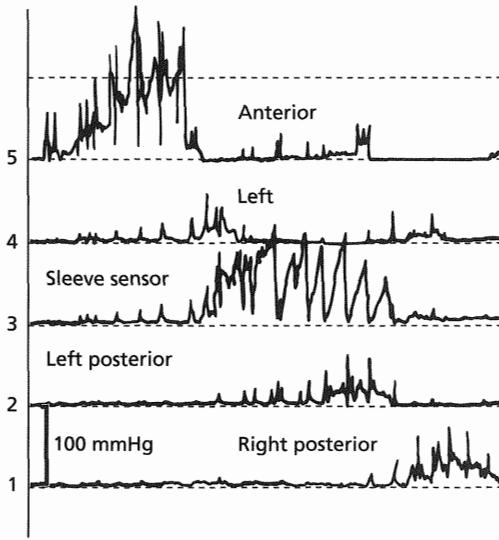
Fig. 6.6 UOS station pull-through recorded from a sleeve sensor and the perfused side holes on the catheter. The sleeve is orientated posteriorly. Note the registration of much greater pressure in the anterior channel than in any of the lateral or posterolateral channels. Note also the slow post-relaxation rise time in the sleeve sensor compared with the perfused side holes. The trace also gives an indication of the UOS axial asymmetry, maximum pressure being registered in the proximal part of the UOS in the posterior plane.

recording sensor should be orientated in the posterior plane in order to register maximum pharyngeal contraction amplitude. It should be borne in mind that there is a pressure trough some 3–5 cm above the UOS.

Computer programs have been devised to assess a great many intervals between different components of the swallow complex. In the absence of a very large number of swallows for analysis, however, many temporal parameters show a great deal of inter-swallow variation and outside the research context it is probably adequate to measure the principal pressure phenomenon as shown in Fig. 6.7.

As with any investigation of pharyngo-oesophageal motility it should be remembered that the bolus characteristics are critical in generating recorded pressure. It is standard to administer 5 ml bolus volumes. This is probably based on studies in the tubular oesophagus. It is clear, however, that the normal bolus volume ingested is at least 20 ml [17]. Upper oesophageal sphincter opening both in terms of area and duration of relaxation is proportional to ingested bolus volume. The literature is inconsistent on the reporting of the effect of bolus consistency on pressure parameters with some workers finding an increase in contraction amplitude in response to a bolus of increased consistency [5] while others find no influence of bolus consistency on recorded pressure measurement [2]. There is no evidence that the inter-swallow interval in the UOS is important in pressure measurement. The events of swallowing are complete within 1 second. Once the events of a single swallow complex have been recorded then it is probably possible to proceed immediately with a second swallow. Convention usually dictates a 20 second interval approximately, however, between swallows as in the tubular oesophagus.
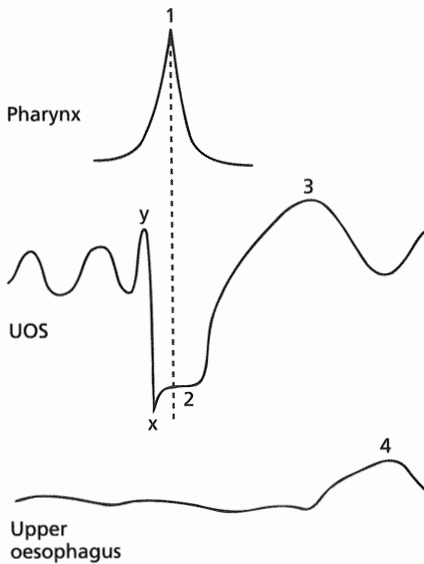
Fig. 6.7 Schematic representation of pharyngo-oesophageal deglutition dynamics. The principal pressure values analysed are: **1** Peak pharyngeal contraction; **2** Nadir of UOS relaxation; **3** UOS after swallow contraction; **4** Upper oesophageal contraction (optional). Note the very transient UOS relaxation point (x). This is taken by some to represent a hypopharyngeal suction pump [27]. The negative pressure is abolished as soon as a bolus flows through the UOS, where the sustained pressure trough is usually about 5 mm relative to intra-pharyngeal zero baseline. The brief, low amplitude pre-swallow UOS pressure augmentation is due to transmission of the tongue bolus—driving force. The peak pharyngeal pressure should occur during UOS relaxation.

Analysis

As in the LOS there is a huge range of possible parameters to describe tonic UOS pressure. As indicated above, however, the optimum is probably an average of the maximum tonic pressure during station pull-through in a number of radially disposed sensors (or alternatively the tonic pressure maximum in a circumferentially sensitive transducers). Averaging the pressure throughout the sphincter length or generating some form of pressure/length index or vector volume analysis seems to have little to offer over and above simple computation of tonic maxima. Pressures obtained during rapid pull-through are comparable (Fig. 6.5).

By assessing swallow dynamics (Fig. 6.8) it should be remembered that some of the measures, particularly temporal parameters, have poor coefficients of variation and it is probably essential to analyse a very large number of swallows to obtain a consistent reading for an individual. As a result the range of data in a group of normal subjects of patients with a particular diagnosis is inevitably wide and it can
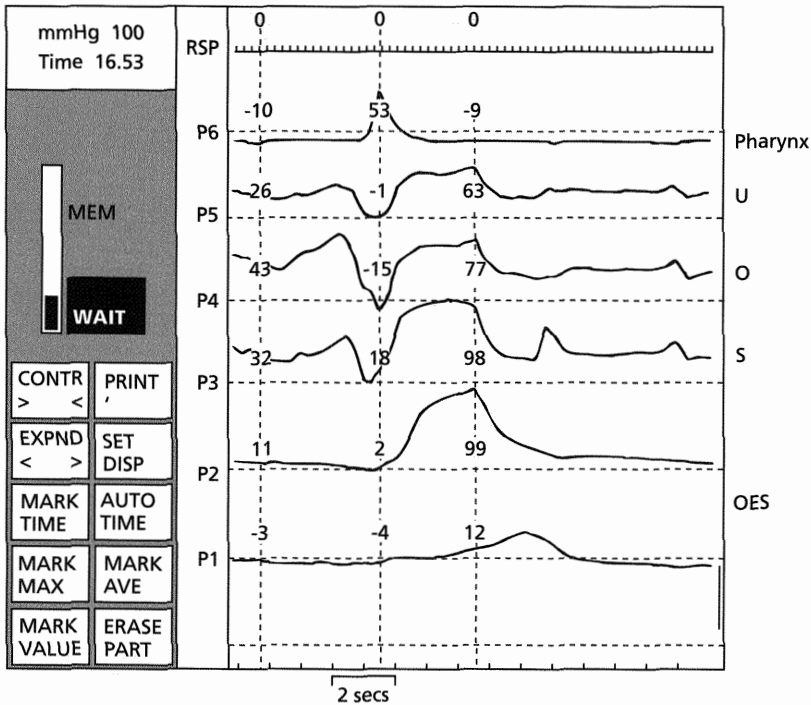
Fig. 6.8 Sample of annotated water swallow computer trace. The duration of contractions and of UOS relaxation may also be calculated.

be quite difficult to define abnormality. Similarly, because of the huge number of recording and biological variables it is very important that each laboratory obtain its own bank of control data, age and sex matched as indicated in the patient groups for study. Published data are widely varying according to the recording system used and are not applicable to other laboratory set-ups.

The account of multiple swallows presents a particular problem (Fig. 6.9a,b). Most normal subjects can perform single water swallows without much difficulty. Semi-solids in particular, however, tend to generate at least a double swallow complex if not triple or quadruple swallows (Fig. 6.9b). Such multiple complexes

Fig. 6.9 *Opposite*. Only a very small minority of healthy volunteers fail to swallow water bolus as a single event. Conversely, many normal subjects swallow equivalent volumes of semi-solid as a double swallow (a) or by a series of multiple swallows (b). Such double or multiple swallow complexes cannot be analysed like single events. The early upper oesophageal sphincter (UOS) relaxations are foreshortened, and the final UOS relaxation after contraction of the quadruple swallow is of increased amplitude. There is a peristaltic response in the striated portion of the oesophagus following two of the four swallows.
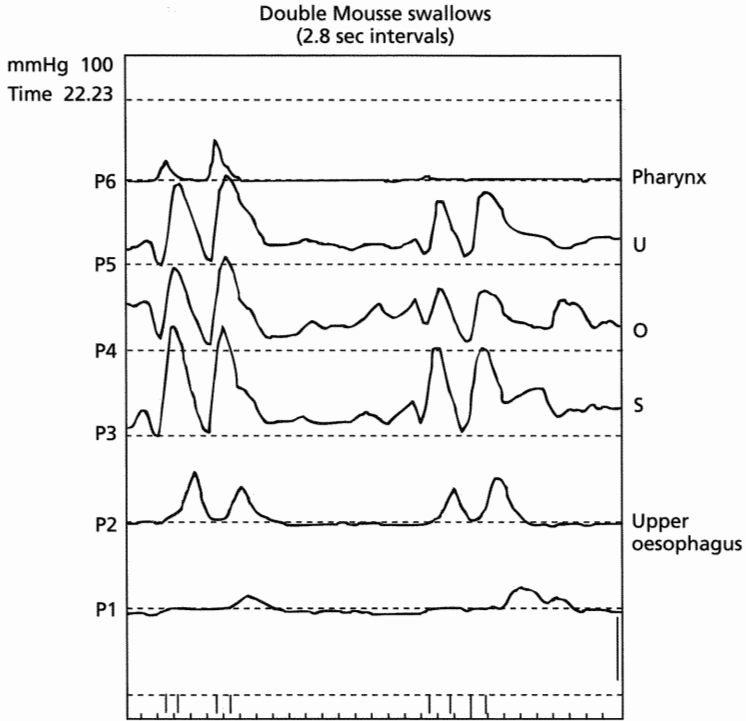
(a)
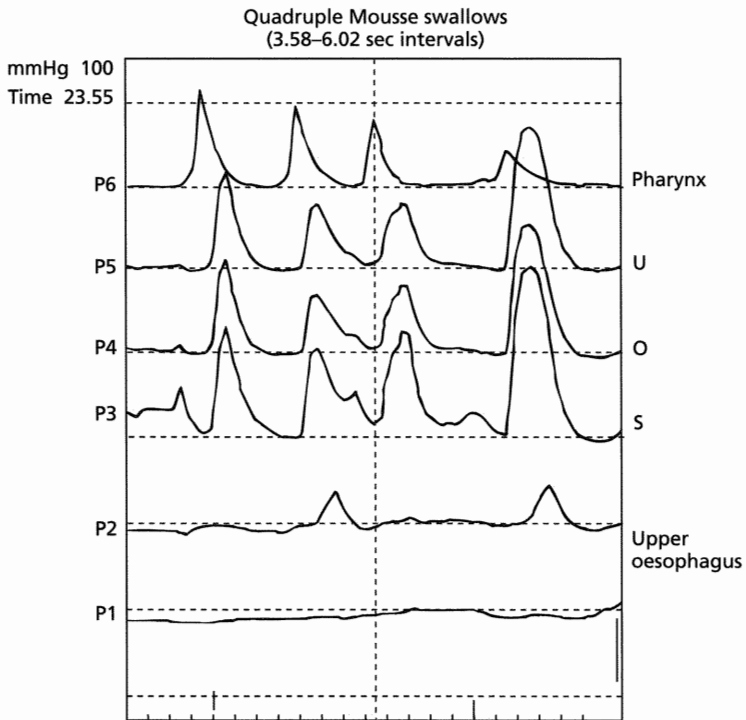
(b)

cannot be analysed as if they were a series of single swallows because the initial events are curtailed as the second and third swallows follow on. None the less, it is one of the key advantages of using manometry in this area that at least a multiple swallow complex can be recognized as such. Conversely, using radiographic analysis the artefacts produced by multiple swallows may not be apparent for what they are, as there is very little attention paid to the timing and number of the patient's swallow movements in many instances.

Computerized analysis [2] has clear advantages in generating more consistent data by allowing analysis of multiple swallow complexes. As with manofluro-graphic studies, detailed swallow analysis shows progressive increase in all time intervals with increasing bolus size from 5 to 20 ml.

Clinical relevance

Crico-pharyngeal impression

Patients complaining of cervical dysphagia are frequently referred for upper oesophageal manometry because of the radiographic detection of a crico-pharyngeal impression (Fig. 6.10a,b). It now appears that these impressions may represent a restrictive defect of UOS opening rather than a true achalasia or UOS spasm [18]. Our own experience is that about one-third of patients with crico-pharyngeal impressions have true hypertonicity as evidenced by two or more parameters of tonic UOS pressure when compared with normal controls [19]. The distinction between a restrictive defect of opening and muscle hypertonicity is probably an important one as the former may respond to balloon dilatation whereas in true hypertonicity crico-pharyngeal myotomy seems a more logical option.

Pharyngeal pouch

Manometric analyses of pharyngeal (Zenker's) diverticula (Fig. 6.11) are frequently hampered by the fact that the recording catheter has a tendency to curl in the pouch rather than to progress down the oesophageal lumen. It is not surprising therefore that there have been very varied reports of manometric findings in pharyngeal diverticula. It must always be remembered that much of the dysphagia and perhaps also of the manometric abnormality may be due to the external compression of the oesophagus by the pouch, i.e. a secondary mechanical problem rather than a primary muscular disorder. There is also little in the demography of the condition (predominance in elderly males) to suggest a primary motor disorder. Rather it seems that anatomical factors may be more important [20]. Manometry probably has little part to play in the assessment of a pharyngeal diverticulum as the treatment is surgical for all but the smaller asymptomatic stages and surgical
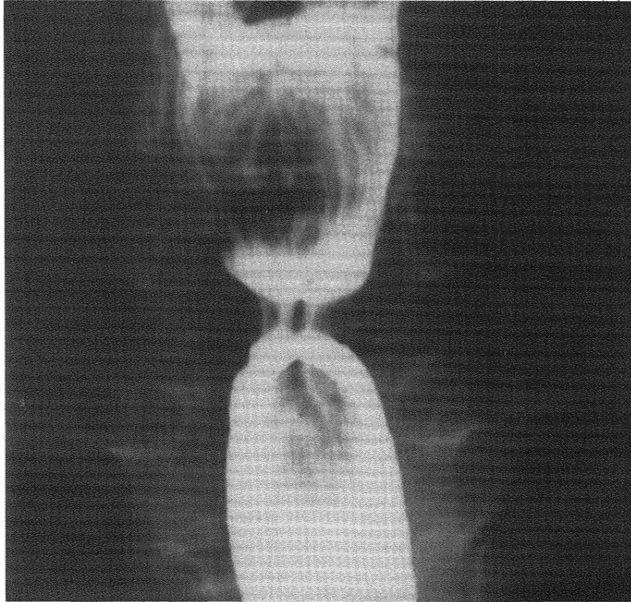
(a)
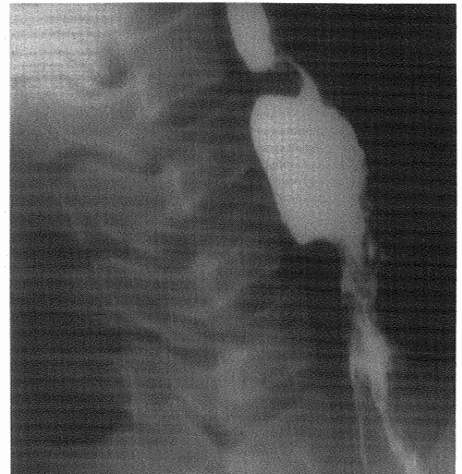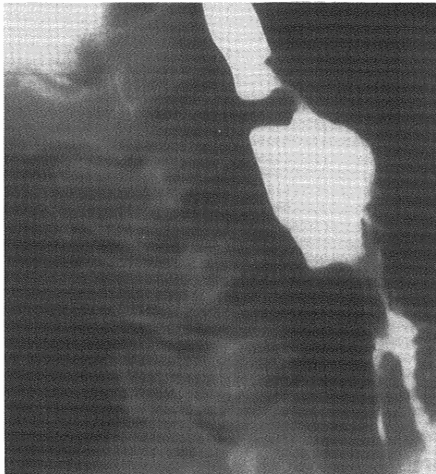
(b)

Fig. 6.10 (a) Anteroposterior and (b) lateral views of a persistent crico-pharyngeal impression on barium swallow examination.

treatment usually entails division of the UOS, whether by external crico-pharyngeal myotomy, or by endoscopic electrocoagulation, stapling or by CO_2 laser ablation.

Globus sensation

The earliest reported manometric data in patients with a feeling of something stuck
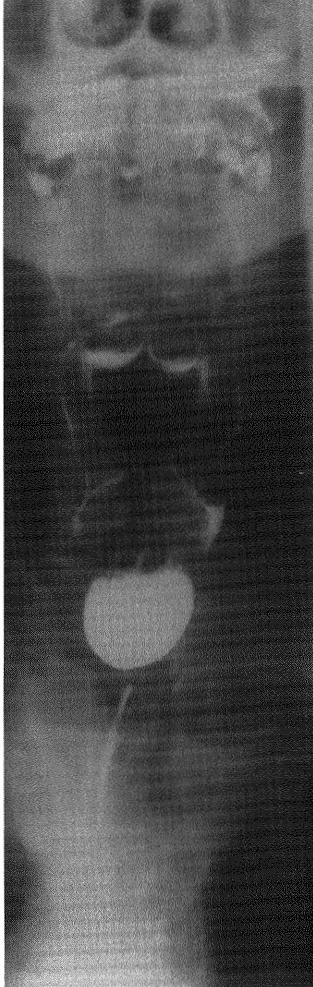
Fig. 6.11 Pharyngeal (Zenker's) diverticulum. On anteroposterior projection the moderate-sized sac is seen as a post-swallow residue. Much of the associated dysphagia is due to mechnical compression by the pouch.

in their throat (globus sensation) suggested marked hypertonicity of the UOS, indeed with no overlap between globus patients and the control group [21]. Subsequent studies have failed to confirm such UOS hypertonicity [22,23]. We have, however, shown certain abnormalities of the swallow complex which are apparent when a large number of globus patients is compared with an equally large number of control subjects (Fig. 6.12). It appears that globus patients generate hypertonic brisk swallows with pharyngeal and upper oesophageal after-contraction amplitudes which are greater than in control subjects. These findings are present in globus patients of both sexes and are an exaggeration of the normally higher after-contraction pressure observed in the sphincter in female patients [22]. It seems likely that this observation represents a secondary response to the sensation that there is something stuck in the throat, i.e. a 'big swallow' is generated to overcome the perceived obstruction.
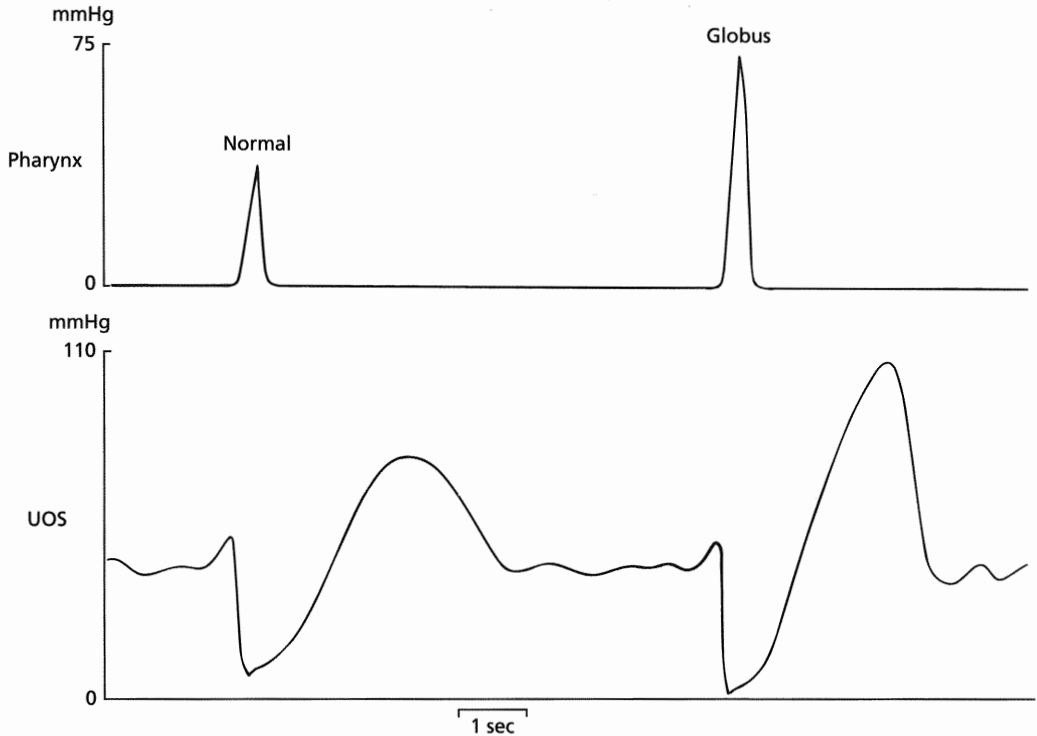
Fig. 6.12 Schematic representation of pharyngo-oesophageal motility in healthy volunteers and patients with a feeling of something stuck in the throat (globus sensation). The globus patients have higher pharyngeal and upper oesophageal sphincter (UOS) after-swallow contraction amplitudes. The swallow complex is also of shorter duration in globus pharyngis.

