

STRENGTH AND FATIGUE OF THE RESPIRATORY MUSCLES
IN MAN

A thesis submitted to the Faculty of Medicine,
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by

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To my late father
Georgios and late uncle
Ioannis Pantazidis

ABSTRACT

The thesis concerns methods for measuring strength and quantifying weakness of the respiratory muscles in man and their relevance to patients. Techniques have also been developed to detect respiratory muscle fatigue.

Body position changes diaphragm length and configuration and hence the mechanical advantage of the respiratory muscles. Binding the abdomen was found to increase transdiaphragmatic pressure (P_{di}) during involuntary (twitches), but not voluntary manoeuvres (Sniffs). Voluntary manoeuvres i.e. Sniff and Static maximum inspiratory ($P_{I_{max}}$) and expiratory ($P_{E_{max}}$) pressures gave higher pressures in the seated position than supine.

Global strength of the respiratory muscles is reflected in the maximum inspiratory and expiratory static mouth pressures. The influence of mouthpiece design was studied in normal subjects and patients. A significant difference was found between a flanged versus a tube mouthpiece: the latter producing higher pressures. The differences are unlikely to be important clinically, provided the appropriate normal range is used. The flanged mouthpiece is more universally applicable.

Maximal voluntary Sniff is a useful manoeuvre to quantify global inspiratory muscle strength but

requires the passage of a balloon catheter to measure oesophageal pressures (Sniff Poes).

Studies were devised and demonstrated that global strength is accurately assessed by measurement of pressures in the upper airways namely in the nasopharynx (Sniff Pnp) and in the oropharynx (Sniff Pmo) during the sniff manoeuvre in both normal subjects and patients with inspiratory muscle weakness, provided lung function is normal.

Respiratory muscle fatigue has been investigated by monitoring Maximum Relaxation Rate (MRR) of Sniff Poes, Pnp and Pmo. It was shown that fatigue of the inspiratory muscles causes marked reduction in MRR of Sniff Poes as well as Sniff Pnp and Pmo. Therefore measurement of Pnp and Pmo pressures and MRR during a sniff may provide a clinically useful, non-invasive technique for quantifying strength and detecting and monitoring fatigue of the respiratory muscles in man.

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PUBLICATIONS

The work described in this thesis has in part been presented by the author at several meetings.

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Papers related to this thesis are:

1. Koulouris N, Mulvey D A, Laroche C M, Green M, Moxham J.
Comparison of two different mouthpieces for the measurement of P_Imax and P_Emax in normal and weak subjects.
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Eur. Respir. J. (submitted)

ABBREVIATIONS

AD - anteroposterior diameter

ATP, ADP, AMP - adenosine tri-, di-, monophosphate

Ca₂ - Calcium ions

Co₂ - Carbon dioxide

DLCO - Lung diffusing capacity for carbon monoxide

EMG - Electromyographic activity

F - Female

FEV₁ - Forced expiratory volume in one second

FRC - Functional Residual Capacity

FT - Fast muscle fibres

FVC - Forced vital capacity

Ht - Height

Hz - Hertz

KCO - Transfer factor

M - Male

MRR - Maximum Relaxation Rate

MVC - Maximum Voluntary Contraction

O₂ - Oxygen

p - Probability

Pdi - Transdiaphragmatic Pressure

Pgas - Gastric Pressure

PEmax - Maximum Static Expiratory Mouth Pressure

PImax - Maximum Static Inspiratory Mouth Pressure

Pnp - Nasopharyngeal Pressure

Pmo - Oropharyngeal Pressure

Pmus - Respiratory Muscle Pressure

PCO₂, PO₂ - Carbon dioxide and oxygen partial pressures

Pi - Inorganic phosphate

Prs - Elastic recoil of the lungs and chest wall

Pcr - Phosphocreatinine

Pst, L - Lung recoil pressure

r - correlation coefficient

SD - Standard Deviation

SE - Standard Error of the mean

SEE - Standard error of the estimate

Se - Seated posture

St - Slow muscle fibres

Su - Supine posture

30s - Semi-supine posture

U - Unbound abdomen

Wt - Weight

X - Mean

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CHAPTER 1

STRUCTURE AND FUNCTION OF THE RESPIRATORY MUSCLES

1.1 INTRODUCTION

Breathing like most other movements of the body depends on muscular action. Around the 3rd century B.C. one of the first known observers of this relationship, Erasistratus of Chios, who sometimes has been called the "Father of Physiology", believed the diaphragm to be the only muscle of breathing (Franklin, 1949). A few centuries later the remarkable Galen realised that not only the diaphragm but also intercostals and various accessory muscles were involved (May, 1968). Until the Renaissance no advances were made, but for Leonardo da Vinci in Italy who made the analogy between the action of breathing and that of a pair of bellows. Later in the 16th century, Vesalius the great Belgian anatomist, observed the movements of the lungs in the living dog by creating a pleural window with careful dissection (Foster, 1901). During the 17th century in England, John Mayow wrote a clear description of the breathing mechanism, (Mayow, 1907). In the 18th century two names stand out; G.E. Hamberger, who presented a geometric model of the action of the intercostal muscles (Hamberger, 1748) and Albrecht von Haller. Hamberger spent much of his efforts disputing with Haller mainly over the action of the internal intercostals. Controversy as to the detailed action of the respiratory muscles, especially of the intercostals, continued

throughout the 19th century. Guillaume Duchenne (1846) studied muscle action by electrical stimulation in both animals and humans (Duchenne, 1959). By this means he did much to clarify the action of the respiratory muscles, especially of the diaphragm. Since then these muscles have been increasingly neglected lying in a grey area, between anatomy and physiology. The description of their function in most textbooks of physiology and anatomy published in the last decade contain very little information and in some of them apologetically in small print (Cambell, Agostoni and Newsom-Davis, 1970; Lockhart, 1984). The respiratory system consists essentially of 2 parts, a gas-exchanging organ, the lung, and a pump to pump gas in and out the gas exchanging part, consisting of the respiratory muscles and chest wall. The lung and its diseases have traditionally been the focal point of interest, whereas pump disorders have received comparatively little attention. This is rather like a cardiologist who ignores the heart. It is surprising that this has happened, particularly because the ancient Greeks regarded the diaphragm as the seat of that part of the soul (Phrenes) that is connected with emotions, desires and sensations, both pleasant and painful. However the respiratory muscles function as a pump, as vital as the heart. Physiologists have recently devoted more attention to the mechanics of breathing and the relevance of the respiratory muscles has become increasingly apparent. For this reason, research on

respiratory muscles has accelerated during the last decade.

1.2 Histology of the Respiratory Muscles

Respiratory muscles are all skeletal muscles having similar fibre composition to the limb muscles. Fibre composition of respiratory muscles is an important factor for their endurance and contractile properties.

1.2.1 Fibre Composition

The classical distinction between red and white muscles (Ranvier, 1873) was based on fibre darkness which is related to their content of myoglobin and mitochondria but a classification of fibres on this basis has limitations. The myosin ATP-ase reaction which has been widely accepted, separates muscle fibres into two groups (Padukula and Herman, 1955). Those staining dark have been shown to possess the largest myosin and actomyosin ATP-ase activities and furthermore to be the fastest contracting as shown in several human experiments. Thus the two fibre types have been called fast (FT) and slow (ST) twitch fibres, respectively. Of the FT fibres, two subgroups named a and b have been identified (Brooke and Kaiser, 1970). With few exceptions, ST and FT fibres are evenly represented in the muscles, however, with a large inter-individual variation (Saltin and Gollnick, 1983). While ST fibres and one group of FT (FTa) show little fatigue with repetitive stimulation, the tension developed by the other type of FT (FTb) fibres is almost

eliminated after 3,000 contractions (Garget et al, 1979). Histochemical and biochemical determinations of oxidative and glycolytic capacity have shown that the ST fibres have the higher capacity for aerobic metabolism and have more capillaries per fibre. With subdivision of the FT fibres in two groups the FTa fibres appear to have the higher oxidative and lower glycolytic potential and to be surrounded by more capillaries. Athletes in endurance events tend to have a predominance of ST fibres and weight-lifters and sprinters to have a predominance of FT fibres. Indirect evidence using partially neuromuscular blocked muscles suggest that FT fibres have the larger electromyographic activity and also the higher mean power frequency when developing a given tension (Secher and Komi, 1984). Human intercostal muscles appear to have approximately 60% ST fibres. In the external intercostal muscles, the number of capillaries and occurrence of FTb fibres is similar to the other muscles. In contrast the internal intercostal muscles placed in the mid-axillary line have no FTb fibres and relatively many capillaries. Thus these expiratory muscles appear to be extensively used. The diaphragms of most mammals, including humans, are composed of all three fibre types. The diaphragm has a high percentage of fatigue-resistant muscle fibres, and most mammalian diaphragms are composed of approximately 60% ST fibres. For a given species, the diaphragm has a greater oxidative capacity and larger blood flow than those of limb muscles and is more resistant to fatigue.

The contractile properties of the diaphragm are predictable from the muscle fibre composition.

Adaptation to training and detraining, as has been observed in greater detail in limb muscles, also occurs in muscle fibres of the diaphragm (Secher, Mizuno and Saltin, 1984).

1.3 Anatomy of the Respiratory Muscles

The main respiratory muscles are the diaphragm, intercostal muscles and muscles of the abdominal wall. The accessory muscles of respiration include the sternomastoid and other muscles of the neck, back and shoulder girdle (Green and Moxham, 1983).

1.3.1 The Diaphragm

1.3.1.1 Anatomy of the Diaphragm

The diaphragm is a structural feature of the mammals (Agostoni and Sant'Abrogio, 1970) and is a complicated muscle anatomically. The main part dome-shaped with a large central fibrous tendon around which are arranged muscles of several fibre groups. These muscular fibres of the diaphragm are grouped into three parts: (i) the vertebral, (ii) the costal and (iii) the sternal. The vertebral fibres arise from the second and third lumbar vertebrae, from the medial arcuate ligaments (psoas) and from the lateral arcuate ligaments (quadratus lumborum). The costal fibres arise from the side and the upper margin of the lower six ribs, interdigitate

with those of the transversus abdominis. The sternal fibres arise from the back of the xiphoid process. All the fibres converge on the central tendon. The costal fibres which constitute the larger part of the diaphragm run directly upwards, parallel and "apposed" to the inner surface of the rib cage. This area of apposition represents up to one third of the surface area of the rib cage at end-expiration (FRC), but diminishes during inspiration (Mead, 1979). Both the origins and insertions of these costal fibres are mobile, and potentially move with respiration. By contrast the crural part does not move with respiration.

1.3.1.2 Innervation of the Diaphragm

Efferent Fibres. The cervical neuromeres contributing the motor fibres to the phrenic nerves are C3, C4 and C5 in man (Hamilton et al, 1962). The fibres coming from the upper segments innervate mainly the ventromedial part, those coming from the lower segments innervate the dorso-lateral part. The diaphragm however contracts as a unit (Sant'Abrogio et al, 1963).

Afferent Fibres. The afferent innervation of the diaphragm is supplied via the phrenic nerves except for the marginal part which is supplied by nerves coming from the T6 to T12 and most of the crura which are supplied by T12 (Rasmussen, 1952; Hamilton et al, 1962). The diaphragm contains relatively fewer sensory end-

organs, and there appear to be more tendon organs than muscle spindles (Corda et al, 1965). There are, however, afferent fibres in the phrenic nerve of the cat, and afferent traffic has been recorded. The paucity of end-organs may reflect the tendency of the diaphragm to contract uniformly so that relatively few sensory endings are necessary to sample accurately its function (Green, Mead and Sears, 1978).

1.3.1.3 Blood Supply to the Diaphragm

The diaphragm receives arterial blood from three major sources: (i) the internal mammary, (ii) the intercostal, and (iii) the inferior phrenic arteries. The superior phrenic, a small artery that lies against the phrenic nerve, also provides a modest portion of the arterial supply. Recently Comptois and colleagues have shown that there is a rich network of anastomotic connections between these vessels (Comptois, Corczyca and Grassino, 1987). These authors found that the internal mammary and phrenic arteries have head-to-head anastomoses, forming an internal arterial circle around the central tendon of the diaphragm. Collateral branches from this circle travel between diaphragm fibres, joining with branches of the intercostal arteries to form costophrenic arcades. Thus larger arteries run perpendicular to the muscle fibres, and arterioles again run at right angles to the muscle fibres. The small muscular arteries form anastomotic loops, except in the costal portion of the diaphragm. The arrangement of

1.3.1.3 large and intermediate size veins is similar to the arterial pattern (Bedd and Baxter, 1960). The anatomical arrangement of the vessels appears to prevent kinking of the blood vessels during diaphragmatic contraction. It has been found that the configuration and branching of the small arteries, arterioles and capillaries of the diaphragm were identical to that of two other skeletal muscles, namely the triceps and intercostals. (Schraufnagel et al, 1983).

1.3.1.4 Lymphatic Drainage of the Diaphragm

The diaphragm is provided with an extensive system of lymphatic vessels that not only remove interstitial fluids and cells from the diaphragm, but also play a major role in the removal of fluids and cells from both pleural and peritoneal cavities. These serous cavities are continuous with the lymphatic vessels of the diaphragm via open pores (stomata) that exist, on its surface. This organisation of lymphatic vessels provides a system of open channels through which fluids and cells may be rapidly removed from the serous cavities. Once fluids and cells are within the lymphatic vessels, contraction of the diaphragmatic muscle fibres would also cause contraction of the lymphatic collecting vessels, compressing their walls and thereby causing the contents to be expelled toward the larger collecting vessels (Leek and Rahil, 1978).

1.3.2 Intercostal Muscles

They are subdivided into two groups: (i) the external and (ii) internal intercostals.

1.3.2.1 Anatomy

The external intercostals extend from the tubercles of the ribs to the costochondral junction where they become continuous to the anterior intercostal membrane. They are thicker posteriorly than anteriorly (Bryce, 1923) and thicker than the internal intercostals (Johnston and Whillis, 1949). Their fibres slope obliquely downwards and forwards from the upper rib to the one below. The internal intercostals extend from the anterior end of the intercostal space to the angles of the ribs posteriorly, where they become continuous with the posterior intercostal membrane. They are thicker anteriorly than posteriorly. The fibres slope obliquely downwards and backwards. The internal intercostals can be subdivided into a posterior or interosseous portion where the ribs slope downwards and forwards and an anterior or intercartilaginous portion (the parasternals) where the costal cartilages slope upwards and forwards.

1.3.2.2 Innervation of the intercostal muscles

The intercostal nerves arise from the first to the twelfth thoracic segments, and are derived from the ventral primary ramus. In man, each main intercostal nerve, which supplies filaments to the intercostal muscles, lies deep to the internal intercostal muscle,

giving off a collateral branch early in its course, a lateral cutaneous branch and a terminal anterior cutaneous branch. The lower intercostal nerves, which supply the abdominal muscles after penetrating the diaphragm (to which they give a few sensory branches), freely communicate with one another over the abdominal wall (Davies, Gladstone and Sibbe, 1932). The intercostal muscles are well supplied with proprioceptors. Histological studies have demonstrated muscle spindles, tendon organs and Pacinian corpuscles (Barker, 1962).

1.3.2.3 Blood Supply to the Intercostal Muscles

The intercostal muscles are supplied by intercostal arteries and branches of the internal mammary arteries, and drained by intercostal veins and branches of internal mammary veins. The intercostal veins drain into the azygos and hemizygous system. As these systems are connected, blood in the azygos vein, which enters the superior vena cava on the right side, represents drainage from the intercostal muscles on both sides.

1.3.3 Abdominal Muscles

The abdominal cavity is bounded by anterior and posterior longitudinal muscles, which connect the thoracic cage to the pelvis and are contained within strong fascial sheaths, together with three muscle sheets which encircle the remainder of the abdomen.

1.3.3.1 Anatomy of the abdominal muscles

External oblique. This muscle arises from the outer surfaces of the lower eight ribs. It is therefore superficial to the intercostal muscles in the lower spaces. The dorsal fibres pass downwards to the iliac crest. The rest of muscle slopes obliquely downwards and forwards, and passes into a fibrous aponeurosis which forms part of the rectus sheath and fuses with its fellow from the other side in the linea alba. The lower border of the aponeurosis forms the inguinal ligament. The internal oblique. The internal oblique muscle passes from the lumbar fascia, iliac crest, and lateral part of the inguinal ligament to an extensive attachment along the costal margin to an aponeurosis contributing to the rectus sheath down to the pubis. The transversus abdominis. The transversus abdominis muscle arises from the costal cartilages of the lower six ribs, the lumbar fascia, the iliac crest and the lateral part of the inguinal ligament. The main part of the muscle passes horizontally forwards into an aponeurosis similar in extent to that of the external oblique. The transversus abdominis is the most deep of these muscles. The rectus abdominis. This covers the external surface of the thoracic cage as it passes vertically downwards from its horizontal line of attachment to the fifth, sixth, and seventh costal cartilages (occasionally the third and the fourth) to its tapering tendinous attachment to the

pubis. The rectus sheath enclose much of the muscle and is derived from aponeurosis of the three lateral muscles (Osmond, 1985).

1.3.3.2 Innervation of the Abdominal Muscles

The external oblique and the rectus abdominis are supplied by the lower 5 intercostal nerves (T7-11), the internal oblique and the transversus by the lower 5 intercostals, the subcostal (T12), the iliohypogastric (L1) and the ilioinguinal (L1) nerves.

1.3.3.3 Blood supply to abdominal muscles

Much less information is known about the arterial supply and venous drainage of the abdominal as well as for the rest of the respiratory muscles.

1.3.4 Accessory Muscles

Of all the so-called accessory muscles of respiration, only the sternomastoids, scaleni and triangularis sterni show significant respiratory activity in man (Cambell, 1954; De Troyer and Estenne, 1988).

1.3.4.1 The Sternomastoids

The sternomastoid arises by two heads from the manubrium sternum and the medial part of the clavicle. The fibres of these two heads fuse into a single one which is inserted into the mastoid process and the occipital bone. The muscle is supplied by the spinal accessory and second cervical nerves.

1.3.4.2 The Scaleni

The scaleni arise from the transverse process of the lower five cervical vertebrae and pass downwards to be inserted into the upper surface of the first rib (scalenus anterior and medius) and second rib (scalenus posterior). The scalenus medius is the largest. They are supplied by the lower five cervical nerves.

1.3.4.3 The Triangularis Sterni

The triangularis sterni fibres originate from the dorsal aspect of the caudal half of the sternum and insert into the inner surface of the costal cartilages of the 3rd to 7th rib. It's motor supply of the muscle comes from the intercostal nerves. It is a flat muscle that lies deep to the sternum and the parasternal intercostals (De Troyer and Estenne, 1988).

1.3.4.4 Other Muscles

There are many other muscles which may participate in the respiratory act. These are trapezius, pectoralis major, pectoralis minor, subclavius latissimus dorsi, serratus anterior, serratus posterior superior, serratus posterior inferior, quadratus lumborum and sacrospinalis. Most of these muscles are unlikely on anatomical grounds to be of importance in the mechanics of breathing (Campbell, 1970).

1.4 MECHANICAL ACTION OF THE RESPIRATORY MUSCLES

1.4.1 Action of the Diaphragm

The contraction of the diaphragm decreases the intrathoracic pressure, and increases the abdominal pressure in normal man. It seems obvious that these pressures are generated by the lowering of the diaphragmatic dome. On the other hand it is difficult to assess whether these effects are facilitated or hindered by the direct action of the diaphragm on the ribs (Cambell, 1970). This problem is a classical cause of arguments. Galen (May, 1968) considered that the diaphragm expands the rib cage, but this view was challenged by Borelli (1680) who reasoned that the diaphragm constricts it. Duchenne (1867) showed that the contraction of the diaphragm expands the rib cage provided that the normal relationships of the diaphragm are preserved and the abdomen is closed. Experiments in dogs have shown that the costal and crural portions of the diaphragm have different actions on the rib cage but the details of segmental innervation and regional activation of the human diaphragm are not wellknown (De Troyer et al, 1982). The shape of the normal human diaphragm at rest is an elliptical cylindroid capped by a dome. The cylindrical portion of the diaphragm apposed to the inner aspect of the lower rib cage and constitutes the "zone of apposition" of the diaphragm to the rib cage (Mead, 1979; Mead and Loring, 1982). The zone of apposition has important implications for diaphragmatic function because when the diaphragm contracts, increased tension within the diaphragmatic muscle fibres causes the

diaphragmatic dome to move caudal relative to its insertions. The fibres are directed axially in the direction of movement of the dome so there is a piston-like axial displacement of the diaphragmatic dome (Rochester, Arora and Braun, 1981; Loring and Mead, 1982). At lung volumes below ^{predicted} TLC in normal humans, the piston analogy probably holds, and the transdiaphragmatic pressure generated by the contracting diaphragm is a function principally of the neural activation of the diaphragm and the force-length and velocity force relationships of diaphragmatic muscle. These principles appear true for humans (Braun, Arora and Rochester, 1982; Rochester, Arora and Braun 1981) and dogs (Kim et al, 1976). When the diaphragm has shortened enough to eliminate the zone of apposition from part of the circumference of the rib cage, or when the apposed diaphragmatic fibres are not parallel to the thoracic axis, the piston analogy breaks down. Under these circumstances the diaphragm force reflects its radius of curvature and anisotropic tension within the diaphragmatic dome.

When the diaphragm contracts, it expands the thoracic cavity and tends to displace the abdominal viscera, resulting in lower pleural pressure and to increase abdominal pressure. The diaphragm also exerts a force at the site of its attachment to the rib cage, a force directed cranially. The fall in pleural pressure has an expiratory effect on the upper rib cage. Inward displacement of the upper rib cage is seen during

diaphragmatic inspiration in tetraplegic subjects (Danon et al, 1979; Mortola and Sant'Ambrogio, 1978; Urmey et al, 1981) and in subjects under spinal anaesthesia extending to T1 (Eisele et al, 1968). The diaphragmatic contraction has two inspiratory effects on the lower rib cage. The first of these has been termed the "appositional" component of the diaphragm's inspiratory action on the rib cage (De Troyer et al, 1982; Mead, 1979; Loring and Mead, 1982) and results from the increase in abdominal pressure acting on the lower rib cage. The second inspiratory effect has been termed the "insertional" component of the diaphragm's action on the rib cage. This force is in the direction of its fibres: towards the head. This force is inspiratory to the ribs, causing them to rotate up and out.

1.4.2 Lung Volume and Diaphragmatic Function

The length of diaphragmatic muscle fibres is closely related to lung volume (Mead and Loring, 1982) and therefore change in lung volume is accompanied by change in the operating length and hence the force of the diaphragm (Braun et al, 1982). The action of the diaphragm on the rib cage is also strongly dependent on lung volume. With increasing lung volume, the fraction of the rib cage exposed to pleural pressure increases as the fraction exposed to abdominal pressure decreases (Mead, 1979; Mead and Loring, 1982) reducing the diaphragm's inspiratory action on the rib cage and increasing its expiratory action through pleural pressure

(Loring and Mead, 1982). At very high volumes, the zone of apposition disappears, and the fibres of the diaphragm can pull inward on their insertions, causing a direct expiratory action on the lower rib cage (Hoover's sign). These effects have been demonstrated in animals (D'Angelo and Sant'Ambrogio, 1974; De Troyer et al, 1982; Sant'Ambrogio and Saibene, 1970).

1.4.3 Mechanical action of the rib cage muscles

To understand the action of particular muscles of the rib cage, we must understand the movement and articulation of ribs. The ribs move about axes defined by their articulation with the vertebral bodies and the transverse processes (Jordanoglou, 1969; Jordanoglou, 1970). The upper ribs rotate so that their anterior parts move cephalad and ventrally during inspiration, the so-called "pump-handle" motion of the ribs. The lower ribs have a prominent lateral as well as ventral movement during inspiration, the so-called "bucket-handle" motion. In the relaxed adult human, the ribs are angled down (Caudad) so that during inspiration, the lower and intermediate ribs move outward, away from the spine, providing an effective ventral and lateral expansion of the rib cage (Jordanoglou, 1969; Jordanoglou, 1970). It is now well established by a variety of studies that intercostal muscles move the rib cage. Patients who have undergone destruction of intercostal nerves on one side of the thorax for treatment of pulmonary tuberculosis, show less respiratory movement of the ribs on the

affected side (Alexander, 1929); in hemiplegic patients, outward displacement of the rib is reduced on the paralysed side (Fluck, 1966). In supine subjects with complete diaphragm paralysis rib cage displacements are exaggerated and belly wall displacements are paradoxical when the abdominal muscles remain relaxed (Kreitzer et al, 1978: Newsom-Davis et al, 1976; Skatrud et al, 1980). The function of the intercostal muscles has been a source of controversy throughout medical history (Cambell and Newsom-Davis, 1970). It is now commonly considered that external intercostal muscles and the interchondral part of the internal intercostal muscles (the parasternal muscles) are inspiratory and serve to raise the ribs, whereas the interosseous part of the internal intercostals are expiratory and act to lower the ribs.

1.4.4 Mechanical action of the abdominal muscles

The abdominal muscles have a number of functions: as rotators or flexors of the trunk, postural and respiratory functions. As respiratory muscles^{they} have expiratory functions as well as inspiratory ones. As expiratory muscles^{they} act in two ways: a) they pull the abdominal wall inward and produce an increase in intraabdominal pressure. Because the abdominal contents are incompressible, this causes the diaphragm to move cranially into the thoracic cavity. This contraction results in an increase in pleural pressure and a decrease

in lung volume. Therefore the abdominal muscles are considered to be powerful expiratory muscles assisting in such activities as forced expiration and coughing. The other function of the abdominal muscles in relation to breathing is to displace the rib cage, acting to pull the lower ribs down and inward, again an expiratory action (De Troyer et al, 1983). They assist inspiration in two ways: a) a direct facilitation of diaphragmatic action by persistent abdominal contraction, as occurs when normal humans adopt the standing position. Their activity is tonic, unrelated to phases of respiration and it is greatest in the dependent regions of the abdomen (Green, Mead and Sears, 1978; De Troyer, 1983; De Troyer, 1984) b) the second mechanism by which the abdominal muscles can assist inspiration is by contracting in phase with expiration. By contracting during expiration and forcing the diaphragm cranially into the thoracic cavity, these muscles can reduce lung volume below the neutral position of the respiratory system. Hence, when they relax at end-expiration, they promote passive descent of the diaphragm, therefore lung volume can increase before the onset of inspiratory muscle contraction. Thus, great activity of the abdominal muscles appears when the ventilation reaches 70-90 l/min (Cambell and Green, 1953; Cambell and Green, 1955; De Troyer and Estenne, 1988).

1.4.5 Mechanical action of the accessory muscles

Many of these muscles have prominently non-

respiratory functions, and many are relatively small or inaccessible. As a result, they have not been extensively studied by respiratory physiologists.

1.4.5.1 Scalene muscles

The importance of the scaleni as muscles of inspiration is disputed but it is now believed that they are true muscles of inspiration and should probably not be called "accessory" (Rapier et al, 1966; De Troyer and Estenne, 1984). Studies using needle electrodes show that the scalenes are active during quiet breathing in upright and supine postures. Others classify them with the sternomastoid as accessory muscles. By their origins and insertions, these muscles must elevate the first two ribs, and therefore, they may be inspiratory but their exact mode of action is not wellknown, because these muscles rarely if ever act individually.

1.4.5.2 Sternocleidomastoid muscles

It has been suggested that the human sternocleidomastoid muscles have a predominantly "pump-handle" action on the rib cage, elevating the first rib and sternum and allowing the resultant decrease in transthoracic pressure to cause inward displacement of the lateral rib cage and abdomen (Danon et al, 1979). The sternomastoids are probably the most important accessory muscles of inspiration and their participation in breathing with dyspnoea is a wellknown clinical observation.

1.4.5.3 The Triangularis Sterni

Most normal subjects when breathing at rest in the supine posture do not activate this muscle unlike cats and dogs (De Troyer et al, 1987). It always contracts during vigorous expiratory efforts such as coughing, laughing and during expiration below FRC. (De Troyer et al 1987; Ninan, Decramer and De Troyer, 1986). During such manoeuvres, the triangularis sterni acts to lower the ribs and increase pleural pressures.

1.4.5.4 Other Muscles

There are other muscles whose origins and insertions suggest that they may have a respiratory function under the right conditions. In particular the trapezii and the platysma as well as some laryngeal muscles contract during inspiration. Despite that they have been considered unimportant to the breathing in normal man (Cambell, 1970; Delhez and Petit, 1966).

1.5 PHYSIOLOGY OF THE RESPIRATORY MUSCLES

The respiratory muscles provide the motive power for breathing. Despite their central role in ventilation their physiology has been relatively neglected, perhaps partly because of the complexity of their function, and the difficulties of studying them (Green and Moxham, 1985). Statics and dynamics of contraction of these muscles are difficult to study in

vivo because force, initial length, velocity of shortening and magnitude of the neural drive of individual muscles are not measurable without invasive methods (Lockhart, 1984). Understanding of the function of the respiratory muscles depends on the relationships of frequency-force, length-tension, force-velocity and fatigability-frequency.

1.5.1 Frequency-pressure relationship

The force developed by a skeletal muscle is a function of the frequency of stimulation. The frequency-force relationships result from the summation of twitch tension during repeated stimulation. This relationship is useful in comparison of force development by different muscles and for the evaluation of high and low-frequency fatigue by the same muscle. Because, in vivo respiratory muscles are inaccessible for the measurement of force directly, their force is measured indirectly as measurement of the pressures generated by them. The frequency-force (pressure) curve for the respiratory muscles is similar to those of other human skeletal muscles. Using the technique of percutaneous stimulation over the motor point of the sternomastoid muscle, it is possible to describe in humans the function of the sternomastoid in the same terms as those used to describe the function of limb skeletal muscles. Similar frequency-force curves were recorded from a strain gauge applied to the mastoid process and from a force transducer (Moxham et al, 1980). The recording of Pdi in

response to electrical stimulation of the right phrenic nerve allows a similar myogram to be obtained from the diaphragm (Moxham et al, 1981; Aubier et al, 1981). When the diaphragm becomes fatigued, its frequency-pressure curve is depressed at all stimulation frequencies.

1.5.2 Force-length relationship

The force-length relationship indicates that when a muscle is stimulated at its optimal resting length, it produces its maximum contractile force. When the muscle is either stretched beyond the optimal resting length or alternatively is foreshortened prior to contraction, supramaximal stimulation of the muscle produces submaximal force. In the case of the diaphragm, there is little or no evidence for compromise of its contractile force by over stretching, but at lung volumes above normal FRC, the diaphragm and other inspiratory muscles are foreshortened and their contractile force is curtailed. In contrast, expiratory muscle contraction force is curtailed at low lung volumes (Marshall, 1962; Evanich, Franco and Lourenco, 1973; Brown, Arora and Rochester, 1982; McCully and Faulkner, 1983; Farkas and Roussos, 1984; Fitch and McComas, 1985; Loring, Mead and Griscom, 1985; Road et al, 1986; Smith and Bellemare, 1987.

1.5.3 Force-velocity relationship

For any muscle length, the maximum contractile force is greatest when the muscle is prevented from

shortening. If the muscle is allowed to shorten during its contraction, its contractile force declines hyperbolically as a function of the velocity with which the muscle shortens. This is termed the force-velocity relationship (Hill, 1938; Wilkie, 1950; Goldman et al, 1978). When both the tension and velocity are normalised to the maximum value, slow muscles show greater curvature than fast muscles. So, this implies that type I (ST) fibres generate less power output than type II (FT). The force-velocity relationship of the diaphragm muscle is intermediate between those of slow (type I) and fast (type II) skeletal muscles (Edwards and Faulkner, 1985).

1.6 RESPIRATORY MUSCLE WEAKNESS

The respiratory muscles are subject to weakness from a variety of processes which affect the motor nerves, neuromuscular junction and muscle cell per se.

1.6.1 Causes of respiratory muscle weakness

Some of the important clinical disorders affecting respiratory muscles are listed below (Pride, 1984):

1. Neuromuscular disease

- a. Neurogenic

- Traumatic teraplegia
- Motor neurone disease
- Poliomyelitis

- b. Neuromuscular junction

- Myasthenia gravis

- c. Muscles

- Dystrophies
- Myotonia
- Polymyositis
- Systemic lupus erythematosus

- 2. Impaired function of respiratory muscles

- a. Metabolic - Endocrine

- Cachexia
- Hypoxia, Hypercapnia
- Thyroid disease, hypocalcemia

- b. "Mechanical"

- Hyperinflation: severe airflow obstruction
- Chest wall diseases: i.e. kyphoscoliosis, obesity, thoracoplasty, pneumonectomy
- Impaired coupling between inspiratory muscles and lung expansion: pleural disease, pneumothorax.

1.6.2 Effect of respiratory muscles weakness on lung volumes

Weakness of these muscles reduces the capacity to generate the negative intrathoracic pressure to expand the lungs with a reduction in total lung capacity (TLC) and a parallel fall in vital capacity (VC). Weakness of

the muscles of expiration, principally the abdominal musculature and the internal intercostals, reduces the capacity to generate positive intrathoracic pressures. This weakness reduces expiratory reserve volume, increases residual volume, and further reduces vital capacity. In these patients the FEV_1/FVC ratio is normal, illustrating a pure restrictive ventilatory defect and the residual volume (RV)/total lung capacity (TLC) ratio is characteristically high. Gas transfer corrected for the reduced lung volume (KCO) is normal or high, and a low KCO implies that muscle weakness is unlikely to be the sole explanation of a respiratory problem (Moxham, 1982).

1.6.3 Effect of respiratory muscle weakness on lung mechanics

Moderate weakness of the inspiratory muscles prevents lung recoil pressure (P_{st} , L) from being developed at full inflation and therefore truncates the upper part of the static pressure-volume (PV) curve of the lung. However in patients with long-standing and severe respiratory muscle weakness pulmonary compliance is reduced also, (De Troyer, Borenstein and Cordier, 1980; De Troyer and Deisser, 1981; Gibson et al, 1977), indicating that the elastic properties of the lung are altered in these patients. The cause of this reduced lung distensibility is not clear. Three factors are theoretically capable of affecting lung compliance (i) dispersed alveolar collapse, undetectable by radiographic

techniques (Prys-Roberts et al, 1967) (ii) generalised increase in the surface tension of the alveolar lining layer (Young, Tierney and Clements, 1970) and (iii) shortening and stiffening of the elastic fibres within the lungs.

1.6.4 Chest wall mechanics in respiratory muscle weakness

Several pathogenic mechanisms are involved in malfunction of the chest wall in patients with neuromuscular disorders. As noted before, FRC is frequently decreased in these patients. It has been suggested that the fall in FRC in these conditions is caused primarily by a decrease in the outward pull of the chest wall. Several studies have shown that chest wall compliance is decreased to about two-thirds of normal values in patients with long-standing neuromuscular disorders. These measurements apply to the entire chest wall, but it seems reasonable to speculate that these changes are primarily due to altered stiffness of the rib cage (Affeldt et al, 1952; Ferris et al, 1952). Further contributory factors can be the development of scoliosis, particularly, in patients with muscular dystrophy, and fibrotic changes and spasticity in the rib cage muscles, as occurs in patients with tetraplegia. In conclusion, the alterations in lung volumes seen in patients with chronic neuromuscular disorders are attributable to a combination of muscle weakness and alterations of the

mechanical properties of the lungs and chest wall (De Troyer and Pride, 1985).

1.6.5 Cough impairment-airway function

The effectiveness of cough is reduced in expiratory muscle weakness because the cough induces dynamic compression and hence the linear velocity of airflow through the large intrathoracic airways. As a result, cough and clearance of secretions is defective in these patients, contributing to the high prevalence of bronchopulmonary infections. Respiratory muscle weakness would be expected to have larger effects on maximum inspiratory rates for two reasons (a) these flow rates depend on the ability of the inspiratory muscles to lower pleural pressure (b) a reduction in lung distensibility which opposes inspiratory flow. Very few studies have been done on maximum inspiratory flow-rates in respiratory weakness (Gal and Arora, 1982; De Troyer and Borenstein, 1980). Similarly, it might be expected that maximum voluntary ventilation (MVV) measured over 15 sec would be reduced disproportionately to changes in FEV₁ in respiratory muscle weakness, but only a small trend in this direction has been found in myasthenia gravis (Ringqvist and Ringqvist, 1971) and in myotonic dystrophy (Serisier, Mastaglia and Gibson, 1982).

1.6.6 Ventilatory drive

Patients with respiratory muscle weakness

breath faster and with a smaller tidal volume than healthy subjects (Begin et al, 1980; Gibson et al, 1977; Newsom-Davis et al, 1976). This tachypnoea may be related to the diffuse microatelectasis, reduction of lung compliance or different signals from the weakened muscles themselves (Begin et al, 1980). Alterations in the central control mechanisms of respiration have been repeatedly suggested in a number of patients with neuromuscular disorders (Plum and Swanson, 1958; Kilburn et al, 1959; Rosenow and Engel, 1978; Bellamy et al, 1975; Carrol et al, 1976). However reductions in the ventilatory responses can be accepted as evidence of damaged medullary respiratory centres only if there are no accompanying abnormalities of lower motor neurone respiratory muscles, or lung mechanics.

1.6.7 Ventilation and blood gases

The main change in blood gases in patients with respiratory muscle weakness is usually a fall in arterial PO_2 (Harrison et al, 1971). Hypoxaemia without an elevated $PaCO_2$ has been reported in patients with acute poliomyelitis during respirator treatment (Affeldt, 1965) and in a number of patients with other neuromuscular disorders (Gibson et al, 1977; Hapke, Meek and Jacobs, 1972; Newsom-Davis and Loh, 1979). In these cases decreased PaO_2 coexists with an increase in alveolar-to-arterial tension difference for oxygen (A-a) PO_2 .

Initially the tachypnoea causes an increase in alveolar ventilation, resulting in alveolar and arterial hypocapnia (Hapke et al, 1972; Harrison et al, 1971). Persistent hypercapnia may be a late and dramatic event and may occur only at a terminal stage of the disease, as in Duchenne's muscular dystrophy. However, hypercapnia may occasionally appear relatively early in the course of some chronic neuromuscular disorders, such as in limb-girdle dystrophy or in myotonic dystrophy.

1.7 RESPIRATORY MUSCLE FATIGUE

The question whether respiratory muscle fatigue causes respiratory failure is over 50 years old but we still have no definitive answer to this question (Macklem and Roussos, 1977).

1.7.1 Physiological classification of fatigue

Muscle fatigue can be defined as the inability to sustain the required or expected force with continued contractions. When exercise ceases or its intensity is reduced, the muscle will recover. Recovery from some forms of peripheral muscle fatigue is complete within seconds, but may be gradual with full recovery taking hours (Jones, 1986). The command chain for voluntary muscular activity involves many steps and force failure i.e. fatigue - can occur as a result of impairment at any one or more links in the chain of command. As a simple practical analysis it is worth separating central from

peripheral fatigue (Edwards, 1981). In the history of human muscle fatigue it was popular in the early years to attribute fatigue to failure of central neural processes (Walker, 1891; Mosso, 1915). Comparisons between forces generated by maximum stimulated contractions and forces by maximum voluntary contraction at different stages of the experiment allowed central fatigue to be assessed (Mosso 1915, Bigland-Ritchie et al, 1978). The importance of peripheral fatigue was first clearly demonstrated by Merton (1954). He showed that force generation was impaired with twitches of the abductor pollicis muscle provided by supramaximal stimulation of the ulnar nerve at the wrist as a result of a sustained maximum voluntary contraction (MVC), during which the muscle became fatigued such that maximum force generation was less than 20% of the force obtained with an MVC with unfatigued muscles (Edwards, 1981).