Neurological dysphagia

Patients suffering from neurological disorders who have high dysphagia usually suffer from a constellation of different defects including problems with oral control and tongue propulsion. The value of pharyngo-oesophageal manometry is thus limited. Also, because of the heterogeneity of most neurological disorders meaning-ful cohort comparison with control groups is difficult. Even the commonest cause of neurological dysphagia—cerebrovascular accident—is not a homogeneous condition. It is possible to generate more consistent data from patients with a clear-cut neurological diagnosis such as motor neurone disease [24]. In such patients, often the most consistent findings may be temporal differences rather than contraction amplitude abnormalities. It is difficult to accrue a very large series of such patients and it remains doubtful whether the manometric observations in any single patient are of particular value. The decision, for example, to carry out a crico-pharyngeal myotomy in a patient with motor neurone disease might be more

reasonably related to the patient's residual tongue function rather than to any registered pressure in the UOS. If a patient has poor tongue propulsion then destruction of a crico-pharyngeal sphincter may in fact be a dangerous procedure and increase the risk of aspiration.

Combination of manometry with other modalities

Limitations of manometry

Some of the limitations of manometry have already been outlined. There are a large number of recording variables and a wide intra-subject variation within the normal population. There are problems with the analysis of adequate numbers of swallows of different types to allow for these variables. Some of the parameters which are important in the performance of the oro-pharyngo-oesophageal segment are not assessed in any way by conventional UOS manometry. Attempts are being made, however, to estimate such parameters as tongue force [25]. Ambulatory manometry may also be combined with dual channel pH-metry (Fig. 6.13). Some patients are, however, somewhat intolerant of the rather bulky combined pressure and pH recording device and in contrast to distal oesophageal acid exposure time measurements, proximal oesophageal pH measurements are very sensitive to the acidity of ingested foods.

Manofluorometry

Radiographic techniques of swallowing give information about bolus control, mastication, palatal closure, vocal cord closure and bolus propulsion, in ways that are not possible with manometry in isolation. For this reason in North America manofluorometry has become increasingly popular since the technique was established in various centres [26,27]. There is no doubt that the use of manofluorometry has greatly advanced the understanding of the physiology of normal swallowing. In particular recent advances in frame grabbing of digital X-ray images has allowed quantification of radiographic images which can then be correlated with measurements from manometry [28] (Fig. 6.14). Such methodology overcomes the fundamental criticism of the radiographic analysis of swallowing—that it is primarily a qualitative investigation with subjective analysis. Manofluorometric techniques are gradually becoming more widely adopted for several reasons. Firstly, more and more X-ray units are equipped with a digital facility. Video-imaging of swallowing is now commonplace particularly when voice therapists are involved in the evaluation of dysphagia. The availability of frame grabbing devices for digitized images is now widespread. Also a similar technology is becoming increasingly used in urodynamic studies and in the ano-rectal segment.
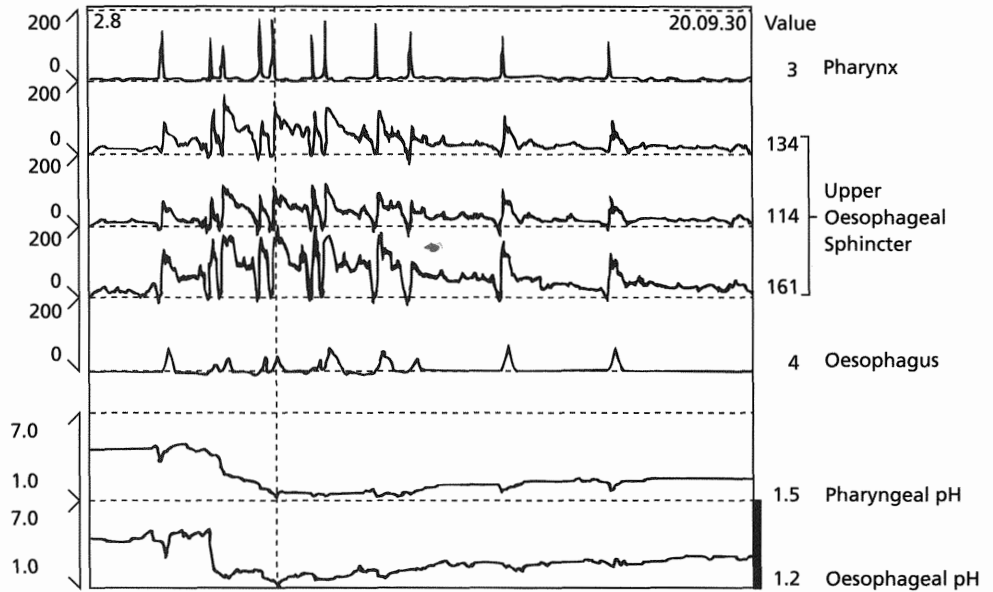
Fig. 6.13 Ambulatory pharyngo-oesophageal pressure and pH-metry. Portion of trace from a healthy volunteer during eating. Note the typical multiple, irregularly timed food swallows. The cursor (values shown to right) marks the peak upper oesophageal sphincter (UOS) after contraction. The pH channels are situated 2 cm above and 8 cm below the triple UOS pressure recorder (pressure 0–100 mmHg). The pH drop seen is due to the ingestion of a low pH food.
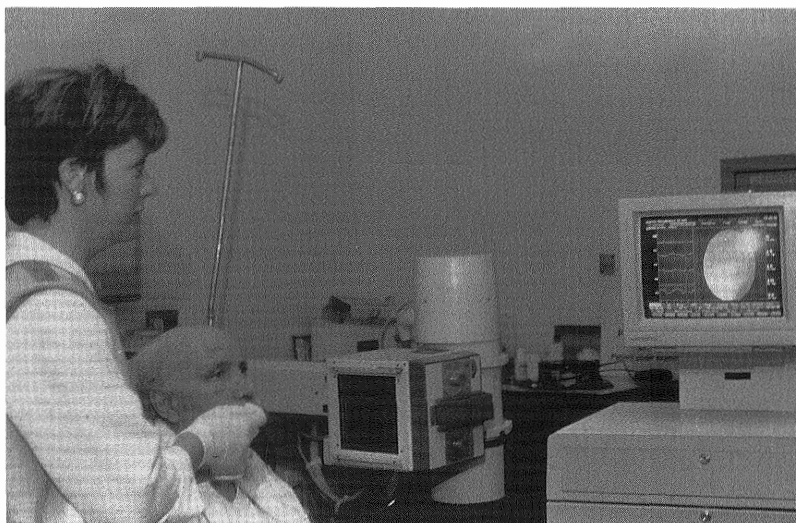
Fig. 6.14 Patient undergoing split screen recording of UOS manometry and videofluoroscopic swallow study.

Video-endoscopic analysis

In oto-laryngological circles, video-endoscopic swallow studies, pioneered in the United States by Bastian [29], have rapidly gained in popularity. The technique uses a standard piece of ear, nose and throat (ENT) equipment, namely the flexible laryngoscope. The technique has the advantage of showing in some detail the anatomy of structures whose normal function is essential to the completion of a normal swallow, in particular closure of the naso-pharynx and apposition of the vocal cords. This, however, can be assessed as a preliminary to the swallow and independent of any other investigation. Alone, video-endoscopic analysis of swallowing is severely limited by the fact that the actual moment of deglutition is obscured by laryngeal movement and the passage of bolus. The bolus should ideally be something which contrasts with the upper aerodigestive tract mucosa, such as milk or a food substance with blue dye added. The technique is particularly useful for detecting aspiration. While limited on its own it has usefully been combined with manometry and electromyography in providing a detailed kinesiological analysis of swallowing [30].

Respiratory parameters

The maintenance of normal swallowing involves circumventing, hundreds of times per day, the natural problem that the air and food passages share a common channel above the level of the supraglottis. For this reason respiration must be suspended during every swallow (deglutition apnoea) and some manometry systems incorporate a respiratory sensor accordingly. Anyone who has tried to speak and swallow at the same time may have experienced the inevitable desynchronization of respiration and swallowing as a piece of food or saliva 'goes down the wrong way'. More detailed attempts to assess the integration of respiration of swallowing have been made by the Exeter group [31]. The three channel Exeter system includes measurement of nasal airflow and registration of the contact between the spoon and our cheek reference electrode. The sounds of swallowing are recorded by a miniature microphone.

Conclusion

In future then it seems as if measurement manometry in isolation will become less popular for the analysis of upper dysphagia. Developing technology will allow the routine integration of manometry with a variety of other measurements to render a more complete evaluation of this most complex of reflexes.

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7 Vector manometry

S. Mark Scott & Sritharan S. Kadirkamanathan

Introduction

The lower oesophageal sphincter (LOS) is the major barrier to reflux of gastric contents in man. A sphincter at the cardia was originally described by Helvetius as early as 1719 [1]. In 1956, Fyke *et al.* [2] were the first to demonstrate a high pressure zone in the distal oesophagus during manometry of the gastro-oesophageal junction. Other manometric studies have also confirmed the existence of a physiological sphincter with an intrinsic pressure extending over 1–4 cm of the distal oesophagus [3]. Since then multiple investigators have tried to correlate LOS pressure to the competency of the cardia and hence resistance to reflux [4]. Although studies have suggested that the resting LOS pressure in patients with gastro-oesophageal reflux and peptic oesophagitis tends to be lower than the LOS pressure in normal subjects [5], the pressure measurements by themselves were found to be insufficient to separate reflux patients from normal subjects as there was a considerable overlap [6]. Because the measurement of LOS pressure alone failed to correlate well with sphincter competence, other sphincter parameters were sought and studied. DeMeester *et al.* demonstrated that the competency of the LOS was also dependent on the total and intra-abdominal length of the sphincter [7,8]. It was therefore suggested that a mechanically defective LOS, identified at standard manometry, had either an inadequate sphincter pressure or a short total or intra-abdominal sphincter length or a combination of these three factors [9]. However, in spite of the inclusion of these new sphincter parameters a significant proportion of reflux patients were still found to have a mechanically sound LOS at manometry. These findings have thus placed oesophageal manometry as an ancillary tool in the management of gastro-oesophageal reflux; its use is limited to finding the position of the LOS for accurate placement of pH sensors (for 24-hour ambulatory pH monitoring), and to exclude oesophageal body motility disorders [10].

Recently, Bombeck postulated that the LOS comprised an aggregation of several contractile units and felt that any method that measures sphincter function should take into account not only the sphincter length and maximal sphincter pressure but also the symmetry of unit contraction around the circumference of the LOS and the distribution of contractile pressures along the entire length of the LOS. He therefore developed a new method of measuring LOS competence called

computerized axial manometry [11] which took into account the various inter-active measurements and was designed to give more information than standard manometry. It has also been suggested that computerized axial manometry, otherwise known as three-dimensional or vector manometry, illustrates the asymmetric nature of the sphincter [12] better than the standard manometry.

Methodology

Manometry

In addition to the LOS, vector manometry of the anal sphincters [13,14] and upper oesophageal sphincter [15] have also been described. In this chapter, we outline the methodology for LOS assessment, although the operating principles are identical for other sphincteric regions.

Vector manometry is performed using a low-compliance Arndorfer-type pneumo-hydraulic capillary infusion system connected to a flexible, multilumen PVC catheter, which is perfused with distilled water at a constant rate (approx. 0.5 ml/min). The catheter assembly comprises 4–8 equidistantly spaced, radially-oriented side holes located at the same level and each lumen is connected to a pressure transducer. Analogue pressure signals are amplified and digitized by a commercially available interface (e.g. PC Polygraph™ HR, Synectics Medical) and
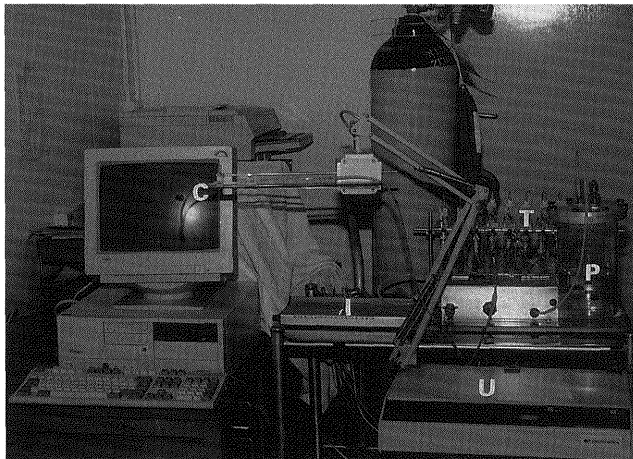
Fig. 7.1 Equipment used for computerized eight-channel manometric assessment of the LOS. The pneumo-hydraulic capillary system (P) perfuses the eight-channel catheter (C), which is withdrawn at a steady rate from the LOS by the mechanical puller unit (U). Pressure signals are relayed via the transducers (T) to the computer interface (I) and personal computer.

transmitted to a personal computer for on-line recording and storage on hard disk. Dedicated software programs (e.g. Synectics Medical) are available for real-time monitoring and subsequent review and analysis of data (Fig. 7.1).

The resolution and sensitivity of the system is enhanced with increased number of side holes, but this also increases the diameter of the catheter, which has a bearing on patient comfort and possible distortion of the sphincteric region. For this reason, the maximum viable number of side holes at present appears to be eight, set at 45° angles to each other (Plate 1).

Procedure

For LOS assessment, the catheter is passed through the nose of fasted subjects and advanced into the stomach, so that a steady gastric baseline is observed. One channel of the probe should be marked over its entire length to check the axial rotation during introduction [16]. Validation studies have shown that the maximum torsion of a standard catheter is less than 20° [17]. Three-dimensional manometric images are obtained by continuous or stepwise pull-back of the catheter across the gastro-oesophageal junction. This is performed using a linear motorized puller unit which withdraws the probe at a constant rate and also maintains its orientation. During recording, on-line display of the eight pressure channels enables the observer to check for artefacts. With slow, continuous pull-back (approx. 1 mm/sec) or stepwise manual pull-back, the patient can breath normally, which enables the respiratory inversion point (RIP) and intra-abdominal portion of the sphincter to be identified. The RIP, and consequently the intra-abdominal sphincter length, are not identifiable with a rapid continuous pull-back technique (2.5–5 mm/sec), during which the patient must hold his or her breath at end-expiration. Whichever technique is preferred, measurements should be taken until a minimum of three satisfactory recordings are obtained [18].

Three-dimensional imaging and vector volume analysis

Three-dimensional images of the LOS high-pressure zone are constructed by the computer program. Each satisfactory pull-through is 'picked-out' manually as a region-of-interest (ROI), and the baselines are set for each channel at gastric pressure (Plate 2). The computer then calculates the pressures in all channels at each station of the pull-back and plots these pressures radially around a zero axis representing the gastric baseline. The three-dimensional pressure-profile of each ROI, or an integrated image of the combined ROIs, can be rotated on screen and viewed from various angles for asymmetry (Plate 3). For visual purposes only, the three-dimensional reconstruction can be enhanced with a cubic curve-smoothing interpolation, which gives a smoother surface to the image [19].

The volume circumscribed by the three-dimensional image is calculated using standard trigonometric formulae, and is the sum of all cross-sectional sphincter pressure areas. The total sphincter pressure vector volume (SPVV) integrates radial pressures exerted over the entire length of the sphincter into one value, and is expressed in units of $mmHg^2 \times mm$.

Vector manometry in normal subjects

In 50 healthy volunteers, without evidence of foregut disorders, the normal SPVV of the LOS was determined to be $5723 \pm 843\,mmHg^2 \times mm$, using a stepwise pull-back technique. The intra-abdominal and intra-thoracic components were 3613 ± 531 and $2050 \pm 319\,mmHg^2 \times mm$, respectively [18]. The three-dimensional image is asymmetric both radially and longitudinally, indicating that the human LOS is not simply a muscular ring.

When comparing three-dimensional images with muscular thickness and architecture at the human gastro-oesophageal junction, Stein and colleagues showed that the asymmetry was due to the pressures exerted by the gastric sling fibres and the semi-circular clasp fibres, and it was these structures that were the anatomic correlate of the manometric LOS (Fig. 7.2) [17].

The role of lower oesophageal sphincter vector manometry in the management of gastro-oesophageal reflux disease

Measurement of sphincter resting pressure and overall and intra-abdominal length at standard manometry is insufficient to identify subtle sphincter defects. The SPVV, which takes into account the pressures exerted over the entire length of the sphincter, better expresses the overall resistance of LOS to reflux of gastric contents. Bombeck *et al.* [11] showed that SPVV was superior to all individual sphincter parameters (measured at standard manometry) in identifying a group of reflux patients who would not respond to medical treatment. It has also been demonstrated that patients with gastro-oesophageal reflux have lower total and intra-abdominal SPVV when compared with healthy volunteers [19]. When compared with standard manometry, measurement of SPVV did not have any significant advantage over standard sphincter parameters in detecting a mechanically defective sphincter in a large population of patients with complicated gastro-oesophageal reflux disease (GORD), i.e. with evidence of mucosal injury. However, in this particular study SPVV did increase the sensitivity of manometry in identifying a defective sphincter in GORD patients *without* mucosal injury [19].

In spite of the slight superiority of three-dimensional manometry in identifying sphincter abnormalities, there is a significant number of patients with increased

Plate 1 Schematic drawing of the manometry catheter used to obtain a three-dimensional pressure profile of the LOS. The cross-section illustrates how the eight ports are radially oriented and set at 45° angles to each other. For each pull-through, it is essential that the orientation of the probe is maintained, where A = anterior, P = posterior and L = lateral. After pulling through the LOS, a computer generated image of each 0.5 cm 'slice' of the sphincter can be created; in this example, pressure is highest in the left anterolateral quadrant. D = dorsal (posterior).
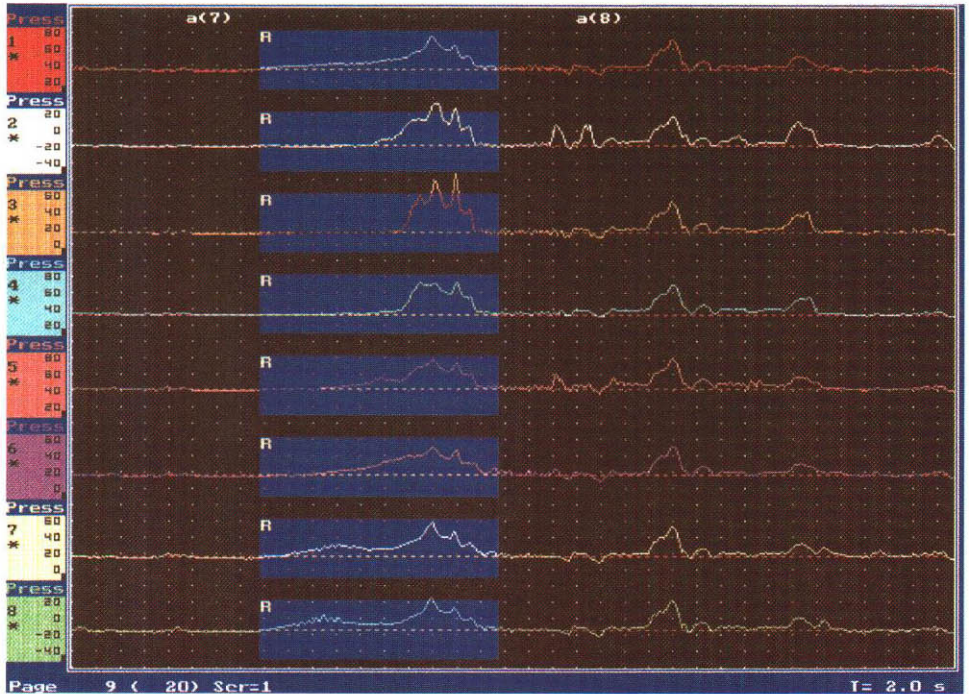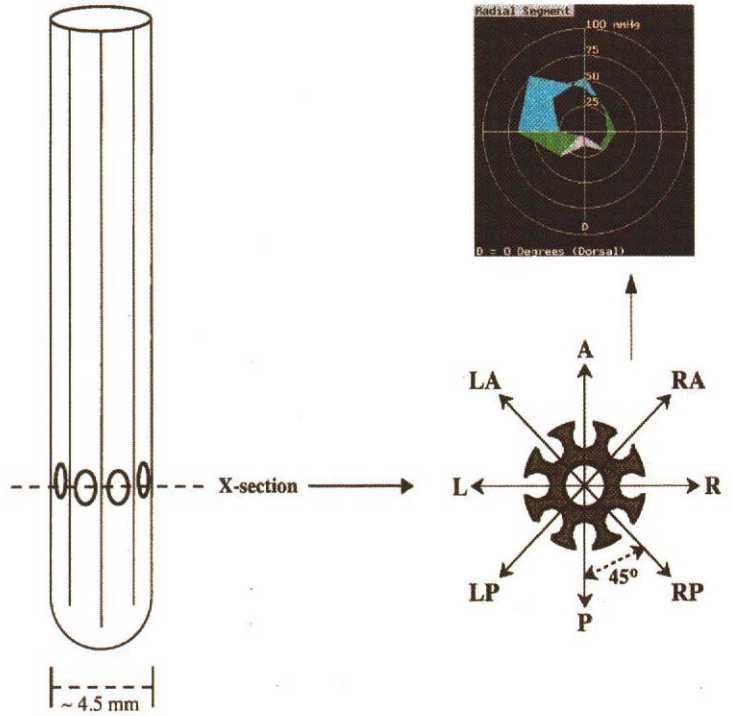
Plate 2 'Raw' eight channel manometric tracing. The high-pressure zone (highlighted area between markers a(7) and a(8)) is demarcated for 3D-display and vector volume analysis. The gastric baseline is to the immediate left of the high-pressure zone.
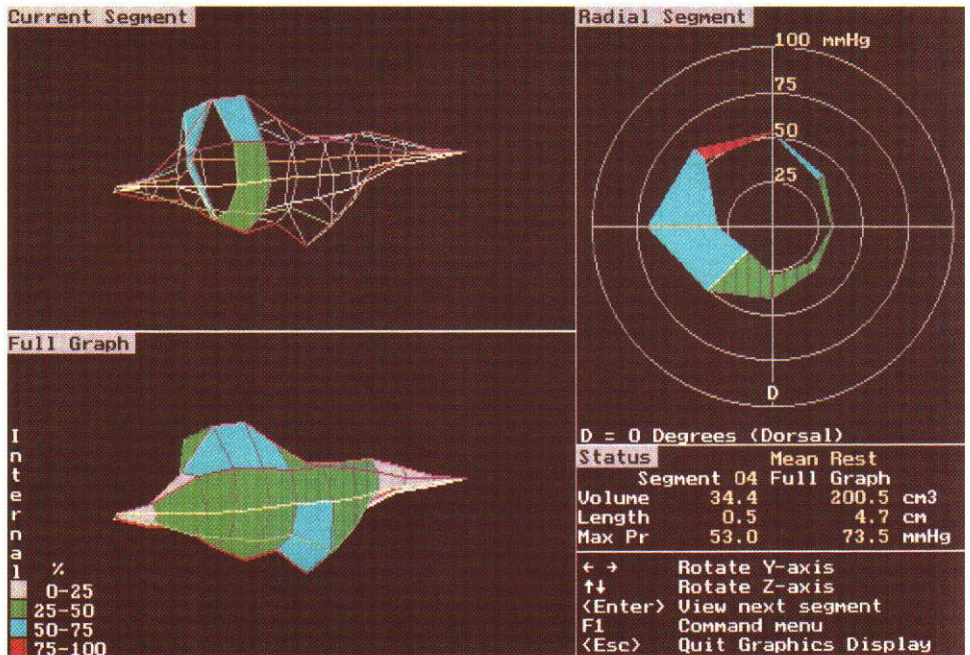
Plate 3 Computer generated three-dimensional image of the LOS. The images are oriented as if the patient were supine; to the left of the high pressure zone is the stomach and to the right the oesophagus. A 'wire-frame' (*top left*) or solid (*bottom left*) representation can be rotated through 360° and re-scaled to facilitate interpretation. Each 0.5 cm segment (highlighted region of the wire-frame image) can be viewed (*top right*) to give an impression of the symmetry/asymmetry of the sphincter. Quantifiable parameters are also depicted (*bottom right*).
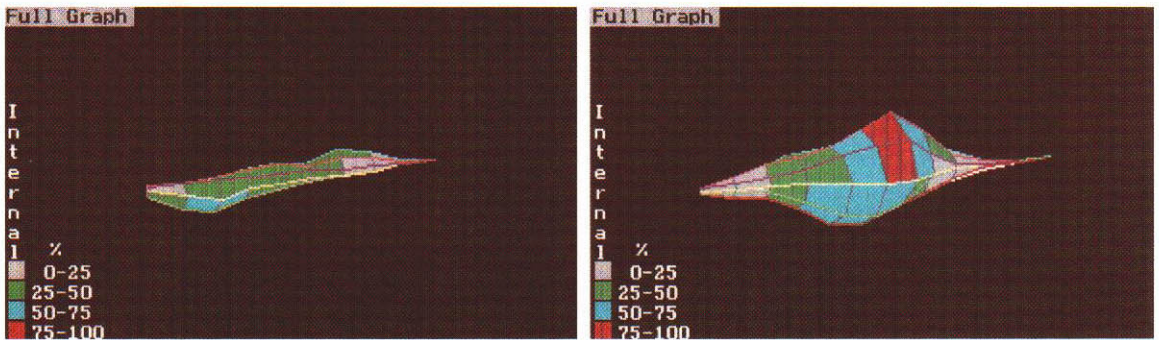
Plate 4 Three-dimensional pressure images of the LOS in a patient prior to laparoscopic fundoplication (*left*) and at one month after surgery (*right*). Note the increase in pressure throughout the length of the sphincter following fundoplication.

Plate 5 Gastro-oesophageal junction or 'Z-line'. The paler oesophageal epithelium joins the redder gastric epithelium.
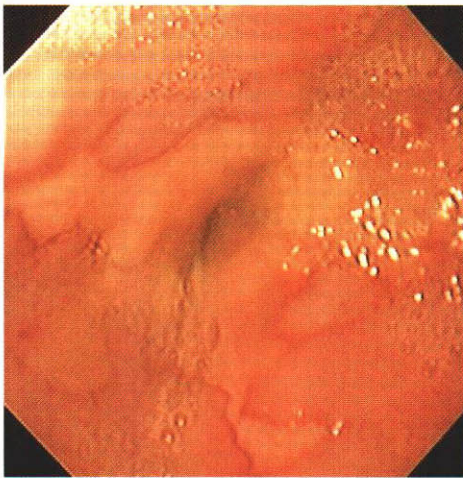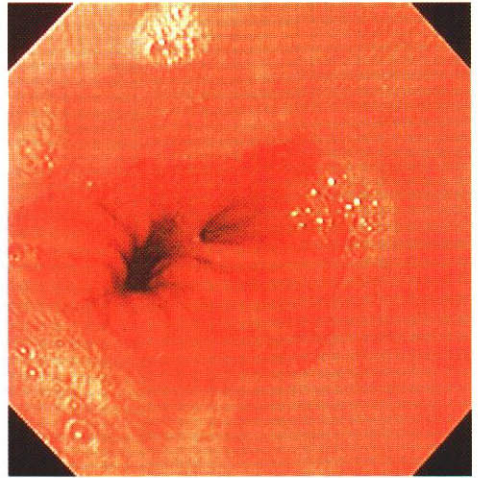
(a)
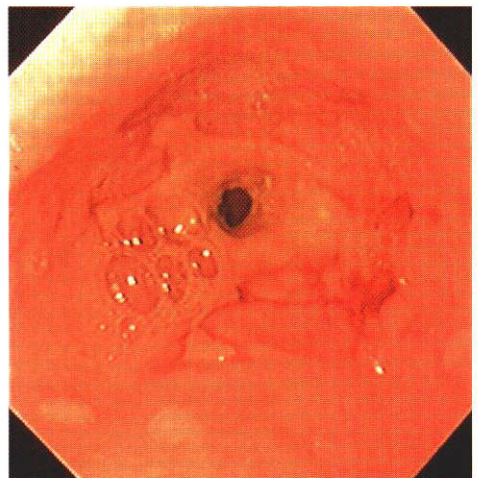
(b)

Plate 6 Lower oesophageal erosions or mucosal breaks due to reflux disease. (a) Confluent erosions. (b,c) Friable linear erosions.
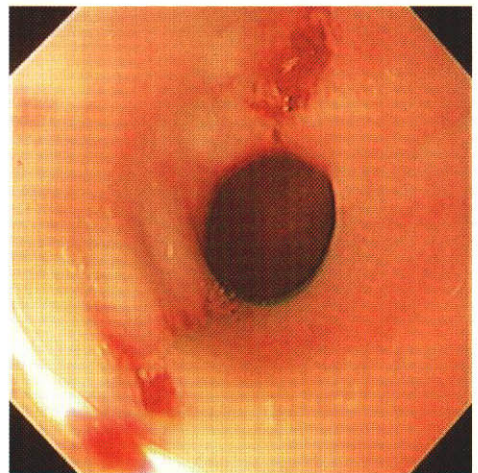
(c)
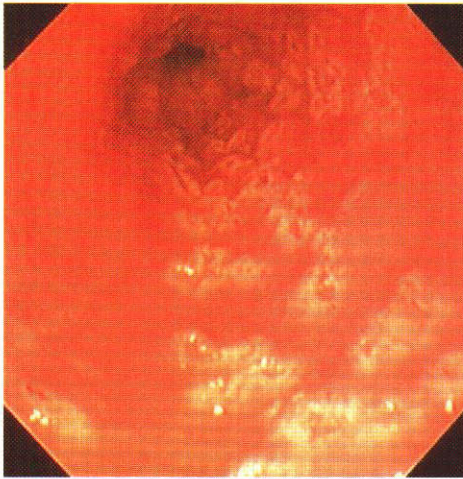
Plate 7 Multiple white non-inflamed erosions due to viral infection.
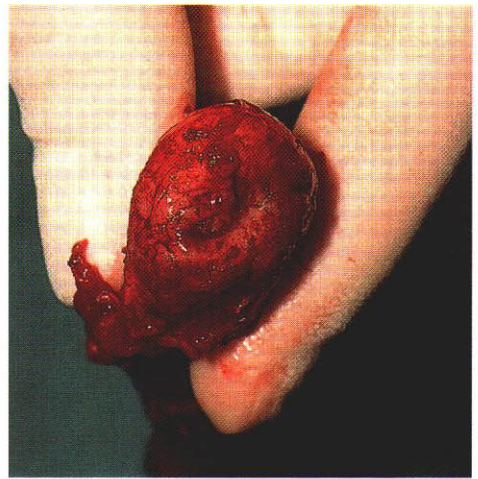
Plate 8 Thickened oesophagus due to corrosive oesophagitis removed at surgery.
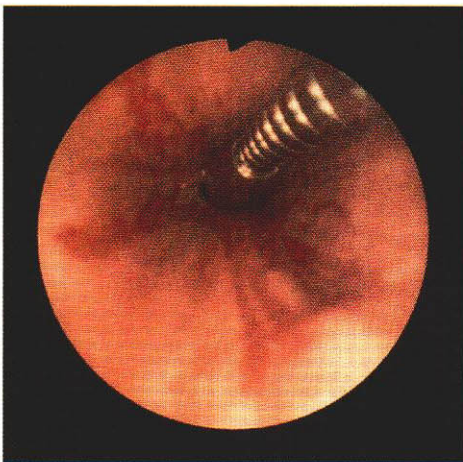
Plate 9 Metal bougie passing through narrow oesophageal stricture.

Plate 10 Example of a summed image recorded from an anterior projection. The path of the tracer can be seen along the oesophagus with a characteristic curve at the cardiac orifice of the stomach. The majority of the activity can be seen in the stomach, however there is some retained activity at the distal end of the oesophagus.

Plate 11 An example of normal oesophageal transit showing activity entering the stomach within the first 30 seconds (*left plot*). Note the oscillatory movement of activity in the stomach over the 10 minute period of the study due to normal respiratory action (*right plot*).

Plate 12 An example of abnormal transit showing prolonged oesophageal spasm with tracer oscillating between the upper and mid oesophagus throughout the entire duration of the 10 minute study (*left plot*, 30 second duration; *right plot*, 10 minute duration).

Plate 13 Condensed image display showing normal swallowing of a Tc-99m-labelled tablet preparation.

Plate 14 Condensed image display showing prolonged swallowing pattern of a Tc-99m gelatin capsule. Momentary stasis of the capsule can be seen in the mid oesophagus.

Plate 15 Pattern of activity resulting from retention of tracer along the entire length of the oesophagus following administration of a radiolabelled medicinal formulation intended to coat the mucosal surface.
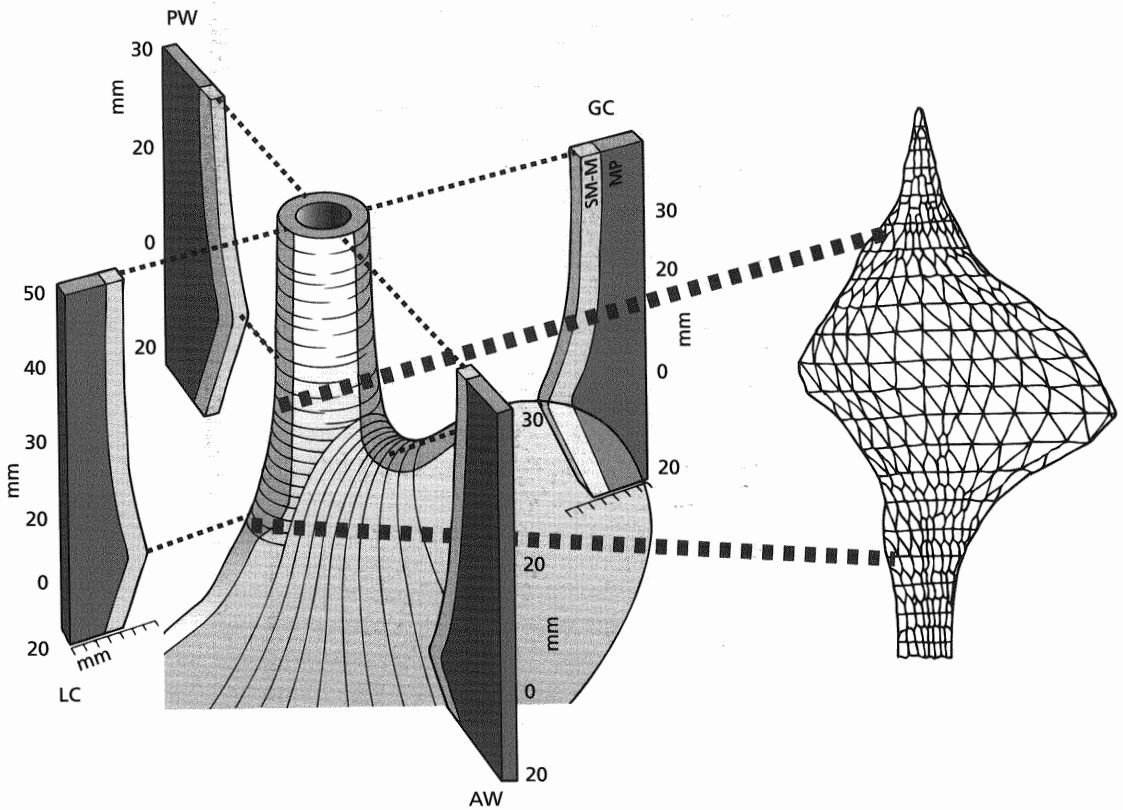
Fig. 7.2 Schematic drawing shows correlation between radial muscle thickness (left) and three-dimensional manometric pressure image (right) at the human gastro-oesophageal junction. Muscle thickness across the gastro-oesophageal junction at the posterior gastric wall (PW), greater curvature (GC), anterior gastric wall (AW) and lesser curvature (LC) is shown in millimetres. Radial pressures at the gastro-oesophageal junction (in mmHg) are plotted around an axis representing atmospheric pressure (from reference [17] with permission).

distal oesophageal acid exposure who have normal SPVV [18]. It is thought that sphincter asymmetry might play an important role in sphincter competence [20], although the relationship between asymmetry of the LOS and the pathogenesis of GORD remains undefined. However, in our series of patients with GORD who underwent successful laparoscopic fundoplication (associated with reduction in distal oesophageal acid exposure), there was a significant reduction in LOS asymmetry from $20.7 \pm 1.0\%$ pre-operatively to $11.7 \pm 0.5\%$ at one month following surgery, where 0.0% is perfectly symmetrical (mean $\pm$ SEM, $n = 87$; $P < 0.001$). The symmetry of the sphincter was maintained at one year ($11.9 \pm 1.0\%$, $n = 35$; $P = \text{NS}$) (unpublished data).

Three-dimensional manometry is being used increasingly to assess the effect of anti-reflux surgery on LOS in reflux patients [21]. Although increases in LOS pressure and length have been demonstrated at standard manometry by some investigators [22], this has not been consistent and there is no clear relationship between post-operative sphincter pressure and success of the operation [23]. Early studies seem to suggest that successful outcome following anti-reflux surgery is better predicted by SPVV than standard manometry [19]. In our series of 87 patients, there was a 226% increase in SPVV following laparoscopic fundoplication after one month ($P < 0.001$; Plate 4), and this was unchanged at one year (unpublished data).

Vector manometry has also been used to evaluate the effect of balloon dilatation [24] and Heller's myotomy [25] on LOS in patients with achalasia. A further novel application is to station the catheter in the oesophageal body, rather than pulling it through the LOS, and to record peristaltic events passing over it. This may enable the assessment of wave characteristics of oesophageal contractions in health and disease (Lowndes & McKirdy, unpublished data).

At present, three-dimensional vector manometry of the LOS remains an interesting investigative research tool. It does give combined functional (pressure measurement) *and* anatomical (three-dimensional profile) information, and has been shown to be more sensitive than standard manometry. Based on current evidence, however, it is not as sensitive as 24-hour ambulatory pH studies in the diagnosis of GORD.

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8 Radiology

Damian Taylor

Introduction

Modern endoscopy has very much transformed the investigation of oesophageal disease. The advent of 'open access' endoscopy has drastically reduced the number of barium studies performed in many X-ray departments, but there remains one area where barium is extremely valuable and that is in the investigation of disorders of pharyngeal and oesophageal motility.

High quality examinations, with attention to fine detail, and the utilization of modern fluoroscopic equipment, video recording, rapid sequence spot films and high density barium preparations are essential.

Detection rates of motility disorders vary from 49% to 95% (95% for achalasia, 75% for diffuse spasm and 50% for non-specific oesophageal motility disorders) [1,2]. It is often important to utilize a solid bolus. In our department a standard 'sweetshop' marshmallow is used, washed down with barium. This is invaluable for demonstrating webs and rings, and may often provoke the patient's exact symptom complex.

As in many fields, a team approach is essential. Clinician, manometry technician, speech therapist and radiologist work together to provide accurate diagnosis and appropriate therapy.

Observations

Swallowing can be subdivided into three phases:
1 Oral phase.
2 Pharyngeal phase.
3 Oesophageal phase.

Oral phase

Observe symmetric tongue elevation delivering the bolus to the oropharynx. The soft palate elevates to appose posterior pharyngeal wall. Also, observe base of tongue retraction which triggers the swallow reflex.

Pharyngeal phase

Observe pharyngeal continence, nasal regurgitation (palatal insufficiency). Confirm normal pharyngeal stripping/constrictor wave.

Figure 8.1 shows a complicated case with a rare glosso-pharyngeal nerve tumour, associated with brain stem infarction. This patient shows gross paralysis and incontinence of the pharynx with gross nasal regurgitation and laryngeal penetration.

Laryngeal elevation

Very important to facilitate a glottic closure. May be impaired in the elderly. Observe hyoid movement.

Crico-pharyngeal opening

Early or late opening or early closure.

Figure 8.2a,b shows the considerable normal variation in the appearance of the crico-pharyngeus during different phases of swallowing.

Laryngeal penetration and aspiration

1   Pre-deglutive.
2   Peri-deglutive.
3   Post-deglutive.

Fig. 8.1 Complicated case with a rare glosso-pharyngeal nerve tumour, associated with brain stem infarction.

(a)   (b)
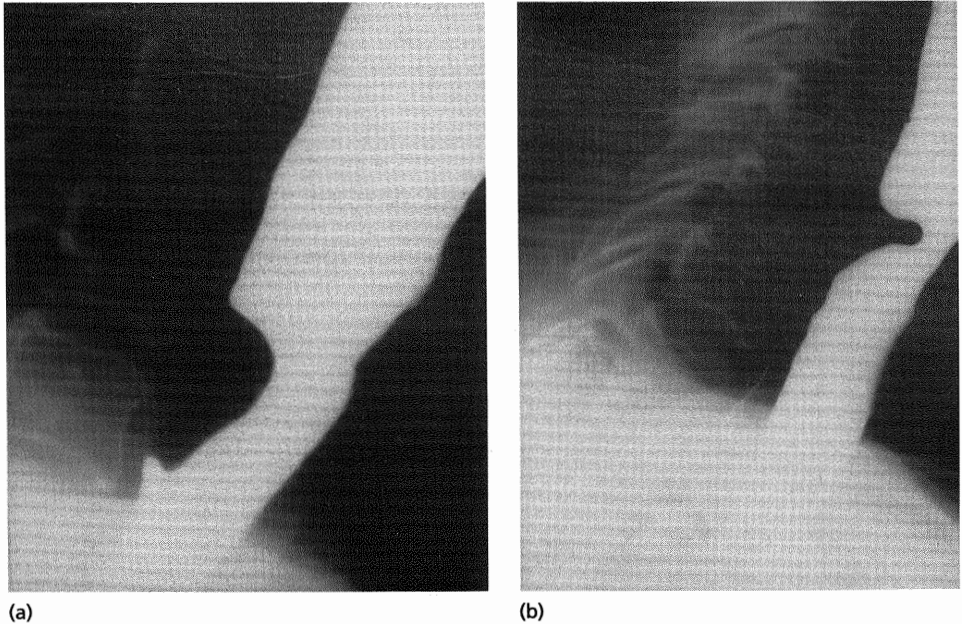
Fig. 8.2 (a,b) The considerable normal variation in the appearance of the crico-pharyngeus during different phases of swallowing.