1.7.2. Causes of peripheral muscle fatigue

Several experimental models have been used to study fatigue: voluntary activation of the muscles, force output or electrical stimulation to determine their contractile properties. There are many possible sites and mechanisms with which fatigue may occur in a peripheral muscle. Changes in membrane electrical characteristics from efflux of potassium ions (Vyskocil et al, 1983; Sjogaard, 1986), or increased cellular water content during exercise, may effect propagation of

the action potential along the muscle membrane and the T-tubule, leading to a reduction in activation and therefore force generation. The excitation-contraction coupling process may be impaired by changes in the amount of calcium stored in or released from the sarcoplasmic reticulum (Jones, 1981). Crossbridge formation can be affected and it may reduce force generation in several ways i.e. the sensitivity of troponin for calcium may be reduced (Hermansen, 1981) as may be the rate (Cook and Pate, 1985) and power output (Kentish, 1986) for each crossbridge cycle. It is often thought that decreased intracellular pH is the cause of muscle fatigue but such relation is not clear. Whilst any increased hydrogen ion concentration reduces isometric force generation in vitro (Metzger and Moss, 1987) reductions in strength in excess of 50% can occur with low-intensity exercise in which no lactic acid is produced and pH is unchanged (Bigland-Ritchie, Cetarelli and Vollestad, 1986). Patients suffering from McArdle's syndrome (myophorylase deficiency) can fatigue with no lactic acid production (Edwards and Jones, 1983). Other metabolic changes i.e. an increase in ADP in combination with a decrease in pH might play a key role in the development of fatigue as these changes have been associated with reductions in force. Furthermore as pH falls the concentrations of phosphocreatinine (Pcr) falls, adenosine diphosphate (ADP), adenosine monophosphate (AMP) and inorganic phosphate (Pi) in diprotonated form increase, the latter

has been found to be directly related to force changes (Nosek, Fender and Godt, 1987). It has recently been proposed that the metabolic determinants of fatigue as well as the recovery from it are related to the nature of exercise used to induce it (Hultmann and Sjoholm, 1986; Green, 1987). When work is sustained for 1-2h, the point of exhaustion is related with the depletion of the glycogen stores of the working muscle (Bergstrom et al, 1967). During heavy exercise large amounts of energy are converted to heat and the subsequent rise in body temperature and fluid loss may impair performance and enhance central fatigue. Eccentric contractions (where the muscle is forcibly extended during activation) produce more profound and longlasting fatigue despite having low metabolic cost (Knuttgen, Bonde-Peterson and Klausen 1971; Newham, 1988)

1.7.3 Respiratory muscle fatigue

By analogy with limb muscles, fatigue could develop in the respiratory muscles and contribute to hypercapnic ventilatory failure (Macklem and Roussos, 1977). Patients with severe lung disease and hyperinflation have reduced force generating capacity of the respiratory muscles. In contrast their ventilatory requirements are increased. These muscles, particularly the inspiratory are subject to large loads with every breath for prolonged periods with little opportunity to rest (Green and Moxham, 1985). In these circumstances,

it appears likely that the respiratory muscles, particularly those of inspiration, can fatigue and precipitate or intensify ventilatory failure (Macklem and Roussos, 1977; Moxham et al, 1981).

CHAPTER 2
MATERIAL AND METHODS

2.1 NORMAL SUBJECTS, PATIENTS AND METHODS

2.1.1 The Patients and Normal subjects

The normal subjects who participated in the following studies were medically qualified and laboratory or hospital workers from The Brompton and King's College hospitals. Only six of them were familiar with the techniques and respiratory manoeuvres employed. The patients who were studied were referred to Dr Malcolm Green, who is known to have a long standing interest in respiratory muscle function for investigation of breathlessness or suspected involvement of respiratory muscles in various lung or systemic disorders. Details for each individual patient are found in the specific studies.

2.1.2 Ethical Approval

Ethical approval has been obtained after submission of a detailed protocol of each study to The Ethical Committee of The Brompton or King's College Hospitals. All patients and normal subjects gave their verbal informed consent to the investigators.

2.1.3 Methods

Basic concepts about methods and technical characteristics of the equipment used are described here. The specific use of the methods, equipment and

experimental set-up are described in the individual chapters.

2.2 MAXIMAL STATIC MOUTH PRESSURES

This widely applied technique is currently used to measure global respiratory muscles strength because it is simple and readily adaptable in clinical practice.

2.2.1 Mouth Pressures and Lung Volume

Subjects must learn how to do the test.

Inspiratory and expiratory pressures are measured during static efforts with minimal air flow. The pressures can be measured at any lung volume, but the maximum inspiratory pressures (P_Imax) are obtained at full expiration (residual volume, RV) whereas the maximum expiratory pressures (P_Emax) are obtained at full inspiration (total lung capacity, TLC) against an occluded airway. Normally RV is about 25% of predicted TLC and the natural breathing position at the end of a quiet breath (functional residual capacity, FRC) is about 50% of predicted TLC. Some subjects are not able to achieve the normal RV or TLC positions and may perform P_Imax test at a higher, and P_Emax at a lower than normal lung volume. It has been suggested that in order to assess how much of the pressure difference regarding normal values is due to true muscle weakness or to the different lung volume the patient's P_Imax and P_Emax must be compared with normal values but corrected for the lung-volume at which the patient performed the test using

the lung-volume relationships (Rochester and Arora, 1983; Rochester, 1988). Pressures measured at the mouth include both the respiratory muscle pressure (P_{mus}) and a component contributed by the elastic recoil of the lungs and chest wall (P_{rs}). P_{rs} must be subtracted from P_{Emax} and P_{Imax} to obtain the proper values for P_{mus} . At FRC P_{rs} is zero, below FRC, P_{rs} is negative and above FRC P_{rs} is positive. Therefore P_{Emax} at TLC overestimates expiratory P_{mus} and P_{Imax} at R_v overestimates inspiratory P_{mus} by about 30%. It has been suggested to measure both P_{Imax} and P_{Emax} from FRC where P_{rs} has little or no effect on the pressures measured (Rochester, 1988.)

2.2.2 Criteria of acceptance

As these tests were concerned with maximal functions, the highest positive and negative pressures recorded were used. The procedures demand a certain technique to avoid extra leakage and to create maximum instantaneous pressures with open glottis. The tests were therefore not interrupted until the investigator considered that a maximal result had been obtained. The criteria used for this were those imposed by Ringqvist (1966), (See also Chapters 3 and 4).

2.2.3 The need for a leak

These manoeuvres may produce artefacts if subjects close their glottis and exert negative or positive pressure with the pharyngeal or cheek muscles

(Ringqvist, 1966; Nochomovitz, Supinski and Kelsen, 1986). In such a situation only minor variations in the volume of comparatively small space may produce large pressure variations according to the equation:

$$P.V = K = (P + \Delta P). (V + \Delta V)$$

The change in pressure may however be more or less avoided by means of a leakage, the volume of which during a short time corresponds to ΔV . The attenuation of the respiratory muscle force due to the leakage should not be more than 1% - 2% (Ringqvist, 1966; Chapter 4)

2.2.4 Measurement

Measurements were made at the highest positive and the lowest negative pressures, each maintained for 1 second (Fig 1). During maximal inspiratory efforts, mouth pressures were sub-atmospheric and thus negative in sign. However, for simplicity, all the pressures are expressed with a positive sign. Normal predicted values for males and females are obtained from Wilson et al (1984) or Black and Hyatt (1969).

2.3 OESOPHAGEAL (POES), GASTRIC (PGAS), AND TRANSDIAPHRAGMATIC (PDI) PRESSURES

Respiratory muscle pressures can also be recorded within pleural and abdominal cavities with suitable balloon catheters. These catheters are introduced via the nose and pharynx into the oesophagus for pleural pressure and into the stomach for abdominal pressure as described in the following section (2.4.3)

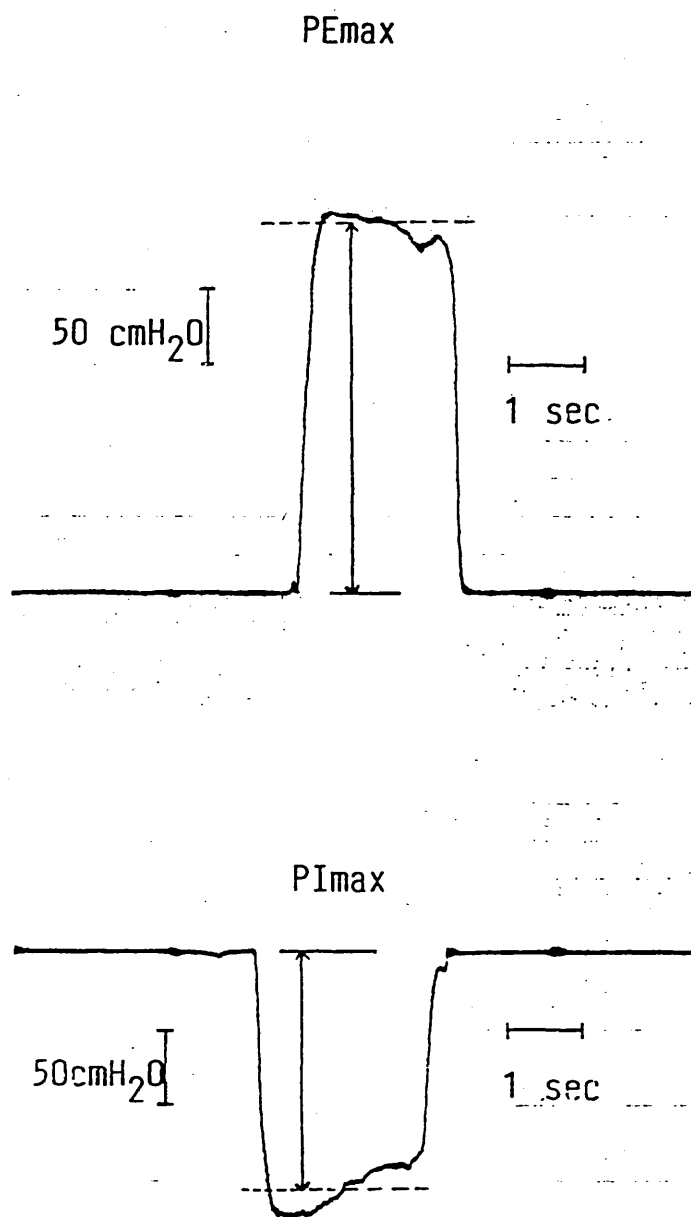


Figure 1 - Measurement of a) PE_{max} and b) PE_{max} from
1 sec plateau

(Mead et al, 1954; Cherniack et al, 1955; Crane, Hamilton and Alfeldt, 1955; Mead and Gaensler, 1959; Knowles, Hong and Rahn, 1958; Milic-Emili et al, 1964; Milic-Emili, Mead and Turner, 1964; Lemen, Benson and Jones, 1974; Beardsmore et al, 1980). Pleural pressures need not be corrected for lung elastic recoil pressure with lung volumes at or below FRC, Poes is only slightly larger than mouth pressures because lung recoil is low. The pressure across the diaphragm (transdiaphragmatic pressure or Pdi) is calculated as $P_{di} = P_{gas} - P_{oes}$ (Agostoni and Rahn, 1960). Pressures were obtained during the sniff manoeuvre (Miller, Moxham and Green, 1985) and percutaneous bilateral phrenic nerve stimulation (twitch Pdi) at the neck (Sarnoff, Sarnoff and Whittenberger, 1951).

2.4 DIFFERENTIAL PRESSURE TRANSDUCERS

Most pressure transducers are designed to measure a pressure applied to one or to both sides of their diaphragm, in which case they measure the difference between the two pressures. A transducer designed for this mode of operation is known as a differential pressure transducer (Sykes et al, 1981). The Validyne MP 45-871 (Validyne CO, Northridge, CA) very low range Differential Pressure Transducer is designed for extremely low pressure measurements (Fig 2). This unit features a small internal volume with low volumetric displacement to achieve high frequency response. The very

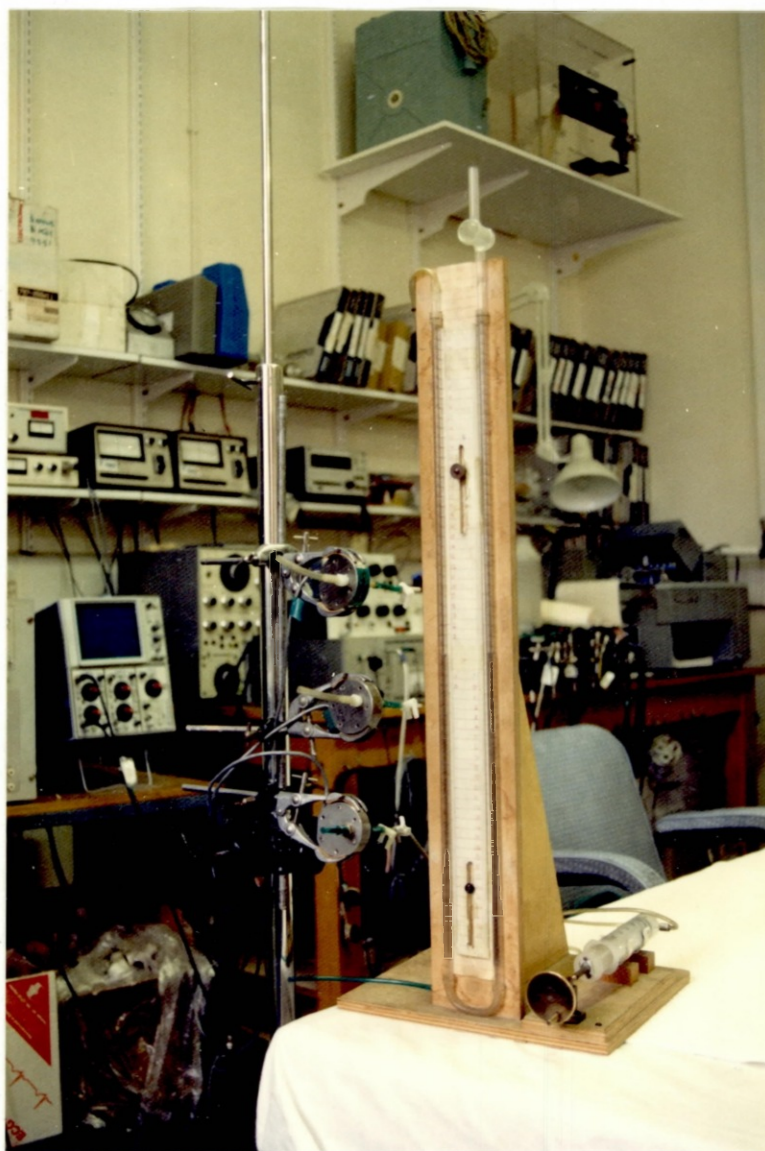


Figure 2 Differential pressure transducers and a U-shaped water manometer for calibrations

rugged construction utilising all stainless steel accepts corrosive media both sides and sustains high mechanical shock and overpressure. The user can replace diaphragm to change operating pressure range. The transducers available in our laboratory were able to measure up to ± 350 cm H₂O. The minimum pressures they could measure were ± 2 cm H₂O. Suitable pressure connections were furnished for the commonly used rubber or plastic tubing. In this pressure transducer shown in simplified form in Fig. 3, a diaphragm of magnetically permeable stainless steel is clamped between two blocks and deflects when the pressure difference is applied through the ports illustrated. An E core and coil assembly is embedded in each block with a small gap between the diaphragm and E core, in a symmetrical arrangement resulting in a condition of equal inductance with the diaphragm in an undeflected position (Fig. 3). The diaphragm's deflection results in an increase in the gap in the magnetic flux path of one core and an equal decrease in the other. The magnetic reluctance varies with the gap determining the inductance value so the effect of the diaphragm motion is a change in inductance of the two coils, one increasing and the other decreasing. When the coils are connected in a bridge circuit and are excited by an AC carried voltage, this output voltage will vary proportionately to the differential pressure applied across the diaphragm. This generation of transducers offer a number of advantages in pressure measurement and

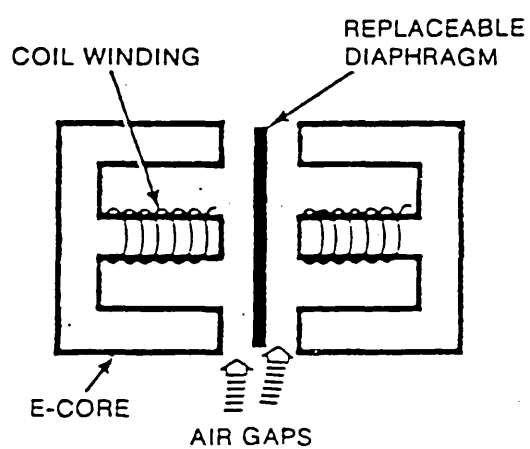


Figure 3 Simplified diagram of a Validyne MP-45
Pressure Transducer

control. These include: a) excellent dynamic response characteristics with gas systems due to high natural frequency, low volumetric displacement and low internal volume. b) Extreme overload tolerance - operator proof. c) Ability to withstand severe shock and vibrations. d) High level output. e) High noise immunity.

2.5 BALLOON CATHETERS

2.5.1 Description

Oesophageal and gastric pressures were measured using standard latex balloon catheters commercially available (P.K. Morgan, Rainham, Kent, UK) 10 cm in length with a wall thickness of about 0.06 cm and perimeter of 3.5 cm. The balloons were sealed over spirally arranged holes drilled at 5 mm intervals along the distal end of a 120 cm long PE-20 polythene catheter, with an internal diameter of 0.1 cm and external diameter of 0.2 cm. The catheters prior to each study were shortened to 100 cm and were marked in 5 cm steps from the tip of the balloon to 70 cm. After emptying the balloons of air by placing them under water to a depth of 5 cm the open ends were attached and sealed to the pressure transducers via three way taps. The balloons were connected to the three way taps with 17 gauge needles cut down to half an inch in length (Fig. 4). The system was considered free of leaks when the initial negative pressure (-5 cm H₂O) was maintained

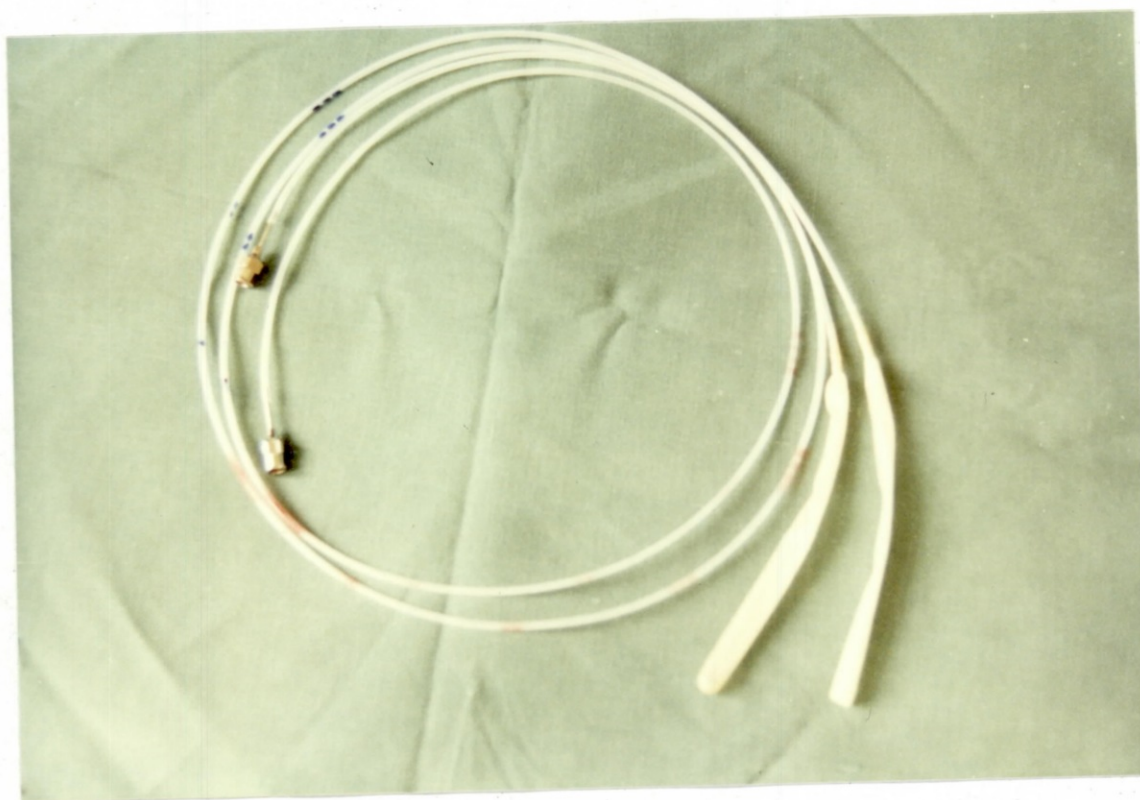


Figure 4 Balloon Catheters

constant for 2-3 min, the balloon being exposed to the atmospheric pressure.

2.5.2 In vitro Technical Characteristics of the Balloon Catheters and Pressure Transducers

Appropriate calibration was made before each test, using a mercury and a water-filled U-shaped manometer (Fig.2). A known pressure was applied to each transducer and the signals recorded by the Mingograph recorder were adjusted to ensure that the same pressure provided an equivalent deflection on the paper trace. All three transducers had a linear response over ± 350 cm H₂O range (Fig. 5). Each transducer was connected to a pressure transducer indicator (Amplifier) model T12 (P K Morgan). The system transducer-indicator has accuracy $\pm 0.5\%$ FS, hysteresis 0.1% of pressure excursion, thermal zero drift 0.01% FS/ $^{\circ}$ F and frequency response flat over 0-1000Hz range (Information given by P K Morgan). The pressure volume characteristics of the balloon-catheters were determined at atmospheric pressure after a balloon was emptied, volumes of air (0.1 ml) were added to the balloon with a glass syringe and the pressure was recorded after each incremental addition. Outside the body, the balloon required 0.4 ml of air to restore pressure to zero inside the balloon. The balloon-catheter system had a pressure volume curve flat over the 0.4-2.8 ml range (Fig 6). The frequency response of the entire system (balloon-catheter-transducer-indicator-

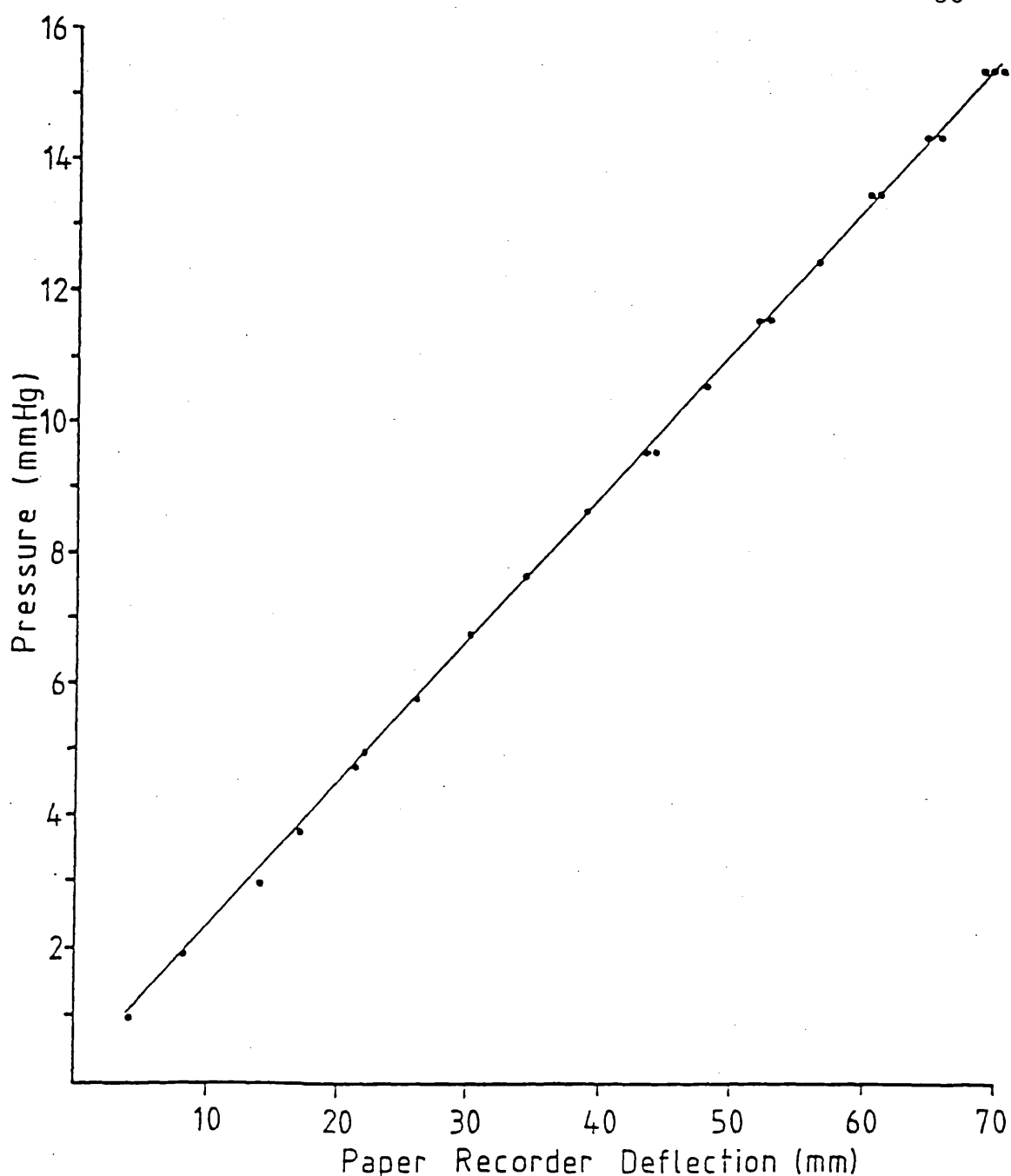


Figure 5 Linearity of the differential pressure transducer. Linear regression analysis showed highly significant relation between paper recorder deflection, measured in mm (X) and pressure calculated in mm Hg(Y).
 $Y = 0.903 + 0.220X$ ($r = 0.999$, $n = 23$, $P < 0.001$)

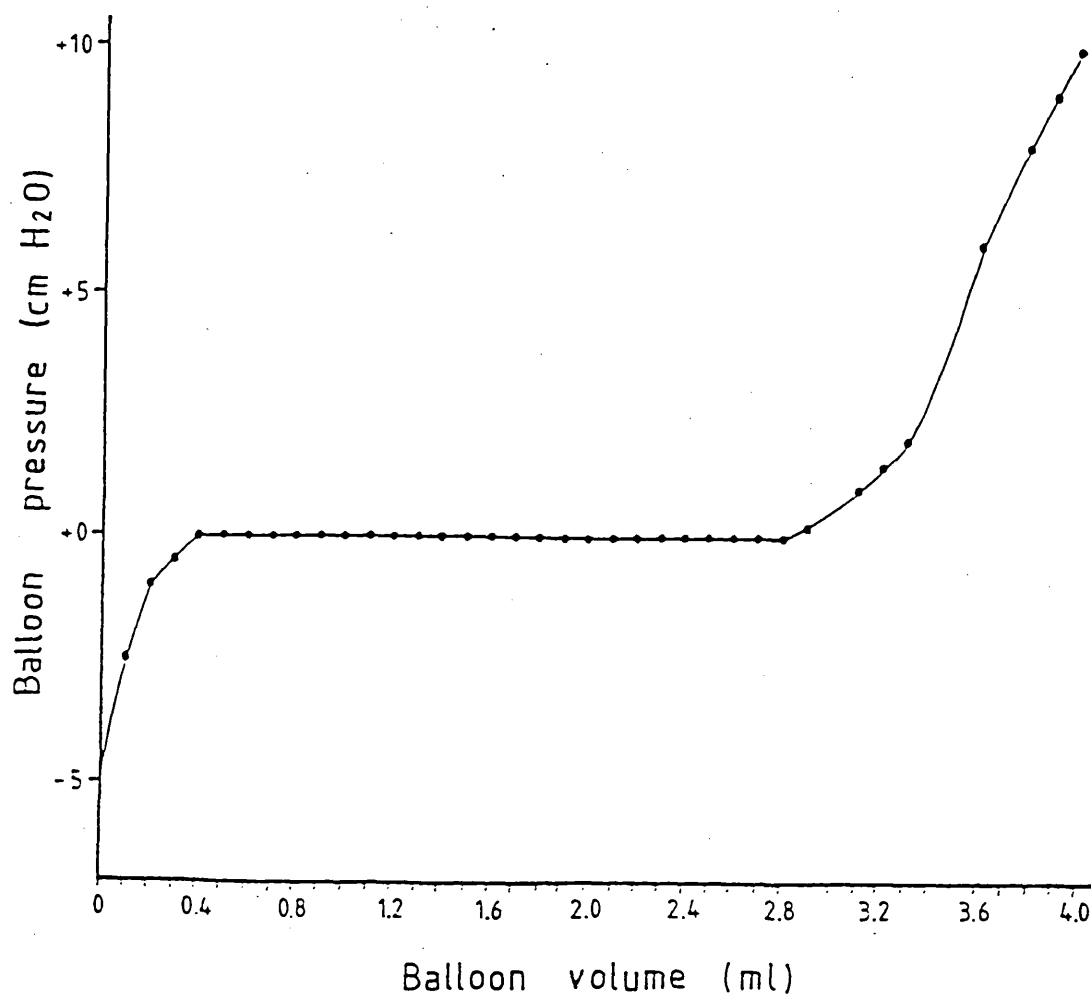


Figure 6 Pressure-volume characteristics of the 10 cm balloon-catheter. The balloon-catheter system has a pressure-volume curve flat when contains air ranging from 0.4 to 2.8 ml.

recorder) was approximately 20 Hz, assessed from the pressure generated by a square wave input obtained by bursting a pressurised balloon with a hot wire "pop test", (Sykes, Vickers and Hull, 1981; Fig. 7)

2.5.3 Positioning of the Balloon Catheters (Cotes, 1977)

To insert the balloon into the oesophagus and stomach the operator first establishes which of the subject's nostrils is widest by asking him to sniff through each in turn; inquiry is made into previous sensitivity to cocaine. The mucosa is then anaesthetised with 1 ml of 4% lignocaine hydrochloride solution (xylocaine). This is administered through a spray fitted with a long nozzle which can be diverted to both the front and back of the nasopharynx. Five minutes is allowed for the anaesthetic to exert its effects. The operator then lubricates the balloons with a tasteless lubricant (e.g. K-Y, Johnson and Johnson xylocaine 2% jelly) and passes it gently into the nose while first the subject makes a series of swallowing manoeuvres. The tubes should now descend into the oesohagus. The passage of balloons is assisted by the subject swallowing water from a glass through a flexible drinking straw which is held between the lips. At this stage it is advisable to check that oesophageal and gastric catheters can be seen passing over the back of the tongue and are not coiled in the oropharynx, as sometimes occurs when a

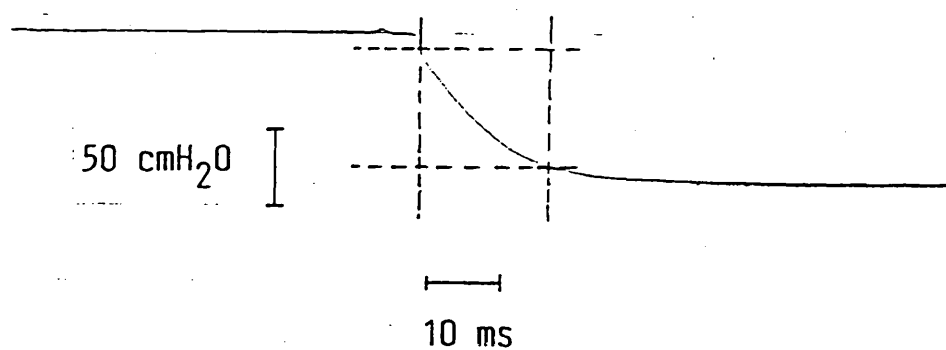


Figure 7 Frequency response of the entire system.

The frequency response of the balloon catheter-transducer-amplifier-recorder system has a maximum frequency response of 20 Hz. From this trace, the 10-90% response time (Tr) is 0.0175. The f3db value was calculated according to the formula

$$f_{3db} = 1/3 \text{ Tr} = 1/3 \times 0.017 = 20\text{Hz}$$

(paper speed 1000 mm/s)

very flexible tube is used. Swallowing is continued until both balloons come to lie in the stomach, where their presence is confirmed by the response to sniffing which should cause a positive pressure in the tubes. Only the oesophageal balloon is slowly withdrawn stopping when sign of pressure sniffing changes i.e. pressure swings in negative direction with inspiration. This occurs when about 1 cm of balloon is in the thoracic oesophagus and serves to measure the level of cardia. Withdrawing the catheter another 10 cm reveals the balloon now lying totally within the thoracic oesophagus with tip about 1 cm above cardia where sniffing causes a fall in pressure. Into the empty gastric balloon 5 mls of air are injected slowly and 3 mls removed leaving 2 mls. Into the empty oesophageal balloon 5 mls of air are injected and 4.5 mls removed leaving 0.5 mls. The gastric balloon should have a positive and the oesophageal a negative deflection with spontaneous inspiration or sniffing. After positioning the balloons it is necessary to check for the tracheal artefact. During a Valsalva and Muller manoeuvre, respectively, lung volume changes only a small amount. Provided the manoeuvres are performed with glottis open and with airway obstructed beyond the pressure tap for mouth pressures the pressure difference from mouth to oesophagus approximates transpulmonary pressure and since volume changes are small the pressure should change little. If, however, the upper part of the balloon is

in the portion of the oesophagus immediately behind the trachea, transpulmonary pressure will appear to change markedly, increasing during Valsalva and decreasing during the Muller manoeuvre. This appears to be the result of impingement of the trachea against the oesophagus. During the Valsalva it is "pulled" away from the oesophagus making oesophageal pressure change in the negative direction. During the Muller manoeuvre the trachea is forced against the oesophagus causing oesophageal pressure to increase. It is important to avoid this artefact because if present oesophageal pressure will change with head position, extension causing negative deflections and flexion, positive deflections. The artefacts can be tested for by having the subject attempt to breathe in and out against an obstructed mouthpiece. If present the artefact is easily demonstrated. The catheter should be inserted further until the artefact disappears. This should happen quite abruptly. If part of the balloon is then in the stomach minimal distortion should result since the relatively more positive pressure in the stomach will displace any air from this portion into the thoracic portion of the balloon and will effectively seal off the gastric portion of the catheter. Attention should be paid to the pressure fluctuations transmitted from the heart (Trop, Peeters and Van De Woestijne, 1970). Another source of error is a rise in oesophageal pressure due to contraction of the oesophageal muscle. Tonic contraction

is particularly liable to occur at near to total lung capacity and is best overcome by waiting. Peristaltic contractions of duration between 2 - 5 s occur especially in the lower part of the oesophagus: their frequency increases during swallowing and before meals. The contractions may be identified by monitoring the pressure on an oscilloscope: those due to the intubation procedure usually disappear after a few minutes (Cotes, 1979).

2.6 The Sniff Manoeuvre

Sniff is defined as a short, vigorous inspiratory effort from FRC, through the nostrils with the mouth closed, usually performed in the seated position. The normal range for sniff Poes for males is 52 - 150 and for females 52 - 140, for sniff Pdi was for males 112 - 204 and females 82 - 182. The peak Pdi, Poes and Pgas was measured at FRC. An example of Sniff Pes, Pgas and Pdi is shown in Fig. 8.

2.7 Phrenic nerve Stimulating (Twitch Pdi, Poes, Pgas)

Human muscle strength may be measured by tetanically stimulating the motor nerve (Merton, 1954). The application of maximal tetanic phrenic nerve stimulation has proved to be difficult particularly if stimulation frequencies greater than 10Hz are employed because of the almost unavoidable co-stimulation and

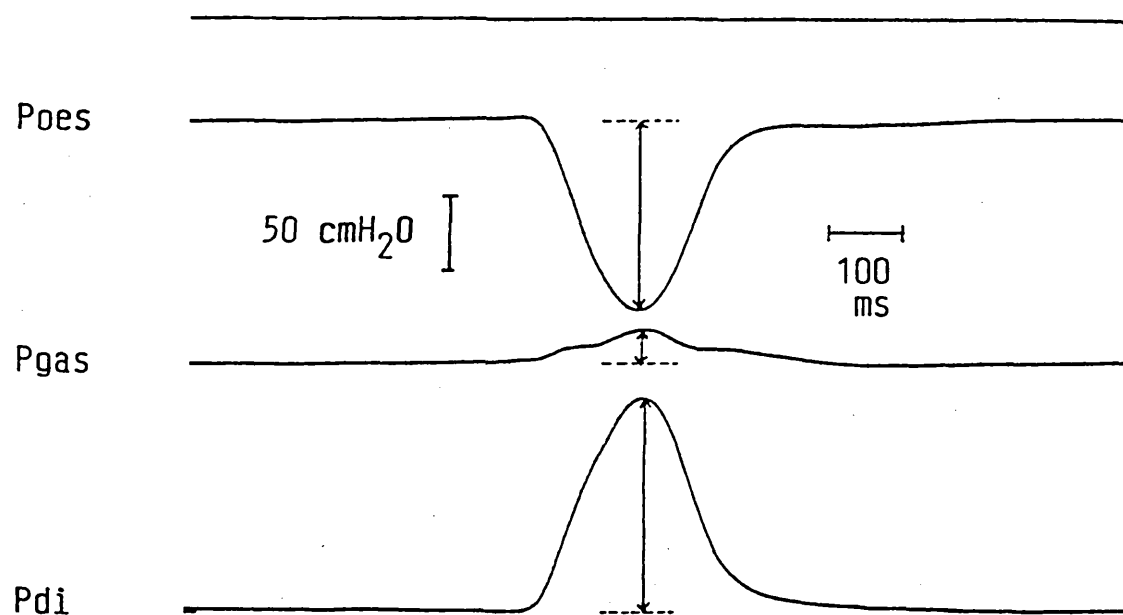


Figure 8 Measurement of sniff Poes, Pgas and Pdi
(paper speed 100 mm/s)

contraction of the neck muscles which displace the stimulating electrodes. However, these problems do not arise when single maximal bilateral electrical shocks are delivered to the diaphragm. It has been shown that bilateral percutaneous phrenic nerve stimulation at 1Hz is a simple objective test to evaluate diaphragmatic muscle strength in man and it is independent of volition (Bellemare and Bigland-Ritchie, 1984). The electrical stimulation was performed with a bipolar nerve stimulating electrode type EC 225 (Medelec Ltd, Surrey, England) which consisted of two felt-tips with surface area at 30 mm² and 30 mm distance between them (Fig. 9) soaked in saline. The stimulation current was delivered from a Digitimer Stimulator type 3072 (Digitimer Ltd, Hertfordshire, England) linked to Dual HV Gated Pulse Generator type 2521 (Digitimer Ltd). The frequency was checked with a feedback Digital Frequency Meter type FM 610 (Feedback Inst. Ltd, Sussex, England; Fig. 10). Supramaximal stimulation was performed with unirectional square wave pulses of 0.5 ms duration. Maximal stimulation was achieved with voltages ranging between 90-150 V. The skin at the neck was carefully cleaned with spirit. Both phrenic nerves were stimulated percutaneously. The electrode was positioned in the supraclavicular fossa, immediately posterior to the sternomastoid border at the level of the cricoid cartilage (Sarnoff, Sarnoff and Whittenberger, 1951; Fig. 17).

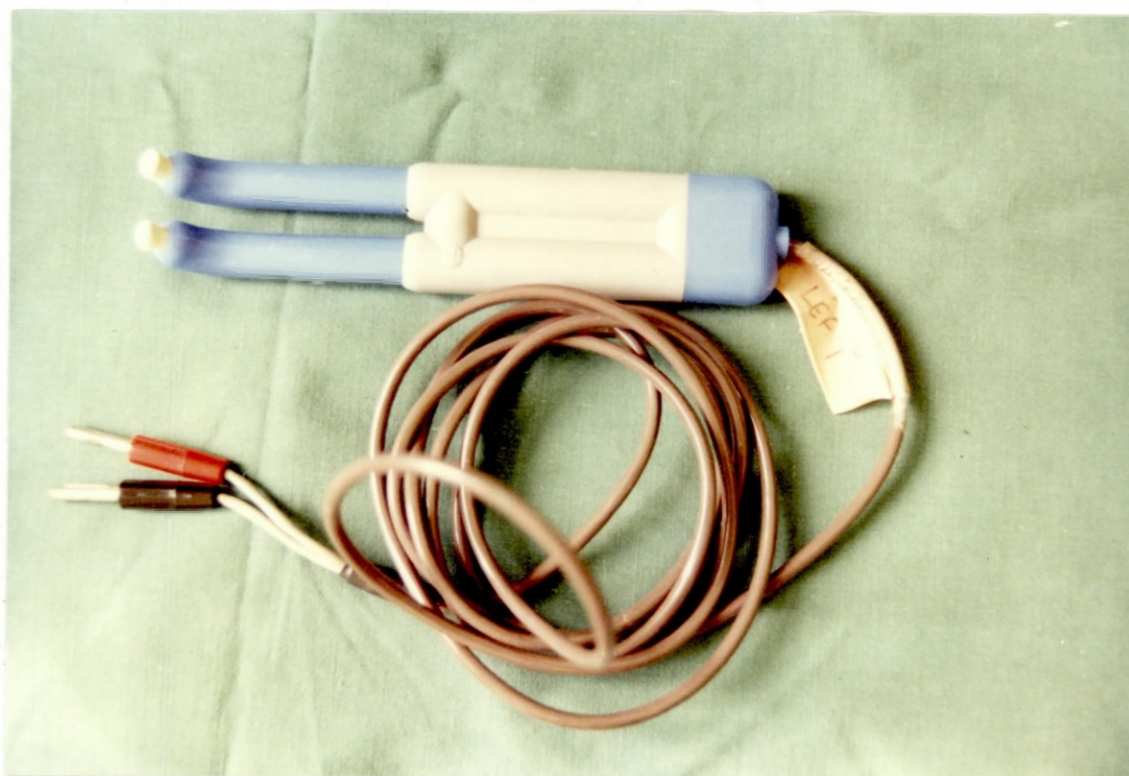


Figure 9 Bipolar electrode used for percutaneous phrenic nerve stimulation. (Medelec Ltd, Old Woking, Surrey)

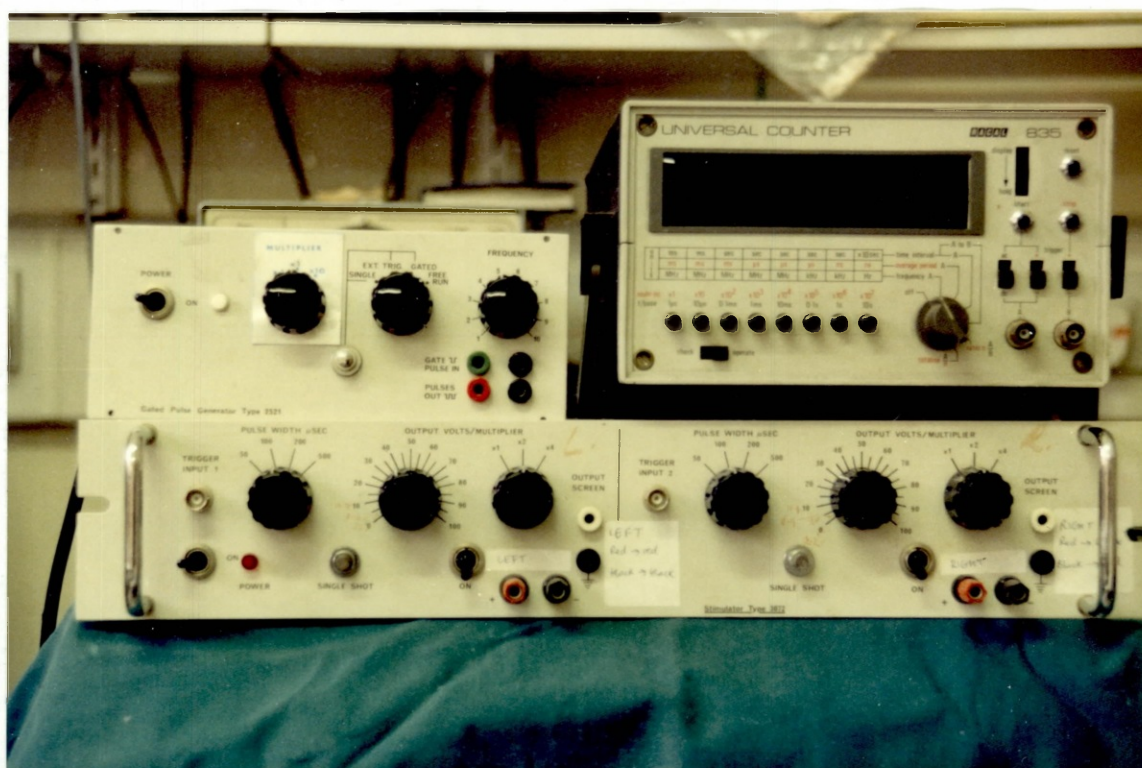


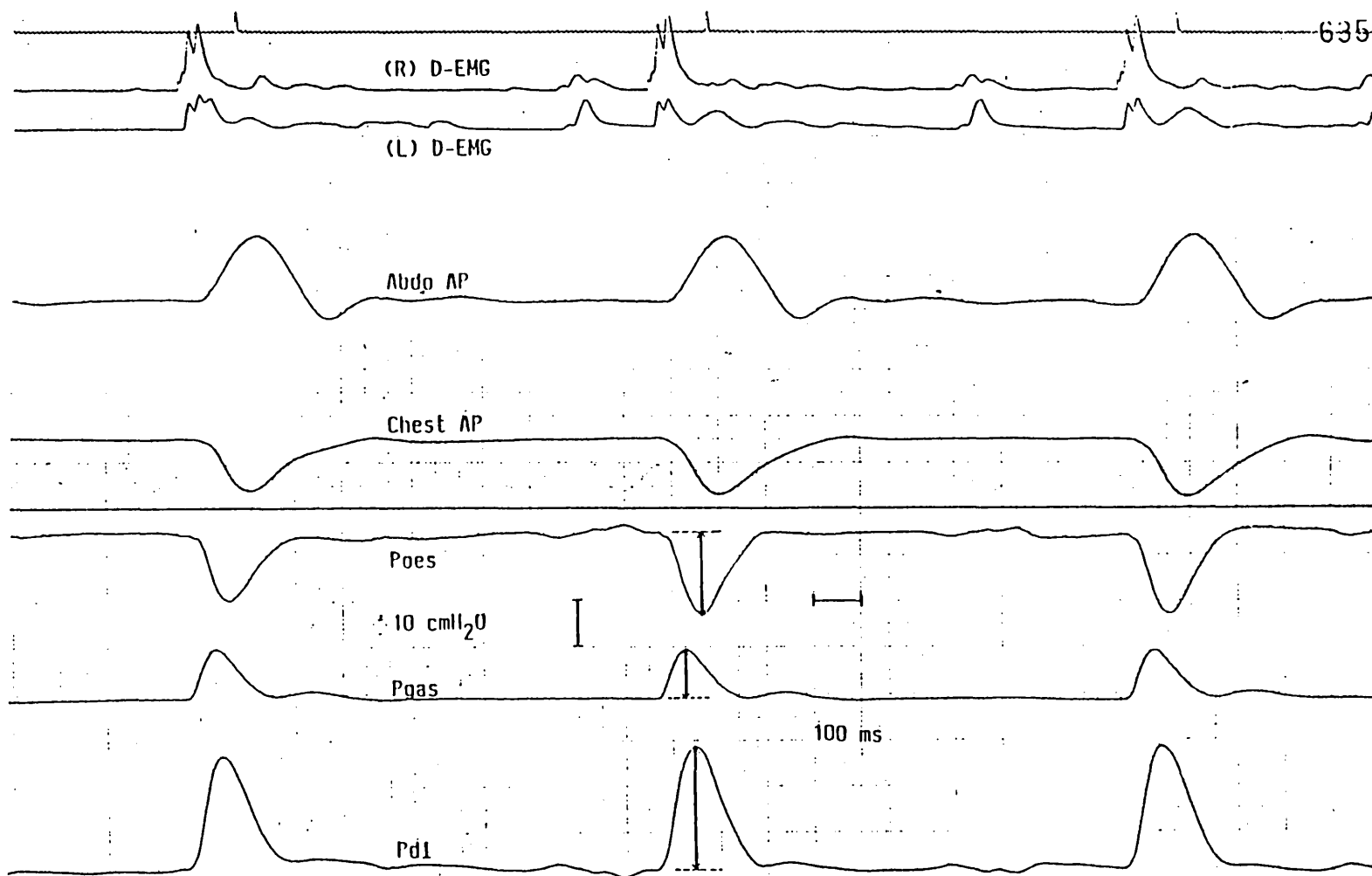
Figure 10 Apparatus used for electrical stimulation of the phrenic nerve: Digitimer Dual Gated Pulse Generator, Universal Counter Digital Frequency Meter, and Digitimer Stimulator (Digitimer, Welwyn, Herts)

Stimulation was usually achieved with the head in the mid-line so that the sternomastoid muscle was completely relaxed. Since the phrenic nerve lies close to the brachial plexus at the point of stimulation, this often initially caused contraction of the upper limb muscles and occasionally paraesthesiae in the cutaneous distribution of the brachial plexus. By positioning the electrode slightly more medially the phrenic nerve could usually be stimulated selectively. Heart rate was monitored throughout the procedure. The voltage of stimulation was increased until there was no further increase in the size of either the diaphragm muscle action potential or twitch amplitude. At this point the stimulation was considered to be maximal. The voltage was then further increased by 10% in order to ensure supramaximal stimulation of the phrenic nerves. The subject wore a nose clip and was instructed to breathe quietly for several breaths and then to relax at FRC with his/her glottis closed. Stimulation was performed for a maximum of 10 seconds, following which the patient breathing again relaxed at FRC, and stimulation was repeated. Adequate rest pauses of 5 - 10 min were taken between runs (Mier, 1986). An example of bilateral twitch Pdi is shown in Fig. 11.

2.8 Electromyography of the Diaphragm (EMG)

EMG's of the left and right hemidiaphragms were recorded with surface electrodes 1.0 cm in diameter,

Figure 11 Measurement of twitch Pdi (Poes = Oesophageal pressure, Pgas = Gastric pressures, Pdi = Transdiaphragmatic pressure, L = Left diaphragmatic EMG, R = Right diaphragmatic EMG, Chest AP = Chest anterioposterior magnet trace, Abdo AP = abdominal anterioposterior magnetic trace)



(Medicotest, England) placed in the 7th and 8th or 8th and 9th intercostal spaces, 1 cm from the costal margins, on either side (Newsom-Davis, 1967; Fig 17). To improve contact of the electrode and reduce impedance, the skin was carefully prepared by rubbing ^{with} an abrasive gauze with alcohol. Position of the electrodes was adjusted so that EMG activity was recorded during quiet inspiration. This was usually easy in thin individuals. Those individuals with no subcutaneous fat were asked to perform maximal sniff to ensure that EMG activity was present. Although contamination from the presence of EMG activity of other muscles could not be excluded, satisfactory diaphragm action potentials were recorded during phrenic nerve stimulation indicating that the electrodes were correctly situated (Fig 12). The EMG signals were processed using an amplifier (Medelec PA 65) and were filtered below 16 and above 1600 Hz (Fig 13).

2.9 OSCILLOSCOPE

The Tectronix-5100 series D13 Dual Beam Storage Display Unit provides a very flexible measurement system with a dual-beam cathode ray tube (CRT) display (Fig 14). A hot cathode produces an electron beam which passes through two deflecting devices, one of which deflects the beam on the X axis and one on the Y axis. The beam then strikes a fluorescent screen where it produces a tracing. The signal may be a pressure tracing from a pressure transducer or diaphragmatic EMG. The advantage of the

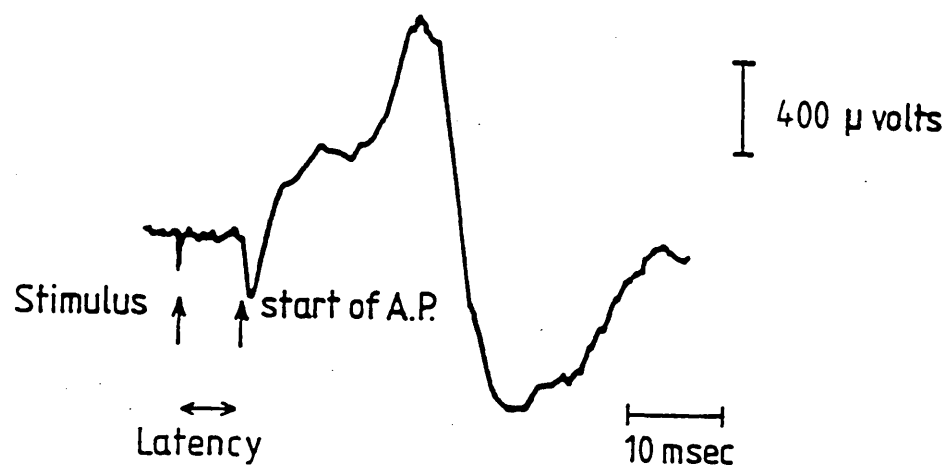


Figure 12 EMG of the hemidiaphragm. The conduction time of the ipsilateral phrenic nerve can be measured from this trace.

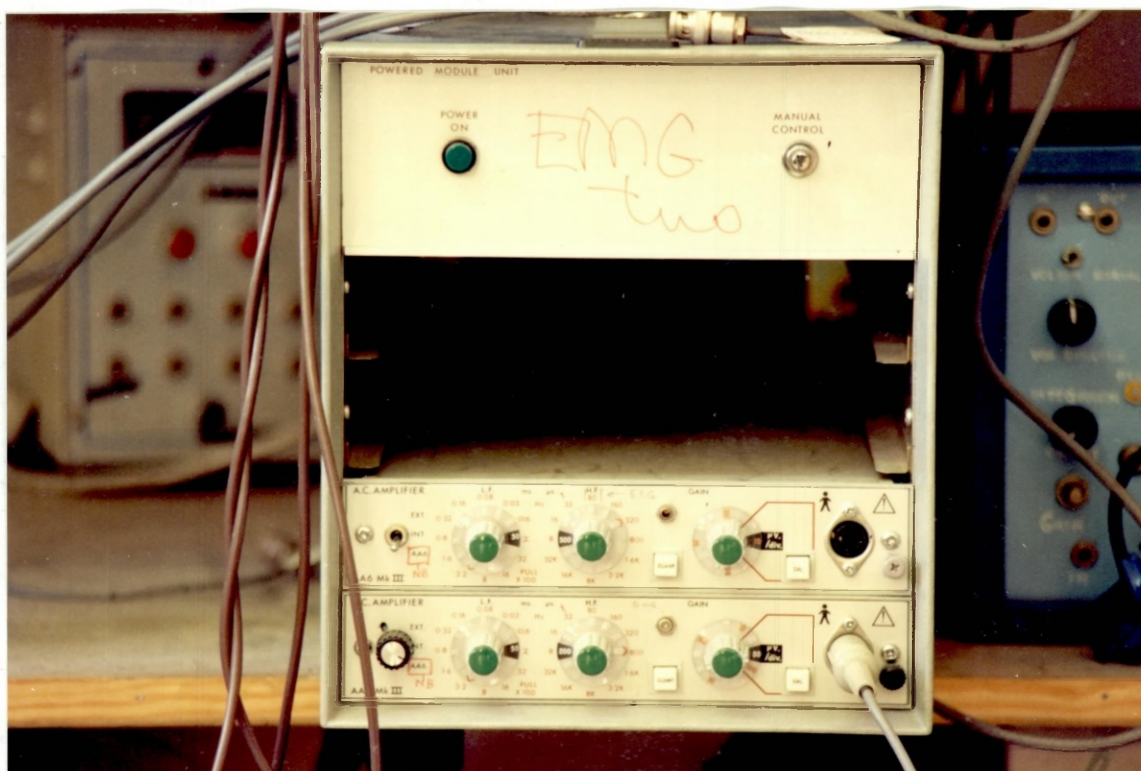


Figure 13 Medelec PA65 EMG amplifier used for processing diaphragmatic or intercostal EMG signals.
(Medelec Ltd, Old Woking, Surrey)

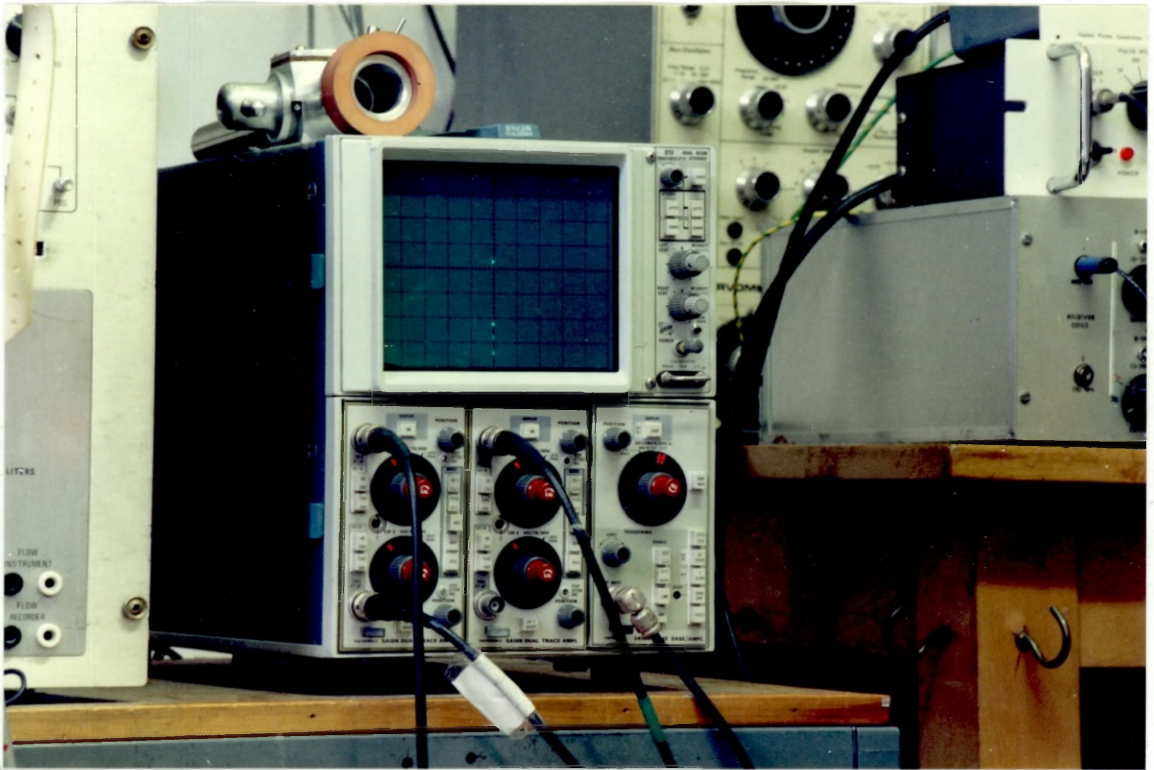


Figure 14 Tectronix 5103N Storage Oscilloscope
(Tektronix Inc, Oregon, USA)

oscilloscope is that the electron beam has negligible inertia, thus leading to a very high frequency response for the apparatus. In addition, there is a continuous display of the signal being monitored. The D13 has a direct-view, bistable storage tube with two 4 X 10 division screens which can be independently controlled for split-screen applications. A variable brightness control permits extended storage time and can be used to integrate fast, repetitive displays. A permanent record of CRT displays can be obtained with an oscilloscope camera system (Tektronix manual; Parbrook, Davis and Parbrook, 1985).

2.10 RECORDER

The mingograf 800 (Siemens-Elema, Sweden) is a multi-channel ink-jet recorder intended for physiological application. It is equipped with up to eight channels for recording of signals from a wide range of pre-amplifiers, pressure transducers or other kinds of instruments. Each recording channel consists of a final amplifier and an ink-jet galvanometer. As recording paper, 210 mm wide, folded paper is used. The final amplifier with the galvanometer can handle frequencies up to 650 Hz. The paper speed varies from 2.5-1000 mm/s (Fig. 15; Sykes, 1981).

2.11 MAGNETOMETERS

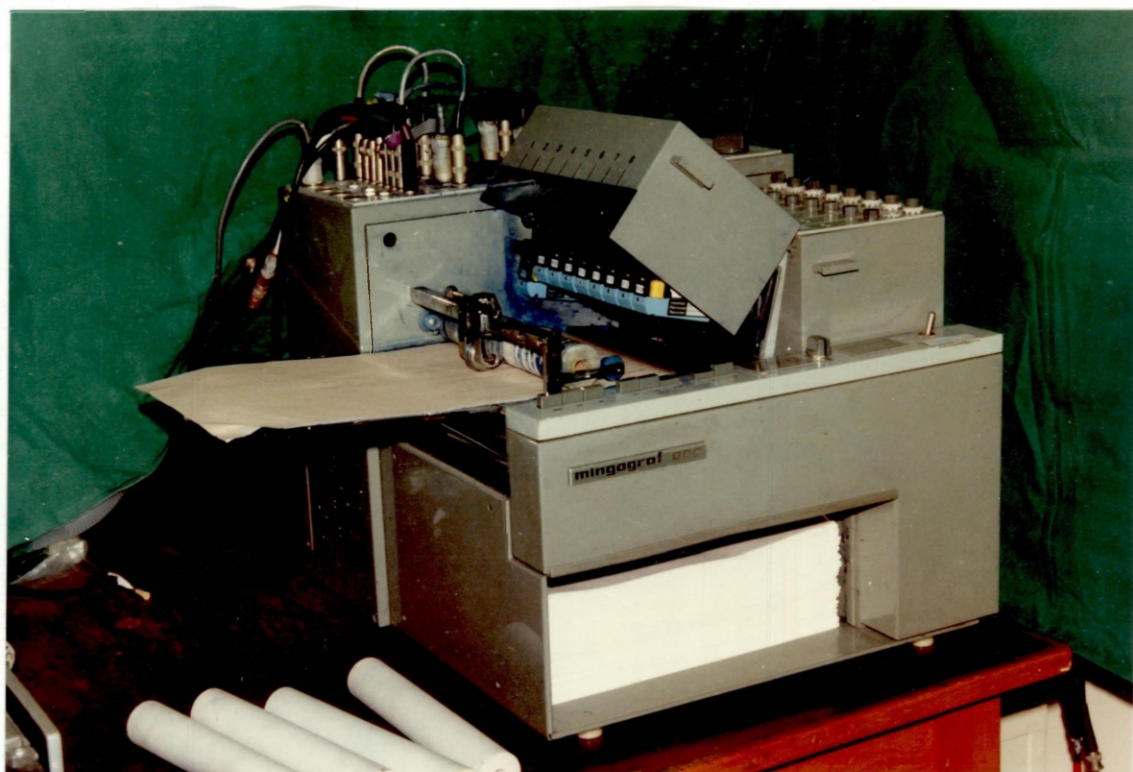
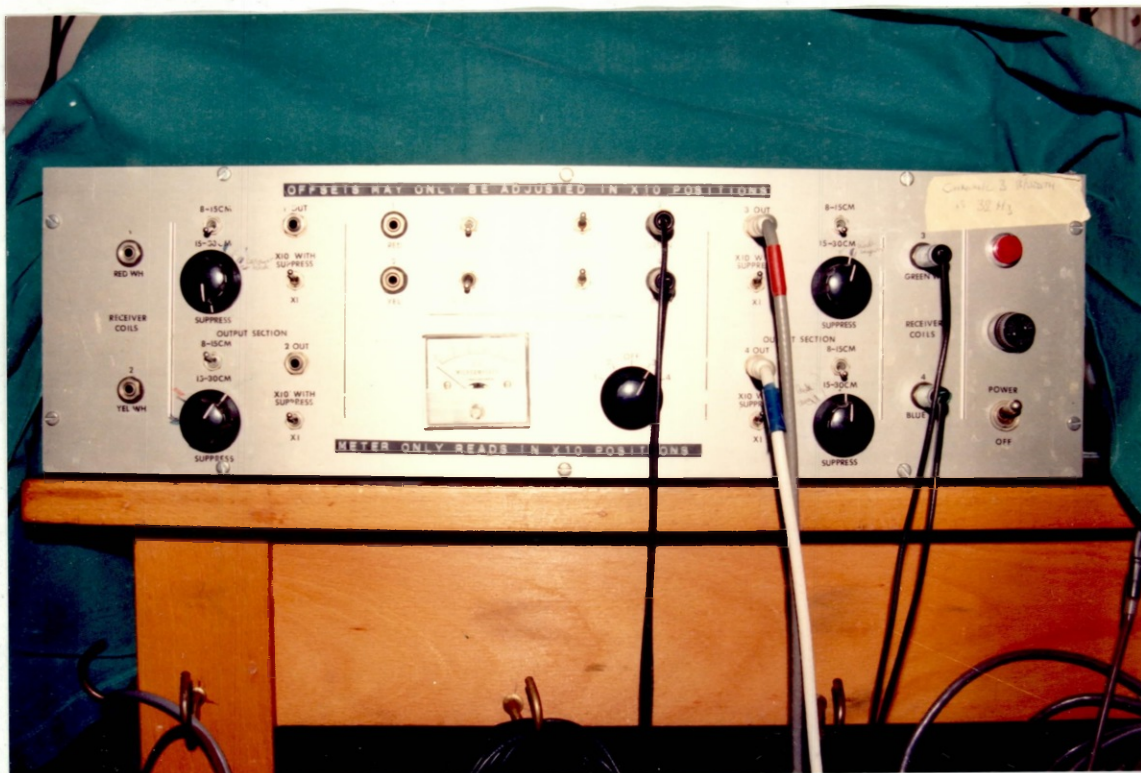


Figure 15 Mingograph 800 ink jet recorder
(Siemens-Elema, Sweden)

2.11.1 Basic Principles:

It is found that a conductor with a current flowing through it can exert a force on another conductor carrying a current. This is the property known as magnetism. The region throughout which a magnet or a current carrying conductor exerts its effects is known as magnetic field and a changing magnetic field induces a flow of electrons in a conductor to produce electric current (Parbrook, 1986). Magnetometers, introduced by Mead and coworkers in 1967 measure changes in anteroposterior or lateral diameters of the ribcage and abdomen during respiration. This technique consists of exciter and receiver coils placed on opposite body surfaces. Alternating current in the exciter coil generates a magnetic field which induces a voltage in the receiver coil. The voltage induced in the receiver coil is universally proportional to the cube of the distance separating the two coils. Since the change in diameter during breathing is small (0.5 cm for resting breathing and 4 cm for vital capacity breathing) relative to the distance between the two coils (15-35 cm) the non-linear relationship between voltage change and diameter change may be approximated to a linear fit (Tobin, 1986). Two pairs of linearised magnetometers (Norman-Peterson, Boston MA) were used to measure changes in ribcage (RC) and abdominal (abdo) configuration (Mead et al, 1967; Fig. 16, 17)

Figure 16 a) Magnetometer Amplifier and b) Two
pairs of linearised magnetometer coils used for monitoring
chest and abdominal anteroposterior diameters (N H
Peterson, Boston, M A)



2.11.2 Positioning

Chest wall anteroposterior diameter was measured at the level of the fifth intercostal space. Abdominal anteroposterior and transverse dimensions were measured at a level of 1 cm above the umbilicus (Fig 17). The magnetometer coils were attached to the subject's skin using double sided stick discs (Medical products, 2181) and were further secured with 2-4 strips of adhesive tape (Micropore). Care was always taken to place the pairs of coils parallel to each other to ensure accurate recording of distance. Interference was minimised by using channels of band frequency 4.23 KHz and 5.91 KHz for ribcage anteroposterior diameter and band frequency of 3.19 KHz and 4.82 KHz for abdominal anteroposterior diameter.

2.11.3 Measurements

Recordings by magnetometers were used only to ensure that normal subjects and patients were at Functional Residual Capacity (FRC) before each manoeuvre and to demonstrate paradoxical motion of the chest wall during respiration. Each set of coils was zeroed at the start of recordings and rezeroed at intervals following changes in posture i.e. sitting, semi-supine and supine positions.

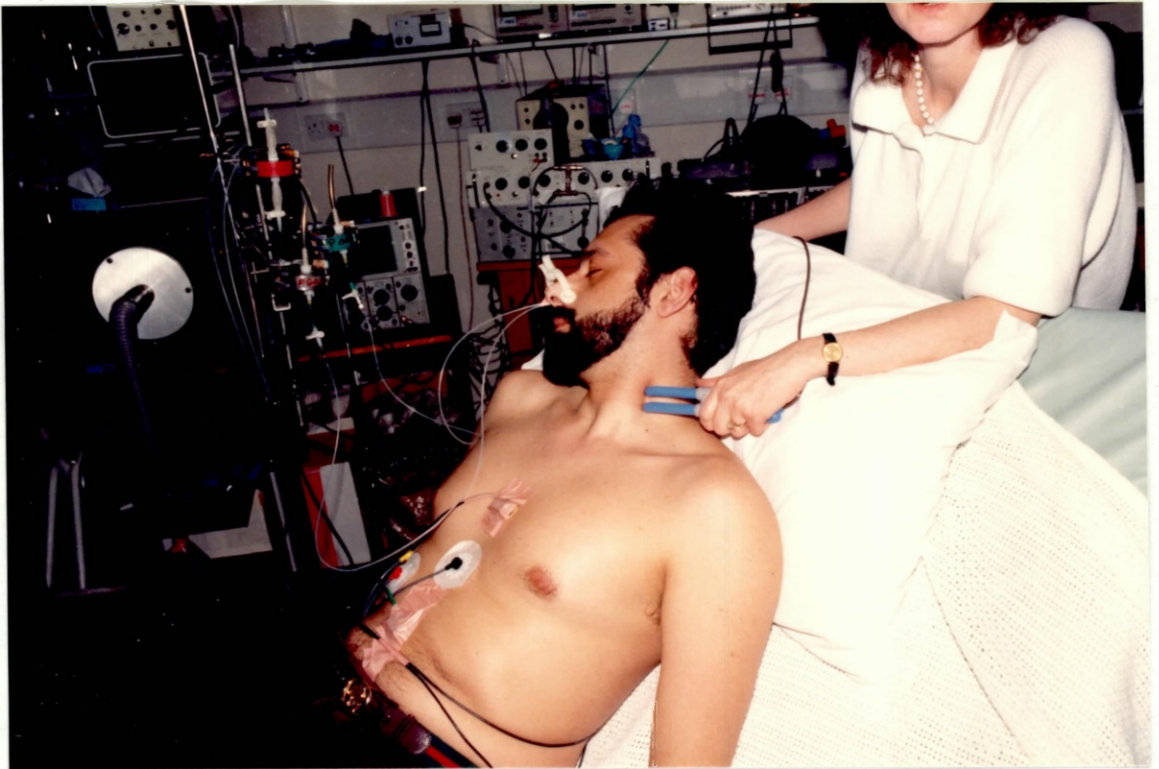


Figure 17 Photograph showing a normal subject (NK) and the operator (CML) stimulating *left* phrenic nerve in the semi-supine posture. The position of the chest and abdominal magnetic coils as well as the right diaphragmatic EMG electrodes are shown.

2.11.4 Frequency Response:

The frequency response of the magnetometers was 32 Hz on the channel which was used to measure abdominal anteroposterior movement and 12 Hz on channel which was used to measure rib-cage anteroposterior changes. The range of frequency response was considered to be adequate for the present studies (Mier, 1986).

2.12 LUNG FUNCTION:

Routine lung function tests were performed for each patient referred to the Respiratory Muscle Laboratory before each study at the Lung Function Laboratory of the Brompton Hospital. The first second expiratory volume (FEV1) was derived from a trace of forced vital capacity (FVC) performed on an Ohio dry spirometer (Spiroflow 131) and flow-volume loops were recorded. Absolute lung volumes were measured by a constant volume body-plethysmograph. Transfer factor (DLGO) and diffusion coefficient (KCO) were estimated with the carbon monoxide technique. Normal values were taken from Cotes (1979) and normal values were considered if they were lying between 85-115% of the predicted values. Partial arterial oxygen (PO_2) and carbon dioxide (PCO_2) tension were analysed by a Corning-170 blood gas analyser.

2.13 VITAL CAPACITY:

Measurements of vital capacity (VC) during

muscle function tests were obtained using an Ohio Dry Spirometer (Fig 18).

2.13.1 Measurement:

Records of VC were first^{made} with the subject in the seated position and subsequently supine. A conventional flanged or cardboard mouthpiece was used. The patient had always a noseclip on. After 4-5 normal breaths the patient was asked to inspire until his/her lungs were fully inflated i.e. to total lung capacity (TLC) and then to expire slowly until no more air could be exhaled, i.e. to residual volume (RV). At least 3-5 recordings were performed in each position until the values were reproducible and ^{the} best was recorded and taken to represent patients data. The supine fall in VC was calculated as the absolute fall taken as a percentage of the VC in the seated position. In few patients who were unable to tolerate the supine posture, "supine" values were obtained at an angle of 20° and they were returned to a more tolerant position as soon as possible.

2.13.2 Calibration

Calibration of the spirometer was performed using a 3 litre commercially available (Vitalograph) air syringe with 500 ml steps.

2.14 STATISTICAL ANALYSIS:

Appropriate statistics were applied which are described in the individual chapters. Data are usually

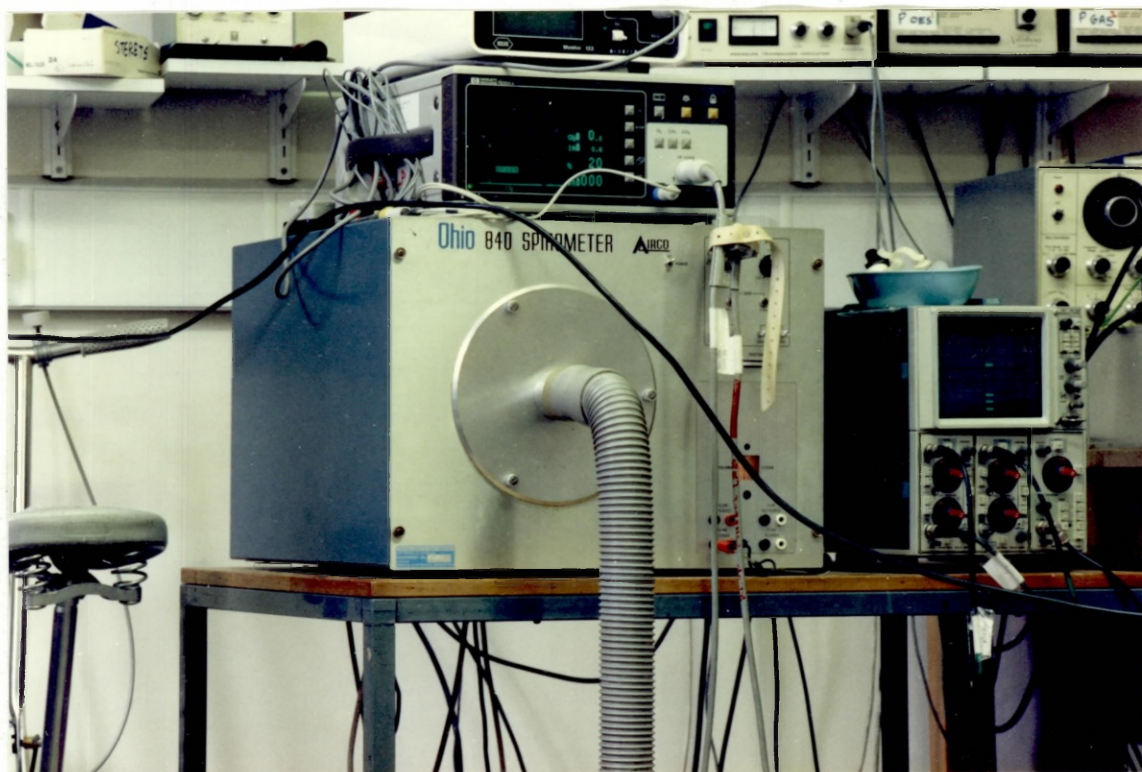


Figure 18 Ohio - 840 Dry Spirometer used for the measurement of VC. (Ohio Medical Products, Wisconsin, USA)

expressed as mean $\pm$ standard error (SE). All statistical analysis was performed by using Minitab (Computer Statistical package data analysis system, Pensilvania State University, 1982).

CHAPTER 3

THE EFFECT OF POSTURE AND ABDOMINAL BINDING ON RESPIRATORY PRESSURES

3.1 INTRODUCTION

Postural changes have profound effects on the chest wall and these changes are mostly due to gravitational factors acting on the abdominal contents. Changes in posture are common in everyday life and exert forces which alter the mechanics of the respiratory system, specifically resting end-expiratory lung volume (FRC) decreases substantially in the supine posture unlike residual volume (RV) or total lung capacity (TLC) which remain unchanged. This change is mainly mediated through the diaphragm which is thought to be passively distended by the abdominal contents. The transition from supine to an erect posture shortens the fibres of the diaphragm. When the operational length of diaphragmatic muscle fibres changes with posture it can produce an alteration of contractility. If uncompensated, a reduction of tidal volume would be expected. However, it is known that tidal volume is maintained by two strategies: (i) increased firing frequency to the diaphragm, (ii) contraction of the expiratory muscles to restore end-expiratory length of the diaphragmatic fibres (Pengelly, Alderson and Milic-Emili, 1971; Kim et al, 1976; Banzett and Mead, 1985). By contrast, little is known about the effect of posture on the generation of maximal respiratory pressures. Occasionally it is necessary to investigate patients who are

unable to assume an upright position, as on the intensive care unit. The aim of this study was to quantify the effect of posture on the following indices of respiratory muscle strength: (i) maximal static inspiratory (P_Imax) and expiratory (P_Emax) mouth pressures (Ringqvist, 1966; Koulouris et al, 1988), oesophageal (P_{oes}) and transdiaphragmatic (P_{di}) pressures generated by (ii) maximal sniffs (Miller, Moxham and Green, 1985; Laroché et al, 1988; Koulouris et al, 1988) and (iii) bilateral phrenic nerve stimulation (Sarnoff, Sarnoff and Whittenberger, 1951; Bellemare and Bigland-Ritchie, 1984; Bellemare, Bigland-Ritchie and Woods, 1986).