Oesophageal phase

Observe peristalsis—normal stripping wave drives the bolus down the oesophagus—look for cephalad escape. Also look for non-propulsive contractions. Observe relaxation of the lower oesophageal sphincter. Check for reflux. Observe gross anatomy—strictures, retro-cardiac compression, vascular rings, etc.

Equipment and procedures

Equipment

The equipment required for accurate radiological assessment of the oropharynx and oesophagus is detailed in Table 8.1.

Procedure

The whole study is recorded on standard VHS video tapes. The patient is screened erect initially (in the infirm or paralysed patient care must be taken to position the

Table 8.1 Equipment required for accurate assessment of the oropharynx and oesophagus.

Good fluoroscopy unit
Video camera
100 mm camera with rapid sequence facility (2–3 films per second)
Appropriate contrast agents—if aspiration is a genuine concern use Isovist (Schering), or similar
Good quality barium, e.g. E-Z HD 100–250%; varibar EZm
'Bendy straw'
Marshmallow, yogurt, biscuit
Water
Opaque wax spheres, 5 mm and 10 mm in diameter [3]
Accurate patient name marker

patient securely, either in a cradle device or supported sitting on the screening table step platform).

The patient takes a mouthful (5 ml to approximately 18 ml maximum) of contrast and holds it in the mouth. Careful observation of oral phase, tongue and palate function is recorded. Phonation views are taken (if assessing speech disorder). Observations and recording of the complete act of swallowing are made. The abnormality may often be very obvious. With more subtle abnormalities, observe at least five individual swallows in the erect and oblique prone positions. If there is a hold-up at the gastro-oesophageal junction, water may be given. This will usually produce a 'wash-through' effect, with good detail of the gastro-oesophageal junction. The patient may require a marshmallow swallow or other textures decided in conjunction with the speech therapist. The marshmallow is washed down with barium. This produces excellent oesophageal distension and may reveal rings and strictures and significant spasm, not seen with liquid barium as well as information on oral and pharyngeal ability (Fig. 8.3a,b).

If there is evidence of achalasia or the study is being performed to evaluate treatment, e.g. post-balloon dilatation, the sphincter size should be documented using an appropriately sized wax sphere [3] (Fig. 8.4a,b).

Spot films

Spot films of the following views are taken for documentation. Oral phase—lateral view. Pharyngeal phase—lateral, anteroposterior and oblique. Oesophageal phase—oblique upper middle and lower third in the erect and prone position. Always check for reflux at the end of the study. (If aspiration occurs, immediate physiotherapy is indicated to clear aspirated contrast.)
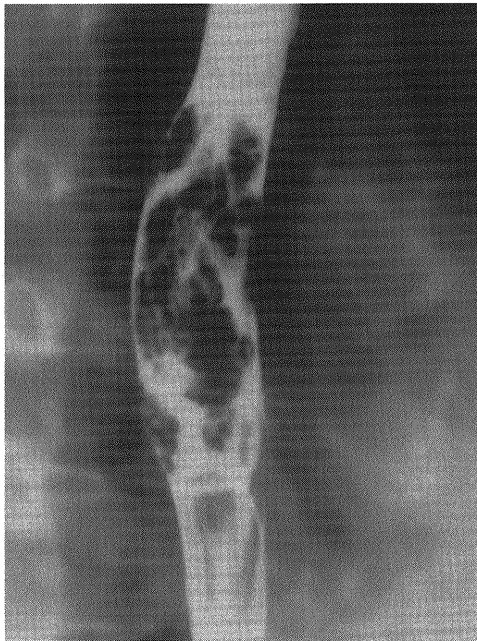
(a)
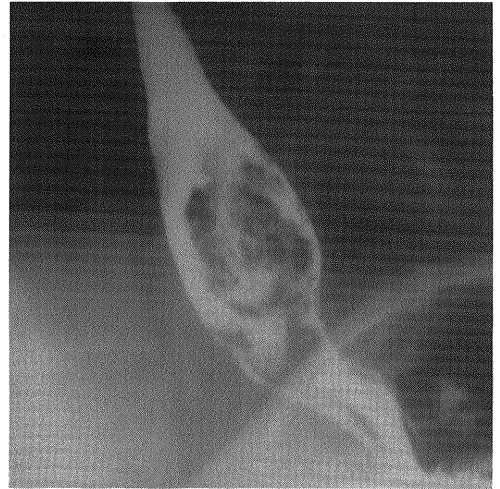
(b)

Fig. 8.3 (a,b) Marshmallow bolus.
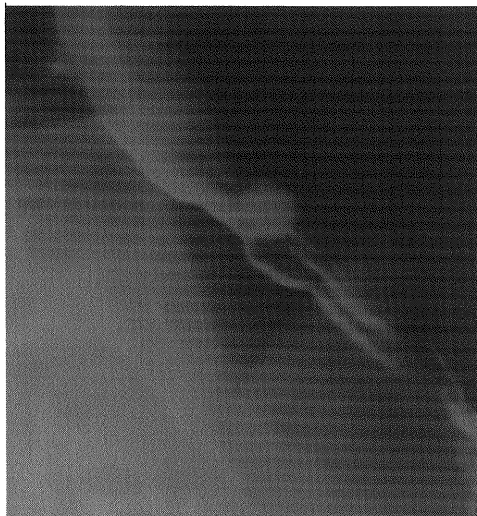
(a)
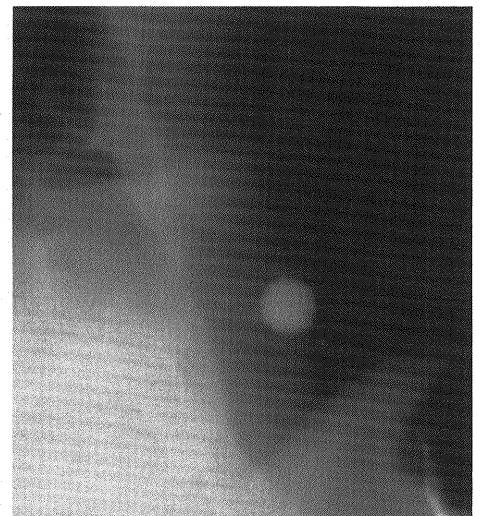
(b)

Fig. 8.4 (a,b) Measuring 10 mm sphere.

Interpretation and clinical relevance, anatomical abnormalities and miscellaneous findings

1 Developmental—duplication—tracheo-oesophageal fistula.
2 Benign tumours, e.g. leiomyoma.
3 Diverticula.
    (a) *Zenker's*. Zenker's diverticulum (posterior hypo-pharyngeal diverticulum superior to crico-pharyngeus) lies in the mid-line. 30% of people have a potential space between the oblique and horizontal fibres of crico-pharyngeus, known as Killian's dehiscence [4,5]. Zenker's diverticulum has also been described as herniating between thyro-pharyngeus and the crico-pharyngeus portion of the inferior constrictor muscle. Figure 8.5 shows a large symptomatic diverticulum.
    (b) *Lateral cervical diverticula*. These occur through the Killian–Jamieson space below the crico-pharyngeus. This is different from Killian's dehiscence. Anatomically the space is bounded superiorly by the crico-pharyngeus muscle, anteriorly by the posterior wall of the cricoid cartilage and infero-medially by the longitudinal tendon of the oesophagus as it inserts into the cricoid-cartilage [6].
4 Rings and webs. Webs are the thin membranes usually found in the proximal oesophagus. They tend to be anterior and may produce symptoms.
5 Schatzki ring (see Fig. 8.6). This represents a thickening of the normal transverse
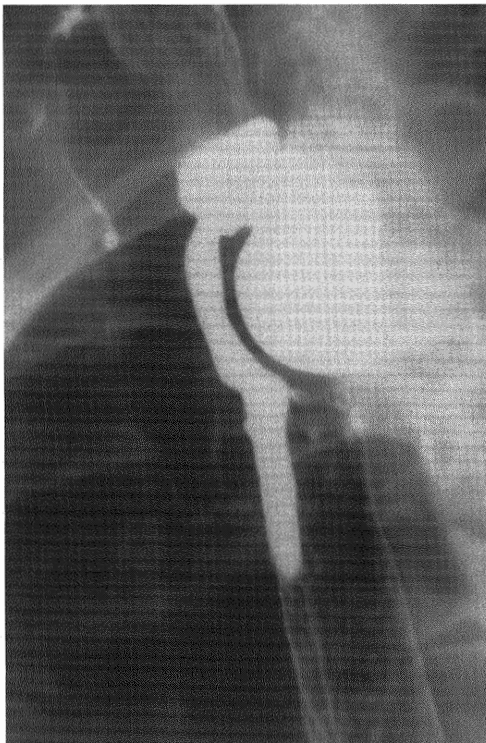
Fig. 8.5 A large symptomatic diverticulum.
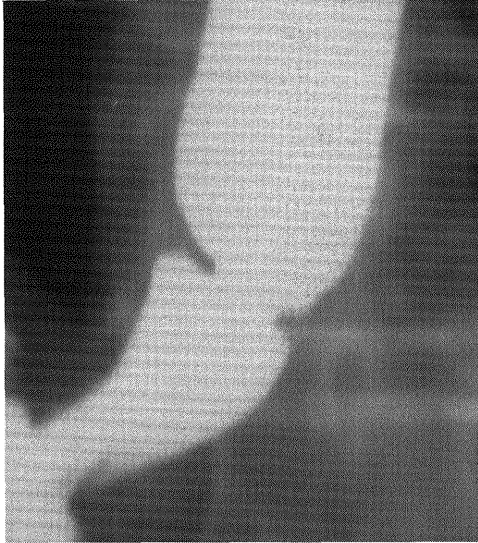
Fig. 8.6 Schatzki ring.

mucosal fold at the gastro-oesophageal junction, producing narrowing. They may be asymptomatic or symptomatic and are often associated with a small axial hiatus hernia and reflux. They may be very difficult to demonstrate if adequate oesophageal distension is not achieved. [7].

6 Strictures. Figures 8.7 and 8.8 show the differences between a benign peptic stricture and typical malignant stricture. Peptic strictures are associated with reflux and hiatus hernias. Stricturing may also occur following corrosive ingestion.

7 Infections. Fungi, yeasts and viruses may be involved and are particularly common in immunosuppressed and AIDS patients.

8 Foreign bodies.

9 Varices.

Motility disorders

Table 8.2 lists the primary and secondary motor and functional disorders that radiologists are able to detect using the various techniques previously described.

Achalasia

(NB. Intrinsic or extrinsic neoplasm may be completely indistinguishable radiologically.) Endoscopic ultrasound (EUS), computerized tomography (CT) and magnetic resonance imaging (MRI) may be helpful in difficult cases.

Figure 8.9 shows chronic achalasia with typical 'sump' effect.

Fig. 8.7 Benign peptic stricture.
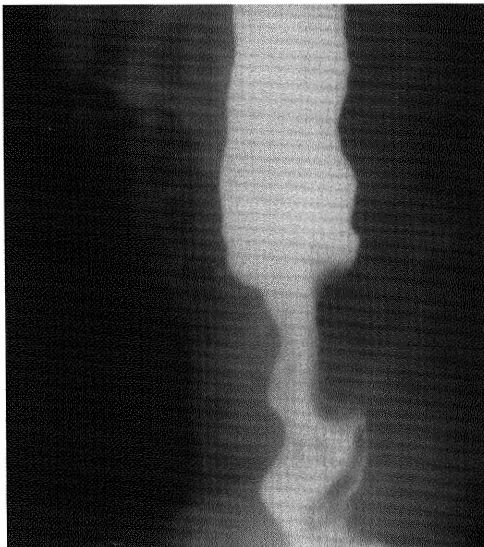
Fig. 8.8 Typical malignant stricture.

Table 8.2 Primary and secondary motor and functional disorders that radiologists are able to detect using the various techniques previously described.

Primary
Achalasia and variants
Diffuse oesophageal spasm
Nutcracker oesophagus
Non-specific motility disorder
Presbyoesophagus

Secondary
Collagen diseases (in particular, scleroderma)
Autonomic neuropathies
Oesophagitis, reflux, drugs, metabolic, endocrine and neuromuscular disorders, radiotherapy

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Fig. 8.9 Chronic achalasia with typical 'sump' effect.

Achalasia is characterized by absence of oesophageal peristalsis, dilatation (often with retained food) and lower oesophagus sphincter dysfunction [8] (Table 8.3). The exact cause is not known.

Destruction of the neuro-muscular plexus to the oesophagus by *Trypanasoma cruzi* (Chagas' disease) produces radiological changes indistinguishable from achalasia.

The risk of carcinoma has been found to be up to 33 times greater than in the general population [9,10]. In a more recent study [11] it was found to be 14.5 times greater. See Figs 8.10–8.12.

Table 8.3 Radiographic features of achalasia and variants.

	Early	Established	Vigorous
Peristalsis	–	–	–
Dilatation	+	+++	++
LOS relaxation	+/–	–	–
Lower oesophageal tapering	+/–	+	+
Non-propulsive contractions	+/–	+	++

NB. Non-propulsive contractions may be absent, intermittent, rippling or spectacular.
+, present; –, absent.

Fig. 8.10 MRI of achalasia after ingestion of 'Abdoscan' contrast agent (Nycomed).

Diffuse oesophageal spasm

This is characterized by intermittent abnormal motility with chest pain and dyphagia, as illustrated in Figs 8.13a,b,c.

Primary peristalsis is present in the upper oesophagus but intermittently absent in the lower oesophagus. Repetitive simultaneous contractions may produce a 'corkscrew' appearance or an 'archipelago' of barium collections (see Fig. 8.14). Occasionally motility disorders may be secondary to a neoplasm at the gastro-oesophageal junction. This must always be considered and excluded.

Nutcracker oesophagus

This is a manometric diagnosis. The patient usually has fairly severe chest pain and dysphagia. It may be radiographically normal or show features very similar to diffuse spasm.

(a)   (b)
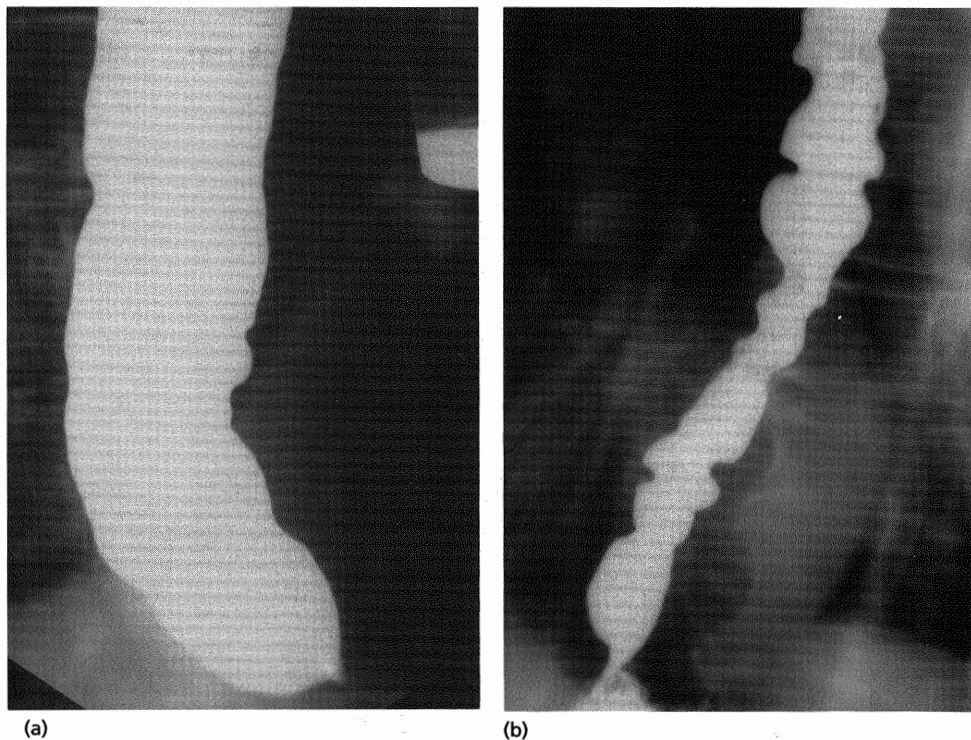
Fig. 8.11 (a) Achalasia pre-treatment showing typical features. (b) Achalasia post-treatment. Note the development of florid non-propulsive contractions.
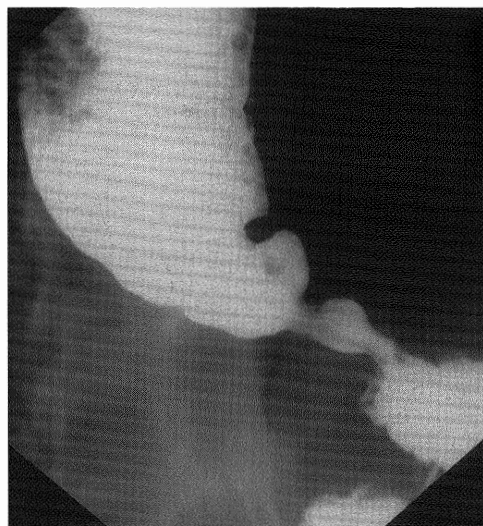
Fig. 8.12 Post-treatment case showing the common indentation above the level of the sphincter, the exact cause for which is unknown.
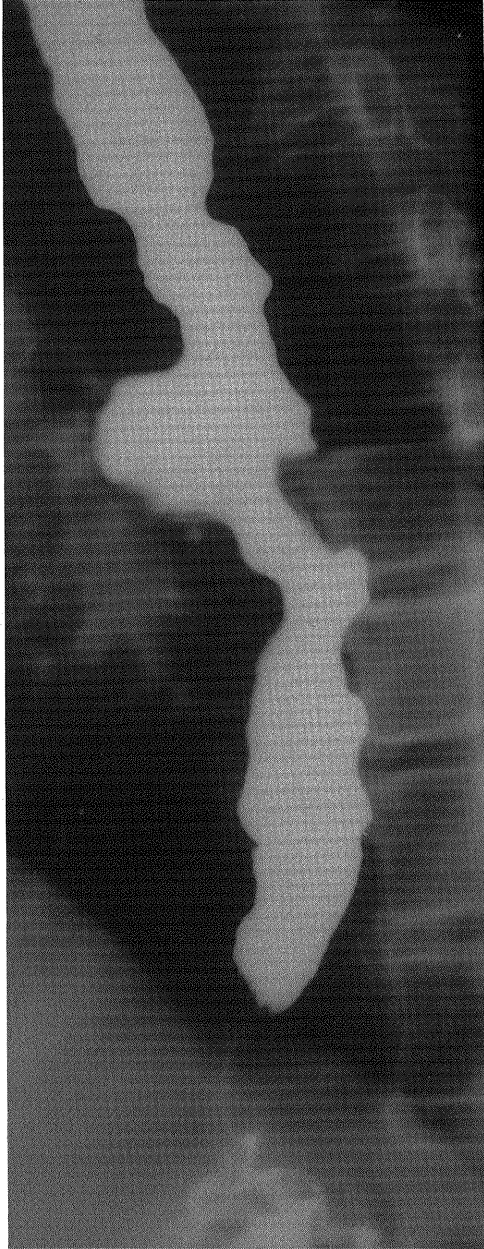
(a)
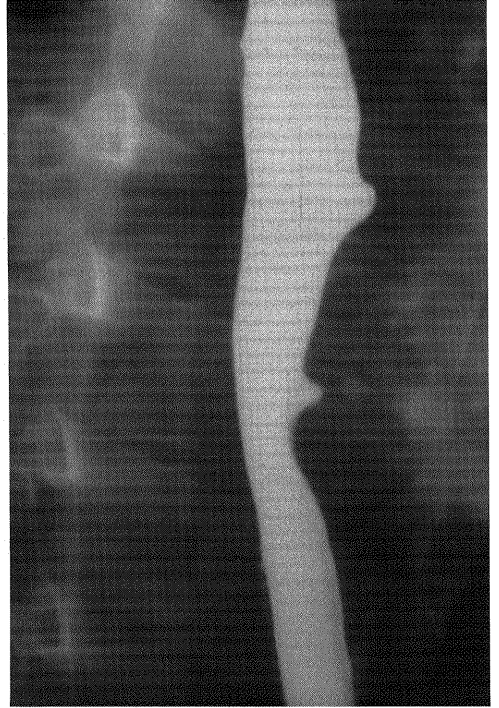
(b)
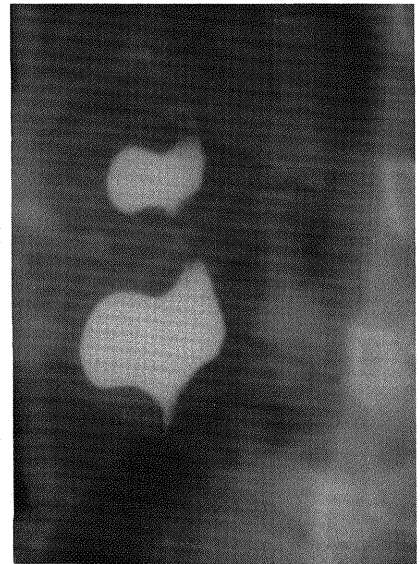
(c)

Figs 8.13 (a,b,c) Diffuse oesophageal spasm.

Non-specific oesophageal motility disorder

Patients may be asymptomatic. Radiographic abnormalities may be absent or subtle, and intermittent, and may overlap with early achalasia, diffuse spasm and particularly secondary motility disorders seen with refluxers.

Presbyoesophagus

This has been an easy option for labelling elderly patients with swallowing disorders or incidental findings of dilatation or peristaltic dysfunction. Studies of healthy elderly individuals show relatively minor deterioration of motility with age [12,13]. Some reduction in laryngeal elevation and a tendency for proximal barium escape is commonly seen. I suspect that most cases of presbyoesophagus have, in fact, a more definable motility disorder.

Scleroderma

This deserves a special mention as it is commonly associated with abnormalities of the oesophagus. It is a systemic disease characterized by fibrosis and degenerative change in the skin, joints, lung and gastro-intestinal tract, including the oesophagus. Involvement occurs in 75–95% of patients. The lower oesophageal sphincter is weak and incompetent, with absent oesophageal peristalsis. There is significant reflux with all its complications.

Conclusion

Benign oesophageal conditions and motility disorders remain a challenging area for the gastro-radiologist and gastro-enterologist. Imaging with clinical correlation is the mainstay of accurate diagnosis. New techniques may be developed and may well prove useful in the future, particularly with the advent of oral MRI contrast agents and rapid MRI scanning techniques.

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9 Endoscopy

John R. Bennett

Introduction

Fibre-optic or video-endoscopy is now the first choice of investigation of the upper alimentary canal. When used for suspected oesophageal disease the limitations and defects of endoscopy (Table 9.1) should always be in the investigator's mind, and for some clinical problems other tests should take priority.

Instruments

The usual instrument is a flexible fibre-optic or (increasingly) video-endoscope with an end-viewing or fore-oblique objective. For patient comfort, and because oesophageal narrowing may be encountered, a slim (less than 10 mm; preferably 8 mm insertion tube) instrument is preferred.

There is still a place for rigid oesophagoscopy but this is mainly for difficult therapeutic procedures. The near-necessity of general anaesthesia and the increased risk of instrumental perforation make rigid endoscopes undesirable as first choice.

Technique of fibre-optic/video-oesophagoscopy

Details of obtaining informed consent, sedation, monitoring, etc. can be obtained from other standard works on endoscopy. This section deals only with some special practical points.

After passage of the scope into the pharynx the crico-pharyngeal sphincter should be observed with the V-shaped glottis beyond (Fig. 9.1). When the subject makes a swallowing attempt the sphincter opens briefly and the scope can be passed through. Neurological disease, or tentative swallowing may cause inadequate opening, or the presence of a pharyngeal pouch may cause difficulty in entering the sphincter. It may then be possible to pass a guide wire (with or without radiological screening) and then the endoscope can be safely introduced over the wire.

The oesophagus

The instrument is passed carefully viewing the lumen at all times. Particular

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(a) Follow the centre of the tongue...

(b) ...past the uvula...

(c) ...and the epiglottis...

(d) ...to pass below the cricoarytenoid on either side
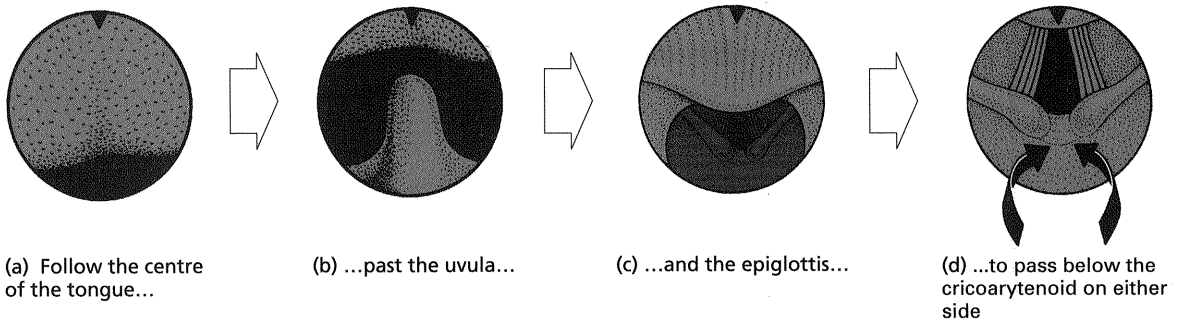
Fig. 9.1 Diagrammatic illustration of passing the endoscope through the glottis (from Cotton PB, Williams CB. Practical Gastrointestinal Endoscopy, 4th edn. Oxford: Blackwell Science Ltd, 1996).

Table 9.1 Problems and limitation of fibre-optic or video-oesophagoscopes.

Mechanical
Pharyngeal diverticulum
Narrowing may prevent passage
Food retention may prevent safe passage

Visual
Inadequate view of pharynx and crico-pharyngeal area
No visual assessment of neurological abnormalities
No visual assessment of most motility problems
Food/fluid may obscure view
Wide rings easily overlooked
Minor reflux changes in mucosa controversial
Significant gastro-oesophageal reflux gives no visible abnormality in 50%

attention should be paid to the gastro-oesophageal mucosal junction ('Z-line') (Plate 5) which is usually just above the narrowing caused by the gastro-oesophageal sphincter and diaphragmatic crura. It may be displaced proximally if there is a hiatus hernia or, more important, if there is a segment of columnar-lined oesophagus (Barrett's mucosa; CLO). The level of the gastro-oesophageal sphincter is noted and the instrument passed through.

The stomach and beyond

Unless some mechanical problem prevents it the examination should include the whole stomach, pylorus and first and second parts of the duodenum, as pathology there may explain some oesophageal symptoms. During withdrawal retroflexion

of the scope to view the fundus is important, and gives an opportunity to assess the cardia from below. It should fit snugly round the instrument.

The oesophagus is again carefully viewed as the instrument is withdrawn; high oesophageal abnormalities in particular may be overlooked as the scope is introduced.

Abnormal appearances

Reflux oesophagitis

This is by far the commonest abnormality in the oesophagus, but the appearances may be hard to describe with confidence. The multiplicity of grading systems (over 30 are in use) reinforces this point. Abnormalities, in order of severity, which have been described are:

1 Mucosal erythema; increased vascular pattern; blurring of the squamo-columnar junction; friability of the junction (these are all often described as 'minor changes').

2 The mucosal erosion (or mucosal break)—a discrete area of reddening, usually round or oval.

3 Erosion with exudate—as above but with part or all of the erosion covered in yellowish material.

4 Linear erosions—longitudinal erosions, often slightly irregular, usually on the summit of a mucosal fold (Plate 6b,c).

5 'Confluent' erosions—linear erosions joined across a mucosal valley (Plate 6a).

6 Circumferential erosions—erosions which cover the whole circumference of the oesophagus.

7 Ulcer—a mucosal break with a perceptible depth of at least 3 mm, usually containing slough.

8 Columnar-lined oesophagus (CLO)—a segment of metaplastic epithelium extending from the gastro-oesophageal sphincter, redder and fleshier than normal squamous mucosa. This may be in the form of tongues, strands or a continuous cylinder; traditionally an extent of 3 cm or more above the oesophago-gastro junction has been required for the term, but new work (on abnormalities of the junction itself) has raised questions about this.

These abnormalities are not always easy to distinguish; few observer-variation studies have been done, and recent observations suggest that even experienced endoscopists differ in their interpretation of these appearances, particularly the less severe ones.

Infective oesophagitis

Oesophageal infection is uncommon. By far the most frequent infection encountered

is moniliasis (candida), characterized by white–yellow cheesy plaques. Herpes simplex causes multiple small vesicles or shallow ulcers (Plate 7). Cytomegalovirus can produce deep linear ulcers, the viral origin diagnosed from characteristic histological appearances in biopsies. Other virus and fungal infections occur rarely.

Such infections are virtually never seen in fit people, and are predisposed to by age, immune failure, malnutrition and corticosteroid and antibiotic treatments. Patients with AIDS are particularly likely to develop them, and the human immuno-deficiency virus (HIV) itself can cause chronic ulceration.

Corrosive oesophagitis

Corrosive ingestion is fortunately uncommon in Britain, but occurs more frequently in developing countries where caustics are used for household cleaning purposes. Strong acid or alkali quickly causes death of the oesophageal mucosa, often over a wide area.

Endoscopy is an essential tool in assessing the extent and severity of damage and can be carried out safely with 48 hours of ingestion. Changes are graded (Table 9.2).

Stricture

Any form of oesophagitis, whether due to reflux, infection or corrosive ingestion, may result in a stricture. Strictures vary greatly in size—both their diameter and the degree to which they encroach on the normal lumen, and their longitudinal thickness.

A ring (Kramer–Schatzki) is thin longitudinally and also wide in diameter, and may easily be overlooked at endoscopy because it is only apparent when the lumen above and below is fully distended. It is also elastic and stretches easily.

Table 9.2 Endoscopic findings in oesophageal burns.

First degree (superficial)	Second degree (transmucosal)	Third degree (transmural)

Non-ulcerative oesophagitis
Mild mucosal erythema
   and oedema
	Shallow to deep ulceration
	   with possible extension to
	   muscularis
	White exudate
	Severe erythema
		Deep ulceration
		   with possible perforation
		Dusky or blackened
		   transmural tissue
		Little remaining mucosa
		Possible obliteration of lumen

More advanced strictures can narrow the lumen to a pin-hole, and their length varies, the longest resulting from the severe diffuse transmural inflammation which follows liquid corrosive ingestion (Plate 8).

The amount of visible mucosal inflammation related to the stricture is determined by the extent of continuing mucosal damage. Thus, corrosive strictures are usually not inflamed, while those resulting from reflux often continue to show the characteristic linear erosions extending above the stricture. The severity of active inflammation is as important as the diameter of the lumen in determining the amount of dysphagia experienced by the patient.

Hiatus hernia

A para-oesophageal (rolling) hernia may be difficult to appreciate endoscopically. It may cause extrinsic compression of the lower oesophagus, or be visible from the fundus with a retroflexed endoscope.

An axial (sliding) hernia is common, and is defined as a segment of stomach visible above the extrinsic compression caused by the diaphragmatic hiatus. Characteristically, the hiatus is visible as a tight narrowing with typical gastric folds running upwards from it to the mucosal gastro-oesophageal junction. It is not always so easy, problems being caused by:

1 a wide hiatus not readily appreciated as such;
2 effacement of gastric folds by over-inflation;
3 an obscure mucosal junction;
4 a Barrett's metaplastic epithelium in continuity with the gastric epithelium.

Motility disorders

The endoscope is not a good tool for diagnosing motility disorders, but the experienced endoscopist may observe some signs to suggest abnormalities of motility.

Widening of the lumen. This is most characteristically seen in achalasia where the lumen can become very capacious and contain food residue.

Absence of peristalsis. Peristaltic waves usually travel down the oesophagus when the patient swallows, or when inflation triggers secondary peristalsis. It may be observed that these do not occur.

Spasm. Multiple concentric rings, of varying diameter, may be seen partly to occlude the lumen along its length.

Narrowing of the cardia. The gastro-oesophageal sphincter usually closes the lumen

gently and it will open with insufflation and gentle advancement of the scope. If the sphincter is non-relaxing (as in achalasia) it may require firm pressure with the endoscope to open it.

Neoplasms

Neoplastic tumours will not be discussed in detail here. However, a neoplasm may cause symptoms similar to those of a motility disorder (especially achalasia) and endoscopy to ensure the absence of such a lesion is essential in the early stages of investigating such patients.

Benign tumours (mainly leiomyomas) have to become very large before causing symptoms, but small malignant growths can cause marked dysphagia. Any endoscopic suspicion will be supported by appropriate cytological and biopsy specimens for confident diagnosis.

Therapeutic endoscopy

Many therapeutic procedures can now be performed effectively and safely by endoscopy, although they require skill and practice. Detailed accounts may be found in books devoted to the topic, but a brief outline will be given here.

Foreign bodies

Swallowed objects may impact in the normal oesophagus but particularly do so if there is an organic narrowing (e.g. stricture or neoplasm) or disturbed motility. They can usually be removed using snares or specially designed forceps, sometimes utilizing an over-tube in the pharynx to facilitate frequent passages of the endoscope.

Bougie dilatation

Organic narrowings can be stretched by passing dilating bougies through them (Plate 9). Usually a guide wire is passed through the stricture under direct vision with the endoscope which is then withdrawn, leaving the wire in place to serve as a 'rail-road' over which bougies are passed. There are several designs of bougies. Usually several bougies of increasing diameter are passed up to the limit considered safe by the operator.

Balloons

Rubber balloons have been used for many years, predominantly for dilating the cardia in achalasia. The introduction of plastic balloons which distend only to a

likelihood of causing perforation at the time, or over-stretching the sphincter leading to reflux at a later time.

Strictures

Balloons can be used instead of bougies to dilate strictures. Balloons of up to 20 mm are used, usually passed 'through the scope' (TTS) and dilatation performed under direct vision. This is a convenient technique but the effectiveness may be slightly less than an equivalent bougie, and balloons are a lot more expensive, so for everyday use bougies are preferred.

Botulinum toxin injection

The toxin from the bacterium *Cl. botulinum* blocks cholinergic nerve conduction and is used frequently to treat blepharospasm and torticollis. It was found that injection of the toxin into the gastro-oesophageal sphincter was an effective treatment for achalasia, and several studies have been published to confirm this. The technique is not difficult, 100 units of toxin being divided between four to eight injection sites around the gastro-oesophageal junction using a standard endoscope needle passed down the operating channel. The results are variable, less predictable and of shorter duration than balloon dilatation.

Percutaneous endoscopic gastrostomy (PEG)

Specially designed kits are available which allow a narrow tube to be passed through the abdominal wall into the stomach where a balloon or flange holds it in place. The endoscope is used to guide the procedure. Through the gastrostomy nutrients can be inserted—continuously if necessary—to support patients' nutrition even if they cannot swallow. It has become a popular technique mainly for neurological problems (such as motor neurone disease or stroke) causing progressive difficulty with the oro-pharyngeal component of swallowing, but it may have uses in any type of swallowing disorder provided that the endoscope can be passed.

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10 Provocation tests

John S. de Caestecker

Introduction

Oesophageal provocation tests are used in an attempt to reproduce symptoms which are believed to arise from the oesophagus since it is rare for these to arise spontaneously in the context of a static oesophageal manometry study. The most usual symptoms prompting investigation are heartburn or non-specific chest pain (perhaps resembling angina). Since the advent of ambulatory oesophageal pH monitoring, there has been less requirement for a test to provoke heartburn. The oldest (recently rediscovered) test is oesophageal balloon distension; the best established and probably still the most useful is oesophageal acid perfusion. The most recent have been a number of pharmacological agents which provoke both symptoms and changes in oesophageal motility.

For any of these manoeuvres being performed for chest pain of undetermined origin, continuous 12-lead electrocardiographic monitoring is an important precaution to ensure that any provoked pain is not due to cardiac ischaemia.

Oesophageal balloon distension

Balloons have a long history of application to the study of oesophageal pain [1]. The use of oesophageal balloons has recently been revived [2–4] after a long lapse, perhaps resulting from the observation that patients with documented ischaemic heart disease could not differentiate between the pain of their exertional angina and that induced by oesophageal balloon distension (despite the lack of electrocardiographic changes during balloon induced pain) [5]. These reservations persist [6]. Oesophageal balloon distension can reproduce pain in 40–60% of patients with non-cardiac chest pain suspected to be of oesophageal origin [3,4]. Furthermore, patients with chest pain tend to get symptoms at lower balloon distension volumes (Fig. 10.1), providing evidence that these individuals have increased oesophageal sensitivity to stretch [3].

Rapid balloon inflation characteristically produces a characteristic proximal stimulation both at and above the balloon with distal inhibition resulting in aboral traction [7,8] (Fig. 10.2). Deschner and colleagues have pointed out that up to
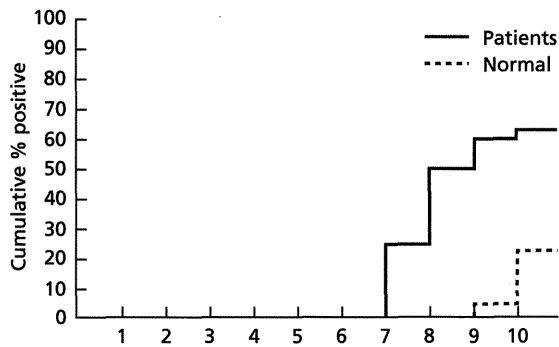
Fig. 10.1 Balloon volumes at which intra-oesophageal distension was perceived as painful. The solid line represents patients with chest pain of undetermined origin, and dashed line healthy controls. The threshold in 50% of patients is below the minimal threshold for controls (9 ml air). (From reference [3].)
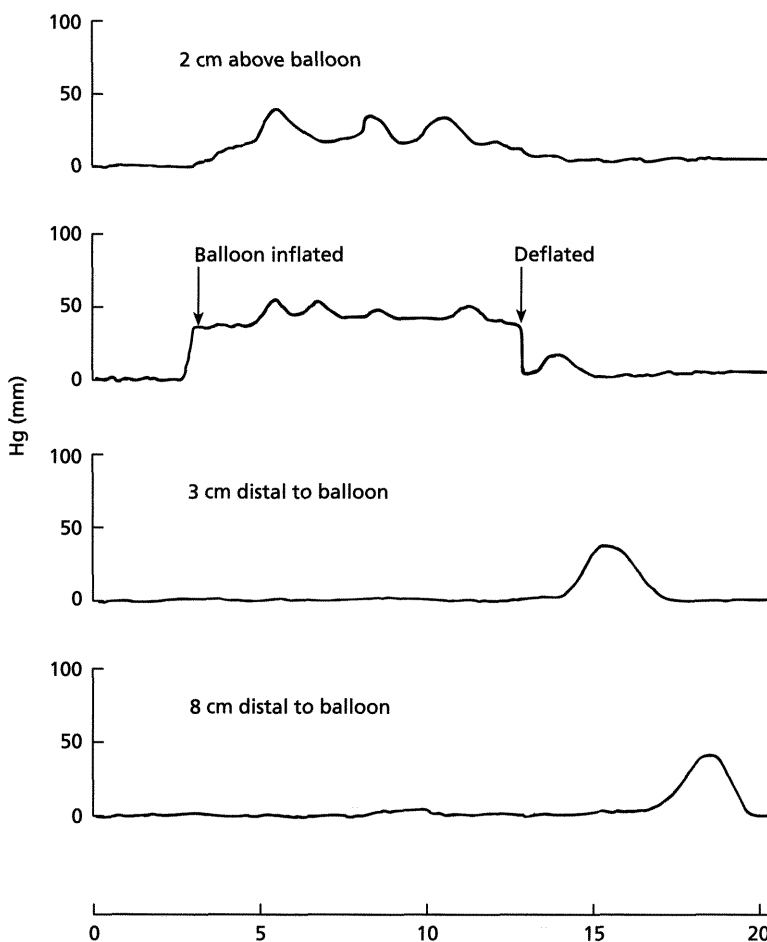
Fig. 10.2 Schematic representation of normal manometric response to intra-oesophageal balloon inflation. Sustained contraction immediately above the balloon (lead 2) produces an aboral traction force. Proximal motor activity does not cross the balloon and motor activity is conspicuously absent distally. A secondary peristaltic wave occurs once the balloon is deflated, beginning at the level of the balloon.
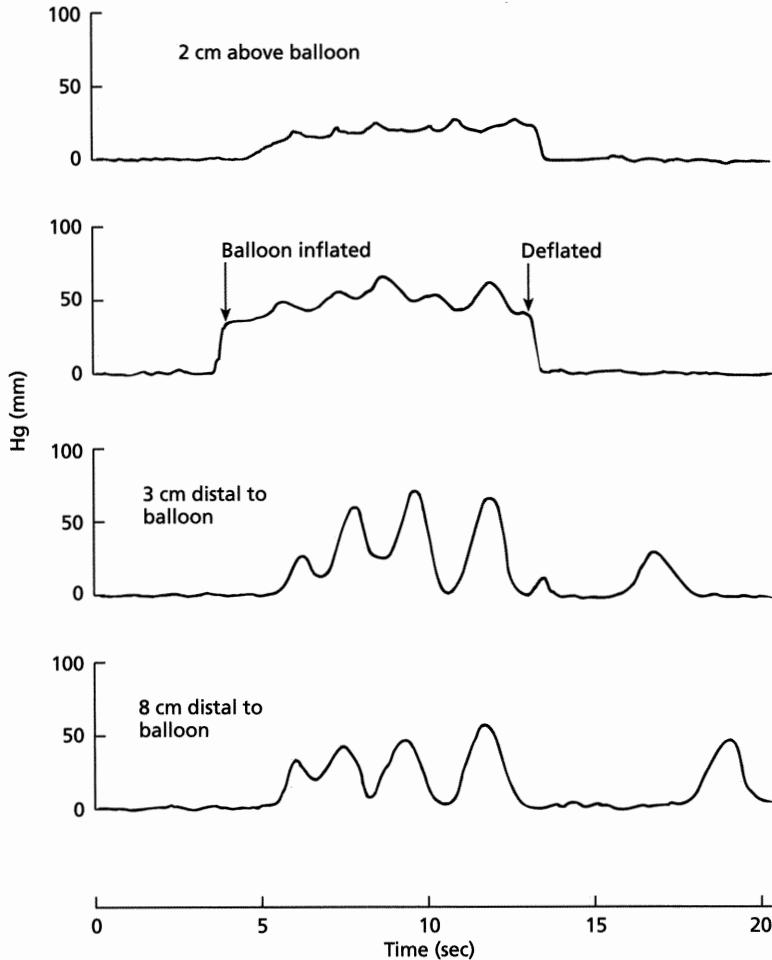
Fig. 10.3 Schematic representation of abnormal response to balloon distension with spasm-like simultaneous waves in the leads distal to the balloon.