3.2 METHODS

The study had the approval of the local Ethical Committee and subjects gave informed consent. We studied six healthy respiratory physiologists (5 male, 1 female, age range 30-45 years). All were highly motivated and very familiar with the techniques to be employed. All pressures were measured using Validyne MP45-1 differential pressure transducers (range $\pm$ 350 cm H₂O, Validyne Co, Northridge, CA). The transducers were calibrated before each study using U-tube water and

mercury manometers as pressure standards. Oesophageal (Poes) and gastric (Pgas) pressures were measured with 10 cm balloons of 3.5 cm circumference, attached to 100 cm polyethylene catheters (PK Morgan, Rainham, Kent) and positioned (Fig 19) in the standard manner (Milic-Emili, 1964). Transdiaphragmatic pressure (Pdi) was derived by electronic subtraction ($Pdi = Pgas - Poes$) using Pdi at resting end-expiration as the zero reference point (Agostoni and Rahn, 1960). The response time of each balloon catheter-recorder system was measured by placing the balloon catheter within a second larger pressurised balloon, and causing a square wave fall in pressure by bursting the larger balloon with a red hot needle ("pop test") (Sykes, Vickers and Hull, 1981)). The pressure signal was recorded at a paper speed of 1000 mm/sec. The 10-90% rise time (Tr) was found to be 0.017 second. The maximum frequency response (f_{3db}) was determined from the equation $f_{3db} = 1/3Tr$ for the critically damped signal (Clayton, 1979), and was 20 Hz (Chapter 2).

Two pairs of linearised magnetometer coils were used to indicate thoracoabdominal movements (Mead, 1967) and to help identify FRC where necessary (Fig 19). Phrenic nerve stimulation was performed percutaneously

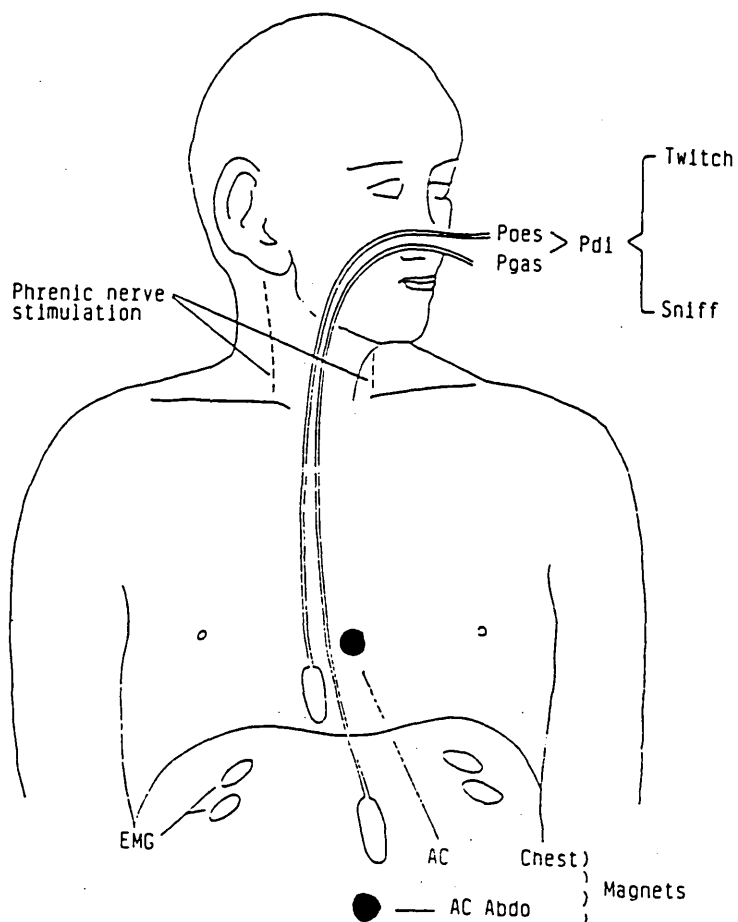


Figure 19 Position of Poes and Pgas balloon catheters, magnetic coils and EMG electrodes

with bipolar electrodes (Medelec Ltd, Old Woking, Surrey) and a constant voltage stimulator (Digitimer, Welwyn, Herts), (Bellemare and Bigland-Ritchie, 1984; Bellemare, Bigland-Ritchie and Woods, 1986). Square wave stimuli of 100 microsecond duration were applied with a frequency of 1Hz at the posterior border of the sternomastoid (Sarnoff, Sarnoff and Whittenberger, 1951). Electrical contact was achieved with saline-soaked felt pads. The electromyogram (EMG) from both hemidiaphragms were recorded using surface electrodes placed in the 7th intercostal space and over the 8th rib (Fig 18, 19) after suitable preparation of the skin (Newsom-Davis, 1967). The EMG signals were integrated by a Neurolog EMG amplifier (Digitimer, Welwyn, Herts) and displayed on a Tektronix 5103N storage oscilloscope (Tektronix Inc, Oregon) (Chapter 2).

A rubber tube mouthpiece was used to obtain P_Imax and P_Emax as maximal pressures were required (Koulouris et al, 1988; Chapter 4). Vital capacity and tidal volume were measured in all postures, bound and unbound, with an Ohio 840 spirometer (Ohio Medical Products, Wis), and dynamic compliance of the lung derived by simultaneous measurement of oesophageal pressure. All calibrated signals were recorded onto paper using a Mingograf 800 ink-jet recorder (Siemens-Elcoma, Sweden).

3.3 PROTOCOL

3.3.1 Body Position and Abdominal Binding

All subjects were studied in three body postures; (a) seated (Se) in a high-backed chair, (b) semi-supine (30s) on a bed with the upper body tilted 30° above the horizontal, (c) totally supine (Su) on a bed without a pillow. Postures were adopted in random order. Static mouth pressures were measured on a separate occasion from sniffs and twitches. Sniff and twitch pressures were measured with the abdomen carefully bound so that ribcage movements were hindered as little as possible, and repeated unbound. The validity of Poes recorded in each posture was confirmed by the simultaneous measurement of sniff oesophageal and sniff mouth (Pmo) pressures (Koulouris et al, 1988: Chapter 5). Where necessary, the position of the oesophageal balloon was adjusted until the ratio sniff Poes/sniff Pmo was within 10% of unity (Baydur et al, 1982; Baydur, Cha and Sassoon, 1987). The abdominal magnetometer trace revealed that movement could be minimised but not completely prevented, particularly when exhaling to RV.

3.3.2 Phrenic nerve stimulation

Bilateral phrenic nerve stimulation was employed as this has previously been shown to retain the normal geometry of the diaphragm (Bellemare, Bigland-Ritchie and Woods, 1986). Supramaximal stimulation was confirmed for each subject in all postures prior to making the definitive measurements. The stimulating

voltage was raised progressively until no further increase in the size of the diaphragmatic M waves could be produced (Bellemare and Bigland-Ritchie, 1984; Bellemare, Bigland-Ritchie and Woods, 1986). Any subsequent decrease in the size of the M waves resulted in rejection of those data. Twitch Pdi was measured at resting end-expiration with a noseclip. Criteria for data acceptance were (Mier, 1986): (a) the diaphragm EMGs showed maximal evoked diaphragm muscle action potential in relation to the twitch Pdi, (b) there was no distortion of the Pdi trace by oesophageal contraction, (c) the M waves were distinct from the electrocardiogram, (d) twitches were performed at FRC as judged by the magnetometers and pre-twitch Poes and Pdi. At least three sets of 10 twitches satisfying these criteria were obtained in each of the three postures, bound and unbound. The 5 biggest twitches were used for analysis.

3.3.3 Maximal Sniff

In this study a "sniff" was characterised by a short, vigorous inspiratory effort through the unoccluded nose from FRC (Laroche et al, 1988; Koulouris et al, 1988; Miller, Moxham and Green, 1985). Ten maximal sniffs were performed in each body posture. Criteria for data acceptance were (Koulouris et al, 1988: Chapter 5): (a) peak pressure maintained for less than 50 millisec, (b) total sniff duration less than 500 millisec, (c) pressure wave had smooth upstroke and decay curves, (d)

sniff performed from FRC as judged by magnetometers and pressure pre-sniff Poes and Pdi. The five biggest sniffs satisfying these criteria were used for analysis.

3.3.4 Maximal static mouth pressures (PEmax and PImax)

Static mouth pressures were measured with a noseclip. All measurements satisfied the criteria of Ringqvist (Ringqvist, 1966) such that: (a) no extra leakage occurred, (b) the three highest pressures recorded were similar (within 5%), (c) subjects felt that they had given maximal efforts. The highest pressure maintained for one second was used for analysis. Loud verbal encouragement was given to the subjects during the voluntary manoeuvres.

3.4 STATISTICAL ANALYSIS

Results of pressures are expressed as mean $\pm$ 1 standard error (SE). Paired t-tests were used to detect statistically significant differences between the pressures obtained in each posture, bound and unbound.

3.5 RESULTS

3.5.1 Twitch Poes, Pgas and Pdi

The coefficient of variation for the twitch Pdi data selected for analysis was less than 7% in all subjects for all postures, bound or unbound (Table 1).

The mean values for bound twitch Pdi were significantly higher than unbound in all postures (Figure 20). Changes of twitch Pdi with binding were mediated through a significant increase in Pgas, Poes remaining unchanged. Posture did not significantly alter twitch Pdi, whether bound or unbound, although Pdi tended to be less in the Se position when unbound. However the changes of posture, Poes and Pgas did change significantly in opposite directions (Table 2).

3.5.2 Sniff Poes, Pgas and Pdi

The reproducibility of sniff Pdi in each posture, either bound or unbound, was similar to that previously reported for the unbound seated position (Miller, Moxham and Green, 1985). For sniff Pdi data the coefficient of variation was less than 8% (Table 3). In contrast to twitch Pdi binding the abdomen did not increase sniff Pdi in any posture. However, moving from the seated to the supine posture resulted in a significantly lower sniff Pdi, whether bound or unbound (Figure 21). The decrease in sniff Pdi in the supine posture resulted from reductions in both Poes and Pgas (Table 4).

3.5.3 Maximum static mouth pressures

Similarly, both PImax and PEmax were significantly lower in the Su posture compared to the Se posture (Figure 22; Table 5).

Table 1
within day coefficient of variation
of twitch Pdi (%) (Best Set)

Unbound			
Subject	Se	30s	Su
N.K.	2.14	2.44	3.11
D.A.M.	3.37	1.73	4.08
M.G.	3.44	3.32	5.83
J.M.	1.57	2.44	2.45
J.G.	6.99	5.15	4.14
C.L.	<u>2.44</u>	<u>0.00</u>	<u>3.03</u>
Mean	3.32	2.51	3.77
Range	(1.57-6.99)	(0.00-5.15)	(2.45-5.83)

Bound			
	Se	30s	Su
N.K.	2.09	3.75	2.44
D.A.M.	5.83	2.64	3.02
M.G.	1.38	1.60	2.32
J.M.	4.91	1.33	1.55
J.G.	4.34	3.35	3.03
C.L.	<u>1.75</u>	<u>0.00</u>	<u>2.26</u>
Mean	3.38	2.11	2.43
Range	(1.38-5.83)	(0.00-3.75)	(1.55-3.03)

Table 2
Results of Pdi, Poes and Pgas during bilateral
Phrenic Nerve Stimulation (cmH₂O, mean $\pm$ SE, N=6)

	Pdi		Poes		Pgas	
	Bound	Unbound	Bound	Unbound	Bound	Unbound
Su	35.9(3.0)	29.7(3.5)	22.5(2.2)	23.9(3.2)	13.7(0.9)	6.3(1.2)
30s	37.9(3.7)	29.4(3.3)	20.9(1.9)	21.0(2.2)	16.9(2.0)	8.4(1.2)
Se	37.0(3.0)	26.4(2.2)	19.4(2.4)	16.13(2.3)	17.6(2.3)	10.2(0.3)

Su = supine, 30s = semi-supine, Se = seated

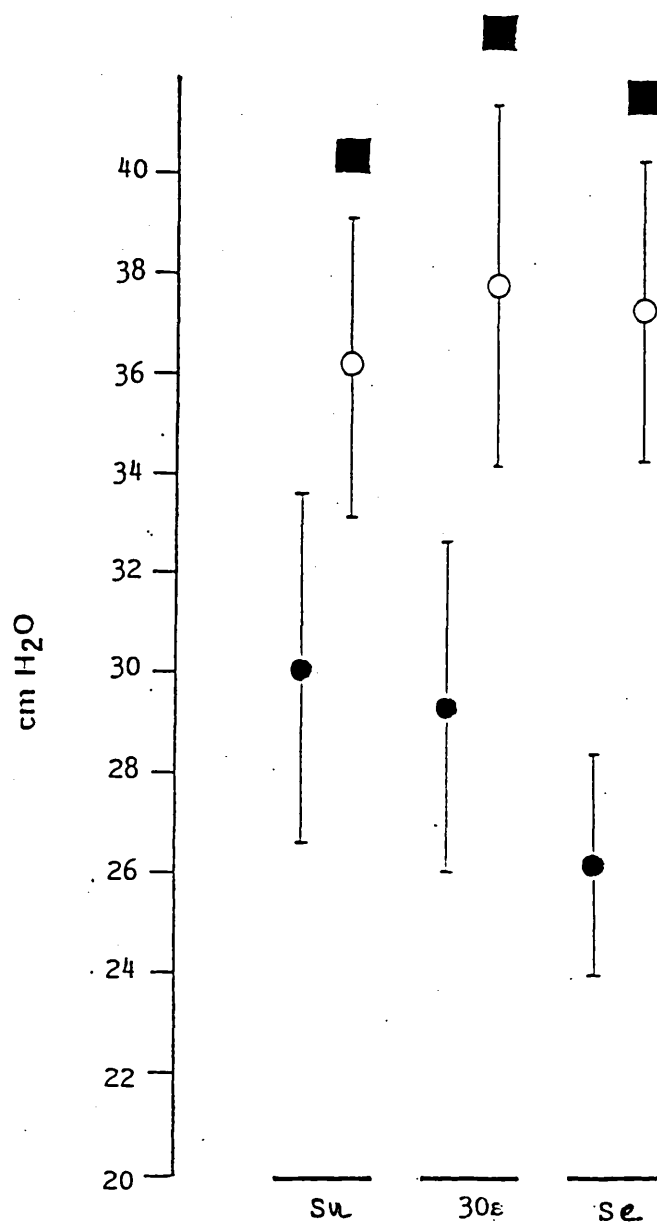


Figure 20 Results of twitch Pdi in 6 subjects (○ bound; ● unbound), in the seated (Se), 30° semi supine (30s) and supine (Su) postures. ■ = significant difference between bound and unbound values ($p < 0.001$).

Table 3
within day coefficient of variation
of Sniff Pdi (%)

Subject	Unbound		
	Se	30s	Su
N.K.	5.70	6.34	3.42
D.A.M.	2.32	1.88	1.58
M.G.	3.49	4.87	4.67
J.M.	0.82	1.21	3.01
J.G.	5.30	7.22	6.00
C.L.	<u>2.44</u>	<u>1.85</u>	<u>3.80</u>
Mean	3.34	3.89	3.74
Range	(0.82-5.70)	(1.21-7.22)	(1.58-6.00)

Subject	Bound		
	Se	30s	Su
N.K.	5.51	4.69	2.14
D.A.M.	1.98	5.92	0.00
M.G.	3.18	0.97	7.75
J.M.	4.70	2.31	1.02
J.G.	1.41	1.64	2.75
C.L.	<u>2.86</u>	<u>1.78</u>	<u>3.55</u>
Mean	3.21	2.88	2.86
Range	(1.41-5.51)	(0.97-5.92)	(0-7.75)

Table 4
Results of Pdi, Poes and Pgas
during a maximal sniff (cmH2O, mean±SE, N=6)

	Pdi		Poes		Pgas	
	Bound	Unbound	Bound	Unbound	Bound	Unbound
Su	109.3(8.15)	116.2(9.1)	98.8(7.6)	105.7(10.2)	10.6(1.6)	10.5(5.0)
30s	120.5(10.6)	120.0(9.9)	103.4(7.5)	109.5(10.6)	17.2(6.7)	10.5(4.2)
Se	132.6(8.0)	129.7(11.8)	108.2(7.2)	110.7(9.1)	24.4(3.6)	19.0(7.2)

Su = supine, 30s = semi-supine, Se = seated

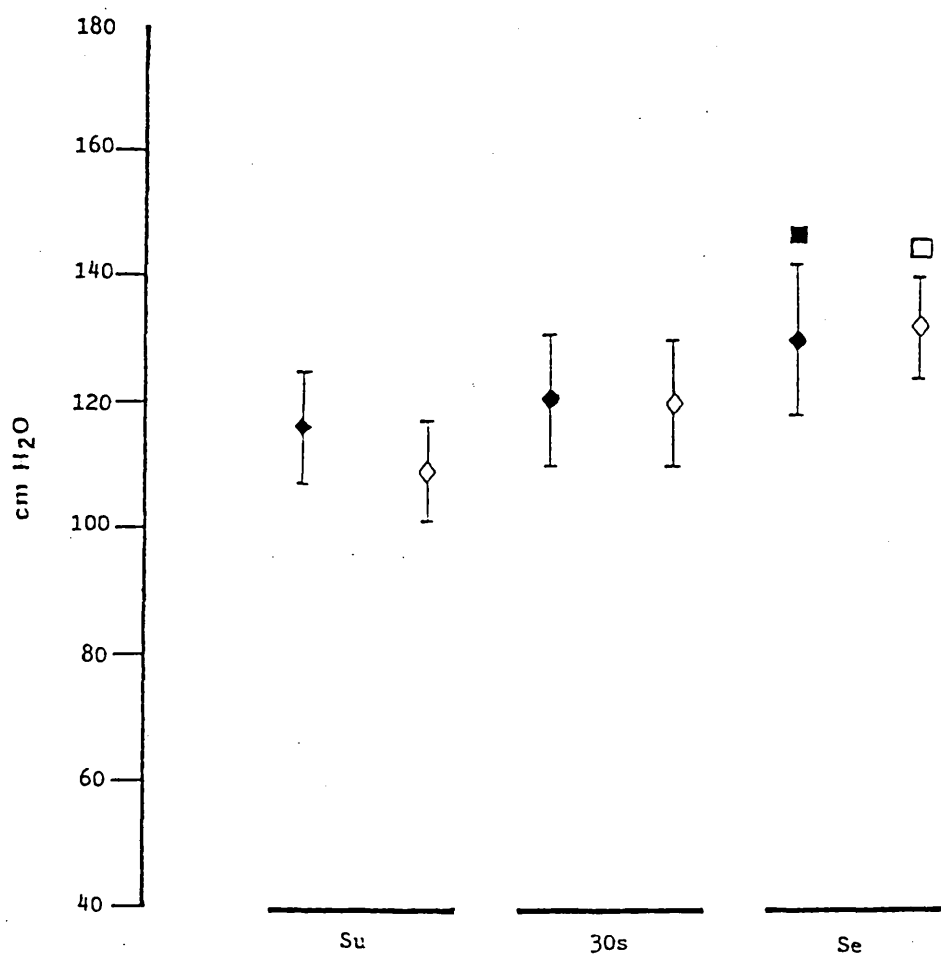


Figure 21 Results of sniff Pdi in 6 subjects ($\diamond$ bound; $\blacklozenge$ unbound), in the seated (Se), 30° semi supine (30s) and supine (Su) postures. $\square$ = significant difference between postures ($p < 0.05$) in the subjects bound; $\blacksquare$ = significant difference between postures ($p < 0.05$) in the same subjects unbound

Table 5
Results of Maximum Static Mouth Pressures (cmH₂O, mean $\pm$ SE, N=6)

	Inspiratory (PImax)	Expiratory (PEmax)
Su	119.16(14.64)	187.08(20.9)
30 ⁰ -s	127.91(13.82)	190(18.11)
Se	131.25(17.12)	209.16(20.54)

Su = supine, 30_s = semi-supine, SE = seated

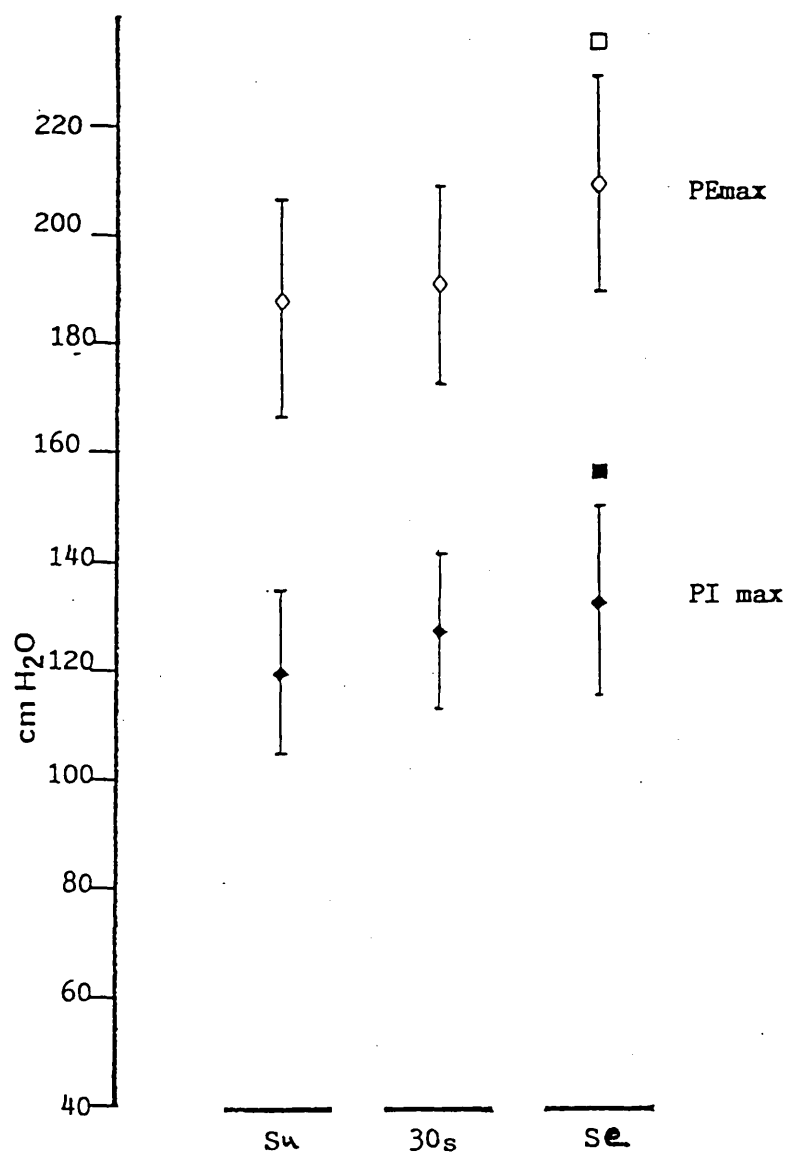


Figure 22. Results of PEmax and PI max in 6 subjects with the abdomen unbound. □ ■ = significant difference between postures ($P < 0.05$).

3.6 DISCUSSION

The results of the present study show that posture and abdominal binding have different effects on voluntary and involuntary respiratory manoeuvres.

3.6.1 Twitch Pdi

These data show that posture has no effect on twitch Pdi and confirm the previous observation that abdominal binding markedly increases this pressure. The present data extend the work of Bellemare and Bigland-Ritchie by comparing the interaction of posture and binding in the same subjects (Bellemare and Bigland-Ritchie, 1984; Bellemare, Bigland-Ritchie and Woods, 1986).

As a human subject rises from supine to upright, the diaphragm moves to a less favourable position on its length-tension curve (McCully and Faulkner, 1983; Braun, Arora and Rochester, 1982; Smith and Bellemare, 1987). Tonic contraction of the abdominal muscles tend to restore the diaphragmatic fibres to the initial resting length (De Troyer, 1983; De Troyer 1984). However incomplete restoration of length is evidenced by a 25-30% increase in FRC that occurs when upright (Colville, Shugg and Ferris, 1955; Davies, San't Ambrogio and San't Ambrogio, 1980). As similar twitch pressures are obtained in the three different postures, compensatory mechanisms additional to the length-tension relationship must be employed.

At a given constant muscle length, the relationship between force generated and velocity attained by contracting muscle is hyperbolic (Fenn and Marsh, 1935; Hill, 1938). When the length of the muscle changes the only way to maintain force is to decrease the velocity of contraction (Fig 23). It has been shown that the velocity of shortening of diaphragmatic fibres is directly dependent on the rate of abdominal wall displacement (Goldman, 1978). Tonic contraction of abdominal wall musculature occurs with moving upright, and would reduce the rate of displacement constraining the diaphragmatic fibres to contract at reduced velocity (Sharp, 1985). By binding the abdomen, the velocity of contraction is further reduced towards the isometric limit with increased pressure generation in a given posture (Bellemare and Bigland-Ritchie, 1984; Bellemare, Bigland-Ritchie and Woods, 1986).

3.6.2 Maximal sniff Pdi, PImax and PEmax

Contrasting results are obtained with the voluntary manoeuvres. Maximal sniff Pdi is not increased by binding the abdomen. Binding markedly increases the stiffness of the anterior abdominal wall while this moves the diaphragm cephalad and maintains it at a more suitable length, binding per se may be the main factor

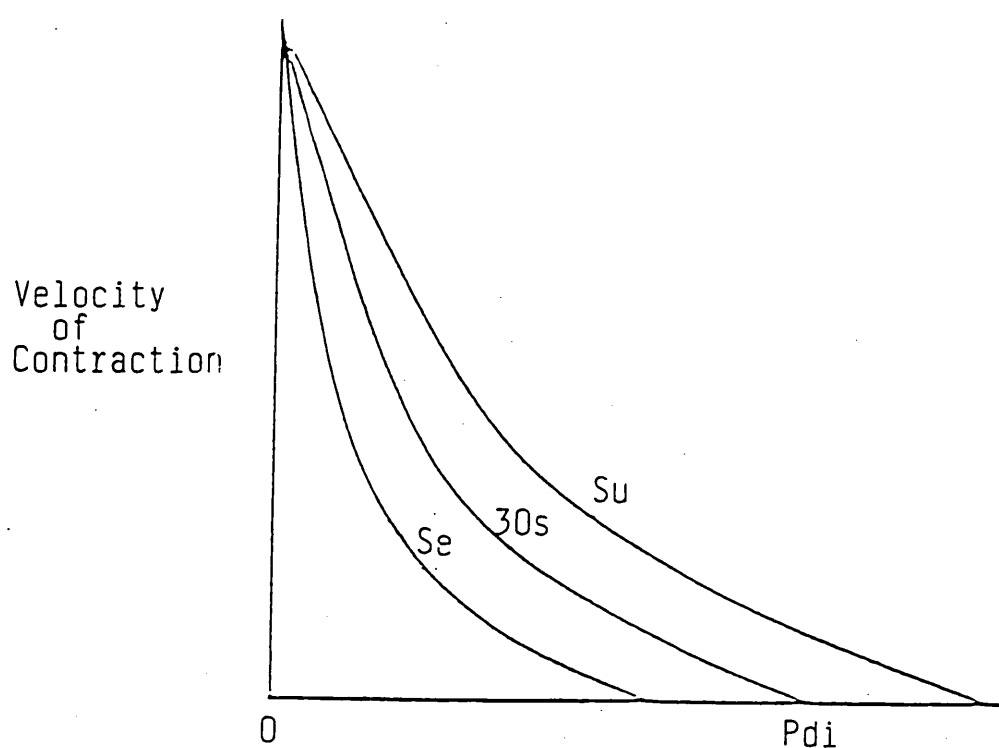


Figure 23. The force-velocity relationship of the diaphragm at three different postures. (Adapted from Sharp, 1985) (Su = Supine, 30s = Semi-supine, Se = Seated)

limiting inspiration by hindering the expansion of the lower chest wall (Green, Mead and Sears, 1978).

Alternatively binding the abdomen may lead to significant reflex inhibition of maximum inspiration due to discomfort. Indeed a preliminary report (Ford et al 1983) has shown that mechanical stimulation of the gallbladder causes inhibition of the inspiratory act. Maximal sniff Pdi, PImax and PEmax are significantly lower in the Su posture, an observation not previously reported. Sniff Pdi in the Se position is higher but this cannot be explained solely by optimization of diaphragmatic length-tension or velocity-tension relationships, as this occurs in all postures. Additionally the length of the inspiratory muscles is unaltered by posture during a PImax effort because residual volume is unchanged. Similarly during the PEmax manoeuvre, the length of the expiratory muscles is unaltered as TLC is unchanged (Colville, Shugg and Ferris, 1955; Sharp, 1985). During maximal volition manoeuvres, muscles other than the diaphragm are recruited (Druz and Sharp, 1981; Estenne, Ninane and De Troyer, 1988). As well as respiratory function, these muscles show postural tonic activity, bracing the ribcage (Duron, 1973; Massion, 1976). The notion of recruitment in muscle physiology is also used to describe the gradation of total muscle force by addition and subtraction of active motor units. It has been shown (Burke, 1986) that under some conditions motor units in

slow, red muscles are recruited more readily than those in fast, white muscles. Conversely preferential recruitment of fast white muscle fibres occurs under other conditions (Denny-Brown, 1929). These orderly patterns of recruitment that occur during voluntary contractions and regulated by the nervous system may favour maximum force generation in the upright posture. The types of contraction of a skeletal muscle can be classified as follows (i) concentric, (ii) isometric and (iii) eccentric. These types of contraction very seldom occur alone in normal humans because various muscles are periodically subjected to impact forces, i.e. gravity which usually lengthens the muscles. In these phases the muscles are usually contracting eccentrically and concentric contraction follows. Thus, the combination of eccentric and concentric contractions forms a natural type of muscle function called the "stretch-shortening cycle" (Norman and Komi, 1979; Komi, 1984). This behaviour allows the final action (concentric contraction) to take place with greater force or power output than a movement initiated by concentric contraction alone. Although there are no systematic studies on the length characteristics of the external (inspiratory) intercostals at various postures they would be expected to increase their length and thus increase force output when they contract in upright posture. Also when an active muscle is under stretch, the activity from both the muscle spindles and the Golgi tendon organs will

increase. The magnitude of the stretch load will then determine which of the following reflexes - facilitatory or inhibitory - will dominate and thus the magnitude of potentiation. This mechanism is called "reflex potentiation" and has been demonstrated in well-trained athletes; preactivation before contact on the ground occurs very late but rapidly and is followed by pronounced increase of EMG activity via a stretch reflex (Komi, 1986). Higher activation (Laporta and Grassino, 1985) and better coordination (Mead, Milic-Emili and Turner 1963) of the ribcage muscles increases the maximal respiratory pressures obtained when upright. Druz and Sharp (1981) thought that the increased ribcage motion characteristic present in the upright posture is due to a combination of increased activation of ribcage inspiratory muscles plus greater activation of the diaphragm that, together with a stiffened abdomen, acts to move the ribcage more effectively during tidal breathing. By analogy, most of the chest wall muscles contributing to generate a maximal Pdi do so by expanding the thoracic volume (intercostals, diaphragm), stabilizing the ribcage (sternomastoid), or optimizing the length of other muscles (as abdominals lengthen the diaphragm) (Coldman and Becklake, 1959). These observations are reinforced by other studies. Goldman et al (Goldman, 1986) demonstrated that sniff Pdi is higher when tetraplegic patients with intact phrenic nerves are supine. Binding the abdomen of a tetraplegic increased

the Pdi obtained when the patient was erect, but it did not reach the supine value.

In the clinical setting, we observe that subjects are most comfortable when phrenic nerve stimulation is performed in the 30s position. The results of this study show that the reproducibility of twitch Pdi is unaltered by posture. When patients or normal subjects were studied, it was much easier to locate the phrenic nerves and maintain stimulus maximality in this posture (Mier, 1987). Any advantage of abdominal binding in producing higher twitch Pdi pressures is offset by patient discomfort and increased breathlessness. It is therefore suggested that stimulation is most convenient in the unbound semi-supine posture, keeping in mind that patients with a weak or paralysed diaphragm may be severely orthopnoeic when totally supine.

It may be concluded that (a) binding the abdomen increases twitch Pdi produced by bilateral phrenic nerve stimulation but confers no clinical advantage, (b) the semi-supine posture is preferable for ease of stimulation, (c) maximal sniff Pdi, PEmax and PImax must be standardised for posture when serial measurements are made in a given patient.

3.7 SUMMARY

We examined the effect of posture on the generation of respiratory pressures in 6 highly trained subjects. Transdiaphragmatic pressure (Pdi) was recorded

during bilateral phrenic nerve stimulation at 1 Hz (twitch Pdi) and maximal sniffs (sniff Pdi), at FRC. Three postures were examined: seated at 90° (Se), semi-supine at 30° (30s), and totally supine (Su). Measurements were made with abdomen bound and unbound. Maximum static inspiratory (PImax) and expiratory (PEmax) mouth pressures were measured with the abdomen unbound. Binding the abdomen significantly increased twitch Pdi in all postures (mean increase: 40% Se, 29% 30s, 21% Su; $p < 0.001$). Sniff Pdi was not increased by binding in any of the subjects. Changes of posture did not significantly alter twitch Pdi, bound or unbound. By contrast sniff Pdi, bound or unbound, and static mouth pressures were significantly reduced in the Su posture. These data suggest that the diaphragmatic function is optimised in the Se position. However voluntary manoeuvres which require a high degree of recruitment coordination and activation of other muscle groups are better performed in an upright position. It may be concluded that posture be standardised for serial comparative measurements of voluntary respiratory pressures in a given subject.

CHAPTER 4

COMPARISON OF TWO DIFFERENT MOUTHPIECES FOR THE MEASUREMENT OF P_{Imax} AND P_{Emax} IN NORMAL AND WEAK SUBJECTS

4.1 INTRODUCTION

Respiratory muscle dysfunction is an uncommon but important cause of respiratory disability. Chest physicians need to be able both to diagnose paralysis and quantitate weakness. It is then necessary to have suitable tests preferably non-invasive and simple for both the clinician and the patient. Certain muscle, metabolic and neurological disorders affect both the respiratory and limb muscles. The latter are amenable to direct measurements unlike the respiratory muscles because it is not currently possible to measure the forces generated by them directly. The number of muscles concerned with ventilatory movements is large and the way they cooperate and affect the respiratory apparatus is very complex. With the exception of the diaphragm it is not possible to quantify the individual contribution of the different muscles with respect to their ventilatory function (Agostoni and Rahn, 1960). The simplest and most widely applied technique for respiratory muscle strength assessment is the measurement of static mouth pressures (Green, 1984). A maximal effort is made against an occluded airway, with a small air leak to prevent glottic closure (Chapter 2). Maximum inspiratory pressure (P_Imax) is usually measured from RV, and maximum expiratory pressure (P_Emax) from TLC. By determining the maximum inspiratory and expiratory pressures at a defined respiratory level an integrated expression of the forces exerted by the inspiratory and expiratory muscles is

obtained. Mouth pressures can be sensitive and specific index of global weakness (Black and Hyatt, 1971; Gillam et al, 1964; Braun and Rochester, 1979; Saunders and Kreitzer, 1979) and are reduced before lung volumes (Moxham, 1982). This reduction in maximum static mouth pressures is often associated with the course of the muscle disease as in Duchenne's Muscular Dystrophy (Inkley, Oldenburg and Vignos, 1973), Amyotrophic Lateral Sclerosis (Kreitzer et al, 1978), Scleroderma (Chausow et al, 1984), Thyrotoxicosis (Siafakas et al, 1987; Wang and Poh, 1986), poorly nourished patients with COPD (Ethemliou et al, 1987), Myasthenia gravis (Radwan, Strugalska and Koziorowski, 1987) Cerebellar atrophy (Mier and Green, 1987), Common cold (Mier et al, 1988) and morbidly obese subjects (Kelly et al, 1988).

Ringqvist reports on a survey of data available in the literature concerning maximum respiratory pressures (Ringqvist, 1966; table 23; p 96-97). The first quantitative observations of respiratory pressures were made during the 18th century by Stephen Hales (1731). He remarks, "I have found by experience that by the bare inspiring action of the diaphragm and dilating thorax, I could scarcely raise the mercury .2 inches. Hutchinson (1846) gives a vague description of the instrument he used to measure "inspiratory" and "expiratory power". The first normal range for men and women is given by Waldenburg (1871) and the second by Taglietti and Agostoni (1958). Ringqvist noticed the

wide variation between normal ranges. He attributed these discrepancies in normal values with respect to most earlier reports in methodological differences. In recent years reference ranges for the normal values of P_Imax and P_Emax have been reported by a number of authors (table 6) but important differences also exist between these commonly quoted ranges. This variation may reflect differences in (a) the cohorts used to establish a normal range, (b) the criteria of measurement, (c) the design of the apparatus and the way it is used. It has even been suggested (Vincken, Ghezze and Cosio, 1987) that the usefulness of static mouth pressures as a test of respiratory muscle strength "is obscured by the failure of a study population to reach the usually quoted standard values". The objective of this study was to assess the importance of mouthpiece design to the pressures obtained, as there has been no standardisation of this variable in previous reports.

4.2 METHODS

4.2.1 Normal subjects and patients

The study was approved by the local ethical committee and subjects gave informed consent. We studied 2 groups (table 7): a healthy volunteer group comprising of 6 respiratory physiologists (RP) and 15 naive subjects

Table 6
Reference Normal Ranges for PEmax and PImax (cmH₂O, mean±SD)

Numbers	PEmax	PImax	Source	Mouthpiece Design
Male				
100	237+46	130+32	Ringqvist 1966	Tube
60	233+42	124+22	Black & Hyatt 1969	Tube
80	216+45	127+28	Arora N.S. 1983	Tube
325	154+82	114+36	Leech et al 1983	Flanged
80	148+34	106+31	Wilson et al 1984	Flanged
46	140+38	105+25	Vincken et al 1987	Flanged
Female				
100	136+38	98+25	Ringqvist	Tube
60	152+27	87+16	Black & Hyatt	Tube
121	138+39	91+25	Arora N.S.	Tube
480	94+33	71+27	Leech et al	Flanged
87	93+17	73+22	Wilson et al	Flanged
60	89+24	71+23	Vincken et al	Flanged

Table 7
Sex and Age Distribution of the 4 Sub-Groups in this Study

SUB-GROUP	MALES		FEMALES	
	number	age range (years)	number	age range (years)
RP(N=6)	4	32-44	2	32-40
NS(N=15)	7	23-34	8	19-32
NP(N=20)	9	21-74	11	25-50
LP(N=20)	13	17-71	7	19-80

RP=respiratory physiologists; NS=naive subjects; NP=patients with normal static inspiratory pressures (Black and Hyatt, 1969); LP=patients with low static inspiratory pressures (Black and Hyatt, 1969)

(NS), and a group of 40 patients referred for respiratory muscle testing. All the volunteer group were non-smokers, and without respiratory disease. The patient cohort was divided into two sub-groups using the normal ranges for P_Imax reported by Black and Hyatt (Black and Hyatt, 1969) for males and females. Those patients with a P_Imax (measured with a rubber tube mouthpiece) less than 2 standard deviations from the mean for their sex were classified into a low-pressure patient group (LP). Those within these limits were classified as a normal-pressure patient group (NP).