60% of patients with chest pain of uncertain origin show failure of distal inhibition during balloon distension, and in 42% this was associated with reproduction of the patients' typical chest pain [4] (Fig. 10.3). Disturbances of the oesophageal response to balloon distension have also been described among patients with dysphagia [9].

There exists a relationship between stimulus intensity and duration for the production of oesophageal pain by balloon distension [10]. This implies that a rapid rate of distension might lower the threshold of stimulus intensity below which pain could not be elicited. Thus the distension threshold for chest pain may be different if a balloon is inflated slowly or rapidly.

Cerebral evoked potentials have been recorded in response to oesophageal balloon distension (Fig. 10.4), and differences in amplitudes of evoked potentials
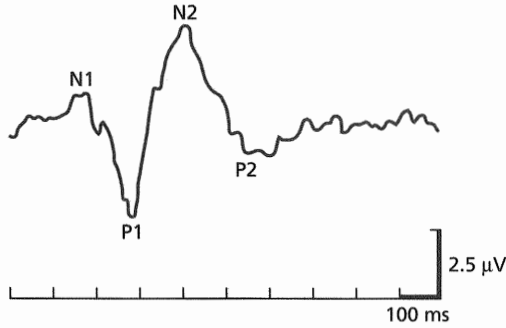
Fig. 10.4 Configuration of cerebral evoked potentials recorded after oesophageal balloon distension in a healthy subject at the point of pain perception. These are averaged signals recorded from 50 very rapid balloon inflations and deflations. Typically, there are two peaks (N1 and N2) and two troughs (P1 and P2). (From reference [11].)

have been found between patients with chest pain and controls [11]. Although this technique adds an objective measure, the technique is not simple and requires a mechanism for very rapid repetitive balloon inflation and deflation. It has not as yet found a role in clinical studies outside the context of research.

Balloon inflation

Equipment

In studies from Castell's group [2,3], a latex balloon approximately 3 cm long was mounted on a standard multilumen oesophageal motility catheter straddling one of the perfused recording channels filled with air (Fig. 10.5); the balloon may be made up from finger cots provided they are made airtight with silicone glue and silk thread. Custom made balloons are now available commercially (Wilson-Cook, UK Ltd).

Fig. 10.5 An inflated 3 cm long latex balloon attached over one of the recording channels of a standard Arndorfer multilumen oesophageal manometry catheter.

Procedure

The balloon, sited 10 cm above the lower oesophageal sphincter, is rapidly (<2 seconds) inflated with air in 1 ml stepped increments maintained for 10 seconds, with complete deflation between steps [2]. The inflations should be randomly interspersed with sham inflations. The end points are the first occurrence of any sensation ('perception threshold') and the point at which the sensation becomes definitely unpleasant or uncomfortable ('pain threshold'). In order not to prompt the patient, a card with categories of sensation should be used and the patient asked to point to the category appropriate to what they are feeling (Table 10.1). It is important that as far as possible the same protocol is adhered to for all studies (though the exact procedure can differ from the one suggested here), as it has been demonstrated that distractions, patient expectation and type of inflation protocol (e.g. random inflations versus stepped inflations) can all alter the pain thresholds [12].

The procedure should be repeated twice and the volume of air recorded for each threshold. Intra-balloon pressure can easily be measured if the balloon channel is connected to an external pressure transducer, but in clinical studies its measurement is not critical. If it is desired to test whether the patient's oesophageal sensory threshold is lowered, a range of values for normal controls is best established in each laboratory since the exact size and compliance of the balloon material used may affect these parameters.

Interpretation of results and potential pitfalls

A positive test requires the reproduction of the patient's usual chest pain. Any other discomfort cannot be regarded as a positive test. The electrocardiogram should show no changes.

Table 10.1 An example of a scale to score sensation evoked by oesophageal balloon distension.

Score	Quality of sensation
0	No sensation
1	Slight sensation, not constant or definite
2	Definite sensation
3	Strong sensation, not uncomfortable
4	Uncomfortable sensation, definitely becoming painful
5	Painful but tolerable
6	Severe intolerable pain

A lower than 'normal' threshold may indicate that the patient has an abnormally sensitive oesophagus. Before this is ascribed to idiopathic sensitization of the oesophageal pain pathways, symptomatic gastro-oesophageal reflux *must* be excluded, as this has been shown to lower the distension threshold [13].

Whether recording of oesophageal motility above and below the site of balloon distension to detect abnormalities of the distension reflex improves the sensitivity and specificity of the test is unclear. Deschner and colleagues have suggested that detection of such abnormalities is useful [4].

It should be borne in mind that it is likely that stretch receptors in the mediastinum may also be stimulated by this manoeuvre; since patients with ischaemic heart disease find it difficult in some cases to differentiate the pain of oesophageal distension from their spontaneous angina [5], the specificity of the test must remain in some doubt.

Perfusion tests

Perfusion tests include iced water, which induces pain but also aperistalsis of the oesophagus [14]. Hypertonic (20%) glucose has been found to precipitate pain in 14% of patients with chest pain of uncertain origin, despite a lack of effect on distal oesophageal motility [15]. Neither of these tests are commonly used in the context of chest pain of uncertain origin.

Acid perfusion test

The acid perfusion test was originally described by Bernstein and Baker as a test for oesophagitis [16]. However, while it is now recognized that it is clearly neither a test for oesophagitis nor for gastro-oesophageal reflux, it does detect oesophageal acid sensitivity [17]. It is often positive in patients with symptomatic gastro-oesophageal reflux (whether presenting with typical heartburn or chest pain of uncertain origin) but may also provoke typical symptoms in patients with chest pain who do not have objective evidence of gastro-oesophageal reflux [18]. These patients may have an 'irritable oesophagus' [19] and indeed often also have a positive edrophonium test [18]. The test may be carried out with concomitant monitoring of oesophageal motility since, at least in patients with chest pain of uncertain origin, motility changes may be observed [18] (see Figs 10.6 and 10.7). Such changes are not observed in patients with simple gastro-oesophageal reflux [20]. In Bernstein and Baker's original description, the test included relief of symptoms by administration of an antacid [16]. It is clear that mere cessation of acid perfusion followed by saline perfusion does not reliably relieve the provoked symptoms [21] and this manoeuvre should not form part of the test.
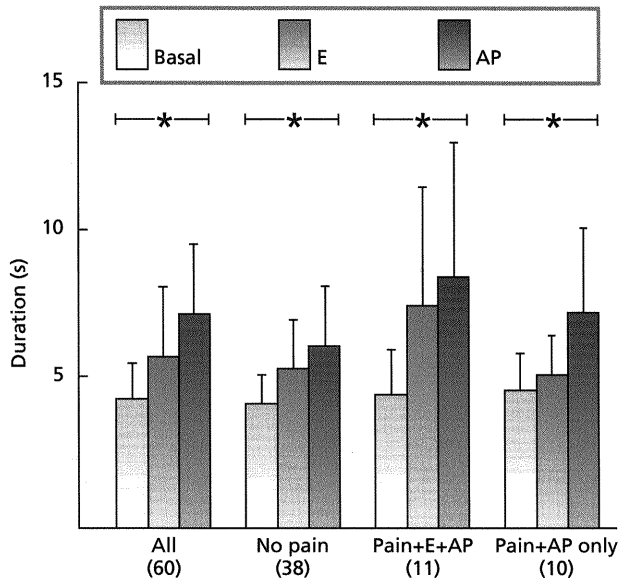
Fig. 10.6 Mean and sD of peristaltic duration during oesophageal manometry in 60 patients with chest pain of uncertain origin, grouped according to whether pain developed during edrophonium administration (E) and/or acid perfusion (AP). *P < 0.01 ANOVA. (From reference [18].)
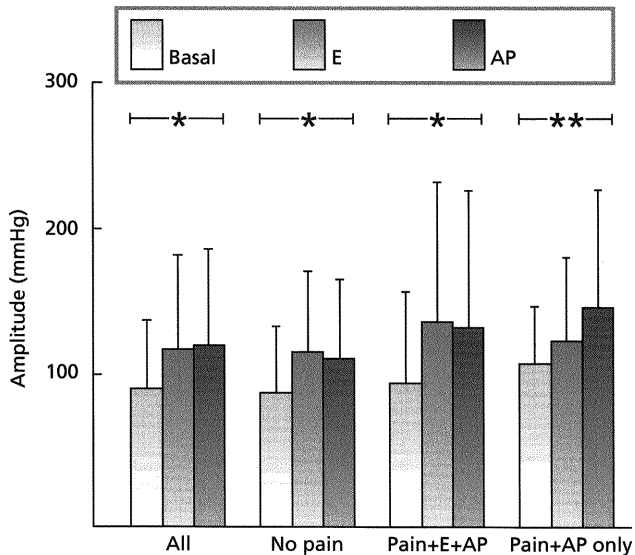
Fig. 10.7 Mean and sD peristaltic amplitude during oesophageal manometry in 60 patients with chest pain of uncertain origin. Groups as for Fig. 10.6. *P < 0.01; **P < 0.05 ANOVA. (From reference [18].)

Equipment

A naso-gastric tube is placed to lie in the mid-oesophagus, normally 30–35 cm from the nares [16]. As originally described, the patient should be sitting in a chair. However, the test is often carried out after oesophageal manometry, with the patient supine. Since the location of the lower oesophageal sphincter has been determined,

the tip of the manometry tube can be positioned 10 cm above this level. If it is desired to monitor oesophageal motility concurrently, two of the recording ports at or above this level can be used [18]. Perfusing solutions, 500 ml each of 0.9 M saline and 0.1 M hydrochloric acid between 20 and 37°C, should be attached using a 3-way tap to the central perfusion port of the oesophageal manometry catheter (or other ports if motility is being monitored) and positioned out of sight of the patient (usually behind them).

Protocol

There have been a number of different protocols of rate and duration of delivery of solutions. Although there are no data to suggest that one protocol is better than another, those using smaller volumes seem to detect few positive results [22], at least among patients with chest pain of uncertain origin. I therefore recommend the protocol adopted by Bennett and Atkinson who found it to discriminate well between cardiac and oesophageal chest pain [23].

Initially perfusion is begun with saline at a rate of 10 ml per minute (150 drops per minute using a standard intravenous administration set) for 10 minutes with the option of increasing to 20 ml per minute for a further 5 minutes. Without the patient's knowledge, the solution is then changed to 0.1 M hydrochloric acid at 10 ml per minute for 15 minutes, increasing if necessary to 20 ml per minute for a further 15 minutes. If positive, the two perfusions should be repeated to verify that the response was genuine [23].

Interpretation of results

A positive result requires reproducible reproduction of the patient's presenting symptom with acid but not saline. Usually if the presenting symptom is heartburn, the positive result will occur within 10–15 minutes. Pain will persist or worsen if the perfusion is continued. If the presenting symptom is chest pain and the patient develops heartburn (which the patient may or may not recognize as a familiar symptom), the result should be regarded as negative. Any patient developing symptoms with both acid and saline should be regarded as having an inconclusive test.

Patients with a presenting symptom of chest pain should have no changes on an electrocardiogram during the test. An electrocardiogram is rarely necessary in patients with a presenting symptom of heartburn.

If the test is positive in a patient with chest pain of uncertain origin, prolonged ambulatory oesophageal pH monitoring should be undertaken to exclude symptomatic gastro-oesophageal reflux.

Acid perfusion is not usually necessary in patients with heartburn, except where other tests have been inconclusive. Such a situation may arise when pH monitoring

shows quantitatively normal or borderline excess gastro-oesophageal reflux and the patient does not develop symptoms during the test (from which a symptom index calculation can be made).

Pharmacological agents

Pharmacological agents were identified on the basis of provocation of new manometric change, usually with symptoms. The most promising pharmacological agents to emerge have been ergometrine (referred to in the American literature as ergonovine) and cholinergic agents or cholinesterase inhibitors. The first was methylcholine, used as an adjunct to the diagnosis of achalasia. It is no longer used, due to an unacceptable side-effect profile.

Ergometrine/ergonovine

Ergometrine can provoke chest pain with oesophageal spasm. Alban Davies and his colleagues [24] were able to provoke pain and manometric change in 22 out of 42 patients with typical angina pectoris but normal coronary angiography, who developed oesophageal spasm with symptoms after ergometrine administration. Despite these encouraging findings, there has been an understandable reluctance to use ergometrine in the setting of an oesophageal motility study, because of the possibility of symptoms being the result of coincident coronary artery spasm and of rare, but serious, side-effects [25].

Bethanecol

Nostrant and colleagues were able to induce chest pain with a manometric change in 46% of 87 patients with chest pain after a single dose of 50 mg per kg body weight of the cholinergic agonist bethanecol given subcutaneously [26]. They found that administration of a second dose of bethanecol increased the proportion to 77%. Side-effects were frequent in patients receiving bethanechol, and recourse to atropine was not uncommon, which has perhaps tempered enthusiasm for the use of this drug.

Pentagastrin

Pentagastrin injected subcutaneously only reproduced chest pain with manometric change in one of 34 patients studied by Benjamin and colleagues [27]; thus this agent has not found any clinical role.

Edrophonium

London and colleagues found that the short acting anticholinesterase edrophonium reproduced chest pain with manometric change in all 10 patients in whom ergometrine had produced a similar response, suggesting that it might be as useful as ergometrine challenge [28]. The value of edrophonium has been confirmed in subsequent studies [22,27,29] with a positive response in about 30% of patients with chest pain. Increased rates of response were found using the higher dose of 10 mg [30]. Side-effects were more likely to be encountered with the higher dose, but were generally mild (light headedness, nausea, abdominal cramps) with occasional bradycardia and hypotension or laryngospasm [29]. If required, these unwanted effects are reversible with atropine. Richter and colleagues [29] found that the drug did not cause coronary artery spasm in patients with normal coronary arteries or coronary artery stenoses observed during coronary angiography.

In summary, ergometrine, bethanechol and edrophonium have been found the most useful pharmacological agents to provoke chest pain with motility disorders in patients with non-cardiac chest pain. Edrophonium has emerged as the most acceptable agent, because of its safety and mild side-effects, at doses between 80 mg per kg body weight and total dose of 10 mg.

Protocol—the edrophonium test

The most widely accepted protocol involves the injection of intravenous edrophonium at a dose of 80 μ per kg administered as a bolus over 5–10 seconds. A saline control injection is an important precaution against false positive responders. A positive response requires reproduction of chest pain. Some feel that new manometric change is required in addition [30], but since increased amplitude and duration of peristalsis (Figs 10.6 and 10.7) occur in both healthy controls and those patients not developing chest pain [29], this is probably unnecessary. Atropine must be available in case of intolerable or distressing cholinergic side-effects.

Since the only indication for this test is in patients with chest pain of uncertain origin, a normal electrocardiogram during provoked chest pain is essential. Although some patients with a positive response have an irritable oesophagus [19], doubt has recently been cast on the value of the test by a study reporting that the chance of a positive response was dependent on the patient's expectation of developing symptoms [31].

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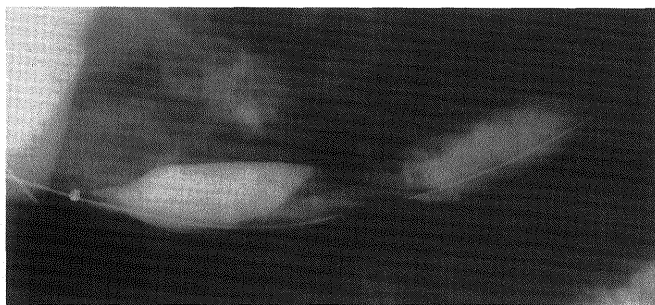
(a)

(b)

Fig. 9.2 Balloon being inflated in oesophageal stricture. (a) Partially dilated; the balloon is indented by the stricture. (b) Fully distended.

fixed maximum diameter has brought other uses, especially as the smaller ones can be passed through the operating channel of the endoscope and inflated under direct vision (Fig. 9.2a,b).

Achalasia

Stretching the non-relaxing gastro-oesophageal sphincter is an effective way to treat achalasia as an alternative to surgical division of the sphincter by cardiomyotomy.

Various balloons are still used, but most operators use the new plastic balloons of guaranteed maximum size. This is best done under radiological screening so that the characteristic waist caused in the partially inflated balloon can be seen and then obliterated. A 30 mm balloon is sufficient for most cases, but sometimes 35 or even 40 mm balloons are used. However, the larger balloons have a greater

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11 Gamma scintigraphy

Alan C. Perkins

Introduction

Unlike most other medical imaging modalities nuclear medicine techniques provide data on physiology rather than anatomy. Radiographic techniques such as the barium swallow and barium meal can provide information on structural abnormalities such as masses and mucosal lesions; however, their capacity for the investigation of functional abnormality is limited since they can only be used for the qualitative assessment of motility. Furthermore, the high density of radiographic contrast agents does not allow the observation of physiologically normal oesophageal motility. Nuclear medicine procedures have been applied extensively throughout the gastro-intestinal tract and possess the capacity to provide a great deal of quantitative information of clinical value to the gastro-enterologist. Oesophageal transit is a routine clinical procedure in nuclear medicine departments, the method being non-invasive and involving minimal discomfort to patients [1–6]. The incorporation of radiolabelled tracers into normal liquid drinks, solid foods and even pharmaceutical dosage forms such as tablets and capsules has provided important information on oesophageal motility.

The scintigraphic technique has been applied since the early 1970s [1,2]. It requires the administration of an appropriately radiolabelled formulation or compound which is imaged using a gamma camera. The camera can record a series of images capable of demonstrating the distribution of the radiolabelled product with time. The images obtained with the gamma camera lack the fine spatial resolution of some other imaging modalities such as magnetic resonance imaging (MRI), X-ray computerized tomography (CT) and ultrasound; however, scintigraphy does have the unique ability of functional quantification. No other imaging modality has the capacity to quantify the regional distribution of an administered product or compound, plot its kinetics with time and express it as a percentage of the administered dose.

This chapter describes the application of gamma scintigraphy in the investigation of oesophageal function as applied in both routine clinical practice and research.

Radiopharmaceuticals

A broad range of radiolabelled foods, liquid suspensions and pharmaceutical dose forms have been used for the investigation of the gastro-intestinal tract [7]. The study of oesophageal motility requires the incorporation of a suitable radiolabelled marker, usually Tc-99m or In-111, into a drink or food product. This enables the swallowing patterns of both liquids or solids to be observed. Non-absorbable compounds radiolabelled with Tc-99m are generally used to study oesophageal motility. Technetium-99m is the radiolabel of choice. This is produced from a molybdenum generator which is routinely available in the radiopharmacy unit of most nuclear medicine departments. It is a pure gamma emitter with a single gamma ray energy of 141 keV and a physical half-life of 6 hours. This results in a low radiation absorbed dose per investigation. Technetium-99m sulphur colloid has mainly been used in the past. This radiopharmaceutical was originally intended for intravenous administration for liver scanning; however, colloid liver imaging is no longer in widespread use. The main agent currently available is Tc-99m-tin colloid. Alternatively, Tc-99m-diethylenetriamine pentaacetic acid (DTPA) may be used as a marker. DTPA may also be radiolabelled with In-111. This radionuclide has a physical half-life of 2.8 days and two gamma ray energies of 171 and 245 keV. Radiation dosimetry is higher than that received with Tc-99m. Indium-111 is commonly used as a second radiolabel for dual radionuclide studies, for example when solid and liquid phase markers are required simultaneously as with the study of oesophageal motility, gastro-oesophageal reflux and gastric emptying.

The nature of the radiolabelled preparation can affect the result of the study [8]. In particular a more viscous material such as gelatin represents more of a challenge to the swallowing process. The use of a radiolabelled solid has been shown to be of greater value than manometry and radiography in the diagnosis of certain clinical conditions [9].

Imaging technique

The technique requires minimal patient preparation. A summary of the procedure is given in Table 11.1. A minimum of a 3-hour fast is recommended prior to the study. The examination may be performed with the patient positioned either erect or supine; however, the supine position is advocated for maximum sensitivity, since this eliminates the effect of gravity on oesophageal clearance [5]. Transit has been found to be more rapid when the study is performed in the upright position. The method of dosing is extremely important. Instructing the patient to make a continuous sequence of swallows or alternatively to pause between swallows may lead to different peristaltic contractions and hence different patterns of transit. It is

Table 11.1 The scintigraphic technique for the measurement of oesophageal motility.