4.2.2 Mouthpiece design

We used two mouthpieces, one was a commercially available semi-rigid plastic flanged type (P K Morgan, Rainham, Kent). This type of mouthpiece is commonly used in pulmonary function laboratories (Fig 24). The other was a simple rubber tube of 4 cm internal diameter and 4.5 cm length (Fig 25), similar to that described by Black and Hyatt in their original paper (Black and Hyatt, 1969). Each of the mouthpieces was fitted to a common stem incorporating a 3-way tap (Figure 24, 25). The common stem was manufactured according to the design of Ringqvist (Ringqvist, 1966). The dimensions of the stem were length 27 cm, internal diameter 2.6 cm. A leak tube of length 3.7 cm and 2 mm internal diameter was

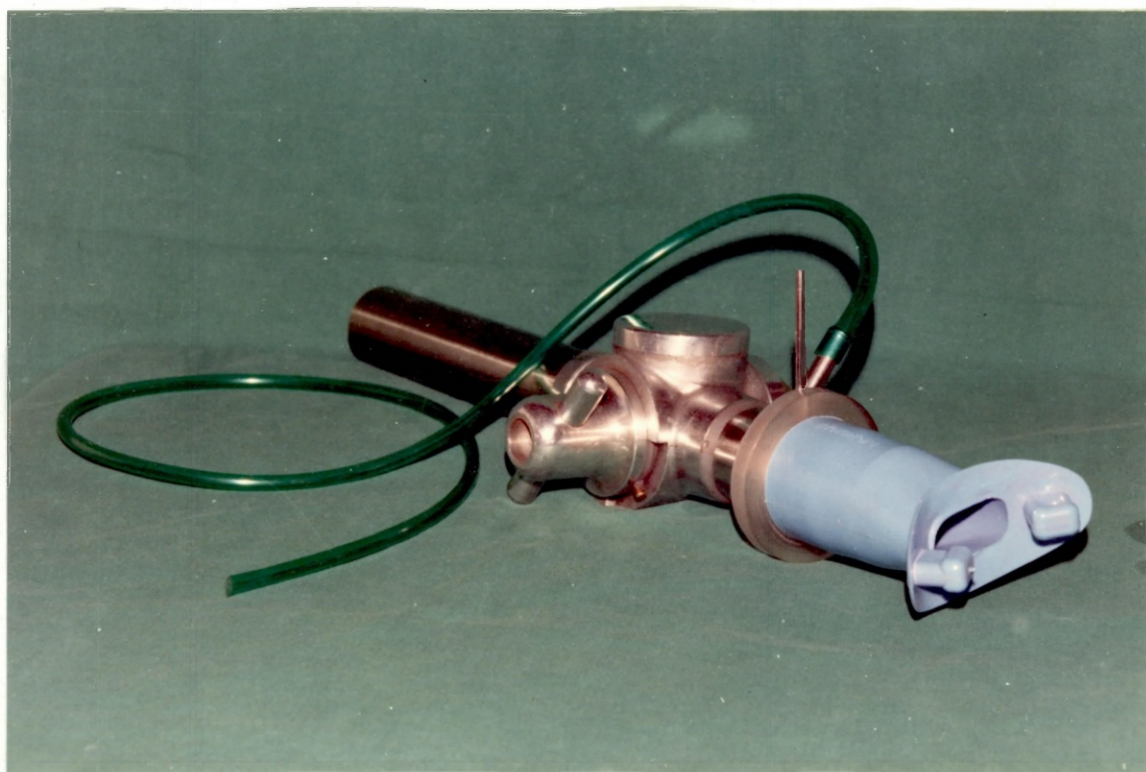


Figure 24 Flanged mouthpiece (P K Morgan) fitted to the common stem.

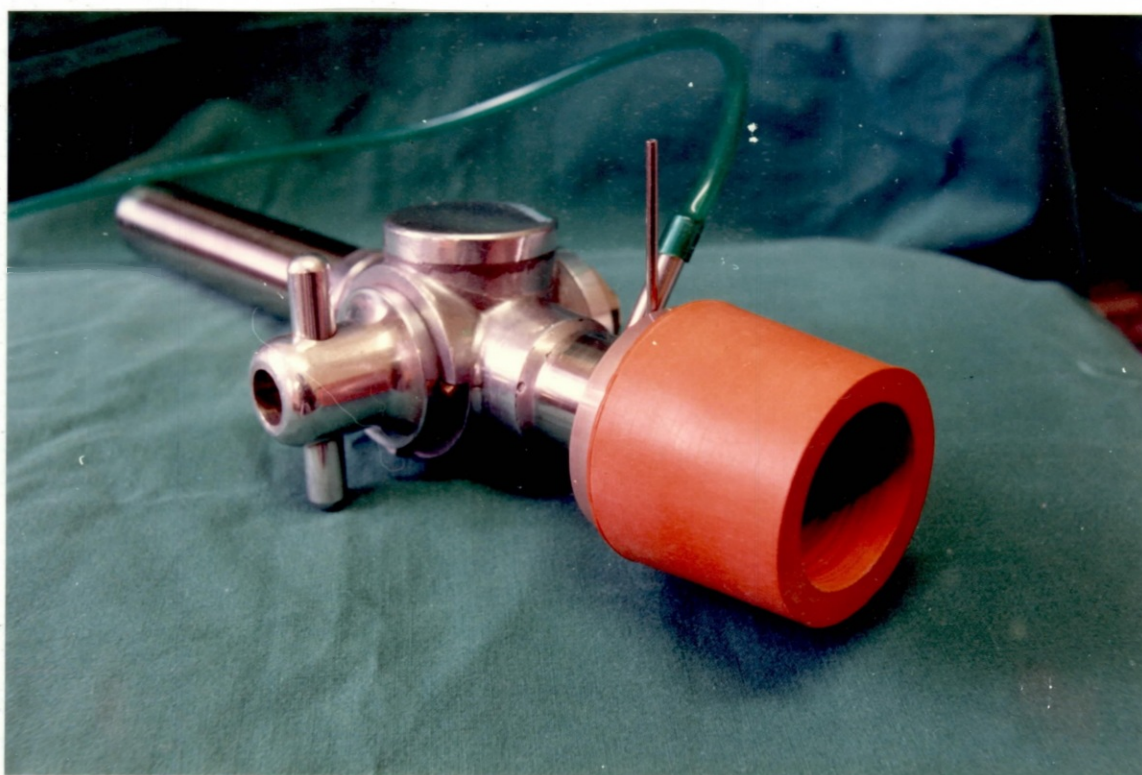


Figure 25. Rubber tube mouthpiece fitted to the common stem. (Manufactured at the Engineering Department, King's College Hospital, London).

incorporated into the stem 3 cm from the point of attachment of the mouthpiece. The 3-way tap was 7 cm from this point. The stem proximal to the 3-way tap was connected by a 70 cm fine polyethylene catheter to a Valindyne MP45-1 differential pressure transducer (range ± 350 cm H₂O, Vali dyne Co, Northridge, CA).

4.3 PROTOCOL

The transducer was calibrated before each study using a U-tube mercury manometer. Pressures were displayed on a Tektronix 5103N storage oscilloscope screen (Tektronix Inc, Oregon) and printed onto paper by Mingograf 800 ink-jet recorder (Siemens-Elema, Sweden). All studies were performed with a noseclip and with the subjects seated comfortably in a high-backed chair at 90° where they could see the oscilloscope screen. The flanged mouthpiece was held in the mouth behind the lips and gripped firmly by the teeth, the operator holding the stem. The subjects used their hands to hold the lips firmly onto the mouthpiece if a leak was noticed. Prior to a PEmax or PImax effort the three way tap was closed by the operator with the subject at TLC or RV respectively. When using the rubber tube mouthpiece, subjects held the stem with the 3-way tap already closed. When RV or TLC was reached, the subjects pressed the tube firmly against their face with the lips inside the tube. All subjects were given verbal encouragement and received uncalibrated visual feedback from the oscilloscope

screen. A period of learning preceded the definitive measurements. The mouthpieces were used in a randomised alternating order to minimise the effect of learning or fatigue on the definitive measurements. All measurements followed the criteria of Ringqvist (Ringqvist, 1966) such that (i) no extra leakage occurred, (ii) the 3 highest pressures recorded were similar (within 5%) and later attempts did not yield higher results, (iii) the subjects felt that they had given a maximum effort. At least 1 minute rest was allowed between efforts. Pressures maintained for less than one second were disregarded. The highest pressure generated by an individual for each mouthpiece was used for analysis.

4.4 STATISTICAL ANALYSIS

Mean values for the four sub-groups studied were obtained and paired t-tests were used to detect statistically significant differences between pressures measured with the 2 mouthpieces.

4.5 RESULTS

For PEmax mean values were significantly higher ($p < 0.02$) for the tube mouthpiece in all 4 subgroups (table 8, Fig 26, 27, 28, 29). For PImax the values were significantly higher ($p < 0.005$) with the tube mouthpiece only in the subgroup of patients (NP) who could generate normal inspiratory mouth pressures (table 8). When all normal subjects and normal patients were compared as a

Table 8
Comparison of Mouthpiece Design in 4 Sub-Groups cmH₂O, mean±S.D.,
*=p<0.02 **=p<0.005 (paired t-test)

Mouthpiece	PI max		PE max	
	Flanged	Tube	Flanged	Tube
RP (N=6)	119.9±36.7	125.5±48.7	140.3±56.5 *	178.6±62.4
NS (N=15)	99.1±31.2	106.±39.5	143.0±38.5 **	165.1±39.7
NP (N=20)	84.4±31.6**	93.1±32.2	117.6±42.8 **	142.5±46.8
LP (N=20)	40.7±13.7	43.6±14.9	84.1±36.2 *	94.7±38.1

RP=respiratory physiologists; NS=naive subjects; NP=patients with normal inspiratory pressures; LP=patients with low maximal static inspiratory pressures (Black and Hyatt, 1969)

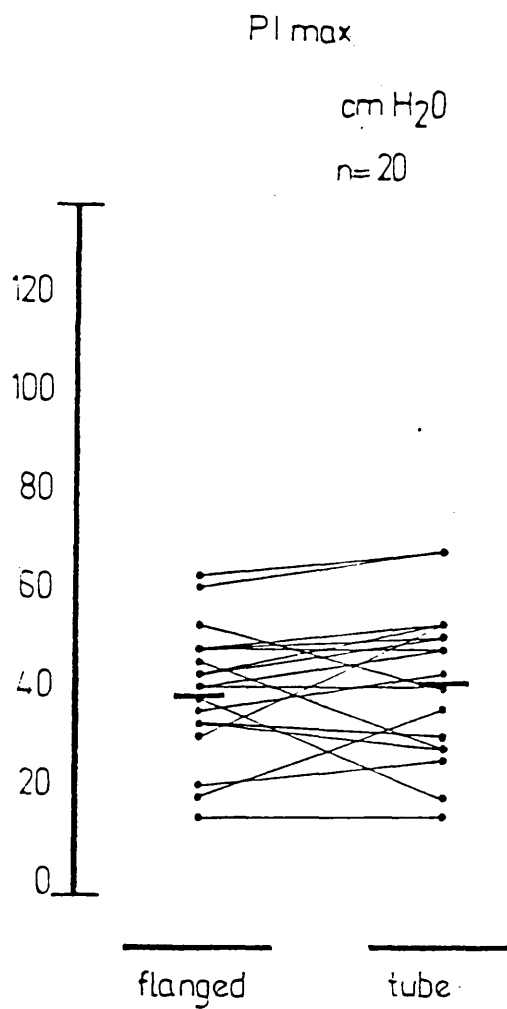


Figure 26 Values of PImax obtained in 20 weak patients (LP) using tube and flanged mouthpieces (paired t-test $t = 1.19$, $p = 0.25$)

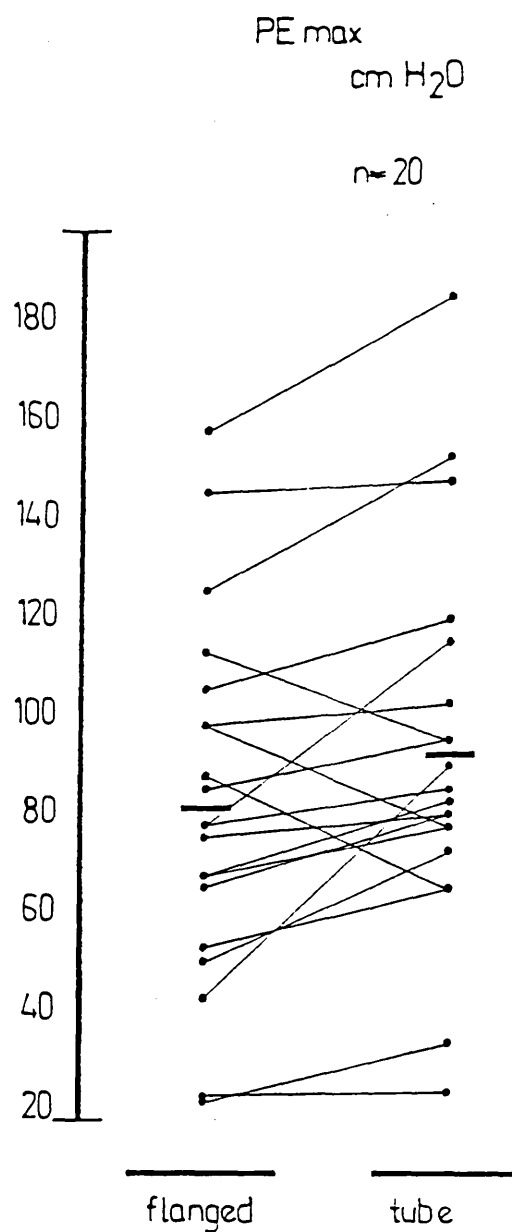


Figure 27 Values of PEmax obtained in 20 weak patients (LP) using tube and flanged mouthpieces (paired t-test, $t = 2.70$, $p = 0.014$).

group (RP, NS, & NP), the values were also significantly higher ($p < 0.005$) with the tube mouthpiece for both P_Imax and P_Emax (table 9; fig 28, 29). The pressures achieved by the males and females in our volunteer group (RP, NS) are given in table 10.

4.6 DISCUSSION

The results of the present study support the hypothesis that the choice of mouthpiece contributes to the differences between the normal ranges of static mouth pressures reported in the literature. When mouthpiece design is taken into account, the standard reference ranges (table 6) are remarkably similar although some variability remains. Our data are complementary to that of Vincken et al (Vincken, Ghezzi and Cosio, 1987) who concluded that such differences in the reference ranges were explained principally by the variation in the subject cohorts used.

Cook (Cook, Mead and Orzalesi, 1964) suggested that higher expiratory pressures would be obtained with a 'tube-type' mouthpiece simply because it prevented unwanted airleaks. In the present study, the absence of extra leakage was one of the criteria for data acceptance therefore this would not explain the differences obtained for P_Emax with the two mouthpieces, and could not explain the differences in P_Imax. Therefore, an important factor must be the manner in which the mouthpieces are used and not simply the prevention of extra leakage. To use a

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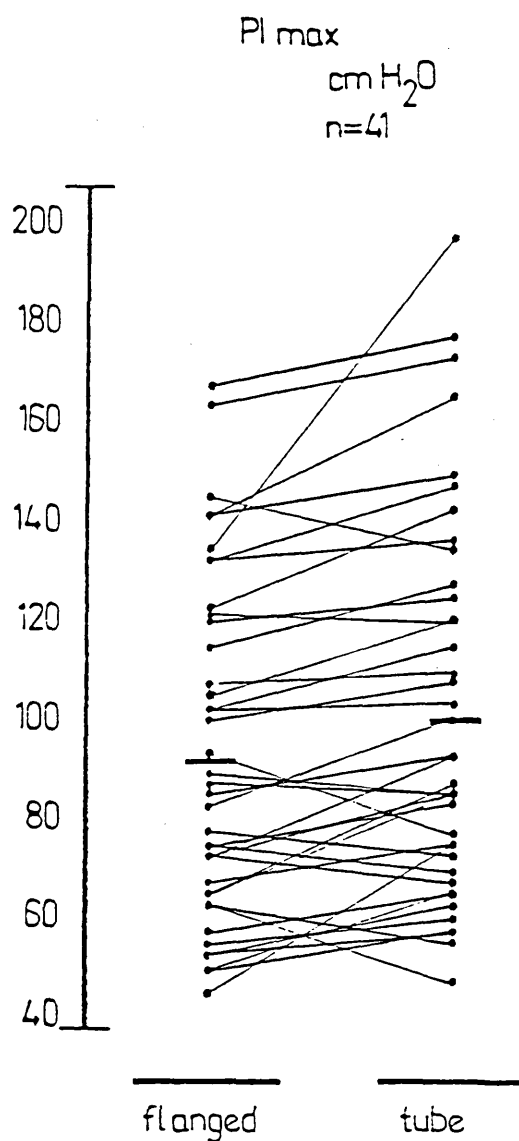


Figure 28 Values of PI_{max} obtained in 41 normal subjects (RP, NS, NP) using tube and flanged mouthpieces. (paired t-test, $t = 3.55$, $p = 0.002$).

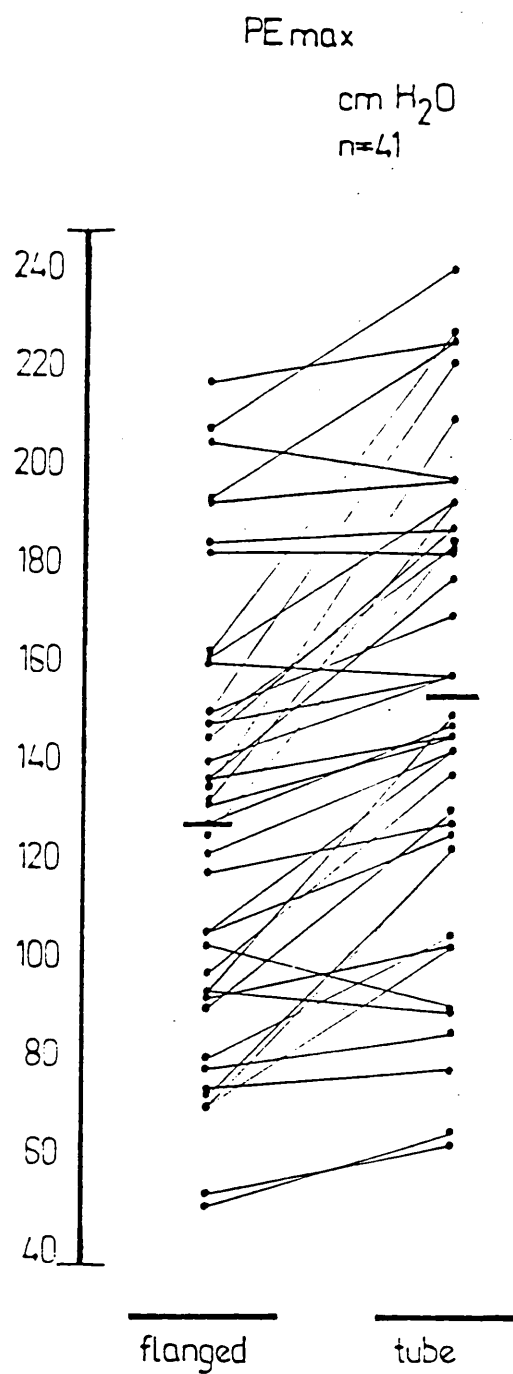


Figure 29 Values of PE_{max} obtained in 41 normal subjects (RP, NS, NP) using tube and flanged mouthpiece. (paired t-test, $t = 4.88$, $p = 0.0000$).

Table 9
Comparison of Mouthpiece Design in all 41 Subjects
without weakness (RP, NS, & NP) cmH₂O, mean±S.D., **=p<0.005

PI max			PE max	
Mouthpiece	Flanged	Tube	Flanged	Tube
	94.4±33.8 **	102.9±38.3	130.2±44.1 **	156.1±47.7

RP=respiratory physiologist; NS=normal subjects; NP=patients with normal static inspiratory pressures; (Black and Hyatt, 1969)

Table 10
Pressures recorded by 21 Normal Volunteers (RP, NS) analysed by Sex
cmH₂O, mean $\pm$ S.D.

		P _I max		P _E max	
		flanged	tube	flanged	tube
FEMALE	(N=10)	85.6 $\pm$ 24.5	89.7 $\pm$ 25.5	117.2 $\pm$ 31.6	144.7 $\pm$ 43.8
MALE	(N=11)	122.3 $\pm$ 31.6	133.5 $\pm$ 44.8	165.1 $\pm$ 38.7	190.6 $\pm$ 36.7

RP=respiratory physiologists; NS=naive subjects

rubber tube mouthpiece as described by Black & Hyatt (Black and Hyatt, 1969), requires the subject to press the apparatus firmly against the face with their arms. This requires the activation and coordination of muscle groups that are not recruited when using the flanged mouthpiece. Activation (Laporta and Grassino, 1985) and coordination (Mead, Milic-Emili and Turner, 1963; Mills, 1950) have been shown to be important determinants of maximal static respiratory pressures. If the flanged mouthpiece is used in a similar fashion to the tube mouthpiece, i.e. pressed by the subject towards the oral cavity, discomfort inhibits the subject's effort and extra leakage occurs during an expiratory manoeuvre as the seal between the lips and mouthpiece is less effective. When the operator holds a tube mouthpiece for the subject, the seal between lips and mouthpiece is often inadequate and lower plateau pressures are recorded. Therefore it is the manner in which the mouthpiece is used, as dictated by its design, that is the critical factor in the differences obtained in this study. Many patients with weak inspiratory muscles also have coexisting generalised muscle weakness. In these patients the recruitment of additional muscles when using the rubber tube mouthpiece may be less effective.

Our results are in contrast to those of Leech (Leech et al, 1983) Vincken (Vincken, Chezzo and Cosio, 1987) and Rubinstein (Rubinstein et al, 1988) who also compared a flanged mouthpiece with a mouthpiece fitting

around the lips in order to prevent a leak, and were unable to show a difference between the pressures obtained. However these authors do not give exact details of the manner in which the mouthpieces were used. I assume that the present tube mouthpiece is similar to the rigid cylindrical mouthpiece used by Vincken et al as these authors quote the paper of Black & Hyatt, upon which our tube design is based. The way in which they describe the use of the mouthpieces is similar to our flange method; it is unlikely that Vincken et al, and Rubinstien and coworkers used the cylindrical mouthpiece in the manner of Black & Hyatt if they could show no difference between it and the flanged mouthpiece. The small number of subjects used in their study would not allow any differences to be detected statistically.

We have 6 patients whose data could not be included in the statistical analysis because they could not hold the common stem due to generalised neuromuscular disease, hand deformity (Fig 30) or quadriplegia. In these 6 patients, no pressures could be obtained with the rubber tube mouthpiece in the manner described by Black and Hyatt (Fig 31). However using the flanged mouthpiece and assisted by the operator, satisfactory mouth pressures could be recorded in these patients (Fig 32).

Other factors contributing to the variability in reference normal ranges must be considered. In the present study, pressures produced by the subjects were recorded onto paper to facilitate the ease with which the



Figure 30 Hand of a patient with Charcot-Marie-Tooth disease.



Figure 31 Patient attempting to perform a PEmax manoeuvre with the tube mouthpiece.



Figure 32 Patient performing a PE and PImax manoeuvre assisted by the operator.

1 second plateau pressure could be identified. Previous studies (Cook, Mead and Orzalesi, 1964; Black and Hyatt, 1969; Rochester and Arora, 1983) estimated the plateau by eye from a pressure dial. It is possible that this led to an overestimation of the plateau value. Both men and women were included in the normal subject groups with the result that the mean mouth pressures recorded with a tube mouthpiece are lower than those of Black and Hyatt for men but greater than those for women. I analysed the present data to take account of sex and found this produced a closer agreement between this data for a tube mouthpiece and the reference normal ranges for both sexes (table 10). Ringqvist's data (Ringqvist, 1966) for males include both military conscripts and naive volunteers. He compared the mean pressures produced by the conscripts to those of volunteers and showed that the former were significantly higher (table 11). Our normal male group were drawn from a similar population to Ringqvist's male volunteers, and record similar pressures (table 10, 11). Thus the subjects selected to construct a normal range must be representative of the population to which it will be applied. It may be preferable for the laboratory wishing to measure mouth pressures to choose one technique applicable to the study population and to establish a local reference range.

We conclude that in the clinical assessment of patients for global respiratory muscle strength, a flanged mouthpiece is more universally applicable.

Table 11
Data of Ringqvist (1966) for Male Sub-Groups
cmH₂O, mean $\pm$ S.D., tube mouthpiece

	PImax	PEmax
male volunteers (N=23)	124.3 $\pm$ 7.1	208.9 $\pm$ 13.2
male conscripts (N=33)	153.9 $\pm$ 13.2	236.9 $\pm$ 12.2

Although values obtained with a flanged mouthpiece are lower, this is not of clinical significance if the appropriate reference ranges (Leech et al, 1983; Wilson et al, 1984; Vincken, Ghezze and Gosio, 1987) are used. However in normal subjects, maximal pressures are obtained with a rubber tube mouthpiece when it is used in the manner described by Black and Hyatt (Black and Hyatt, 1969). A rubber tube mouthpiece would seem appropriate in physiological studies when truly maximal pressures are needed. The differences reported in the literature for normal ranges of P_Imax and P_Emax may be explained in part by the choice of mouthpiece and the way in which it is used.

4.7 SUMMARY

I investigated the effect of mouthpiece design on maximum static expiratory (P_Emax) and inspiratory (P_Imax) mouth pressures. I measured P_Emax from TLC and P_Imax from RV in 21 healthy volunteers, and in 40 patients referred for respiratory muscle testing. I compared two different mouthpieces, a semi-rigid plastic flanged type fitting inside the lips and a 4 cm diameter rubber tube held against the lips. The tube mouthpiece gave significantly higher values for P_Emax ($p < 0.02$) in all subjects. P_Imax was also significantly higher ($p < 0.005$) with the tube mouthpiece in subjects who recorded normal pressures. It can be concluded that (1) maximum pressures are obtained in all normal subjects

with the rubber tube mouthpiece, (2) differences in quoted normal ranges of maximum static respiratory pressures reflect in part the design of the mouthpiece and the way in which it is used.

CHAPTER 5

THE MEASUREMENT OF INSPIRATORY MUSCLE STRENGTH BY SNIFF OESOPHAGEAL, NASOPHARYNGEAL AND MOUTH PRESSURES

5.1 INTRODUCTION

Assessment of respiratory muscle strength should be included in any comprehensive clinical evaluation of patients with dyspnoea and respiratory failure. Serial measurements can provide the framework for following the time course of any reduction in strength caused by muscle or respiratory diseases and efficacy of any therapeutic interventions. In practice respiratory muscle weakness frequently goes unrecognised although with careful clinical assessment and simple measurements it is possible to detect it. Therefore, measurement of respiratory muscle strength is a logical necessity since weakness is defined as a failure to generate force (Edwards, 1982). The contractile force of human respiratory muscles is usually evaluated by measuring the pressures that the muscles generate during voluntary contractions (Rochester, 1988). The simplest approach and most widely applied technique is the measurement of the maximal mouth pressure sustained for one second during an inspiratory effort (PI_{max}) from residual volume (RV), and an expiratory effort (PE_{max}) from total lung capacity (TLC) (Chapter 2 and 4). During static manoeuvres PI_{max} is very similar to oesophageal pressure (P_{oes}), therefore static P_{oes} measurements confer no advantage in describing weakness. Miller, Moxham and Green (1985) compared oesophageal pressures during the sniff and PI_{max} manoeuvres in healthy volunteers of both sexes. They showed that P_{oes} measured

during a maximal sniff was higher than Poes during the static effort. In addition sniff Poes had a narrower normal range with a higher lower limit of normal, and was more reproducible than Poes measured during the static inspiratory effort. These results suggest that sniff Poes may be more useful than a static inspiratory manoeuvre in the detection of mild to moderate degrees of inspiratory muscle weakness. Laroche (Laroche et al, 1988) recently showed that sniff Poes discriminated patients who have a low PImax due to poor technique or lack of motivation from those with true inspiratory muscle weakness. In this study oesophageal pressure generated during a maximal sniff (sniff Poes) was compared with mouth pressures generated during a maximal inspiration against a closed airway (PImax) in sixty-one patients referred for investigation of respiratory muscle function. Sniff Poes was greater than PImax in fifty-five of the sixty-one patients. In thirty-six patients sniff Poes and PImax were both normal whereas in thirteen patients were both low. In eleven patients PImax was low, but sniff Poes was normal. Only one patient had a reduced sniff Poes but a PImax at the lower limit of normal. These eleven patients also had a normal or moderately reduced Pdi, suggesting that PImax was falsely low, perhaps because of difficulties with the technique. It therefore appears that the measurement of oesophageal pressure during a maximal sniff is a useful test of

inspiratory muscle strength and overcomes the difficulty some patients have with the static manoeuvres. However, the value of sniff Poes in detecting inspiratory muscle weakness can be offset in some subjects by the need to pass an oesophageal balloon.

The aim of this study was to establish whether pressures in the mouth (Pmo) or nasopharynx (Pnp) reflect Poes during a maximum sniff and if their measurement provides a minimally invasive technique for the discriminatory assessment of inspiratory muscle strength.

5.2 METHODS

5.2.1 Normal subjects and patients

The study had approval of the local ethical committee and all subjects gave informed consent. We studied 10 normal healthy caucasian volunteers (6 men aged 29-44; 4 women aged 28-38) and 12 caucasian patients (8 men aged 20-72; 4 women aged 25-59) with respiratory muscle weakness. All patients experienced breathlessness which was either unexplained or disproportionate to the severity of the co-existing lung pathology.

5.2.2 Lung function

The volunteer group had forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) measured from a forced expiration into a spirometer (Ohio 840, Ohio Medical Products, Wis.). The patient

group had formal assessment of lung function in the hospital laboratory. All predicted lung function values were derived from a computer programme based on the data of Cotes (Cotes, 1979).

5.2.3 Pressure measurements

Validyne pressure transducers (MP-45, range ± 350 cm H₂O, Validyne Co, Northridge, CA.) were used to measure pressure waveforms during both static and dynamic manoeuvres. The transducers were calibrated before each study using U-tube water and mercury manometers as pressure standards. Uncalibrated pressure traces were displayed on a storage oscilloscope screen (Tektronix 5103N, Tektronix Inc, Oregon) for visual feedback. Calibrated signals were recorded onto paper using an ink-jet recorder (Mingograf 800, Siemens-Elema, Sweden) at a paper speed of 100 mm/sec.

Maximal static inspiratory (P_Imax) and expiratory (P_Emax) mouth pressures were measured in all subjects using a plastic semi-rigid flanged mouthpiece (PK Morgan, Rainham, Kent). The mouthpiece was attached to a metal stem manufactured according to the design of Ringqvist (Ringqvist, 1966) incorporating a 3-way tap, and a leak tube of 37mm length and 2mm internal diameter, necessary to prevent glottic closure. The operator held the stem for the subject and closed the 3-way tap when the static measurement was to be made (Chapter 4; Koulouris et al, 1988). P_Imax was performed from RV and

PE_{max} from TLC, with a noseclip. The highest recorded pressures maintained for one second were used for analysis.

Oesophageal pressure was measured using commercially available balloons 10 cm long, 3.5 cm circumference attached to 100 cm long fine polythene catheters (PK Morgan) and filled with 0.5 ml of air (Chapter 2). Gastric pressure (P_{gas}) was measured in the patient group with a second balloon of the same dimensions but containing 2 ml of air. This allowed transdiaphragmatic pressure (P_{di}) to be derived electronically by subtraction of P_{gas}-P_{oes} (Agostoni and Rahn, 1960) but using P_{di} at resting and expiration as the zero reference point. Nose and mouth pressures were measured with a 10 cm balloon reduced in length to 5 cm by taping over the proximal end (Fig 33). The optimum volume of air for the small balloon was 0.7 ml determined from its pressure-volume characteristics measured both in vitro and in vivo (Appendix 3). The response time of each balloon catheter-recorder system was measured by placing the balloon catheter within a second larger pressurised balloon, and causing a square wave fall in pressure by bursting the larger balloon with a red hot needle ("pop test"). The pressure signal was recorded at a paper speed of 1000 mm/sec. The 10-90% rise time (Tr) was found to be 0.017 second. The maximum frequency response (f_{3db}) for the large balloon (Appendix 3 for the small

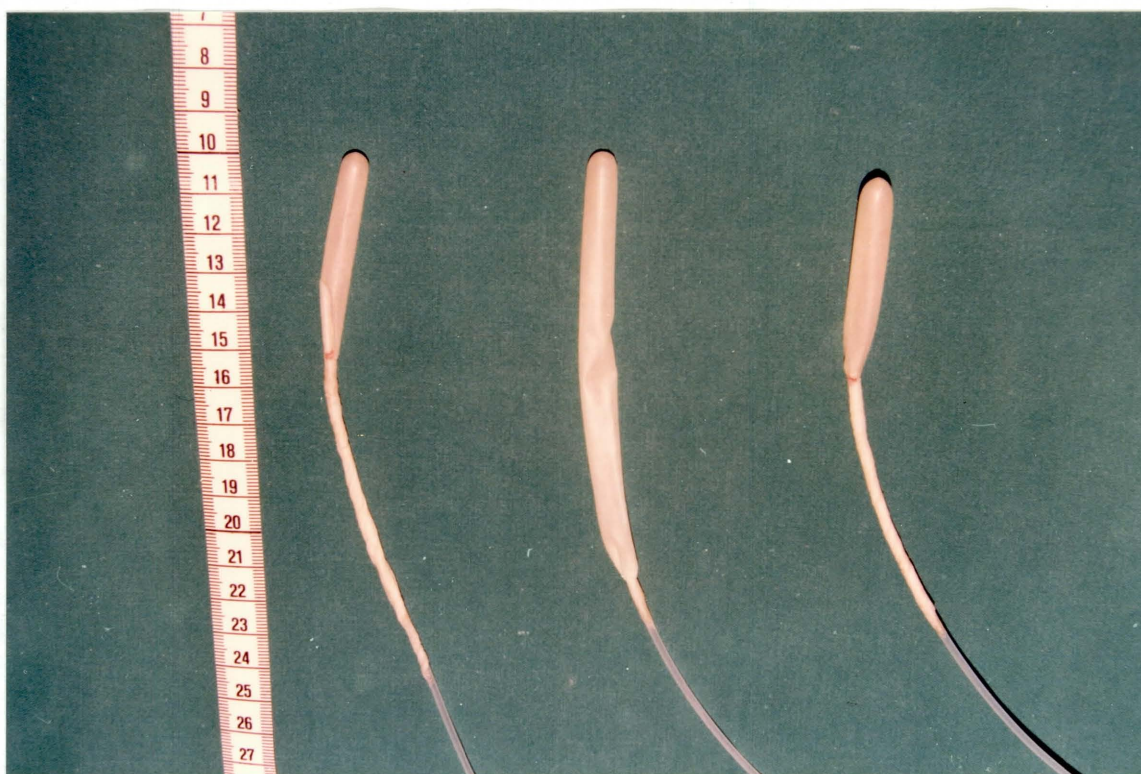


Figure 33 Photograph of the 5 cm and 10 cm balloons.

balloon) was determined from the equation $f_{3db} = 1/3T_r$ for the critically damped signal (Beardsmore, 1980; Clayton, 1979) and was 20 Hz. No phase difference was found between Poes and Pnp or Pmo waveforms in either of the subject groups (figure 34).

5.3 PROTOCOL

The normal subjects performed maximal sniffs during which Poes, Pnp and Pmo were measured simultaneously. In the patient group Poes, Pgas and Pnp or Pmo were measured simultaneously to allow sniff Pdi to be calculated. A "sniff" was characterised by a short, sharp, voluntary inspiratory effort from FRC, without a noseclip, through the nostrils with the mouth closed. Periods of rest were allowed between individual sniffs. The oesophageal balloon was passed through one nostril after topical anaesthesia of the nasal mucosa (lidocaine spray 2%), and lubrication of the catheter (lidocaine gel 2%), and was swallowed by the subject with iced water. The oesophageal balloon was passed into the stomach and then withdrawn whilst observing the pressure signal until it was in the middle third of the oesophagus (Cotes, 1979). Nasopharyngeal pressure (Pnp) was measured with a 5 cm balloon, advanced through the anaesthetised nose into the nasopharynx. When the subject could just feel the balloon at the back of the throat during swallowing, it was withdrawn 1 cm so that the tip of the balloon was approximately 10 cm from the anterior nares. Pressure in

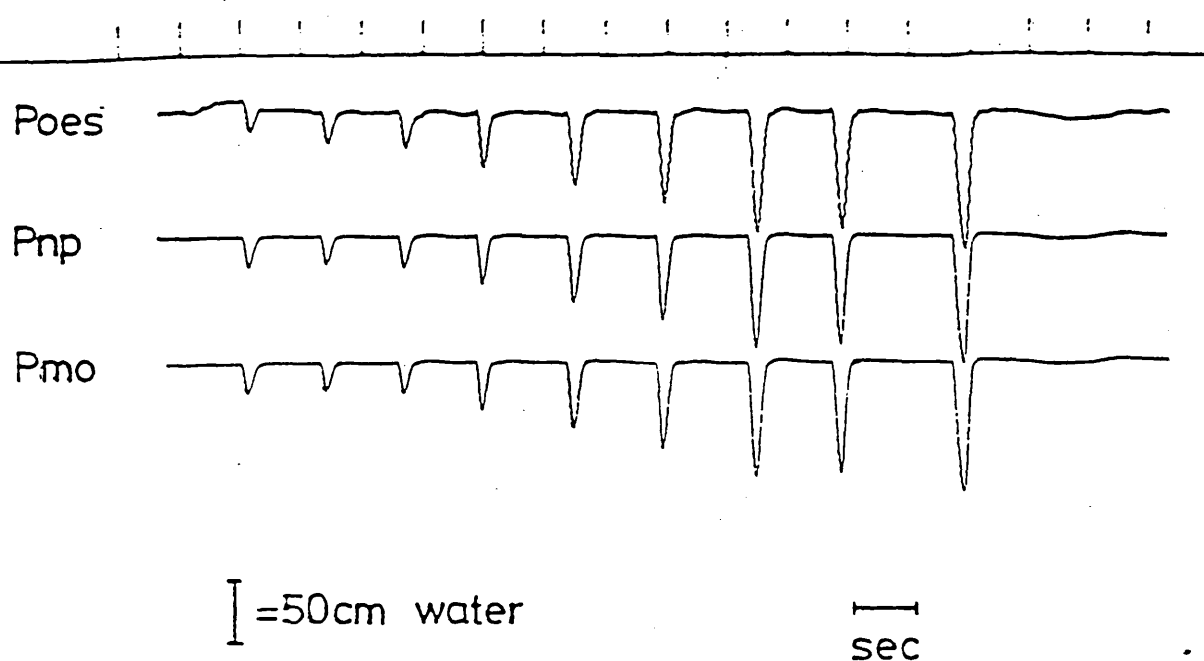


Figure 34 Simultaneous pressure waveforms from oesophageal (Poes), nasopharyngeal (Pnp), and mouth (Pmo) balloons in a single normal subject performing sniffs of increasing effort. Paper speed 10 mm/sec for this illustration.

the mouth (Pmo) was also measured with a 5 cm balloon, held in the oral cavity with the lips closed; subjects were instructed not to bite the catheter, or compress, or apply suction to the balloon with the tongue during the sniff (Fig 35).

Magnetometers (Mead, 1967) were used to monitor the anteroposterior diameters of the chest and abdominal walls to ensure that the subjects performed sniffs at FRC. Measurements were made with the subject sitting in a firm upright chair with arm rests, facing the oscilloscope screen. Body movement was not restricted and the pattern of sniffing was not imposed. The subjects were asked to perform single, short maximal sniffs, and when a plateau value of sniff Poes was reached (usually within 6-10 sniffs) a further 8-10 maximal sniffs were performed to ensure no further increase. The subjects were repeatedly encouraged to try as hard as possible, and visual feedback was given from the oscilloscope screen. Subsequently the normal subjects performed 30 sub-maximal sniffs of varying intensity to simulate the sniffs of weak patients. Within day reproducibility was assessed by the normal subjects repeating maximal sniffs three times at 0, 20 and 40 minutes. Day to day reproducibility of sniff pressures was determined by repeating studies in three normal subjects on three separate days.

Criteria used to select those sniffs suitable for analysis were (a) peak pressure maintained for less



Figure 35 Lateral skull x-ray to show relative positions of nasopharyngeal and mouth balloons. Balloons filled with CONRAY 420 contrast medium. (X-ray Department, Brompton Hospital).

than 50 msec (b) total sniff duration less than 500 msec (c) pressure waveform of sniff displayed smooth upstroke and decay curves (d) sniff performed from FRC as judged by the magnetometer traces and presniff Poes. In normal subjects data were occasionally rejected because sniffs were not performed at FRC. In patients, the rejection rate was higher but still less than 2-3% of sniffs recorded.