Radiopharmaceutical
10–15 MBq Tc-99m non-absorbable marker, e.g. tin colloid or DTPA administered in 10–20 ml water

Effective radiation dose
Tc-99 m, 0.022mSv/MBq (equivalent to 0.3 mSv for 15 MBq administered activity)

Patient preparation
3–4 hour fast

Patient position
Supine or erect with the gamma camera positioned to include the oro-pharynx and upper stomach (diagnostic studies are normally undertaken with the patient in a supine position)

Administration
The solution is given through a straw and the patient asked to hold the solution in the mouth. The images are started as the patient is asked to swallow. The patient should then perform dry swallows every 30 seconds to clear any retained activity from the oro-pharynx

Image acquisition
Anterior dynamic images in 64×64 image matrix of 0.5 second's duration for 2 minutes followed by slower frame rate over a total imaging time of 10 minutes

Image processing
The dynamic images are viewed to determine the position of the oro-pharynx, oesophagus and stomach. Regions of interest are defined to include the upper, mid and lower third of the oesophagus. Time activity curves are produced for each region. The condensed image format is the most suitable display format for the image data

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DTPA, Tc-99m-dimercaptosuccinic acid.

important to standardize the study procedure to obtain consistent and reproducible results.

The procedure should be fully explained to the patient to relieve any anxiety and to ensure good compliance with the test. A practice swallow with 10 ml water is useful prior to the commencement of the study. The radiopharmaceutical should be administered into the mouth using a syringe with a plastic tip or quill. The solution is placed in the patient's mouth and the patient asked not to swallow. The computer acquisition is started and the patient instructed to swallow the test solution followed by dry swallows every thirty seconds. The patient then remains still under the camera until the data have been collected. The images may then be recorded continuously for a period of 10–15 minutes or intermittently over a few hours in the study of gastro-oesophageal reflux.

A gamma camera having a large field of view is required to ensure inclusion of the entire oesophagus from the oro-pharynx to the lower oesophageal sphincter

and fundus of the stomach. Clinical systems having either a circular or rectangular field of view with a diameter or width of at least 40 cm are generally suitable. Images recorded in a 64 × 64 matrix are adequate for studies of oesophageal motility. The frame acquisition rate may vary from centre to centre. It is necessary to include rapid short frames of 0.2–0.5 seconds' duration over the first 2 minutes to determine the pattern of bolus transport followed by frames of longer duration of, for example, 5–20 seconds over a total time of 10 minutes. A suggested protocol would be 60 × 0.5 second frames followed by 38 × 15 second frames to give a total 10 minute study period. The images may then be viewed as a dynamic sequence to observe the passage of the activity from the mouth to the stomach. Since there is some variability in the occurrence of patient symptoms it is recommended that the procedure is repeated before the investigation is finished [10]. Once the integrity of the images has been checked the patient is allowed to leave. It is good practice to archive the image data prior to undertaking any data analysis.

Data analysis

The images may be displayed on the computer screen or image work station in either black and white, or using a colour display, to observe the passage of the tracer from the mouth to the stomach. A colour display is usually preferred since this provides the maximum range of information available from the image data. The lower threshold and upper saturation levels (window) of the colour display should be altered to show any activity which may be retained in the oesophagus. The dynamic sequence of images may be viewed as a series of individual frames or they may be shown in a rapid sequence to provide a ciné display.

In situations where the transit is not significantly delayed a simple measurement of the bolus transit time through the oesophagus may be made by observing the position of the activity in each of the frames in the study. This would simply be given by:

Oesophageal transit time = $(F_{st} - F_{oro}) \times F_d$ seconds

where: F_{st} = frame number when activity is observed in the stomach; F_{oro} = frame number when activity is in oro-pharynx; and F_d = the duration of each frame in the dynamic sequence in seconds.

Further analysis may be undertaken by adding the pixel values in the whole sequence of frames to produce a summed image (Plate 10). This will provide an image of the oro-pharynx, oesophagus and stomach and may then be used to define regions of interest (ROI) to identify the position of the upper and lower limits of the oesophagus. The oesophagus is commonly divided into three regions to define the upper, mid and lower portions. Once the ROIs have been defined the count rates within the regions for each frame in the study may be calculated to

produce time activity curves. Once the curves have been generated it is possible to separate the rapid component of the main bolus and the residual component according to a two component model. It is also feasible to calculate a mean transit time for the swallowed activity [11].

The preferred method of display is the computer generated condensed image format [12,13]. A schematic diagram of the production of the condensed images is given in Fig. 11.1. The display is produced by adding the count rates in the collected data across the image matrix to produce a single column of data one pixel wide for each frame. By placing all columns of data in sequence from left to right the condensed image is produced. This has the advantage of providing both positional and temporal information in a single graphical plot. Lateral movement from left to right or right to left is of no interest, hence movement from the mouth to the stomach is shown in the vertical axis and time is displayed along the horizontal axis.

Interpretation

Scintigraphic studies of the oesophageal motility have been well investigated and validated for the investigation of motor dysfunction, dysphagia, heartburn and chest pain [14–19]. The technique is sensitive for the detection of the major disorders of oesophageal function including achalasia and scleroderma. Oesophageal spasm, stasis and gastric reflux can be detected with a high degree of accuracy. Less severe motility disorders such as lower oesophageal sphincter and non-specific motor disorders are less easily determined due to the lack of any clear difference with normal transit.

Once swallowing occurs the constricting peristaltic wave takes the majority of the contents into the stomach, the remainder being cleared by secondary waves. A normal swallow would result in the administered activity rapidly entering the stomach. An example of a normal study is given in Plate 11. Normal transit is considered to occur within 15 seconds. Once in the stomach the activity may be seen to oscillate slightly up and down due to respiratory motion of the stomach. Following quantification up to 10% of the bolus may be retained in the lower oesophagus in normals. In cases of abnormal motility the activity will be retained within the oesophagus. This may be seen as a variety of patterns of swallowing, stasis and retrograde movement of the tracer.

In cases of oesophageal spasm, for example in achalasia, the activity will oscillate up and down (Plate 12). Achalasia may be differentiated from scleroderma by repeating the procedure in the upright position [3]. The test is also of value in the follow-up of patients with achalasia after treatment [20]. Gastro-oesophageal reflux may also be identified as activity enters the stomach and subsequently passes back into the oesophagus [21,22].
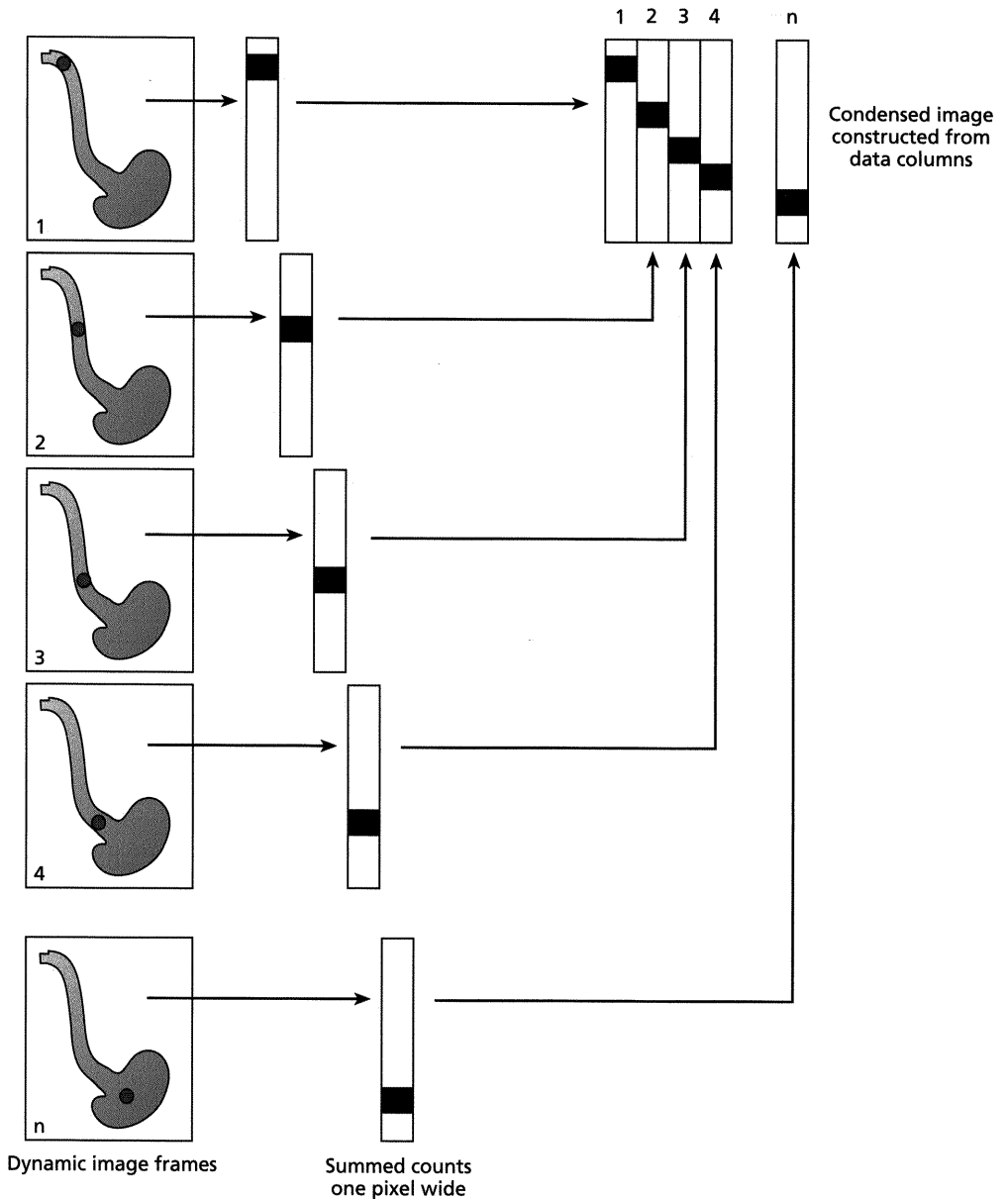
Fig. 11.1 Schematic diagram showing the generation of the condensed image display. Count rates are summed in the horizontal direction for each frame in the image to give a column of data one pixel wide. The columns are then placed in increasing frame order to form the condensed image. This is now the accepted method for presentation of scintigraphic studies of oesophageal transit.

Research applications

The ease of the procedure together with the low radiation dosimetry makes oesophageal scintigraphy a suitable research tool for use in specific patient groups [22] including children [23] and for investigation in normal subjects [24]. The technique has been used in a range of clinical conditions; however, it is perhaps not used as widely as would be expected. A logical extension of the diagnostic technique is in the assessment of the transit of oral dose formulations such as tablets and capsules. For example, the method has previously been used to examine the influence of posture and co-administration of water on swallowing patterns [7].

The scintigraphic technique is especially important in the study of patient populations at high risk of oesophagitis through long-term medication of drugs with potential for causing mucosal injury. This has been observed with a wide range of substances including tetracycline, emepronium bromide, slow release potassium chloride and NSAIDs. Most injuries are seen in the mid–lower oesophagus, where it has been shown that certain formulations tend to lodge [25]. Prolonged mucosal contact of many drugs may be toxic through a range of mechanisms including low or high pH as well as high osmolarity [26–28]. This leads to the importance of the shape and size of tablets and capsules on the swallowing of oral medications [29].

The author has previously undertaken such studies to compare the transit of tablet and capsule formulations [30]. A prerequisite of the technique is the satisfactory radiolabelling of the formulation under investigation. For such purposes it is essential that the radiolabelling does not adversely affect the contact surface or properties of the preparation. Tablets and capsules may be radiolabelled by the administration of radiolabelled ion exchange resins. Tablets can be clamped and drilled at one edge using a 1.5 mm diameter drill bit sterilized with alcohol and the hole filled with radiolabelled resin. Radiolabelling of capsules may be performed by the addition of 5 mg Tc-99m-labelled amberlite resin to the contents, replacing the cap and inverting to mix the contents. In each case units should be weighed prior to and after radiolabelling. Examples of different swallowing patterns of tablets and capsules observed in the same subject are given in Plates 13 and 14.

The technique is also well suited to the investigation of the retention of medicinal products such as cough mixtures and antacids which are intended to coat the oesophagus. An example of a radiolabelled formulation showing coating of the oesophagus is given in Plate 15. This shows a uniform deposition of tracer along the length of the oesophagus throughout the period of the study. Views may be recorded over many hours to assess the duration of action of such preparations.

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detector which is placed externally over the oesophagus to monitor the reflux of radiolabelled food in ambulant subjects. Although the detector cannot image reflux episodes it detects the amount of radiolabel which is refluxed within its window.

Equipment

The equipment consists of a highly collimated cadmium telluride detector which is worn in a harness on the chest wall (Fig. 12.1). The gamma detector uses a collimator which is designed to register the counts from radiolabelled food which is refluxed, but excludes counts from the stomach. This detector can be used in conjunction with a glass oesophageal pH electrode to study the correlation between acid and food reflux. Both the gamma detector and pH probe are attached to a small, dual-channel, battery-powered solid state recorder which can be worn on a belt.

Procedure

A test meal is administered to the subject which is labelled with a suitable dose of technetium-99m, usually in the form of tin colloid added to egg prior to cooking. The labelling technique is similar to that described for standard gastric emptying studies (see Chapter 11). Although data can be gathered for up to 24 hours, the test meal normally has a 50% residence time in the stomach of only $2.4\,h \pm 0.38\,h$ [10], and therefore measurements typically extend to 4–5 hours.
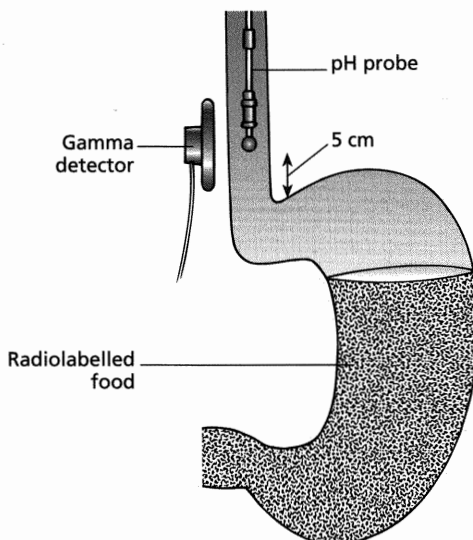
Fig. 12.1 Relative positions of the oesophageal gamma detector and pH probe to each other. The gamma detector measures the amount of gamma radiolabel as it is refluxed past it.

12 Ambulatory scintigraphy

Neena Washington

Introduction

The use of ambulatory gamma monitoring for the investigation of gastro-oesophageal reflux is still relatively novel; however, the more traditional technique of gamma scintigraphy has been used as early as 1982 to study this disease [1]. Early scintigraphic studies assumed that the refluxed material was merely acidified food, and that the addition of a radiolabel to the food would allow a non-invasive method of detecting reflux, conferring an immediate advantage over 24-hour pH monitoring. Unfortunately, scintigraphy demonstrated a surprising lack of correlation between the reflux of radiolabelled food and/or drink and acid reflux detected by the accepted 'gold-standard' of pH monitoring. This led to the conclusion by Seibert and co-workers in 1983 that scintigraphy simply was not sensitive enough to detect the reflux phenomenon [2].

Later studies demonstrated that the use of acidified food increased the correlation of food and acid reflux, leading to the conclusion that gamma scintigraphy was detecting the reflux of neutral materials which could not be detected by pH monitoring [3,4]. By 1986, largely due to the work of Kaul and co-workers, scintigraphic reflux could be detected in 92% and 79% of the patients with and without histological evidence of oesophagitis, respectively [5]. By 1990, the lack of correlation between pH monitoring and reflux of radiolabelled gastric contents as measured by scintigraphy became accepted, and the conclusion was drawn that extended pH monitoring and scintigraphy measured different pathophysiological phenomena detecting reflux under different conditions [6,7]. It has been suggested that the two tests are complementary and that they may be of greatest value when used together to enhance the sensitivity and specificity of the diagnostic evaluation [6].

It is known that restricting a patient's movement, for example, in a hospital situation, reduces the number of reflux episodes observed when compared with patients allowed to resume normal daily activities, and hence ambulatory tests for the measurement of 24-hour oesophageal pH are now the norm [8,9]. A major drawback with the use of gamma scintigraphy to monitor reflux is that the patients are required to be still as the images are acquired. In Nottingham, we are pioneering the technique of using a small, highly collimated, portable gamma

Studies from healthy volunteers

Figure 12.2 shows typical simultaneous food and acid reflux obtained from the technique in a healthy volunteer. A study of 37 subjects (Fig. 12.3) revealed that simultaneous food and acid reflux occurred for less than 1% of the recording time which is in general agreement with earlier scintigraphic studies. The time the oesophageal pH fell below 4 was 3.2 (+8.6/–2.3)% (mean ± SD) of the recording time. Food reflux alone occurred for 17.8 (+53.2/–13.8)% of the recording time. Not every reflux event detected by a fall in pH was seen as an increase in counts as a result of reflux of food, and vice versa. Another interesting finding is that the majority of food reflux does not occur immediately after ingestion of a meal, but 1–2 hours later, a phenomenon which has also been reported by Bennett [11].

Studies in patients with endoscopically proven oesophagitis

Similar patterns of reflux were observed in a group of 12 patients with endoscopic evidence of reflux oesophagitis (Fig. 12.4). This study was the first to use the combined techniques of pH monitoring and gamma monitoring in patients with endoscopically proven grades I and II oesophagitis. As with previous studies carried out in volunteer subjects, food and acid reflux events were found to occur independently of each other [12,13]. The patients with grades I and II oesophagitis
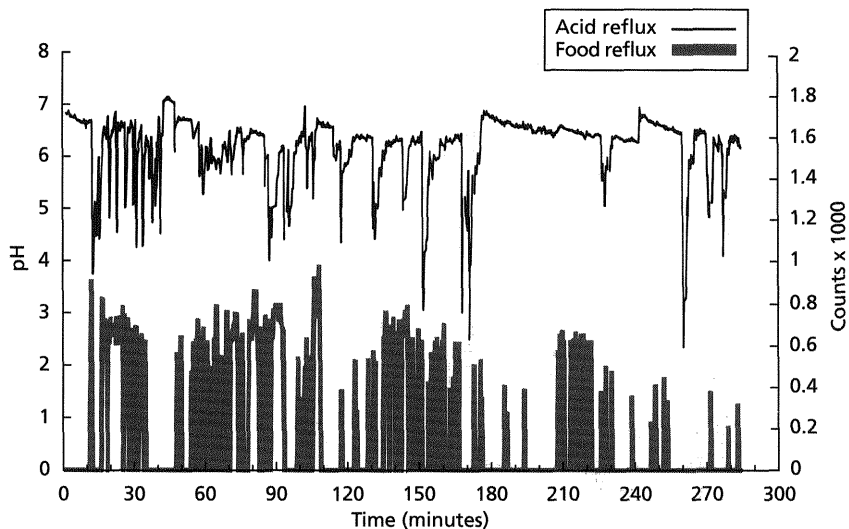
Fig. 12.2 Typical trace showing food (thicker grey line) and acid reflux (thinner black line) from one normal volunteer.
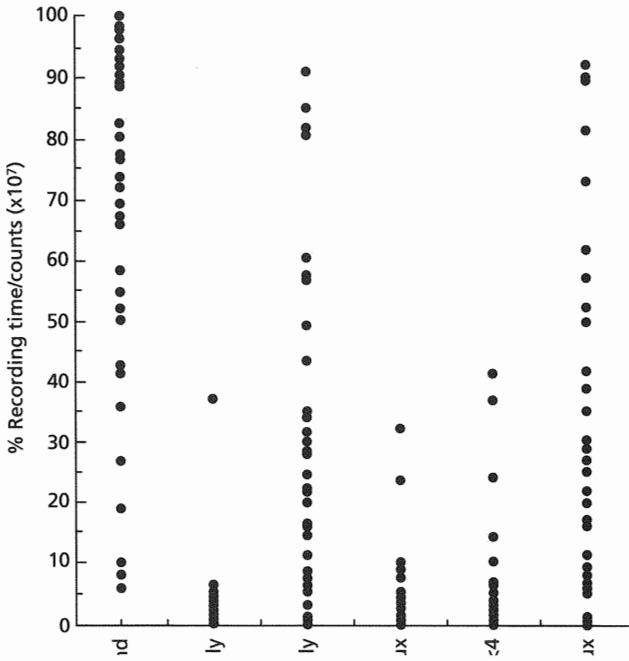
Fig. 12.3 Data from 37 healthy volunteers examining the spread of values for food and acid reflux.
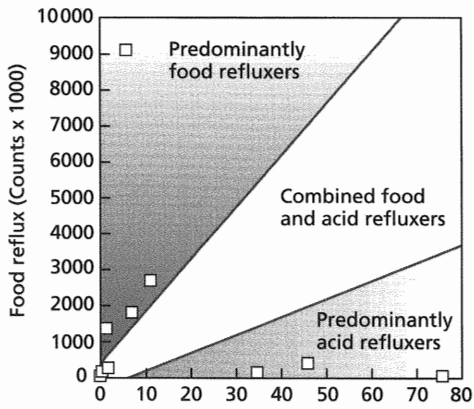
Fig. 12.4 Correlation of food and acid reflux from 12 patients with grades I–III oesophagitis.
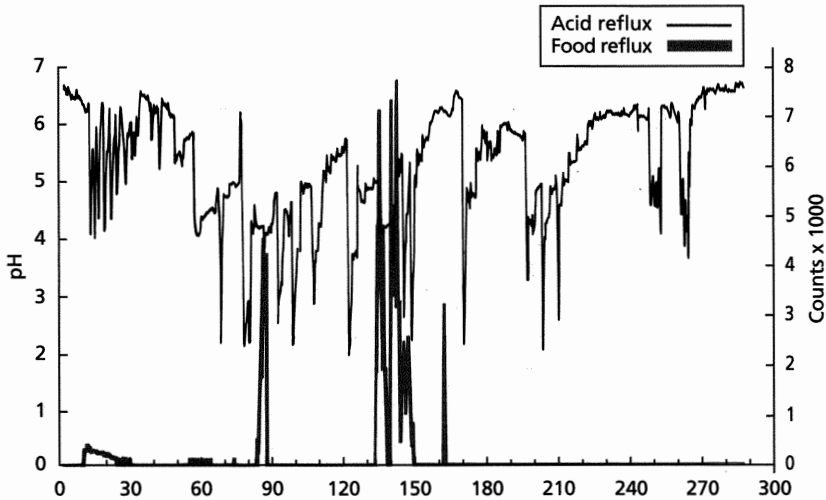
Fig. 12.5 Trace from a patient with grade II oesophagitis showing classical patterns of acid reflux with fewer, but large episodes of food reflux.

refluxed acid for approximately 15% of a post-prandial period, whereas healthy volunteers refluxed acid for 3% of the 4-hour post-prandial recording time. Food reflux occurs for 21% of the post-prandial period compared with 18% in healthy volunteers. Only four of the group demonstrated classical patterns of post-prandial acid reflux associated with this disease (Fig. 12.5), but interestingly, two patients with endoscopically proven oesophagitis did not reflux acid during the post-prandial period and four others refluxed acid for less than 5% of the recording time (Fig. 12.6). This wide variation could be attributed to several factors:

1 These patients could be mainly nocturnal acid refluxers.

2 The meal did not contain the exact ingredients which stimulated reflux for each particular patient. It may be necessary to use patient questionnaires to identify the foods which precipitate the onset of symptoms.