5.4 STATISTICAL ANALYSIS

Mean values, standard errors (SE), correlation coefficients (r), and regression analyses were obtained using the "Minitab" statistical computer programme (Minitab Inc, State College, PA).

5.5 RESULTS

5.5.1 Normal subjects

Descriptive data for the normal subjects are (mean $\pm$ SE), age 34.7 ± 1.8 years, height 174.3 ± 2.7 cm, weight 66.5 ± 3.4 kg, FEV₁ $103.7 \pm 5.9\%$ predicted, FVC $99.7 \pm 5.4\%$ predicted, FEV₁/FVC $84.3 \pm 2.2\%$ (Table 12). In the normal subjects, sniff Poes ranged from 79-156 cm H₂O, sniff Pnp from 70-146 and sniff Pmo from 75-146. The mean ratio Pnp/Poes for ten maximal consecutive sniffs for each of the ten subjects as 0.92 ± 0.006 (mean $\pm$ SE), and Pmo/Poes 0.95 ± 0.006 . The mean values for Pnp and Pmo for each subject, compared to Poes are shown in table 13 and figures 36, 37. The correlation

TABLE 12
DESCRIPTION OF NORMAL SUBJECTS

Subject	Sex	Age (years)	Ht (cm)	Wt (kg)	<u>FEV1</u>		<u>FVC</u>		<u>FEV1</u> FVC %
					(L)	%pred	(L)	%pred	
1	M	31	179	77	4.5	108.9	5.1	101.5	88.2
2	F	38	156	55	1.76	67.9	2.2	72.7	80.0
3	F	38	178	60	3.49	109.6	4.0	97.2	85.3
4	F	28	169	53	3.23	100.5	3.23	82.3	100.0
5	M	44	175	73	4.28	119.9	4.8	107.1	88.2
6	M	42	175	61	4.66	128.6	5.6	123.1	82.8
7	F	28	166	58	2.96	94.7	3.9	105.6	74.4
8	M	29	183	79	4.83	111.9	6.1	116.5	78.5
9	M	33	184	67	3.37	79.8	4.0	77.1	83.4
10	M	<u>36</u>	<u>178</u>	<u>82</u>	<u>4.5</u>	<u>114.8</u>	<u>5.5</u>	<u>113.2</u>	<u>81.8</u>
	Mean	34.7	174.3	66.5	3.76	103.7	4.44	99.63	84.3
	SE	1.83	2.69	3.35	0.31	5.85	0.38	5.43	2.21

Table 13
Results for Normal Subjects,
Sniff Pressures in cmH₂O
(mean±SE)

Subject	Poes	Pnp	Pmo	Pnp/Poes	Pmo/Poes
1	155.65±1.34	145.90±1.37	145.95±1.56	0.94	0.94
2	108.85±1.73	103.45±1.38	100.90±1.72	0.95	0.93
3	103.20±1.36	95.05±1.44	97.05±1.51	0.92	0.94
4	78.50±1.38	60.90±1.00	74.75±1.20	0.89	0.95
5	126.15±1.71	112.80±1.72	121.30±1.61	0.89	0.96
6	148.50±1.83	138.50±1.35	144.80±1.90	0.93	0.98
7	97.38±1.07	90.18±0.91	95.42±1.10	0.93	0.98
8	130.70±1.04	119.00±0.60	120.00±0.61	0.91	0.92
9	131.40±0.99	118.42±0.77	124.15±0.95	0.90	0.94
10	120.70±1.18	110.70±0.92	115.60±0.88	0.92	0.95
Mean				0.92	0.95
± S.E.				0.006	0.006

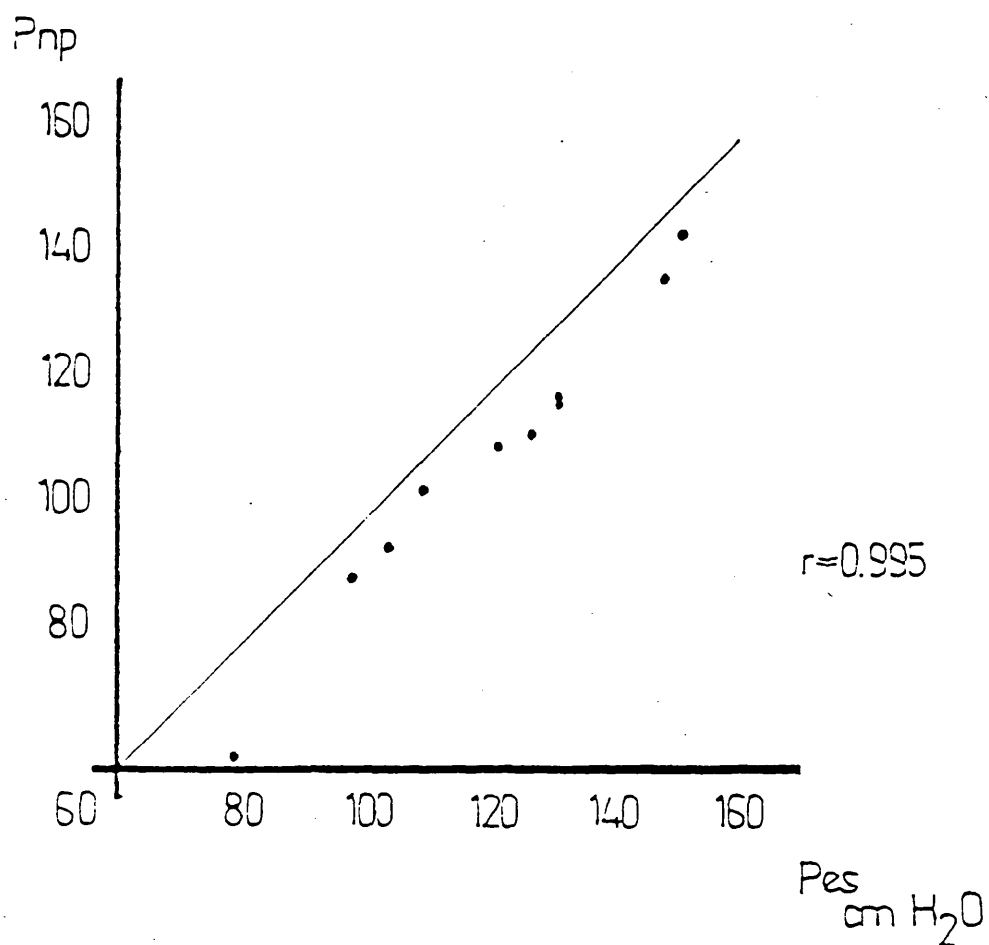


Figure 36 Comparison of Poes with Pnp. Each value represents the mean of 10 maximal sniffs in each of the 10 normal subjects. $P_{oes} = 4.57 + 1.05 P_{np}$. ($R^2 = 98.9\%$, $SEE = 2.42$)

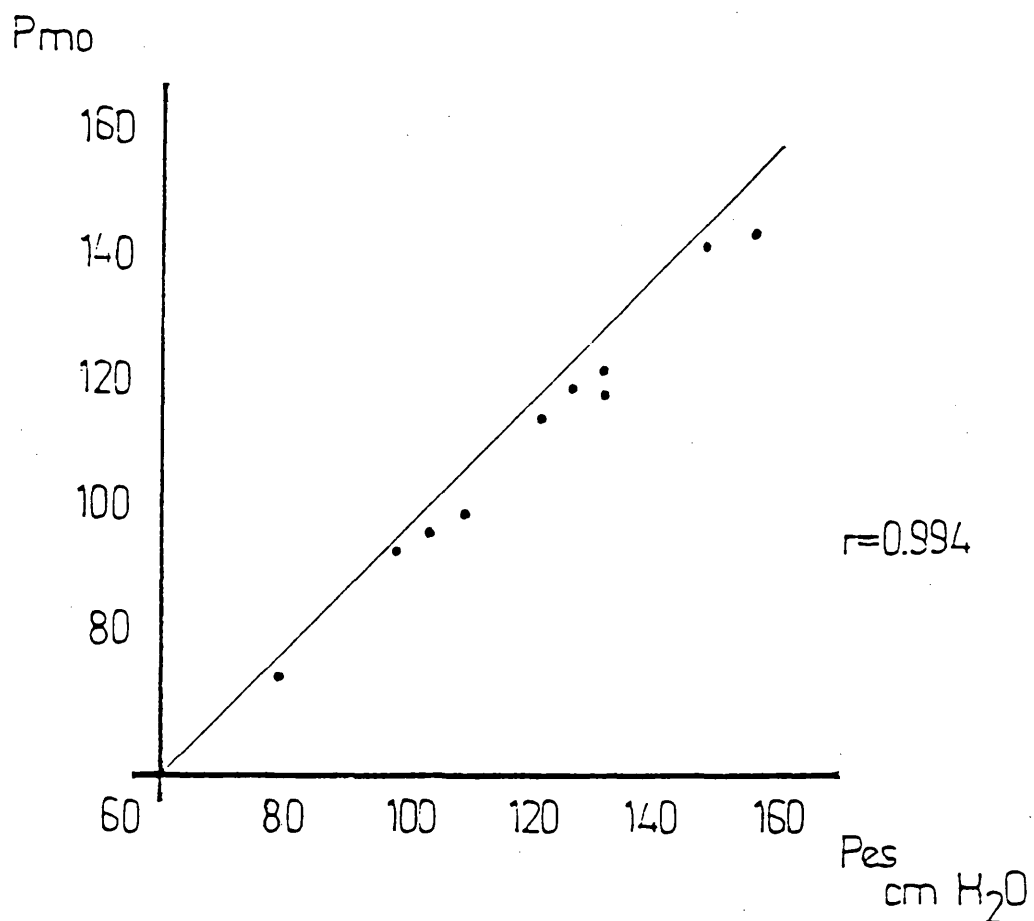


Figure 37 Comparison of Poes with Pmo. Each value represents the mean of 10 maximal sniffs in each of the normal subjects $P_{oes} = 0.741 + 1.05 P_{mo}$ ($R^2 = 98.7\%$, SEE = 2.7).

coefficient of the sniff Poes and sniff Pnp was $r = 0.995$; $p < 0.001$, and of Poes and Pmo $r = 0.994$; $p < 0.001$. Regression analysis showed that $\text{Poes} = 4.57 + 1.05 \text{ Pnp}$ ($R^2 = 98.9\%$, standard error of the estimate (SEE) = 2.42) and $\text{Poes} = 0.74 + 1.05 \text{ Pmo}$, ($R^2 = 98.7\%$, SEE = 2.7).

Within day mean coefficient of variation as assessed in the 10 subjects for the three study sessions was 5.2% for Poes (range 4.1 - 8.4), 5.0% for Pnp (range 3.4 - 8.2), and 5.0% for Pmo (range 3.2 - 8.1) (Table 14). The day to day coefficient of variation studied in three subjects on three different days was 4.5% for Poes (range 2.4 - 5.1), 3.3% for Pnp (range 1.8 - 4.8), and 3.9% for Pmo (range 2.1 - 5.2) (Table 15).

Analysis of 30 sub-maximal sniffs from each normal subject showed that the mean ratio Pnp/Pes was 0.90 ± 0.002 and Pmo/Pes was 0.92 ± 0.002 . Poes correlated with Pnp ($r = 0.995$, $p < 0.001$) and Pmo ($r = 0.995$, $p < 0.001$) (figures 38, 39). Regression analysis for sub-maximal sniffs showed that $\text{Poes} = 2.47 + 1.07 \text{ Pnp}$, ($R^2 = 98.9\%$, SEE = 2.81) and $\text{Poes} = 2.62 + 1.04 \text{ Pmo}$ ($R^2 = 99.0\%$, SEE = 2.67).

5.5.2 Patients

Descriptive data for the patients are given in table 16 lung function data in table 17 and respiratory muscle function in tables 18, 19. Predicted static mouth pressures were calculated from the data of Wilson (Wilson et al, 1984) as a flanged mouthpiece had been used to

Table 14
Within day coefficient of variation for maximal
sniffs in 10 normal subjects (%)

Subject	Poes	Pnp	Pmo
1	5.56	5.58	4.94
2	8.40	8.19	8.11
3	5.12	5.07	5.26
4	4.69	4.02	4.73
5	4.10	4.43	5.46
6	5.79	6.62	5.82
7	4.13	3.42	3.84
8	4.80	5.04	4.15
9	4.71	4.40	5.09
10	4.48	3.95	3.16
Mean	5.178	5.072	5.056
Range	(4.10-8.40)	(3.43-8.19)	(3.16-8.11)

Table 15
Day to day coefficient of variation for
maximal sniffs in 3 normal subjects at
3 different days (%)

Subject	Poes	Day 1	
		Pnp	Pmo
1	4.15	4.77	4.93
2	2.72	2.97	3.37
3	3.90	3.09	4.15
		Day 2	
1	1.84	3.01	2.89
2	2.40	2.31	3.63
3	5.14	4.37	5.21
		Day 3	
1	2.38	1.82	2.08
2	3.21	3.44	3.80
3	4.50	4.28	4.66
Mean	4.5	3.34	3.85
Range	(2.40-5.14)	(1.82-4.77)	(2.08-5.21)

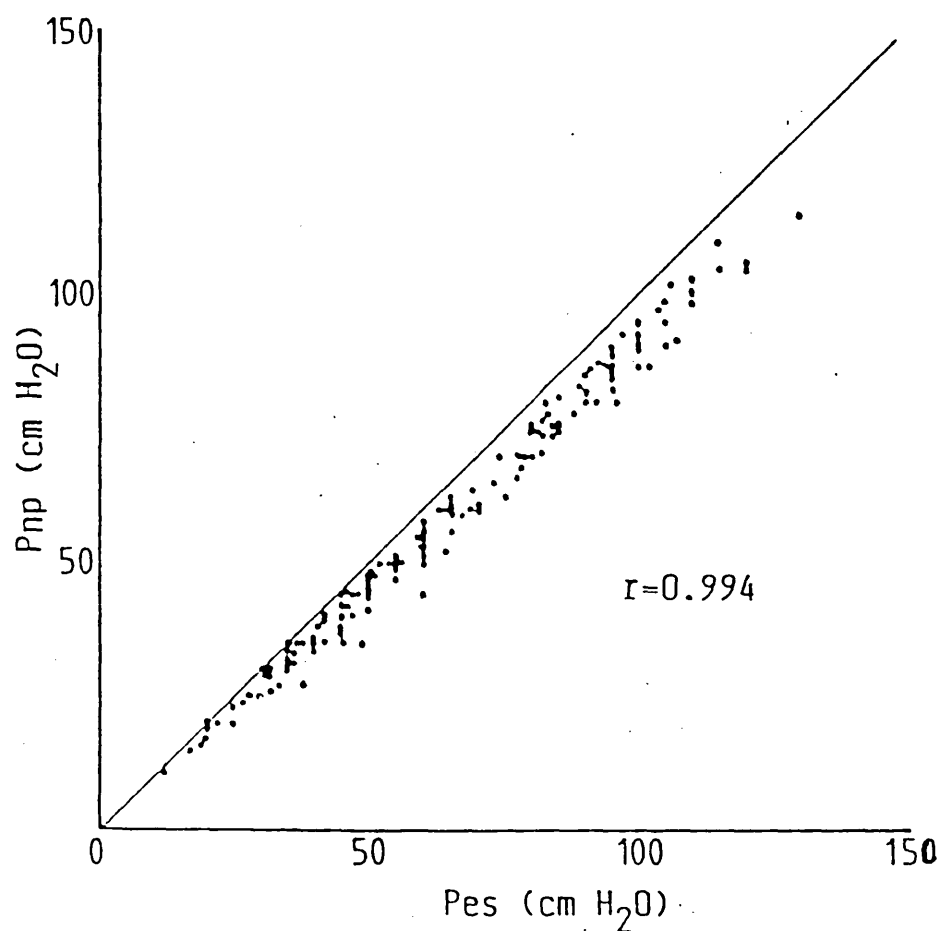


Figure 38 Comparison of Poes with Pnp for submaximal Sniffs. For clarity 30 sniffs from 6 of the 10 normal subjects are shown.

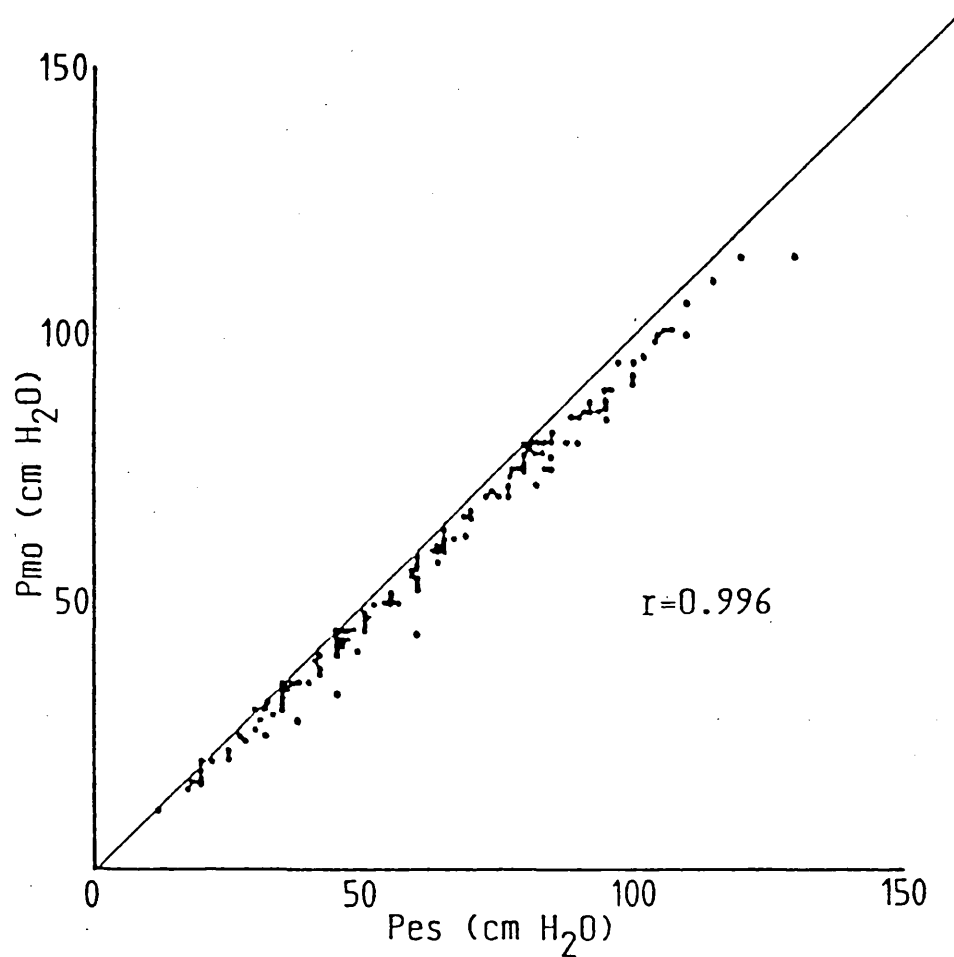


Figure 39. Comparison of P_{es} with P_{mo} for submaximal sniffs. For clarity, 30 sniffs from 6 of the 10 normal subjects are shown.

Table 16
Descriptive data for 12 patients
* Data unavailable

PT	DIAGNOSIS	SEX	AGE (yrs)	HT (cm)	WT (Kg)
1	BUA	M	57	187	54.5
2	Lambert-Eaton	M	71	154	64.5
3	BDE	M	59	173	82
4	CMT	M	59	183	73
5	Steroid myopathy	M	63	175	59
6	CFA/UDE	M	55	174	73
7	SLE	F	28	172	79.5
8	MCTD	F	25	161	59
9	Myopathy/Asthma	F	49	155	81
10	Tetraplegia	M	20	*	*
11	BUA	F	59	165	74
12	UDE	M	72	180	98.5
Mean			51.4	171	72.6
± SE			5.1	3.3	3.9

Abbreviations - BUA - Breathlessness of unknown aetiology
 - BOE - Bilateral diaphragm elevation
 - UDE - Unilateral diaphragm elevation
 - CFA - Cryptogenic fibrosing alveolitis
 - SLE - Systemic lupus erythematosus
 - MCTD - Mixed connective tissue disease
 - CMT - Charcot Marie Tooth Disease

Table 17 - Lung Function Data for 12 patients

. Data unavailable

PT	FEV1 (ml)	FVC (ml)	<u>FEV1</u> FVC %	TLC (ml)	RV (ml)	DLCO (SI)	KCO (SI)
1	1250	1460	86	.	.	.	.
2	1280	1930	66	3720	1620	4.96	1.6
3	1350	2660	51	5380	2680	5.69	1.43
4	1280	1790	72	4060	2210	4.42	1.98
5	2360	3550	66	5430	2130	3.99	0.89
6	2260	2920	77	4890	1890	5.42	1.47
7	1870	2100	89	3270	1170	5.36	1.94
8	2640	2730	97	3920	1420	5.88	1.86
9	1610	2120	76	4070	2020	4.75	1.47
10	1550	1950	79	.	.	.	.
11	2800	3650	77	4970	1350	8.19	1.78
12	2420	3210	75	5020	1670	6.37	1.47

make the measurements (Chapter 4). All patients had weak inspiratory muscles as judged by these criteria, and 7 of the 12 had weak expiratory muscles (table 18). For the 12 patients, P_Imax was $43 \pm 6.4\%$ predicted (mean $\pm$ SE), and P_Emax was $62 \pm 8.7\%$ predicted. Global inspiratory muscle and diaphragm weakness was confirmed by the measurement of sniff P_{oes} and sniff P_{di} respectively (Miller, Moxham and Green, 1985). For the 12 patients sniff P_{oes} was $50.7 \pm 4.3\%$ predicted, and sniff P_{di} $42.3 \pm 5.4\%$ predicted. In the patient group, sniff P_{oes} ranged from 25.1 - 63.4 cm H₂O, sniff P_{np} from 20.9 - 59.6, and P_{mo} from 16.2 - 59.0 (table 19). The mean ratio P_{np}/P_{oes} was 0.9 ± 0.02 (mean $\pm$ SE), and P_{mo}/P_{oes} was 0.87 ± 0.03 . The correlation coefficient of sniff P_{oes} and P_{np} was $r = 0.949$; $p < 0.001$, and of P_{oes} and P_{mo} $r = 0.936$; $p < 0.001$. Regression analysis showed that P_{oes} = $5.12 + 1.0$ P_{np}, ($R^2 = 89.1\%$, SEE = 3.96) and P_{oes} = $11.2 + 0.882$ P_{mo} ($R^2 = 86.1\%$, SEE = 4.8) (Fig 40, 41). Combined data for all the 22 subjects are presented graphically in figures 42 and 43.

5.6 DISCUSSION

The results of the present study indicate that sniff P_{oes} may be predicted from sniff P_{np} and sniff P_{mo} in both normal subjects and in patients with inspiratory muscle weakness. The measurement of sniff P_{np} and P_{mo} does not require the passage of an oesophageal balloon, the principal disadvantage of the sniff P_{oes} measurement.

TABLE 18
Respiratory Muscle Strength: Results in 12 patients *data unavallable

Patient	Sex	<u>PI max</u>		<u>PE max</u>		<u>Sniff Pdi</u>	
		cmH ₂ O	% pred.	cmH ₂ O	% pred.	cmH ₂ O	% pred.
1	M	16.0	15.1	24.0	16.2	*	*
2	M	35.0	33.0	100.0	67.6	48.75	33.0
3	M	42.5	40.1	160.0	108.1	36.5	25.0
4	M	25.0	23.6	52.5	35.5	15.4	10.0
5	M	35.0	33.0	45.0	30.4	52.5	35.0
6	M	37.5	35.4	80.0	54.1	57.8	39.0
7	F	50.0	68.5	80.0	86.0	72.03	59.0
8	F	52.5	71.9	52.5	56.5	74.53	61.0
9	F	22.5	30.8	87.5	94.1	67.50	56.0
10	M	85.0	80.2	85.0	57.5	72.50	49.0
11	F	30.0	41.1	80.0	86.0	71.66	59.0
12	M	45.0	52.1	80.0	58.5	52.25	35.2
Mean		39.67	43.72	77.21	62.54	56.49	41.93
± SE		5.20	5.85	9.79	7.91	5.93	4.94

Normal values mean (SD)

M	148(34)	106(31)	148(24)
F	93(17)	73(22)	121(25)

PE max, PI max - Static maximum expiratory and inspiratory pressures measured at the mouth; Sniff Pdi - Transdiaphragmatic pressure measured during a short, sharp maximal sniff.

TABLE 19
RESULTS FOR 12 PATIENTS

Mean Sniff Pressures cmH₂O *data unavailable

PT	Pnp	Pes	Pnp/Pes	Pmo	Pes	Pmo/Pes
1	39.02	40.32	0.97	34.5	40.32	0.86
2	42.22	47.72	0.88	38.26	46.21	0.83
3	40.5	55.25	0.73	35.7	53.1	0.67
4	20.88	25.1	0.83	16.23	21.21	0.77
5	41.87	45.47	0.92	*	*	*
6	51.38	54.00	0.95	55.24	58.8	0.94
7	59.64	63.4	0.94	59.06	63.28	0.93
8	60.00	62.66	0.96	51.96	53.21	0.98
9	52.25	61.00	0.86	43.12	53.59	0.80
10	54.83	63.33	0.87	58.0	60.0	0.97
11	33.05	37.15	0.89	32.71	36.36	0.90
12	45.57	48.07	0.94	*	*	*
Mean			0.896	Mean		
± SE			0.02	± SE		
				0.864		
				0.03		

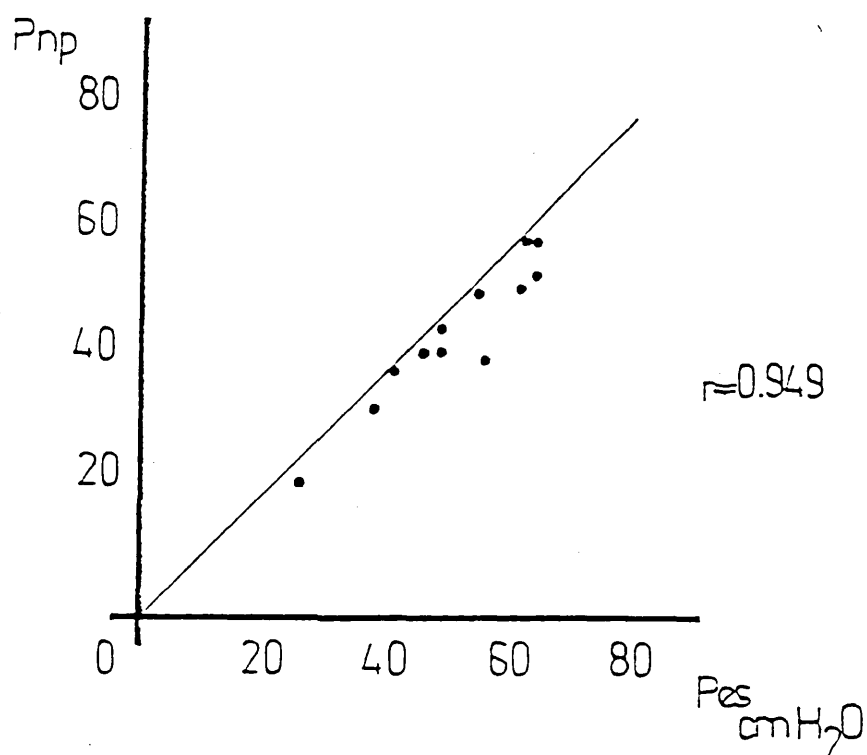


Figure 40 Comparison of Poes with Pnp in patients with respiratory muscle weakness ($Poes = 5.12 + 1.0 Pnp$, $R^2 = 89.1\%$, $SEE = 3.96$, $n = 12$)

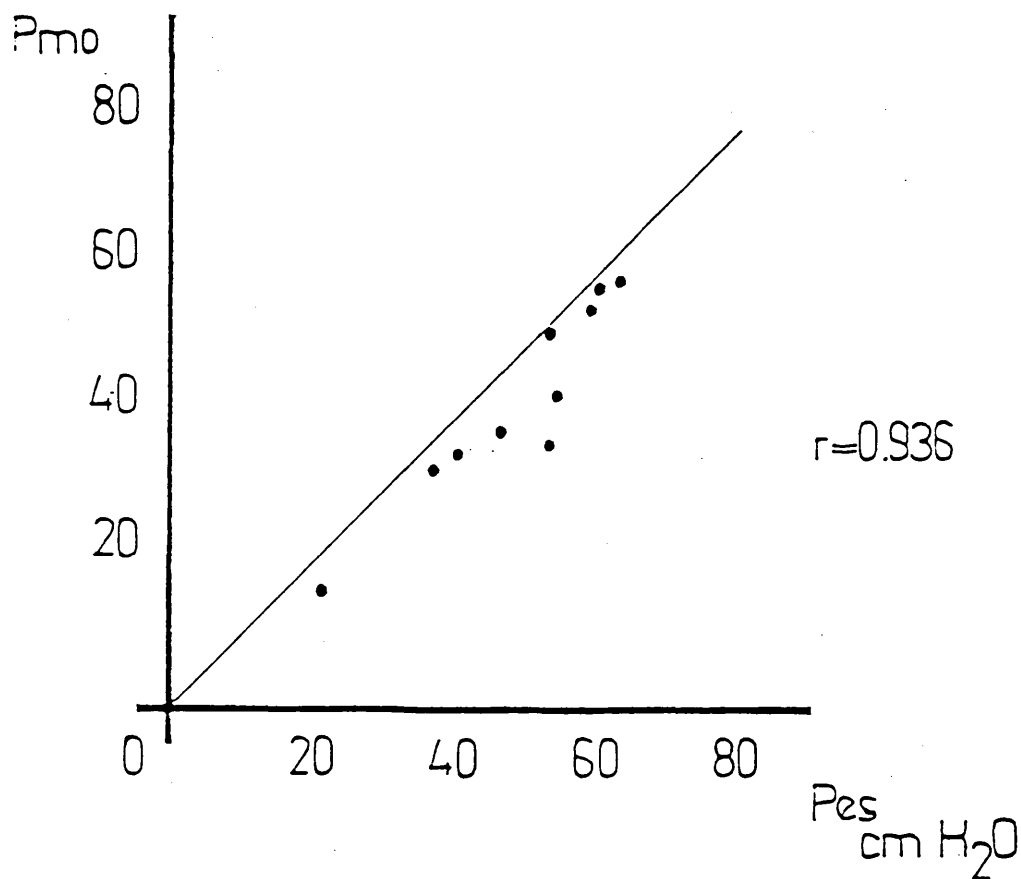


Figure 41 Comparison of P_{oes} with P_{mo} in patients with respiratory muscle weakness ($P_{oes} = 11.2 + 0.882 P_{mo}$, $R^2 = 86.1\%$, $SEE = 4.8$, $n = 10$).

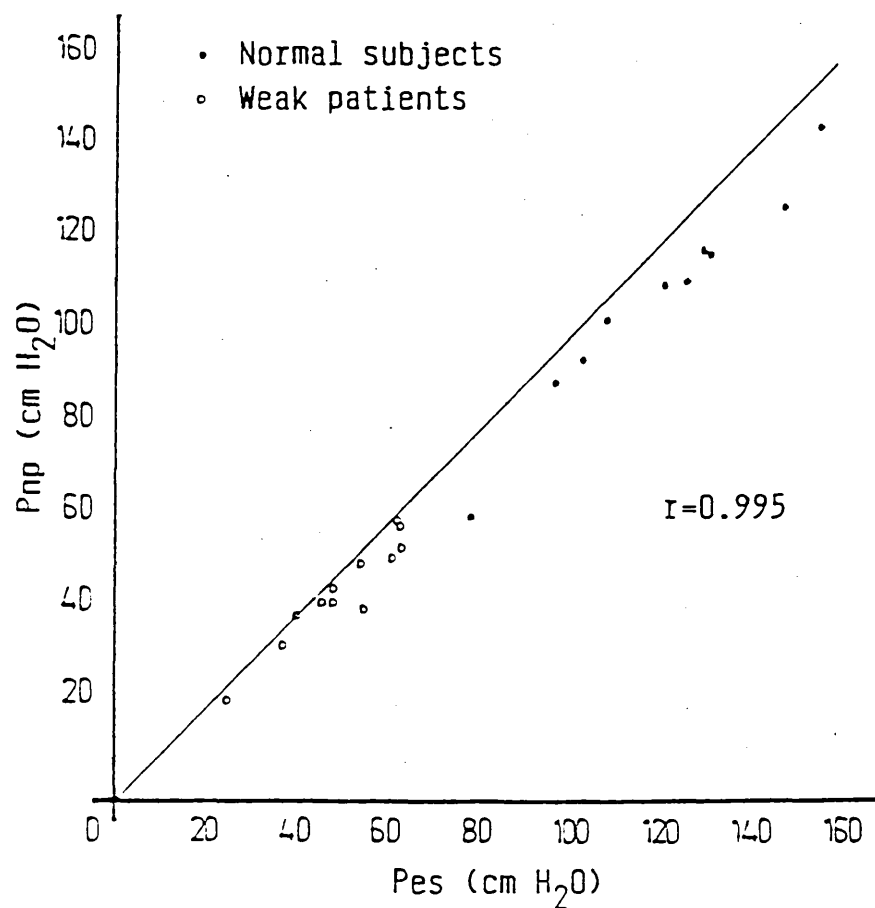


Figure 42 Comparison of Poes with Pnp. Values for normal subjects (closed circles) and for weak patients (open circles). Regression analysis for the pooled data showed: $Poes = 3.37 + 1.06 Pnp$ ($R^2 = 99.0\%$, $SEE = 4.06$, $n = 22$).

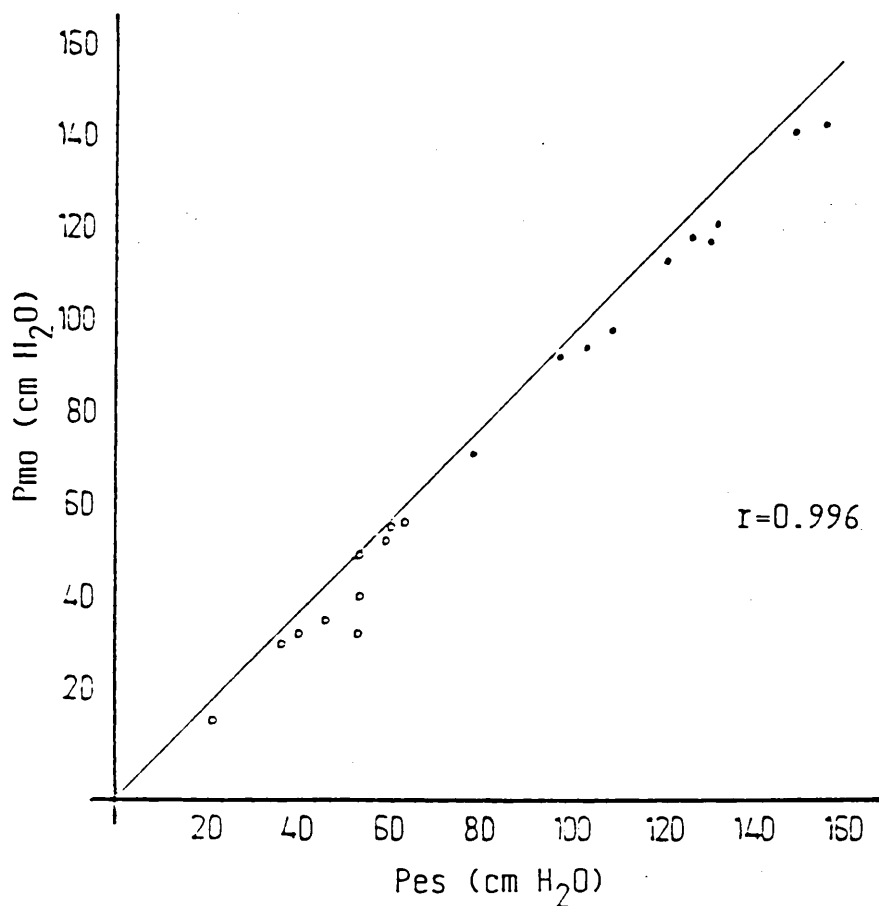


Figure 43 Comparison of Poes with Pmo. Values for normal subjects (closed circles) and for weak patients (open circles). Regression analysis for the pooled data showed: $Poes = 6.11 + 1.00 Pmo$ ($R^2 = 99.1\%$, $SEE = 3.93$, $n = 20$)

This makes the sniff test more acceptable to patients, and circumvents the occasional problem with oesophageal pathology or a patient who has difficulty in swallowing an oesophageal balloon.

The similarity of upper airway and oesophageal pressures during respiratory manoeuvres has previously been described by Milner in neonates (Milner, Saunders and Hopkin, 1978) and by Baydur (Baydur et al, 1982) and Marazzini in normal adult subjects. All groups showed a high degree of correlation between Poes and Pmo during occluded inspiratory efforts. In these three studies, airflow at the time of pressure measurement was negligible, with the result that minimal pressure gradient existed between the mouth and pleural space. Our results also show a high degree of correlation between Poes and both Pnp and Pmo during a sniff. The reason for the similarity of upper and lower airway pressures during a dynamic manoeuvre may be deduced from previous studies. There is good evidence that during the sniff manoeuvre the nostrils behave as a Starling resistor, rapidly collapsing under the influence of negative nasal pressures (Bridger, 1970; Bridger and Proctor, 1970; Haight and Cole, 1983). Bridger and Proctor (1970) used fine catheters to explore intranasal pressure gradients during vigorous inspiratory efforts. They were able to identify a point of occlusion in the region lying between the junction of the pyriform aperture, and the upper and lower lateral cartilages.

When a critical pressure gradient (estimated at 10-12 cm H₂O) exists across this region, occlusion occurs. Beyond the point of occlusion the upper and intrathoracic airways can be regarded as being in continuity with little pressure gradient between them. Rhinologists are aware of the narrowing which occurs at the site of the "nasal valve" during deep inspiration (Fig 44). Bridger and Proctor in 1970 noticed that on deep inspiration through one nostril, nasal airflow increases as the pressure drop across the nose (ΔP) increases until a critical transnasal pressure is reached ($\Delta P'$) at which point nasal airflow becomes constant. Greater inspiratory effort (increasing ΔP beyond the point where $\Delta P = \Delta P'$) does not increase nasal airflow. These findings are compatible with the nose having a collapsible or flow limiting segment (FLS) acting as a Starling resistor. Such a situation has already been described in the tracheobronchial tree on expiration (Jordanoglou and Pride, 1968). In a more detailed analysis Bridger (1970) reported that during rapid inspiration (and by analogy in the sniff manoeuvre) a pressure difference is established between the nasopharynx (P_{np}) and the atmosphere, and the pressure in the nasal airway decreases towards the nasopharynx. The nasal airway is subjected to a negative, lateral intraluminal pressure which will cause deformation except where the anatomy is sufficiently rigid to withstand this

THE NASAL MODEL

Bridger GP Arch Otolaryng
1970;92:543-553

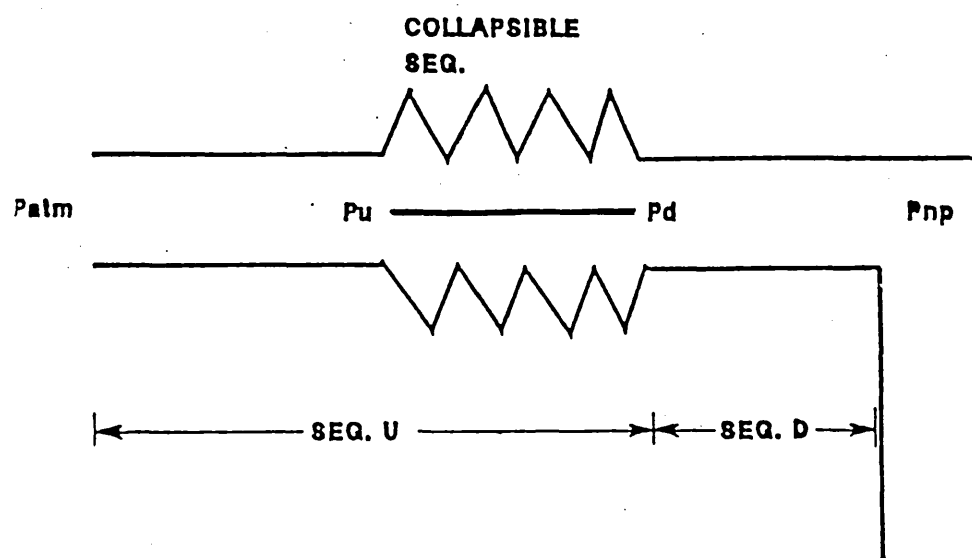


Figure 44 Nasal model of a flow limiting segment (FLS). A collapsible segment is shown. As the FLS is elastic and has a tendency to stay open, it requires a negative pressure to produce collapse. On vigorous inspiration a pressure difference is established between the atmosphere (P_{atm}) and the nasopharynx (P_{np}) causing the FLS to flutter as negative pressure exceeds critical pressure. (P_u = pressure upstream, P_d = pressure downstream).

negative pressure. The nasal cavity may be considered in two parts: a rigid main osseous nasal cavity and a less rigid ventral cartilaginous vault, the vestibule. The vestibule is designed to withstand the range of negative pressures encountered during normal breathing. When subjected to the increased negative pressure of rapid inspiration (e.g. a sniff) the upper lateral cartilages are sucked onto the septum and the aperture of the nasal valve is reduced to a small orifice. This narrowing can be observed in most people on vigorous and rapid inspiration. Bridger was able to demonstrate this by x-rays of nasal passages during rapid inspiration through one nostril after outlining the vestibule with radio opaque tantalum dust. Almost total obliteration of the nasal lumen occurred. The critical transnasal pressure gradient is approximately 10-12 cm water, at which point airflow becomes constant. During a maximum sniff, even in the weakest of patients, Pnp is greater than the critical transnasal pressure and Pnp therefore reflects Poes, both pressures depending on the contractility of the inspiratory muscles. The presence of this flow limiting mechanism explains both the close agreement between sniff Poes, Pnp and Pmo, and the high pleural pressures developed during a sniff (Miller, Moxham and Green, 1985). The sniff could be considered a less isometric technique than PImax because a volume change occurs. Pertuze (Pertuze et al, 1987) has shown that the mean volume change occurring during a maximal sniff

is 500 mls, similar to the likely volume change accompanying a P_Imax effort due to gas expansion and the permitted air leak preventing glottic closure (Ringqvist, 1966). The flow during a sniff is greater, a factor that would reduce peak pressure due to the force-velocity relationship of respiratory muscle (Rochester, 1982). However Miller, Moxham and Green (1985) demonstrated that sniff P_{oes} was greater and more reproducible than P_{oes} measured during a static manoeuvre. Although P_Imax is the most widely applied technique for the assessment of inspiratory muscle strength, it does have certain limitations. The manoeuvre is not difficult for cooperative subjects who perform the test reproducibly after suitable training. However, Mead and co-workers (Mead, Milic-Emili and Turner, 1963; Mills, 1950) have reported that the antagonistic contraction of the abdominal muscles may limit the development of high inspiratory mouth pressures in untrained subjects. Patients, particularly the elderly or those with coexisting weakness of the mouth and cheek muscles, can have particular difficulties with this static technique (Green, 1984). The reference ranges for P_Imax in normal subjects (Chapter 4; table 6) are wide with very low lower limits in some age groups. The limitations of P_Imax are such that Leech (Leech et al, 1983) concluded "...in the clinical context, some caution is required before low inspiratory pressures are attributed to muscle weakness".

Predicting sniff Poes from Pnp and/or Pmo simplifies the application of the sniff technique which has the advantage of being familiar to nearly all subjects as a natural manoeuvre. It has been reported that the firing rates to a given muscle decrease more rapidly under strict isometric conditions than during movement, suggesting that inhibitory impulses from tension receptors play a role (Grimby, 1986). Pmo is a better predictor of Poes than Pnp in normal subjects, but either could be used to measure inspiratory muscle strength in physiological studies. The converse was true for the patients, Pnp being the better predictor of Poes. This may have been due to the inability of the upper airway muscles to resist collapse of the walls of the oral cavity under application of negative airway pressures (Suratt, 1987). The nasopharynx being a semi-rigid structure resists such collapse better in the erect posture with the result that Pnp is closer to Poes during the sniff.

Two of the twelve patients did not produce satisfactory sniff Pmo waveforms due to sucking on the balloon, and therefore the traces obtained were discarded. It is possible that sniff Pnp will be the more universally applicable test in patients.

The lung function data shows that only one of our 22 subjects (patient no 3) had moderate obstructive airways disease and this patient had the lowest upper

airway/oesophageal ratios. Similarly none of the subjects had a significant restrictive pulmonary defect. Alterations of lung mechanics are known to reduce the transmission of alveolar pressure to the upper airways (Marazzini et al, 1978; Murciano et al, 1982; Gibson 1983), as would functional obstruction of the upper air passages (Stauffer et al, 1987; Suratt, Wilhot and Cooper, 1984). Further studies are required to quantify the effect of these factors on Pnp/Poes and Pmo/Poes ratios.

We conclude that in both normal subjects and patients with pure respiratory muscle weakness, Pnp and Pmo reliably predict Poes during the sniff manoeuvre. Measurement of sniff Pnp and Pmo is simple, minimally invasive, reproducible, well tolerated by all subjects and may provide a clinically useful technique for the assessment of inspiratory muscle strength.

5.7 SUMMARY

Sniff oesophageal pressure (Poes) is a useful measurement of global inspiratory muscle strength although it does require passage of an oesophageal balloon. I investigated the relationship between nasopharyngeal pressure (Pnp) or pressure within the mouth (Pmo) and Poes during the maximal sniff from FRC without a noseclip. I measured Poes, Pnp and Pmo simultaneously in 10 normal volunteers, and in 12

patients with inspiratory muscle weakness. In both groups Pnp and Pmo were slightly less but very close to Poes. In normal volunteers the mean ratio Pnp/Poes was 0.92 ± 0.006 (mean $\pm$ SE) and Pmo/Poes was 0.95 ± 0.006 . Regression analysis showed $\text{Poes} = 4.57 + 1.05 \text{ Pnp}$ ($r = 0.995$, $p < 0.001$) and $\text{Poes} = 0.74 + 1.05 \text{ Pmo}$ ($r = 0.994$, $p < 0.001$). Similar relationships between Pnp, Pmo and Poes were found over a wide range of pressures generated by submaximal sniffs in normal subjects. In patients the mean ratio Pnp/Poes was 0.90 ± 0.02 and Pmo/Poes 0.87 ± 0.03 . Regression analysis showed $\text{Poes} = 5.12 + 1.0 \text{ Pnp}$ ($r = 0.949$, $p < 0.001$) and $\text{Poes} = 11.2 + 0.882 \text{ Pmo}$ ($r = 0.936$, $p < 0.001$). It is concluded that Pnp and Pmo predict Poes during a maximal sniff in both normal subjects and patients with inspiratory muscle weakness. Sniff Pnp and/or Pmo may provide a useful and less invasive method of measuring maximum inspiratory pressures during a sniff.

CHAPTER 6

MAXIMUM RELAXATION RATES OF OESOPHAGEAL, NOSE AND MOUTH PRESSURES DURING A SNIFF REFLECT INSPIRATORY MUSCLE FATIGUE

6.1 INTRODUCTION

Clinical observations supports the view that patients can become exhausted and their respiratory muscles fatigued (Roussos and Macklem, 1982). However, the great difficulty is in deciding how important respiratory muscle fatigue is as a clinical problem and how commonly it occurs (Moxham, 1984). The answer to these questions will only be known when we have methods that can reliably detect muscle fatigue in patients with ventilatory failure. In recent years, the problem of respiratory muscle fatigue has been investigated using three separate techniques (Moxham, 1984). (i) Electromyogram (EMG). When skeletal muscle is subjected to a load that cannot be sustained indefinitely, there is a change in the EMG signal with a reduction in the amount of power at higher frequencies and a relative increase in the power at lower frequencies (Lindstrom, Magnusson and Petersen, 1974). If a high frequency and a low frequency band are analysed, the shift towards lower frequencies in the EMG power spectrum is reflected by a fall in the EMG high/low ratio. Although this technique has been used extensively to study fatigue in the respiratory muscles (Bryan, 1979; Gross et al, 1979), it has its limitations as an indicator of muscle fatigue. The relationship of the change in the EMG to the decline of force generation is complex. Thus during a sustained maximum voluntary

contraction of a limb muscle, force generation falls slowly. The EMG high/low ratio falls very rapidly in advance of any detectable loss of force, whereas later in the sustained contraction when force is still gradually falling there is no further change in the EMG high/low ratio. The time constant of decay of H/L varies widely among subjects when Poes or Pgas predominate whereas is consistent among subjects only when Poes = Pgas. Such a situation is very rare in clinical settings (Bradley et al, 1988). It is of interest that low frequency fatigue can persist for many hours at which time the electromyogram has returned to normal. Thus at a time that is obvious low frequency fatigue and very small twitch responses the EMG including the EMG power spectrum and EMG high/low ratio is normal (Moxham et al, 1982).

(ii) Frequency-fatigue relationship. The measurement of muscle force following electrical stimulation is particularly useful. Such techniques clearly demonstrate that following exhaustive muscular exercise, twitch tension can be greatly reduced (Merton, Mill and Morton, 1981). For the diaphragm, contraction force is measured in terms of transdiaphragmatic pressure measured by oesophageal and gastric balloons. The diaphragm is activated by stimulating the phrenic nerve in the neck using surface electrodes. , With stimulation, the pressure response obtained is very similar to the force response for any skeletal muscle (Moxham et al, 1981). Force-curve is characteristic with a rapid increase in force up to a stimulation frequency of approximately 40

Hz, after which a plateau is reached. With fatigue the shape of the curve can be altered, so that repeated high load muscle contraction may lead to a reduction in the forces generated at high stimulation frequencies (i.e. high frequency fatigue) and/or a reduction in the forces generated at low stimulation frequencies (i.e. low frequency fatigue), shifting the frequency force curve to the right. High frequency fatigue which is associated with a defect of neuromuscular transmission and depolarisation of the muscle cell causes a reduction of the muscle EMG, and recovers rapidly. With low frequency fatigue depolarisation of the muscle cell is normal and the EMG is not affected, but the force generated for each action potential is reduced reflecting an impaired response of the muscle fibre itself. Low frequency fatigue can last a long time, sometimes persisting for many hours (Edwards et al, 1977). Low frequency fatigue is believed to be of particular importance as the firing frequency of motor neurones during everyday activities is low (5-30 Hz) and therefore on the steep part of the frequency force curve. Even for a sustained maximum voluntary contraction the firing frequency of motor neurones falls to below 30 Hz within a few seconds. Low frequency fatigue has been documented for the sternomastoid and diaphragm in normal subjects following inspiratory loading and also in the sternomastoid of patients with stable airways obstruction who have been stressed with sustained maximum voluntary ventilation

(Moxham et al, 1981; Wilson et al, 1984). However the observations of this type of fatigue in patients with ventilatory failure in whom fatigue has occurred spontaneously are very few (Moxham et al, 1981). In severely ill patients it is difficult to use the invasive techniques that are necessary to detect low frequency fatigue. This problem greatly limits the usefulness of stimulation techniques and as yet it is not known how frequently low frequency fatigue is an important problem in clinical practice.

(iii) Relaxation rate. The most recent technique used to study the importance of muscle fatigue is the measurement of the relaxation rate of the respiratory muscles (Esau et al, 1983; Esau, Bye and Pardy, 1983; Levy et al, 1984). During fatigue a universal finding is that skeletal muscle becomes slower (Edwards, Hill and Jones, 1972). It is likely that the measurement of relaxation rate will provide useful information about the development of respiratory muscle fatigue and it may establish its importance in respiratory failure (Moxham, 1984). Relaxation rate can be described in terms of the half time and time constant of the pressure decay curve following voluntary or stimulated contraction of muscle (Edwards, Hill and Jones, 1972; Edwards et al, 1977; Edwards, 1982). A third measurement of relaxation rate is the slope of the tangent to the early part of the pressure decay curve. Maximum relaxation rate (MRR) is the ratio of slope/peak pressure and is expressed as % during pressure fall/10

msec (Wiles, 1981). The measurement of MRR during occluded inspiratory efforts is not always successful. Recently an attempt has been made to measure MRR of the respiratory muscles non-invasively at the mouth following brief inspiratory efforts against an occluded airway (Levy et al, 1984). However 25% of normal subjects could not perform the manoeuvre satisfactorily and were excluded from the study. By contrast a sniff (Miller, Moxham and Green, 1985; Laroche et al, 1988; Koulouris et al, 1988) is a natural manoeuvre, easily performed by both normal subjects and patients. The aim of this study was to investigate MRR of oesophageal pressure (Poes) generated by voluntary sniffs, and to determine if MRR decreases with inspiratory muscle fatigue. We also investigated whether the MRR of sniff nasopharyngeal (Pnp) and mouth pressure (Pmo) reflect MRR of sniff Poes.

6.2 METHODS

The study had approval of the local ethical committee and subjects gave informed consent. In this study a 'sniff' was characterised by a brief voluntary inspiratory effort with the lips closed, through the nostrils without a noseclip, from functional residual capacity (FRC) (Miller, Moxham and Green, 1985; Chapter 5). Body movement was not restricted and no special instructions were given regarding thoraco-abdominal movements.

Oesophageal pressure was measured using commercially available balloons, 10 cm long and 3.5 cm in

circumference attached to 100 cm long fine polythene catheters (PK Morgan, Rainham, Kent) and filled with 0.5 ml of air (Milic-Emili et al, 1964; Milic-Emili, 1984; Beardsmore et al, 1980). Nose and mouth pressures were measured using similar balloons reduced in length by taping the proximal 5 cm. The optimum volume of air for the small balloon was 0.7 ml determined from its pressure-volume characteristics measured both in-vitro and in-vivo. (Chapter 5; Appendix 3).

The oesophageal balloon was passed through one nostril after topical anaesthesia of the nasal mucosa (lidocaine spray 2%), and lubrication of the catheter (lidocaine gel 2%), and was swallowed by the subject with iced water. The oesophageal balloon was passed into the stomach and then withdrawn whilst observing the pressure signal until it was in the middle third of the oesophagus. Nasopharyngeal pressure (Pnp) was measured with a 5 cm balloon, advanced through the anaesthetised nose into the nasopharynx. When the subject could just feel the balloon at the back of the throat during swallowing, it was withdrawn 1 cm so that the tip of the balloon was approximately 10 cm from the anterior nares.

Pressure in the mouth (Pmo) was also measured with a 5 cm balloon, held in the oral cavity with the lips closed; subjects were instructed not to bite the catheter, or compress, or apply suction to the balloon with the tongue during the sniff. (Fig 45).

Each balloon catheter was connected to a Validyne MP-45 pressure transducer (range ± 350 cm H₂O,

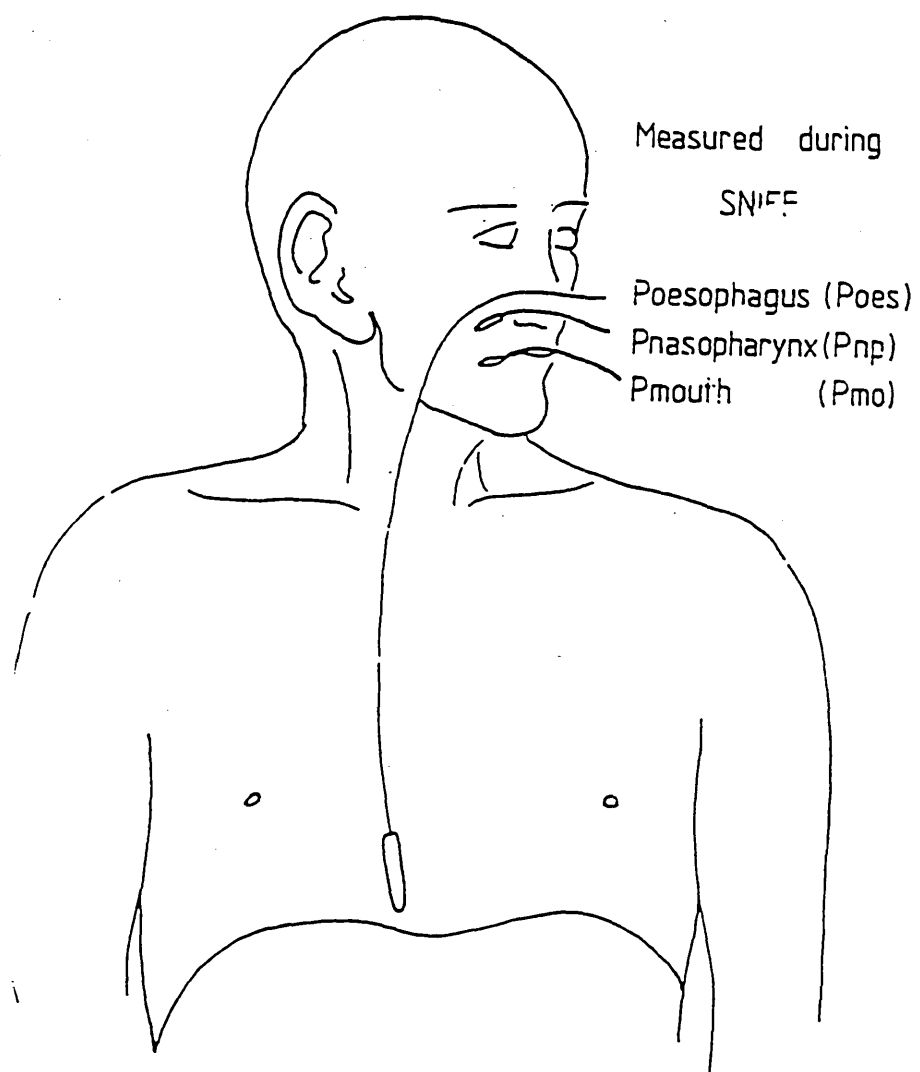


Figure 45 Diagram showing the simultaneous measurement of Poes, Pnp and Pmo pressures during a sniff manoeuvre.

Validyne Co, Northridge, CA). Transducers were calibrated before each study using U-tube water and mercury manometers as pressure standards. Uncalibrated pressure traces were displayed on a Tektronix 5013N storage oscilloscope screen (Tektronix Inc, Oregon) and calibrated signals were recorded onto paper using a Mingograf 800 ink-jet recorder (Siemens-Elema, Sweden) at a paper speed of 100 mm/sec. The response time of each balloon catheter-recorder system was measured by placing the balloon catheter in a second larger pressurised balloon and bursting the latter with a hot needle to create a square wave fall in pressure ("pop test"). The pressure signal was recorded at a paper speed of 1000 mm/sec. The 10-90% rise time (T_r) was found to be 0.017 sec. The maximum frequency response (f_{3db}) was determined from the equation $f_{3db} = 1/3T_r$ for the critically damped signal and was 20 Hz (Sykes, Vickers and Hull, 1981; Clayton, 1979).

Magnetometers (Mead et al, 1967) were used to monitor anteroposterior diameters of the thoracic and abdominal cavities to ensure that the subjects performed sniffs from FRC. In addition the pre-sniff oesophageal pressure was examined to confirm the subject was at FRC.

6.3 PROTOCOL

6.3.1 Normal subjects

MRR was determined in 10 normal healthy caucasian subjects (6 male, 4 female, aged 27-44), all

members of the laboratory staff. Within day reproducibility was assessed by the subjects performing 3 sets of 10 maximal and 10 sub-maximal sniffs at 0, 20 and 40 minutes. Control sub-maximal sniffs were performed to confirm that any reduction in the post-fatigue sniff amplitude could not cause a change in MRR (Wiles et al, 1979). Day to day reproducibility was determined by repeating these measurements in 3 subjects on three separate days.

The slope of the pressure decay curve was determined from a tangent drawn to the steepest portion of the curve (Figure 46). MRR is the ratio slope/peak pressure and is expressed as % pressure loss in 10 msec (Wiles et al, 1979; Edwards, Hill and Jones, 1975; Jewell and Wilkie, 1960). In this way sniffs of varying peak pressures can be compared. Criteria used to select those sniffs suitable for analysis were (a) peak pressure maintained for less than 50 msec (b) total sniff duration less than 500 msec (c) sniff pressure wave had smooth decay curve (d) sniffs were performed from FRC, since MRR may change with lung volume (Levy et al, 1984) (e) when sub-maximal sniffs were analysed, a peak pressure of at least 60% of maximum, since MRR slows when skeletal muscle is only partly activated during voluntary contractions (Wiles et al, 1979). By these criteria 94% of the sniffs were available for analysis.

6.3.2 Inspiratory loading

We investigated the change of MRR of sniff

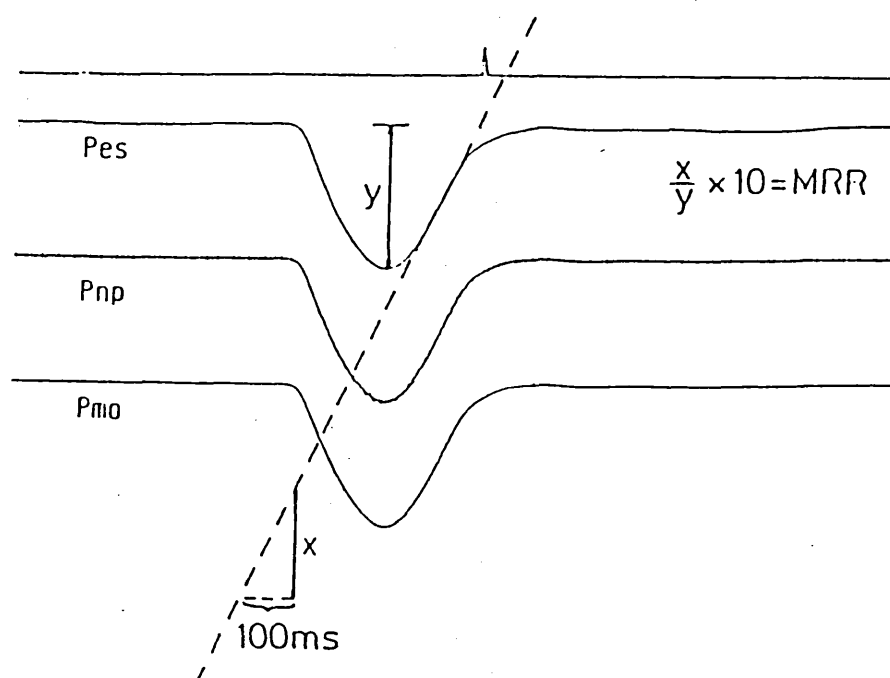


Figure 46 Measurement of maximum relaxation rate
(MRR) expressed as % pressure fall in 10 msec

Poes, Pnp and Pmo with the development of inspiratory muscle fatigue. Four of the ten normal subjects (3 male, 1 female, aged 31-44) participated in the fatiguing protocol. All were respiratory physiologists familiar with the techniques used.

These subjects fatigued their inspiratory muscles by breathing through a partially occluded 2-way valve of high alinear inspiratory resistance, expiration being unloaded. Arterialised venous blood (Forster et al, 1972) samples were drawn from a warmed hand vein throughout the study. The oesophageal and nasopharyngeal balloons were placed in position before the fatigue run. Maximum Poes was determined from a static inspiratory effort maintained for one second against an occluded mouthpiece. Target Poes was set at 80% of this value, marked on an oscilloscope screen in front of the subject, and each subject then generated the target pressure with each breath for as long as possible (3-6 mins). Fatigue was defined as the point at which the subject could no longer reach and maintain the target for six consecutive breaths. At this point subjects came quickly off the mouthpiece, placed the small balloon in their mouth and performed a series of maximal and submaximal sniffs from FRC. Sniffs were performed at 5-10 sec intervals for the first 5 minutes, and then at 10 minutes after fatigue.

6.4 STATISTICAL ANALYSIS

Mean values, correlation coefficients,

regression analyses and paired t-tests were obtained using the "Minitab" statistical computer (Minitab Inc, State College, PA)

6.5 RESULTS

6.5.1 Normal subjects

Maximal sniff Poes, Pnp and Pmo MRR were closely related (table 20). Correlation coefficients were; Poes and Pnp MRR $r = 0.977$, $p < 0.001$, Poes and Pmo $r = 0.947$, $p < 0.001$. Regression analyses showed that Poes MRR = $-1.19 + 1.09$ Pnp MRR ($R^2 = 94.9\%$, SEE = 0.299), and Poes MRR = $-0.62 + 1.03$ Pmo MRR ($R^2 = 88.4\%$, SEE = 0.451) (Fig 47, 48). Paired t-tests revealed no statistically significant difference between the results for maximal and sub-maximal sniff MRR in the ten subjects (table 21).

Within day coefficients of variation (CV) for maximal sniffs as assessed in ten subjects for three study sessions were 5.7% (range 1.8 - 8.5) for Poes, 5.4% (range 1.4 - 8.0) for Pnp, and 5.5% (range 3.2 - 7.7) for Pmo (table 22). Day to day CV's as assessed in three subjects on three different days, were 6.1% (range 5.6 - 8.5) for Poes, 6.3% (range 4.6 - 8.5) for Pnp and 6.8% (range 6.6 - 7.3) for Pmo (table 23). For sub-maximal sniffs in 10 subjects, within day CV's were 5.6% (range 3.2 - 10.1) for Poes, 5.2% (range 1.9 - 7.6) for Pnp, and 5.7% (range 1.9 - 9.8) for Pmo (table 24). Day to day CV's were 9.2% (range 7.9 - 10.1) for Poes, 8.1% (range

Table 20
Normal Values (mean $\pm$ SE) for Maximal Sniff MRR
(% pressure loss/10 msec)

Subject	Poes	Pnp	Pmo
1	10.587 $\pm$ 0.15	11.028 $\pm$ 0.70	11.072 $\pm$ 0.26
2	9.07 $\pm$ 0.27	10.096 $\pm$ 0.28	10.335 $\pm$ 0.28
3	9.200 $\pm$ 0.23	9.660 $\pm$ 0.28	9.470 $\pm$ 0.18
4	9.89 $\pm$ 0.17	9.792 $\pm$ 0.15	9.663 $\pm$ 0.14
5	10.010 $\pm$ 0.22	9.837 $\pm$ 0.20	9.730 $\pm$ 0.18
6	6.730 $\pm$ 0.20	7.290 $\pm$ 0.18	7.010 $\pm$ 0.20
7	9.890 $\pm$ 0.17	10.400 $\pm$ 0.16	10.490 $\pm$ 0.17
8	8.000 $\pm$ 0.17	8.210 $\pm$ 0.16	8.030 $\pm$ 0.19
9	8.150 $\pm$ 0.18	8.750 $\pm$ 0.22	8.730 $\pm$ 0.20
10	7.060 $\pm$ 0.16	7.910 $\pm$ 0.20	8.280 $\pm$ 0.20
Mean	8.901	9.297	9.287
$\pm$ SE	0.421	0.379	0.397

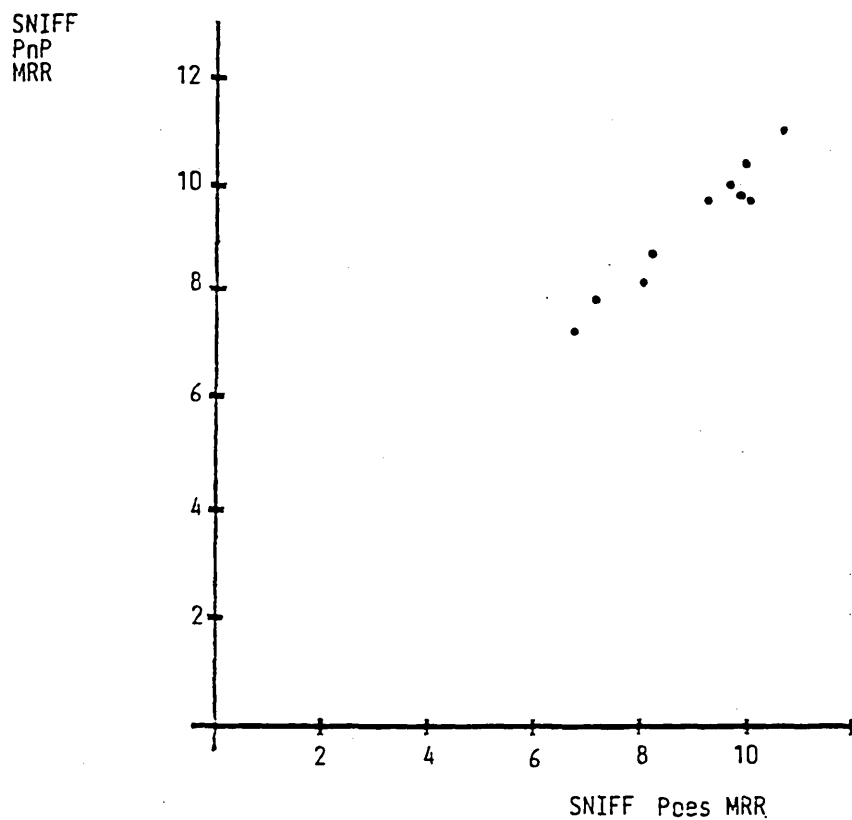


Figure 47. Comparison between Poes and Pnp MRR in ten normal subjects obtained during maximal sniffs
(Poes MRR = $-1.19 + 1.09$ Pnp MRR, $R^2 = 94.9\%$, SEE = 0.299
n = 10)

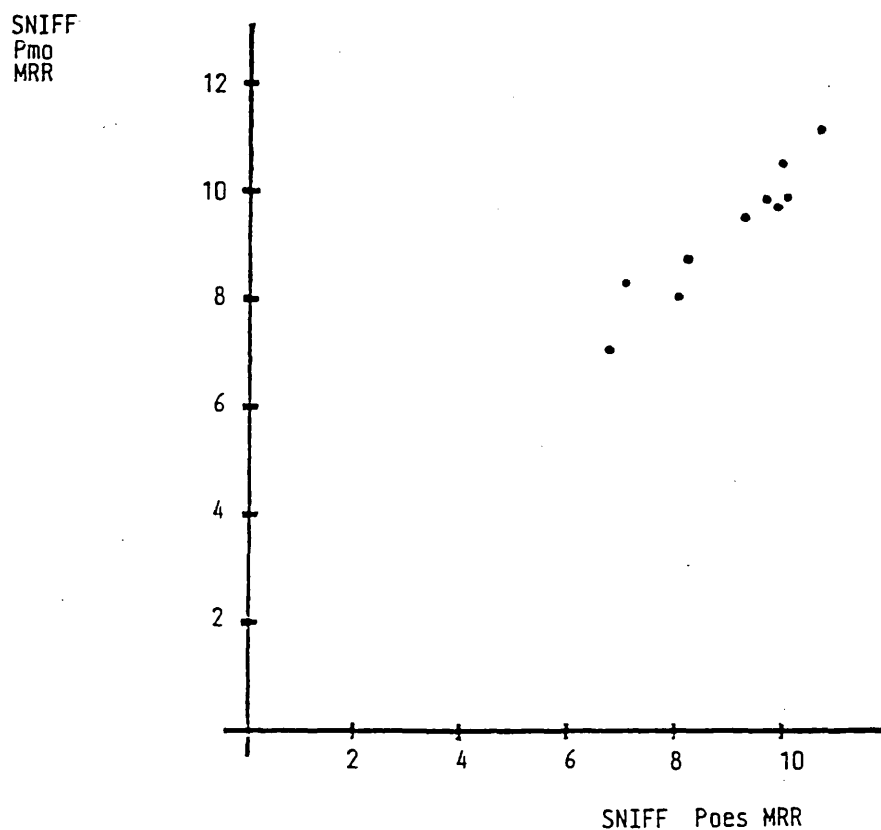


Figure 48 Comparison between Poes and Pmo MRR in ten normal subjects obtained during maximal sniffs (Poes MRR = $-0.62 + 1.03$) Pmo MRR ($R^2 = 88.4\%$, SEE = 0.451, n = 10).

Table 21
Normal values for Submaximal Sniff MRR
($>60\%$ sniff Poes)

Subject	Poes	Pnp	Pmo
1	10.18 $\pm$ 0.31	10.06 $\pm$ 0.42	9.98 $\pm$ 0.42
2	9.40 $\pm$ 0.42	9.89 $\pm$ 0.33	9.92 $\pm$ 0.43
3	10.09 $\pm$ 0.49	10.72 $\pm$ 0.45	9.73 $\pm$ 0.60
4	8.76 $\pm$ 0.19	8.59 $\pm$ 0.11	8.47 $\pm$ 0.08
5	9.65 $\pm$ 0.21	9.85 $\pm$ 0.13	9.79 $\pm$ 0.11
6	7.48 $\pm$ 0.21	8.13 $\pm$ 0.07	7.90 $\pm$ 0.28
7	9.12 $\pm$ 0.14	9.93 $\pm$ 0.33	10.07 $\pm$ 0.21
8	7.93 $\pm$ 0.15	7.86 $\pm$ 0.22	7.83 $\pm$ 0.12
9	7.74 $\pm$ 0.16	8.28 $\pm$ 0.19	8.64 $\pm$ 0.19
10	6.75 $\pm$ 0.21	7.17 $\pm$ 0.17	7.12 $\pm$ 0.16
Mean	8.710	9.043	8.945
$\pm$ SE	0.370	0.371	0.343

Table 22
 Within day coefficient of variation for
 Maximal Sniffs MRR in 10 normal subjects

Subject	Poes	Pnp	Pmo
1	7.90	6.60	7.70
2	7.44	5.44	6.22
3	5.77	6.66	4.41
4	1.79	1.40	4.95
5	8.49	8.05	5.98
6	7.37	6.27	7.07
7	3.62	3.16	3.21
8	4.96	4.51	5.31
9	4.47	5.19	4.70
10	5.17	5.75	5.47
Mean	5.69	5.35	5.50
Range	(1.79-8.49)	(1.4-8.05)	(3.21-7.70)

Table 23
Day to day coefficient of variation for maximal
sniff MRR in 3 normal subjects

Subject	Poes	Pnp	Pmo
1	5.58	4.64	6.64
2	7.08	7.33	6.63
3	8.48	8.53	7.25
Mean	6.09	6.85	6.84
Range	(5.6-8.5)	(4.6-8.5)	(6.6-7.3)

Table 24
 Within day coefficient of variation for Submaximal
 Sniff MRR (>60% of Sniff Poes) in 10 normal subjects

Subject	Poes	Pnp	Pmo
1	5.41	7.07	6.56
2	10.11	7.55	9.82
3	5.09	5.92	9.54
4	4.45	2.67	1.89
5	5.38	3.30	2.90
6	5.70	1.93	7.11
7	3.20	6.76	4.30
8	3.80	5.73	3.09
9	5.57	6.16	6.03
10	7.05	5.10	5.27
Mean	5.576	5.249	5.651
Range	(3.20-10.11)	(1.93-7.55)	(1.98-9.82)

7.0 - 8.9) for Pnp, and 9.5% (range 8.1 - 11.2) for Pmo (table 25).

6.5.2 Inspiratory loading

Maximum relaxation rates (% pressure loss /10 msec) for pre-fatigue maximal sniffs in 4 subjects were 10.0 ± 0.2 (mean $\pm$ SE) for Poes, 10.2 ± 0.3 for Pnp, and 10.1 ± 0.3 for Pmo. All subjects showed a substantial decrease in MRR after fatigue (figures 49, 50, 51) at 30 seconds sniff Poes MRR decreased by 34% (range 20-41); Pnp MRR by 31% (range 18-43); and Pmo MRR by 32% (range 21 - 42) (table 26, 27, 28, 29). Recovery of MRR was rapid and exponential (figure 51); MRR and the natural logarithm of time showed a straight line relationship (sniff Poes MRR $r = 0.985$, Pnp $r = 0.961$, Pmo $r = 0.954$, $p < 0.01$) (figures 51, 52). The decrease in MRR was no longer statistically significant by the third minute of recovery. Repeated studies in the four subjects showed closely similar results.

Arterialised blood samples showed no change in pH, P_{CO_2} and P_{O_2} between control and fatigue values (table 30).