3 Reflux disease is cyclical and can have periods of relative quiescence. Generally, the period of symptoms is triggered by a particular event such as eating a food which is a stimulant of reflux or overeating or over indulgence in alcohol, etc.

Implications of the findings from ambulatory gamma monitoring

The independent reflux of food and acid observed using the technique of ambulatory gamma detection is supported by Shay and co-workers [14] and Vandenplas and co-workers [15]. Shay's group concluded that the two methods agreed in only 25% of total reflux events. Scintigraphy was superior for the detection of reflux of
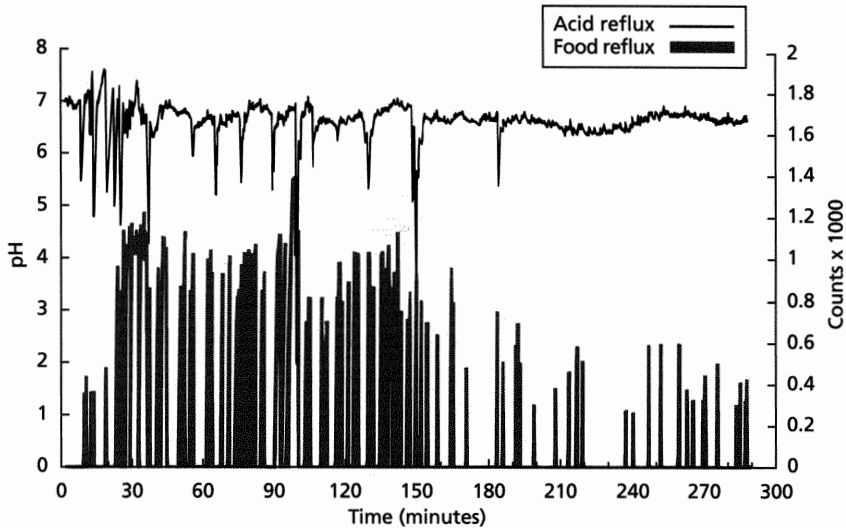
Fig. 12.6 Trace from a patient with grade I oesophagitis showing normal acid reflux with numerous small episodes of food reflux.

buffered gastric contents and detection of additional reflux events during acid clearing intervals, whereas only the pH probe detected reflux events after gastric emptying had occurred. Vandenplas's group reported that out of 123 reflux episodes recorded with both techniques, only six occurred simultaneously. Significantly more reflux episodes were recorded by scintigraphy, particularly during the first half-hour period ($n = 62$), when compared with the number of pH drops greater than 1 unit, even at pH levels higher than 4 ($n = 41$; $P < 0.05$). Scintigraphy has been shown to be superior to pH monitoring in the detection of reflux of gastric contents resulting in aspiration pneumonia in tube-fed elderly patients [16] and pulmonary aspiration of gastric contents in asthmatic adults [17], again demonstrating differences in food and acid reflux. In 1984, Cargill in France found that scintigraphy could be used to evaluate the reflux of food in the development of pulmonary disorders [18].

The most likely interpretation of the results from the cadmium telluride detector studies, and those performed using scintigraphy, is that the poor correlation of food and acid reflux implies incomplete mixing of the two within the stomach. Recent evidence using magnetic resonance imaging has clearly demonstrated that food and liquid form two distinct layers in the fundus of the stomach where there is very little in the way of motility patterns which could mix the two phases (Fig. 12.7) [19,20]. Formation of chyme, which is a homogeneous mixture of food, liquid and gastric secretions, occurs in the antrum from where it is emptied into the duodenum. This further highlights the inadequacy of reflux diagnosis methods that depend on pH detection alone.
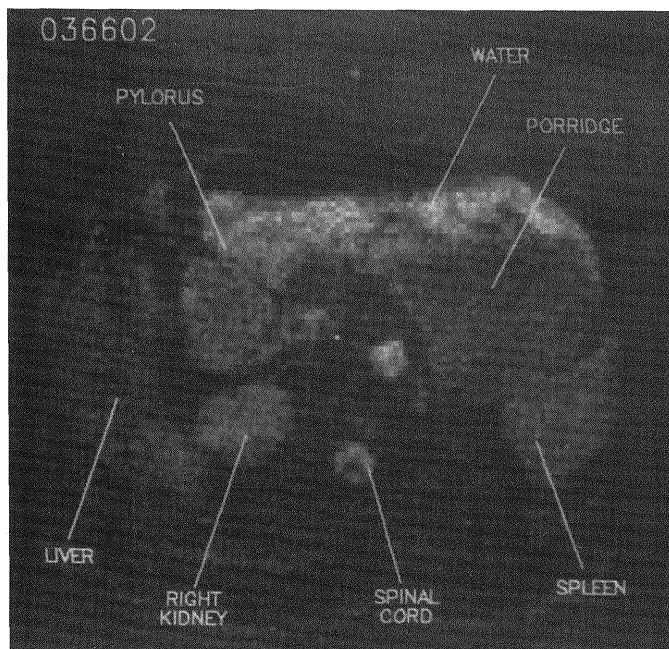
Fig. 12.7 Image of a cross-section through the stomach obtained by magnetic resonance imaging showing water floating on the porridge. Note that the subjects are supine. (Photograph kindly supplied by Mr Jeff Wright.)

The observation that food and acid reflux independently may shed some light onto patients who have reflux symptoms, but have normal patterns of acid reflux [21]. The potential variability of the refluxate was highlighted by Fiorucci [22], who suggested a division into three different types of oesophageal reflux: (i) acid refluxes, defined as a drop in oesophageal pH to values below 4 together with a gastric pH below 4; (ii) mixed refluxes, defined as a drop in oesophageal pH from baseline to values above 4 associated with rises in gastric pH above 4; (iii) alkaline refluxes, defined as a rise in oesophageal pH to above 7 associated with a simultaneous increase in gastric pH to above 4. It is often assumed that simultaneous increases in gastric and oesophageal pH indicate that bile reflux has occurred; however, recent evidence suggests that there is no correlation between oesophageal pH and the bile acid contents of the refluxate [23].

Although it is not disputed that acid plays a major role in the aetiology of gastro-oesophageal reflux disease, it has long been recognized that symptoms of reflux oesophagitis correlate poorly with both the results of 24-hour oesophageal pH and pressure monitoring and with the degree of endoscopic lesion [24]. To add a further dimension to the mystery, in recent years a small group of patients has been identified whose reflux disease is resistant to proton pump inhibitor therapy which is known to virtually abolish acid production [25]. It is possible that in this group

the major aggressive factor in the refluxate is not acid and this may be true of other reflux sufferers but to a lesser degree. Other components of refluxate, such as the gastric enzymes, e.g. pepsin, and biliary components from duodeno-gastric reflux, have all been implicated in oesophageal damage. However, the major problem is the collection and assay of these materials. Duodeno-gastric reflux is usually inferred from the occurrence of alkaline transients; however, it has been postulated that stimulation of saliva production by the presence of the catheter could be mistaken for alkaline reflux since this raises both oesophageal and gastric pH, as it is rich in bicarbonate [26]. Also, it is often speculated that increases in oesophageal pH above 7 are caused by an artefact when antimony electrodes are used. The methodological difficulties have given rise to conflicting reports in the literature as to the importance of duodeno-gastric bile reflux [27,28]. There is evidence, however, that the presence of duodeno-oesophageal reflux increases the frequency and changes the histological type of oesophageal cancer in nitrosamine-treated rats, suggesting that it plays a role in the development of oesophageal adenocarcinoma [29]. The cadmium telluride detector is currently being used to assess the reflux of bile using the radiolabelled tracer technetium-99m HIDA which is a bile imaging agent. This technique should be more sensitive and reliable than aspiration of oesophageal contents and pH monitoring.

Despite the fact that gastro-oesophageal reflux disease is a common problem with an estimated 12–36% of people experiencing heartburn at some point in their life, it still represents a major challenge in both diagnosis and therapy. The use of new techniques such as ambulatory gamma or pressure monitoring in conjunction with pH monitoring will give us greater insights into what was once considered a relatively simple disorder.

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13 Propulsive force

Mounes Dakkak

Introduction

There are several techniques available to assess oesophageal function of transporting food towards the stomach. They include radiology, scintigraphy and manometry. None of these techniques offers a direct assessment of the aboral force generated by the action of the smooth muscle of the oesophagus. The measurement of this force may offer further information in patients with dysphagia that cannot be obtained by other techniques.

Attempts have been made to measure oesophageal aboral forces by hanging weights, outside the body, on the catheter of an inflatable balloon [1–3], but this was cumbersome and only provided a crude assessment of the oesophageal aboral force. In 1972 Pope developed a transducer, consisting of a mercury-in-silastic strain gauge attached to a plastic sphere, which could be swallowed, allowing direct measurement of oesophageal forces for the first time [4]. Using the same concept, a more modern device devoid of mercury was commercially manufactured (Gaeltec Ltd, Scotland).

Definitions

The purpose of the measurement is to quantify the oesophageal peristaltic propulsive force which is exerted by the oesophageal smooth muscle on a bolus (represented by a balloon) as a result of a peristaltic wave induced by swallowing. The force is aboral (the direction is towards the stomach and away from the mouth). It was described by Pope and Horton in 1972 [4]. This is not the same as the oesophageal non-peristaltic propulsive force which was described by Winship and Zboralske in 1967 [3]. The Winship and Zboralske aboral force has been described as an oesophageal response to the distension of a balloon and not related to peristaltic activity. There does not appear to be any other work describing this force and we have failed to observe this force in our laboratory.

Equipment and procedures

Equipment

The device which is used to assess oesophageal propulsive force is a miniature transducer measuring 4.2 mm in diameter and 12 mm in length. It can easily be passed through the nostril and the pharynx down the oesophagus. It consists of an electronic strain gauge mounted on a catheter to which a silicone extension is attached by inelastic Kevlar threads (Fig. 13.1).

The transducer is supplied without a balloon or specific instructions. Different researchers in this field tend to attach a balloon in different ways and needless to say several sizes and designs of balloons have been employed. The balloon, which is used in this unit, is made of specialized silicone rubber which is resistant to distortion. This is attached to the end of the transducer and can be inflated through a catheter running alongside the assembly (Fig. 13.2).

The electrical output of the device needs to be amplified before being recorded on a polygraph chart (Fig. 13.3). In our department, the propulsive force and the peristaltic activity are recorded simultaneously on the same chart.

The transducer provides a linear relationship of output to applied traction force between 0 and 200 g. Regular calibration needs to be performed before and after each study, using known weights within the range of the transducer.
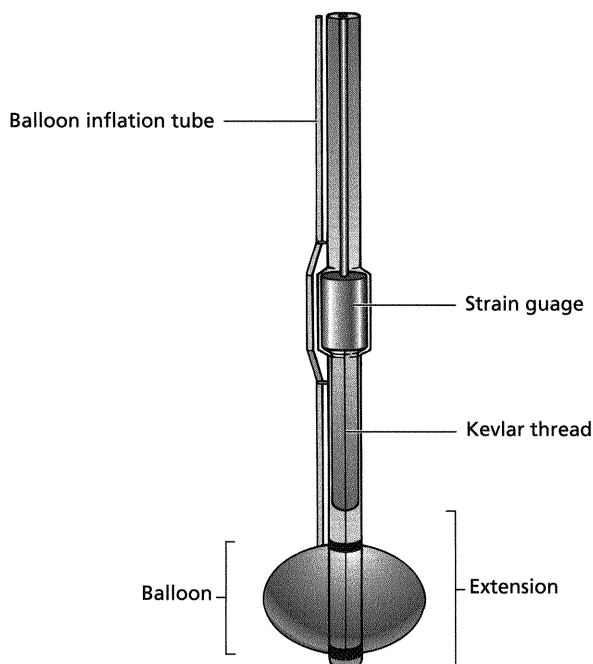
Fig. 13.1 The design of the propulsive force transducer.
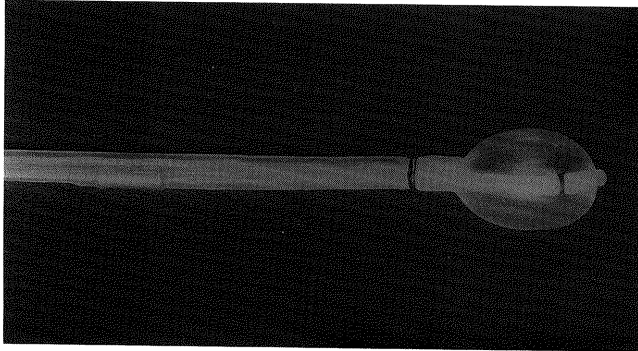
Fig. 13.2 The propulsive force transducer.
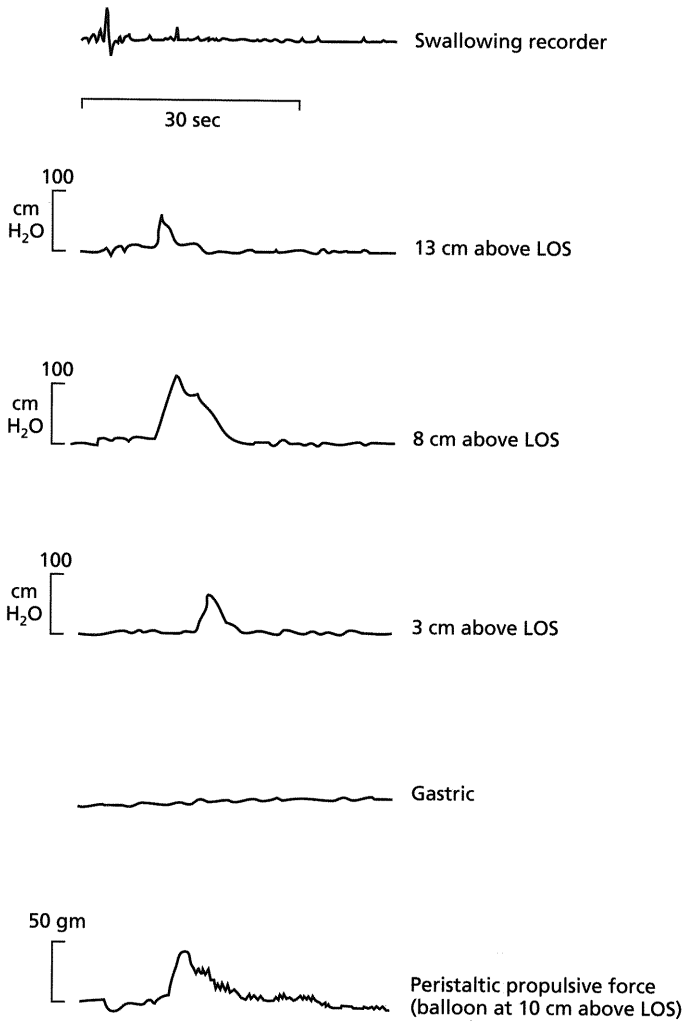
Fig. 13.3 A chart demonstrating a record of the propulsive force.

A standard manometric probe can be passed through the other nostril to provide simultaneous information about oesophageal peristalsis. We use a multilumen water perfused catheter. The catheter, which has several side holes 5 cm apart, is attached to a pneumo-hydraulic perfusion system. Each channel transmits pressure changes in the oesophagus, where the side hole is positioned. These are recorded on a polygraph chart.

Procedure: measuring the propulsive force

After the position of the lower oesophageal sphincter is established manometrically, the measurement of the oesophageal force is undertaken (Fig. 13.4).

When using the Manchester technique the balloon used is filled with an increasing volume of air. The diameter of the balloon may be difficult to predict if inflated with a standard volume of air when the rubber material of the balloon is altered. We prefer to rely on the actual diameter of the balloon, regardless of the volume of air or the type of rubber.

After the balloon is inflated at 5 cm above the sphincter to a diameter of 15 mm, the subject is given 5 ml of water and is asked to swallow. The force transducer will record any traction exerted on the balloon as a result of the swallow. This can be repeated at the same position with a balloon diameter of 20 mm and at 10 cm above the sphincter when the ballon can be inflated to 15 mm and 20 mm.

Interpretation of results

There are a few points to take into account when the propulsive force is interpreted.
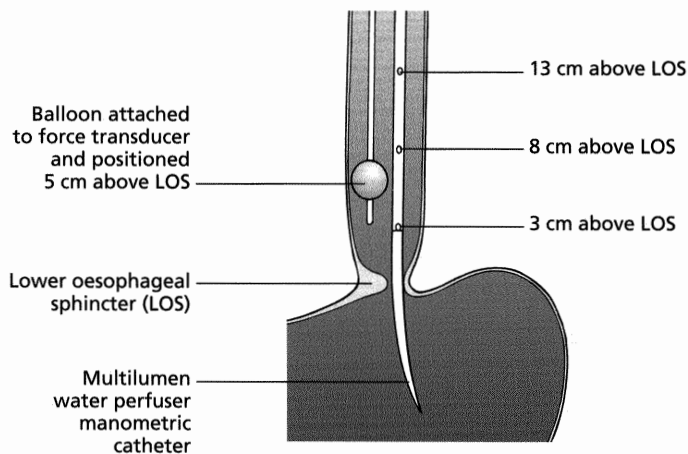
Fig. **13.4** The manometric catheter and the propulsive force transducer in the oesophagus.

Variability. The value of the peristaltic propulsive force is remarkably variable among individual subjects. There is great overlap between normal subjects and patients, thus making it very difficult to draw practical clinical conclusions in individual cases.

Balloon diameter. The peristaltic propulsive force is larger when the balloon diameter is increased.

Propulsive force and peristaltic activity. A poor correlation exists between the values of peristaltic propulsive force and the peristaltic wave amplitude.

Individual groups. The propulsive force is shown to be diminished in patients with oesophagitis [5] and also in patients with benign oesophageal stricture [6]. The force may recover after healing oesophagitis [7].

Discussion and clinical relevance

Traditional manometric studies have their limitations. Although they provide a measurement of oesophageal peristalsis, these peristaltic waves are produced by the circumferential squeeze of the oesophagus during its contraction. The peristaltic propulsive force is a direct measure of oesophageal peristaltic ability to move a bolus aborally. The inflammatory and fibrotic changes in patients with oesophagitis and benign oesophageal stricture are probably responsible for the lower propulsive force. In some cases of benign oesophageal stricture the propulsive force several centimetres above the stricture can be increased, probably reflecting the oesophageal muscle's attempt to overcome the stenosis.

Doubts were expressed in the past [8] that manometric intra-oesophageal pressures do not correlate with oesophageal clearance. It has been suggested that a peristaltic amplitude below a certain threshold may represent an ineffective peristaltic wave [9]. In our work, there was little relationship between peristaltic wave amplitude and the peristaltic propulsive force. This may reflect the fact that each of these parameters measured a different aspect of oesophageal peristaltic activity. It is uncertain which parameter provides a better indication of oesophageal peristaltic activity.

Although it is tempting to recommend radical changes in the way oesophageal peristaltic activity is recorded and to suggest a wide scale introduction of peristaltic propulsive force measurement, our work and that of other groups merely indicates that we now have another method to measure oesophageal motility. This is an alternative and not a substitute for traditional manometric techniques.

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Index

Alphabetization is letter-by-letter. Greek letters are ignored in alphabetization: δP is found under P. Page references in *italic* refer to illustrations; page numbers in **bold** refer to tables. Abbreviations used: LOS, lower oesophageal sphincter; UOS, upper oesophageal sphincter.