6.6 DISCUSSION

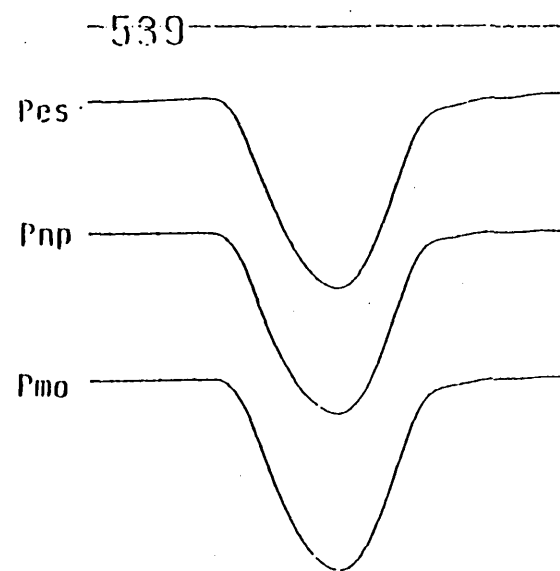
The results of the present study show that the MRR of sniff oesophageal pressure is reduced with fatigue, and could therefore be a valuable technique for the detection of inspiratory muscle fatigue although

Table 25
Day to day coefficient of variation for Submaximal
Sniff MRR (>60% of Sniff Poes) in 3 normal subjects

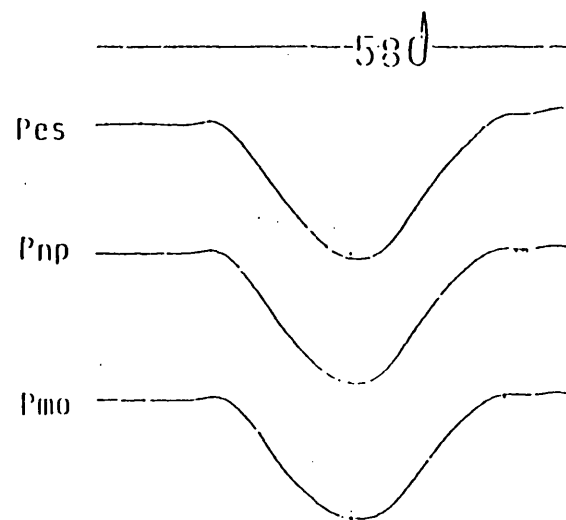
Subject	Poes	Pnp	Pmo
1	10.069	8.355	8.090
2	9.479	8.863	9.282
3	7.929	6.961	11.202
Mean	9.159	8.058	9.464
Range	(7.92-10.06)	(6.96-8.86)	(8.09-11.20)

Figure 49 Sniff wave forms before and after fatigue
in one subject

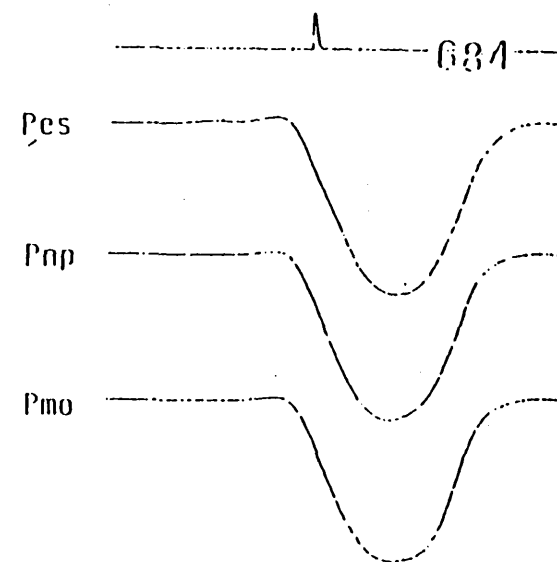
Before fatigue



30 seconds after



10 minutes after fatigue



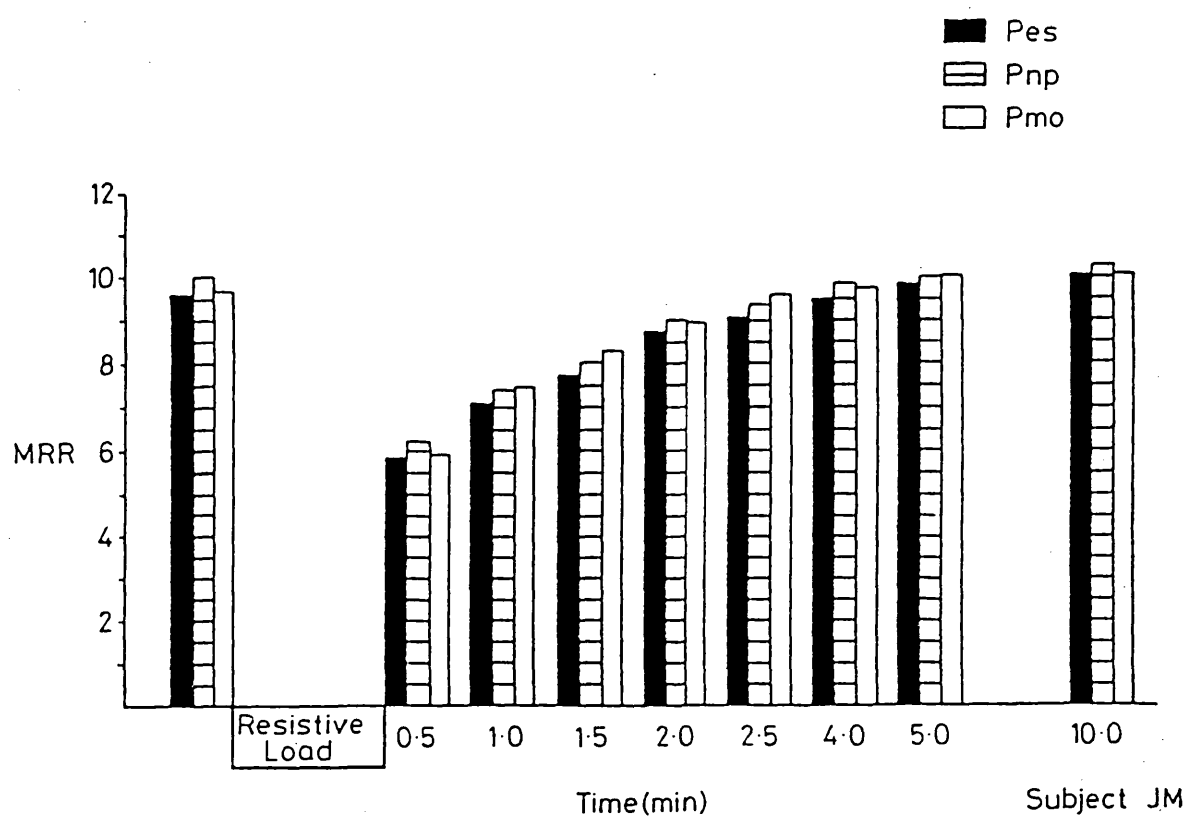


Figure 50 MRR values before and after fatigue for sniff Poes, Pnp and Pmo in one subject (JM)

Table 26
MRR of Sniff Poes before and after fatigue, and
during recovery (mean $\pm$ SE)

Sub- jects	Before	30"	1'	2'	3'	4'	5'	10'
LV	9.79 $\pm$ 0.17	7.87 $\pm$ 0.19	8.15 $\pm$ 0.10	8.74 $\pm$ 0.24	9.31 $\pm$ 0.25	9.40 $\pm$ 0.13	10.37 $\pm$ 0.24	10.18 $\pm$ 0.22
NK	10.58 $\pm$ 0.15	6.20 $\pm$ 0.15	7.36 $\pm$ 0.30	8.49 $\pm$ 0.16	9.55 $\pm$ 0.33	9.204 $\pm$ 0.33	10.06 $\pm$ 0.08	9.86 $\pm$ 0.21
MG	10.01 $\pm$ 0.22	5.99 $\pm$ 0.23	6.17 $\pm$ 0.35	7.07 $\pm$ 0.30	8.05 $\pm$ 0.30	9.39 $\pm$ 0.35	8.11 $\pm$ 0.17	10.68 $\pm$ 0.21
JM	9.57 $\pm$ 0.17	6.47 $\pm$ 0.35	6.38 $\pm$ 0.29	8.25 $\pm$ 0.29	9.37 $\pm$ 0.339	9.51 $\pm$ 0.27	9.87 $\pm$ 0.14	10.45 $\pm$ 0.32
Mean	10.013	6.632	7.019	8.142	9.072	9.128	9.606	10.297
$\pm$ SE	0.219	0.424	0.459	0.369	0.343	0.254	0.506	0.178

Table 27
MRR of Sniff Pnp before and after fatigue, and
during recovery (mean $\pm$ SE)

Sub- jects	Before	30"	1'	2'	3'	4'	5'	10'
LV	9.79 $\pm$ 0.15	7.98 $\pm$ 0.27	8.18 $\pm$ 0.008	8.74 $\pm$ 0.25	9.26 $\pm$ 0.25	9.20 $\pm$ 0.13	10.24 $\pm$ 0.27	10.20 $\pm$ 0.24
NK	11.02 $\pm$ 0.20	6.25 $\pm$ 0.14	7.47 $\pm$ 0.33	8.75 $\pm$ 0.23	9.91 $\pm$ 0.33	9.34 $\pm$ 0.07	9.94 $\pm$ 0.16	9.92 $\pm$ 0.29
MG	9.83 $\pm$ 0.20	6.50 $\pm$ 0.23	6.61 $\pm$ 0.30	7.80 $\pm$ 0.28	8.96 $\pm$ 0.25	8.32 $\pm$ 0.30	8.35 $\pm$ 0.19	10.84 $\pm$ 0.17
JM	9.99 $\pm$ 0.24	6.96 $\pm$ 0.33	6.69 $\pm$ 0.30	8.48 $\pm$ 0.25	9.65 $\pm$ 0.30	9.91 $\pm$ 0.14	10.05 $\pm$ 0.11	10.73 $\pm$ 0.31
Mean	10.157	6.922	7.237	8.442	9.445	9.192	9.695	10.422
$\pm$ SE	0.290	0.381	0.369	0.223	0.209	0.328	0.436	0.218

Table 28
MRR of Sniff Pmo before and after fatigue, and
during recovery (mean $\pm$ SE)

Sub- jects	Before	30"	1'	2'	3'	4'	5'	10'
LV	9.66 $\pm$ 0.14	7.62 $\pm$ 0.25	7.79 $\pm$ 0.16	8.61 $\pm$ 0.23	8.78 $\pm$ 0.28	9.09 $\pm$ 0.09	9.97 $\pm$ 0.24	10.20 $\pm$ 0.24
NK	11.07 $\pm$ 0.26	6.46 $\pm$ 0.16	7.58 $\pm$ 0.27	8.73 $\pm$ 0.19	10.01 $\pm$ 0.37	9.43 $\pm$ 0.09	10.09 $\pm$ 0.11	10.14 $\pm$ 0.23
MG	9.73 $\pm$ 0.18	6.30 $\pm$ 0.35	6.78 $\pm$ 0.22	7.08 $\pm$ 0.22	8.08 $\pm$ 0.28	8.31 $\pm$ 0.35	8.04 $\pm$ 0.19	10.56 $\pm$ 0.20
JM	9.85 $\pm$ 0.18	6.97 $\pm$ 0.33	6.58 $\pm$ 0.36	8.66 $\pm$ 0.28	9.84 $\pm$ 0.42	9.84 $\pm$ 0.27	10.13 $\pm$ 0.14	10.57 $\pm$ 0.29
Mean	10.081	6.837	7.186	8.275	9.183	9.172	9.559	10.276
$\pm$ SE	0.332	0.297	0.296	0.397	0.455	0.324	0.507	0.180

Table 29

Sniff MRR: mean ($\pm$ SE) (n=4)* $p < 0.02$, ** $p < 0.01$, *** $p < 0.001$

Time in min	Pes	Pnp	Pmo
Control	10.0 $\pm$ 0.2	10.2 $\pm$ 0.2	10.2 $\pm$ 0.3
0-1 mins	7.0 $\pm$ 0.4**	6.9 $\pm$ 0.2***	7.2 $\pm$ 0.3***
1-2 mins	8.1 $\pm$ 0.4**	8.3 $\pm$ 0.2*	8.3 $\pm$ 0.4*
2-3 mins	9.1 $\pm$ 0.3	9.4 $\pm$ 0.3	9.2 $\pm$ 0.5
3-4 mins	9.1 $\pm$ 0.3	9.2 $\pm$ 0.3	9.2 $\pm$ 0.3
4-5 mins	9.6 $\pm$ 0.5	9.3 $\pm$ 0.4	10.3 $\pm$ 0.2
9-10 mins	10.3 $\pm$ 0.2	10.4 $\pm$ 0.4	10.3 $\pm$ 0.2

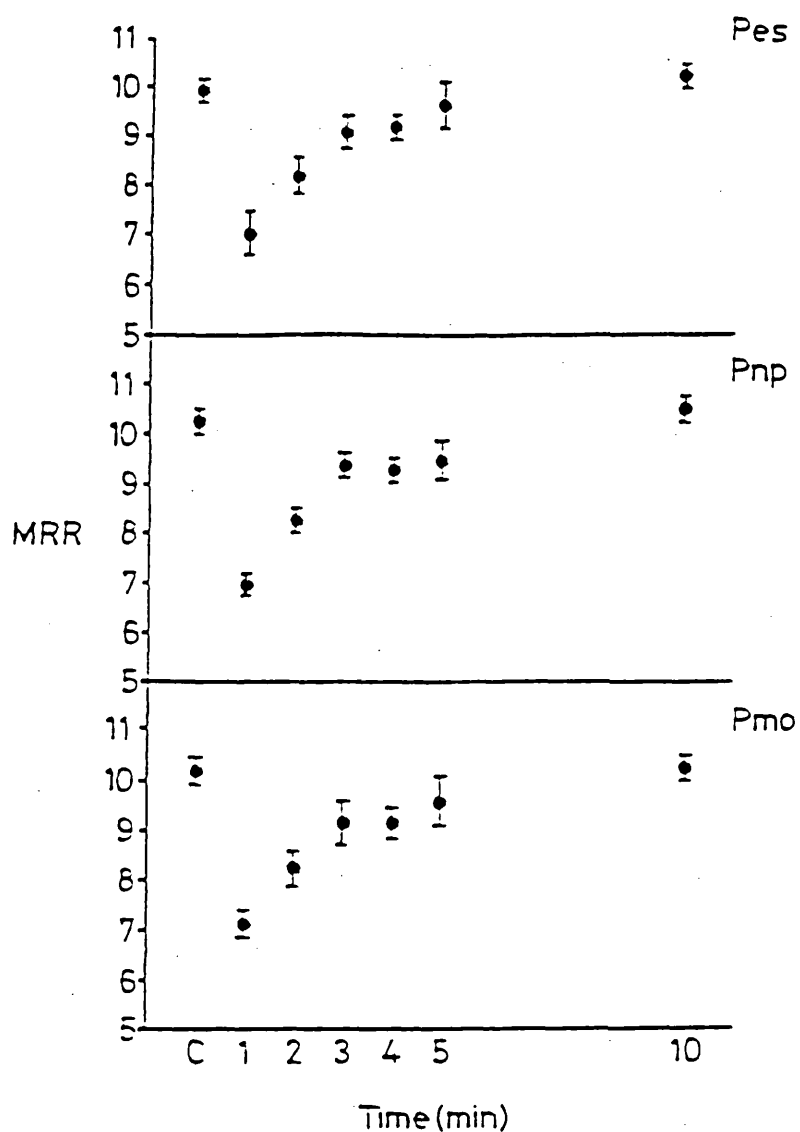


Figure 51 MRR of sniff pressures before and after fatigue and during recovery. Each circle represents mean $\pm$ SE data for 4 normal subjects

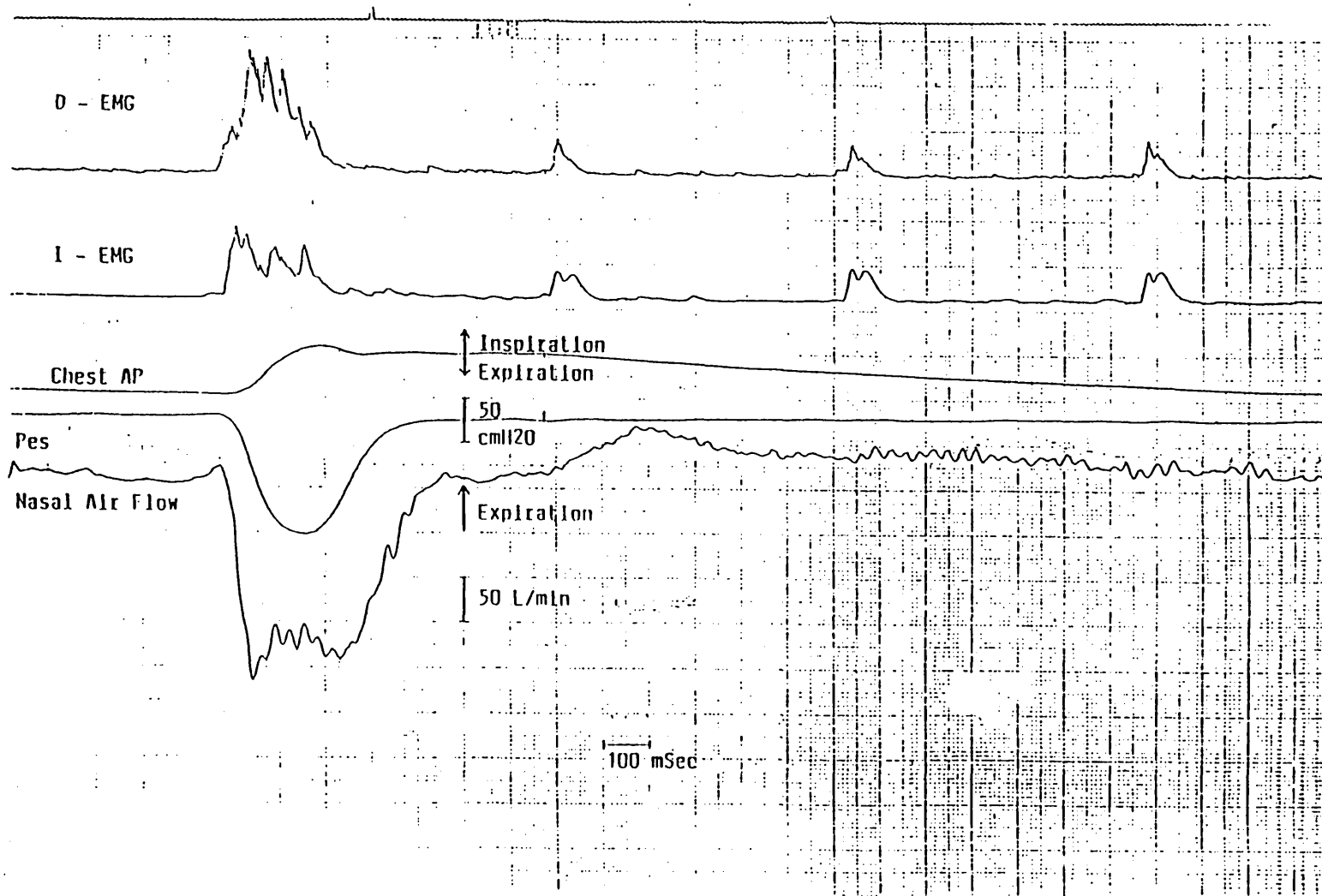
Table 30
Arterialised Venous Blood
(mean $\pm$ SE, n=4)

	At rest	At point of fatigue	
pH	7.43 $\pm$ 0.01	7.41 $\pm$ 0.01	N.S.
PCO ₂ (mm Hg)	37.3 $\pm$ 1.23	35.9 $\pm$ 1.97	N.S.
PO ₂ (mm Hg)	78.9 $\pm$ 3.28	73.5 $\pm$ 5.55	N.S.

requiring the passage of an oesophageal balloon. The MRR of sniff Pnp and Pmo accurately reflect the decrease in Poes MRR with fatigue, and the rapid return to control values in an exponential fashion by 3-4 mins.

The absolute values and rate of recovery following fatigue of sniff Poes, Pnp and Pmo MRR were similar to those documented for transdiaphragmatic and mouth pressures during occluded inspiratory efforts (Esau et al, 1983; Esau, Bye and Pardy, 1983; Levy et al, 1984) and for other non-respiratory skeletal muscles (Wiles, 1981; Wiles et al, 1979a; Wiles et al, 1979b). The conclusion that MRR can be measured from sniff pressures is based on the assumption that the decay part of the sniff pressure wave corresponds to the relaxation phase of respiratory muscle contraction. The diaphragm and intercostals are relaxing as judged by the EMG recordings (figure 52). The A-P diameter of the upper chest, as recorded by magnetometers, returns more slowly to FRC values, suggesting that the chest wall and lung relaxation rate was much slower and that the pressure curve is most likely to reflect relaxation of the respiratory muscles. This view is supported by data available in the literature (Lorino et al, 1982; Sharp et al, 1967) indicating that the constant of stress adaptation of the lungs and chest wall is several orders of magnitude greater than the time constant of relaxation of skeletal muscle. The reason for the similarity of upper and lower airway pressures and MRR's during a

Figure 52 Simultaneous recording of changes in
nasal airflow (flow) oesophageal (Poes), thoracic
anteroposterior diameter (Chest AP) intercostal (I - EMG)
and diaphragmatic (D - EMG) integrated electromyograms
during a sniff



dynamic manoeuvre such as a sniff may be deduced from previous studies as described in the previous chapter. There is good evidence that during the sniff manoeuvre the nostrils behave as a Starling resistor, rapidly collapsing under the influence of negative nasal pressures. Bridger and Proctor (Bridger and Proctor, 1970) used fine catheters to explore intranasal pressure gradients during vigorous inspiratory efforts. They were able to identify a point of occlusion in the region lying between the junction of the pyriform aperture and the upper and lower lateral cartilages. When a critical pressure gradient (estimated at 10-12 cm H₂O) exists across this region, occlusion occurs. Beyond the point of occlusion the upper and intrathoracic airways can be regarded as being in continuity with little pressure gradient between them. The presence of this flow limiting mechanism explains both the close agreement between sniff pressures and relaxation rates measured in the three sites, and the high pleural pressures developed during a sniff. These features of the Starling mechanism during a sniff are seen in figure 52.

The normal values of MRR for the respiratory muscles vary considerably between subjects and there can be marked overlap between fresh and fatigued values. Although the absolute values of MRR were very similar in our small group of subjects (table 20) it is probable that in some circumstances single values or MRR will not be sufficient to demonstrate the presence or absence of

fatigue. Serial measurements of MRR would then be needed to detect the onset of fatigue or the recovery from it. Technique may also affect MRR; when the MRR for unobstructed sniffs is compared with the values for inspiratory gasps, the latter are slower, such that the relaxation rate of the diaphragm is at the lower limit of normal for skeletal muscle (Levy et al, 1984). The lung volume at which MRR is determined may also be of importance (Levy et al, 1984); our normal subjects performed sniffs from FRC as judged by the megnetometer trace and pre-sniff values of Poes. In patients any alteration in lung volume must be taken into account when performing serial measurements.

Inspiratory muscle fatigue may precipitate or intensify ventilatory failure (Roussos and Macklem, 1982). Hypoxia and hypercapnic acidosis consequent to ventilatory failure may slow muscle relaxation directly and offset the value of MRR as an index of fatigue in this clinical context. However, the data to support this view has been obtained from in-vitro studies (Dawson, Gadian and Wilkie, 1980; Esau, 1987). A recent in-vivo study (Vianna et al, 1988) has shown no direct effect of acute hypoxia and hypercapnia/acidosis on MRR in human subjects. It is therefore concluded that sniff Poes MRR could be used in respiratory failure as an index of muscle fatigue.

Other metabolic influences on MRR of skeletal muscle include thyroid (Wiles et al, 1979b; Laroche et

al, 1988) and nutritional (Chan et al, 1986) status. The measurement of upper airways pressure and relaxation rates is simple and relatively non-invasive and may provide a quantitative index of response to therapeutic interventions.

Assessments of inspiratory muscle fatigue is difficult with the currently available techniques. Power spectral analysis of the diaphragmatic electromyogram (EMG) (Lindstrom, Magnuson and Peterson, 1974) reveals the frequency composition. With fatigue, there is an early alternation of the EMG such that high frequency activity is reduced and there is an increase in power at low frequencies, referred to as a reduction in the high/low ratio. This change in diaphragmatic EMG has been used as a marker of muscle fatigue, and the fall in relaxation rate of occluded inspiratory efforts shows a similar time course during the onset of fatigue (Esau et al, 1987). However, the time constant of decay of H/L varies widely among subjects when Poes or Pgas predominates, whereas is consistent among subjects only when Poes = Pgas. Such a situation is very rare in clinical environment (Bradley et al, 1988). Similarly our results for the recovery of sniff MRR agree with the data for high/low ratio recovery (Bellemare and Grassino, 1982). However, the cause of the shift in power spectrum or slowing of MRR is not known, nor is the relationship between these changes and force failure understood. Attempts have been made to document the contractile

properties of muscle by recording the force response as a function of the frequency of electrical stimulation (frequency/force curve) (Aubier et al, 1981; Moxham et al, 1981; Moxham, Wiles and Edwards, 1980). With fatigue the shape of the curve can be altered with a reduction in the forces generated at high stimulation frequencies (high frequency fatigue) and/or at low frequencies (low frequency fatigue). However it is difficult to apply high frequency stimulation techniques in sick patients. By contrast the measurement of upper airways sniff MRR provides a simple and minimally invasive technique (Chapter 5).

It may be concluded that (a) a fatiguing pattern of contraction causes a reduction in MRR of sniff oesophageal pressure, (b) these changes in Poes MRR are reflected in nasopharyngeal and mouth pressures during the sniff, (c) these measurements may prove to be useful for detecting and monitoring inspiratory muscle fatigue in both physiological and clinical settings.

6.7 SUMMARY

Maximum relaxation rate (MRR, % pressure fall/10 msec) of the inspiratory muscles is reduced with fatigue. I have investigated whether MRR of oesophageal pressure (Poes) generated by voluntary sniffs is decreased by fatigue, and whether sniff nasopharyngeal (Pnp) and mouth (Pmo) MRR reflect these changes. In 10 normal subjects, control MRR of sniff Poes correlated

closely to Pnp MRR ($r = 0.977$, $p < 0.001$) and Pmo MRR ($r = 0.947$, $p < 0.001$). To produce inspiratory muscle fatigue, 4 highly motivated subjects breathed to exhaustion (3 - 6 minutes) through a high inspiratory resistance. MRR was determined from 10 sniffs for Poes, Pnp and Pmo before fatigue, and at intervals up to 10 minutes after fatigue. The subjects showed a mean decrease in sniff Poes MRR of 34% (range 20 - 41) immediately following fatigue which returned exponentially to control values within 3-4 minutes. The mean changes in Poes MRR were reflected by similar changes in Pnp MRR, 31% (range 18-43) and Pmo MRR, 32% (range 21 - 42). Studies were repeated in the 4 subjects with closely similar results. It may be concluded that fatigue of the inspiratory muscles reduces MRR of sniff Poes, and that this is reflected in Pnp and Pmo. Sniff Poes, Pnp and Pmo MRR measurements may provide a useful method for detecting and monitoring fatigue; Pnp and Pmo have the advantage of being less invasive.

CHAPTER 7
CONCLUSIONS

The primary function the respiratory muscles have to accomplish together in a coordinated manner is to displace the rib cage and the abdomen to pump gas into and out of the lungs.

The mechanics of breathing is a problem requiring on one hand the detailed knowledge of a classical anatomist and on the other hand the analytic understanding of an engineer (W O Fenn). Therefore for the sake of better understanding the function of this vital pump, some of the most relevant features are stressed in the chapter one. A brief description of the techniques and equipment currently available to test the respiratory muscles is given in chapter two.

In the last ten years there has been considerable increase in interest and research in respiratory muscle physiology and pathophysiology. This implies the necessity of refinement of old and invention of new techniques to investigate various aspects of respiratory muscle function.

Muscle configuration and length are major determinants of diaphragmatic contractility; the length of the diaphragm is increased in the supine posture with a theoretical improvement in mechanical advantage. The transition from supine to upright posture shortens the diaphragmatic fibres compromising force generation. Little is known about the effect of posture on the generation of maximal respiratory pressures. The aim of the study in Chapter three was to quantify the effect of

body position on the following indices of respiratory muscle strength (i) transdiaphragmatic pressure (Pdi) generated at FRC during percutaneous bilateral phrenic nerve stimulation at 1Hz, (ii) maximal sniffs and (iii) maximal static mouth pressures (PImax and PEmax). Studies performed in six highly trained normal subjects. Sniffs and twitches were performed with abdomen bound and unbound. Three postures were examined: seated (Se), semi-supine (30s) and supine (Su). Binding the abdomen significantly increased twitch Pdi in all postures by 40% in Se, 29% in SS and 21% in Su but any advantage in producing higher pressures is offset by patients discomfort and increased breathlessness. Changes of posture did not significantly alter twitch Pdi. In the clinical setting, I observed that subjects are most comfortable when phrenic nerve stimulation is performed in the 30s position. It is also easier to locate the phrenic nerves and maintain stimulus maximality in this position. By contrast sniff Pdi and static mouth pressures were significantly reduced in Su posture. Therefore voluntary manoeuvres give higher pressures in seated position than supine despite a theoretical reduction in mechanical advantage of the diaphragm. This improvement is not seen in involuntary manoeuvres. It may be that in voluntary manoeuvres a better recruitment, activation and coordination of the respiratory muscles can be achieved. From a practical viewpoint serial measurements of respiratory pressures during voluntary

manoeuvres should be carried out in a standard posture.

Important differences exist between reference ranges for the normal values of P_Imax and P_Emax. This variation may reflect differences in the cohorts used to establish a normal range, the criteria of measurement, the design of the apparatus and the way it is used. The latter hypothesis therefore was investigated in Chapter 4 i.e. differences reported for normal ranges reflect the use of different mouthpieces. I compared two mouthpieces, a rigid plastic flanged type fitting inside the lips (flange) and a rubber tube held against the lips (tube). It was concluded that for subjects able to use the tube, pressures may be higher. A rubber tube mouthpiece would seem appropriate in physiological studies when truly maximal pressures are needed. The flange is more widely applicable as pressures can be obtained by the assistance of the investigator in patients who are unable to use the tube owing to neuromuscular disease, hand deformity or quadriplegia. The choice of the mouthpiece does contribute to the variability in the reported normal ranges for P_Emax and P_Imax. The differences are unlikely to be important clinically, provided the appropriate range is used. It may be preferable for a laboratory wishing to measure mouth pressures to choose one technique applicable to the study population and to establish a local reference range.

Oesophageal pressure measured during a maximal sniff from FRC without a nose clip discriminates patients

with suspected weakness of the respiratory muscles who have a low P_Imax due to poor technique or lack of motivation from those with total inspiratory muscle weakness. However the usefulness of sniff Poes in detecting inspiratory muscle weakness can be offset in some subjects by the need to pass an oesophageal balloon. The aim of the studies in chapter 5 was to establish whether pressures in the mouth (P_{mo}) or nasopharynx (P_{np}) reflect Poes during a maximum sniff and if their measurement provides a minimally invasive technique for the discrimination assessment of inspiratory muscle weakness. It was found that in both normal subjects and patients with pure inspiratory muscle weakness, P_{np} and P_{mo} accurately predict Poes during the sniff manoeuvre. Measurement of sniff P_{np} and P_{mo} is therefore a simple minimally invasive, reproducible, well tolerated by all subjects and may provide a clinically useful technique for the assessment of inspiratory muscle strength.

The most recent technique used to detect fatigue of the respiratory muscles has been slowing of Maximum Relaxation Rate (MRR). It has been shown (chapter 5) that P_{np} and P_{mo} accurately reflects Poes during a sniff. The aim of the studies in chapter 6 was to investigate MRR of sniff oesophageal pressure, to determine if MRR decreases with inspiratory muscle fatigue and whether MRR of sniff P_{np} and P_{mo} reflect MRR of sniff Poes. It was found that a fatiguing pattern of contraction causes a significant reduction in MRR of

sniff Poes and these changes are reflected in sniff Pnp and Pmo MRR. All changes in MRR returned exponentially to control values within 3-4 minutes. These measurements i.e. sniff Poes, Pnp and Pmo MRR may prove useful for detecting and monitoring respiratory muscle fatigue; Pnp and Pmo have the advantage of being minimally invasive.

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APPENDICES

Appendix 1a
Pressures obtained during Bilateral Phrenic Nerve Stimulation
at various postures (cmH₂O, mean $\pm$ SE, n=5)

Subjects	Pdi		Poes		Pgas	
	Bound	Unbound	Bound	Unbound	Bound	Unbound
Su D.M.	34.2 $\pm$ 0.49	26.8 $\pm$ 0.49	20.60 $\pm$ 0.59	20.80 $\pm$ 0.49	13.60 $\pm$ 0.24	7.40 $\pm$ 0.36
M.G.	43.0 $\pm$ 0.44	39.40 $\pm$ 1.03	28.20 $\pm$ 0.37	32.40 $\pm$ 0.92	14.80 $\pm$ 0.37	7.00 $\pm$ 0.44
J.M.	28.7 $\pm$ 0.20	23.3 $\pm$ 0.25	16.00 $\pm$ 0.00	16.60 $\pm$ 0.24	12.70 $\pm$ 0.20	6.60 $\pm$ 0.29
N.K.	44.80 $\pm$ 0.40	36.6 $\pm$ 0.51	28.40 $\pm$ 0.20	27.60 $\pm$ 0.40	16.40 $\pm$ 0.40	9.00 $\pm$ 0.31
J.G.	39.7 $\pm$ 0.53	35.7 $\pm$ 0.66	24.70 $\pm$ 0.80	31.60 $\pm$ 0.40	15.00 $\pm$ 1.00	4.10 $\pm$ 0.45
C.L.	27.0 $\pm$ 0.27	16.50 $\pm$ 0.22	17.10 $\pm$ 0.40	14.40 $\pm$ 0.29	9.90 $\pm$ 0.29	2.10 $\pm$ 0.10
30s D.M.	36.4 $\pm$ 0.43	25.8 $\pm$ 0.20	20.20 $\pm$ 0.58	17.60 $\pm$ 0.24	16.20 $\pm$ 0.46	8.20 $\pm$ 0.37
M.G.	44.0 $\pm$ 0.31	39.2 $\pm$ 0.58	25.20 $\pm$ 0.49	26.60 $\pm$ 0.40	18.80 $\pm$ 0.37	12.60 $\pm$ 0.40
J.M.	31.40 $\pm$ 0.18	23.3 $\pm$ 0.25	16.00 $\pm$ 0.18	16.50 $\pm$ 0.22	15.40 $\pm$ 0.10	6.80 $\pm$ 0.25
N.K.	44.6 $\pm$ 0.74	34.20 $\pm$ 0.37	25.60 $\pm$ 0.67	25.60 $\pm$ 0.24	19.00 $\pm$ 0.31	8.60 $\pm$ 0.51
J.G.	46.7 $\pm$ 0.70	35.5 $\pm$ 0.82	23.40 $\pm$ 1.22	24.90 $\pm$ 0.33	23.30 $\pm$ 1.25	10.60 $\pm$ 0.67
C.L.	24.0 $\pm$ 0.00	18.5 $\pm$ 0.00	15.2 $\pm$ 0.37	14.60 $\pm$ 0.18	8.80 $\pm$ 0.37	3.90 $\pm$ 0.18
Se D.M.	33.40 $\pm$ 0.87	24.8 $\pm$ 0.37	16.90 $\pm$ 0.33	15.00 $\pm$ 0.54	16.50 $\pm$ 0.74	9.80 $\pm$ 0.49
M.G.	39.60 $\pm$ 0.24	29.0 $\pm$ 0.44	27.00 $\pm$ 0.44	19.40 $\pm$ 0.51	12.60 $\pm$ 0.24	9.60 $\pm$ 0.40
J.M.	30.50 $\pm$ 0.67	22.5 $\pm$ 0.15	12.30 $\pm$ 0.53	11.10 $\pm$ 0.10	18.20 $\pm$ 0.25	11.40 $\pm$ 0.10
N.K.	42.60 $\pm$ 0.40	33.00 $\pm$ 0.31	25.80 $\pm$ 0.20	20.60 $\pm$ 0.24	16.80 $\pm$ 0.20	12.40 $\pm$ 0.40
J.G.	47.60 $\pm$ 0.92	30.9 $\pm$ 0.96	19.50 $\pm$ 0.63	20.10 $\pm$ 0.66	28.10 $\pm$ 0.95	10.80 $\pm$ 0.33
C.L.	28.5 $\pm$ 0.22	18.3 $\pm$ 0.20	14.90 $\pm$ 0.24	8.20 $\pm$ 0.20	13.60 $\pm$ 0.40	10.10 $\pm$ 0.33

Appendix 1b
Pressures obtained during Maximal Sniffs at different
postures (cmH₂O, mean $\pm$ SE, n=5)

Subjects	Pdi		Poes		Pgas	
	Bound	Unbound	Bound	Unbound	Bound	Unbound
Su D.M.	125.0 $\pm$ 0.006	132.00 $\pm$ 0.94	117.00 $\pm$ 2.00	131.50 $\pm$ 1.00	8.00 $\pm$ 2.00	0.50 $\pm$ 0.50
M.G.	106.00 $\pm$ 3.67	122.00 $\pm$ 2.55	93.00 $\pm$ 4.06	112.00 $\pm$ 2.00	13.00 $\pm$ 1.22	10.00 $\pm$ 1.58
J.M.	109.5 $\pm$ 0.50	117.50 $\pm$ 1.58	97.00 $\pm$ 3.39	84.00 $\pm$ 1.70	12.50 $\pm$ 3.71	33.50 $\pm$ 1.27
N.K.	128.00 $\pm$ 1.22	130.50 $\pm$ 2.00	115.00 $\pm$ 1.58	128.00 $\pm$ 3.00	13.00 $\pm$ 2.00	2.50 $\pm$ 1.12
J.G.	121.50 $\pm$ 1.50	123.50 $\pm$ 3.32	110.50 $\pm$ 2.00	110.50 $\pm$ 1.46	11.00 $\pm$ 1.00	13.00 $\pm$ 3.91
C.L.	77.00 $\pm$ 1.22	72.00 $\pm$ 1.22	73.00 $\pm$ 0.93	68.00 $\pm$ 2.89	4.00 $\pm$ 0.61	4.00 $\pm$ 3.41
30s D.M.	128.50 $\pm$ 3.41	145.50 $\pm$ 1.20	121.50 $\pm$ 2.18	150.00 $\pm$ 1.58	7.00 $\pm$ 2.00	4.50 $\pm$ 0.50
M.G.	114.50 $\pm$ 0.50	123.50 $\pm$ 2.69	97.00 $\pm$ 1.84	112.00 $\pm$ 1.22	17.50 $\pm$ 1.37	11.50 $\pm$ 1.87
J.M.	103.12 $\pm$ 1.20	118.75 $\pm$ 0.72	93.75 $\pm$ 3.75	93.75 $\pm$ 2.39	9.37 $\pm$ 3.29	25.00 $\pm$ 2.70
N.K.	139.00 $\pm$ 2.92	141.00 $\pm$ 4.00	116.50 $\pm$ 4.94	129.50 $\pm$ 6.04	22.50 $\pm$ 1.58	11.50 $\pm$ 3.50
J.G.	131.60 $\pm$ 0.97	128.00 $\pm$ 4.14	117.50 $\pm$ 1.37	114.50 $\pm$ 4.77	14.10 $\pm$ 0.55	13.50 $\pm$ 2.57
C.L.	76.50 $\pm$ 0.61	74.00 $\pm$ 0.61	74.00 $\pm$ 0.61	71.50 $\pm$ 0.61	2.50 $\pm$ 0.00	2.50 $\pm$ 0.79
Se D.M.	138.00 $\pm$ 1.22	140.50 $\pm$ 1.46	122.00 $\pm$ 1.46	139.00 $\pm$ 1.70	16.00 $\pm$ 2.32	1.50 $\pm$ 1.50
M.G.	131.50 $\pm$ 1.87	128.00 $\pm$ 2.00	94.00 $\pm$ 3.76	106.00 $\pm$ 2.45	37.50 $\pm$ 3.54	22.00 $\pm$ 2.00
J.M.	133.75 $\pm$ 3.15	150.62 $\pm$ 0.62	115.62 $\pm$ 1.57	104.37 $\pm$ 4.37	18.12 $\pm$ 4.61	46.25 $\pm$ 3.89
N.K.	149.00 $\pm$ 3.67	144.00 $\pm$ 3.67	118.00 $\pm$ 4.64	125.00 $\pm$ 4.47	31.00 $\pm$ 5.99	19.00 $\pm$ 7.64
J.G.	148.50 $\pm$ 0.94	143.00 $\pm$ 3.39	120.50 $\pm$ 2.00	116.50 $\pm$ 2.18	27.50 $\pm$ 1.37	26.50 $\pm$ 1.50
C.L.	95.50 $\pm$ 1.22	72.50 $\pm$ 0.79	78.96 $\pm$ 2.30	73.50 $\pm$ 1.00	16.54 $\pm$ 3.40	1.00 $\pm$ 1.00

Appendix 1c
Maximum Static Mouth Pressures
P_Imax, P_Emax at various postures (cmH₂O, Best attempt data)

Posture	Subjects	P _I max	P _E max
Su	D.M.	130.00	185.00
	M.G.	127.50	190.00
	J.M.	115.00	190.00
	N.K.	165.00	230.00
	J.G.	122.50	235.00
	C.L.	55.00	92.50
30s	D.M.	140.00	195.00
	M.G.	135.00	190.00
	J.M.	130.00	190.00
	N.K.	167.50	245
	J.G.	130.00	210.00
	C.L.	65.00	110.00
Se	D.M.	150.00	210.00
	M.G.	140.00	232.50
	J.M.	130.00	210.00
	N.K.	170.00	235.00
	J.G.	147.50	255.00
	C.L.	50.00	112.50

Appendix 2a
Maximum Static Mouth Pressures in trained
and naive subjects (cmH₂O, Best attempt)
(a) flanged, (b) tube mouthpiece

Highly Trained

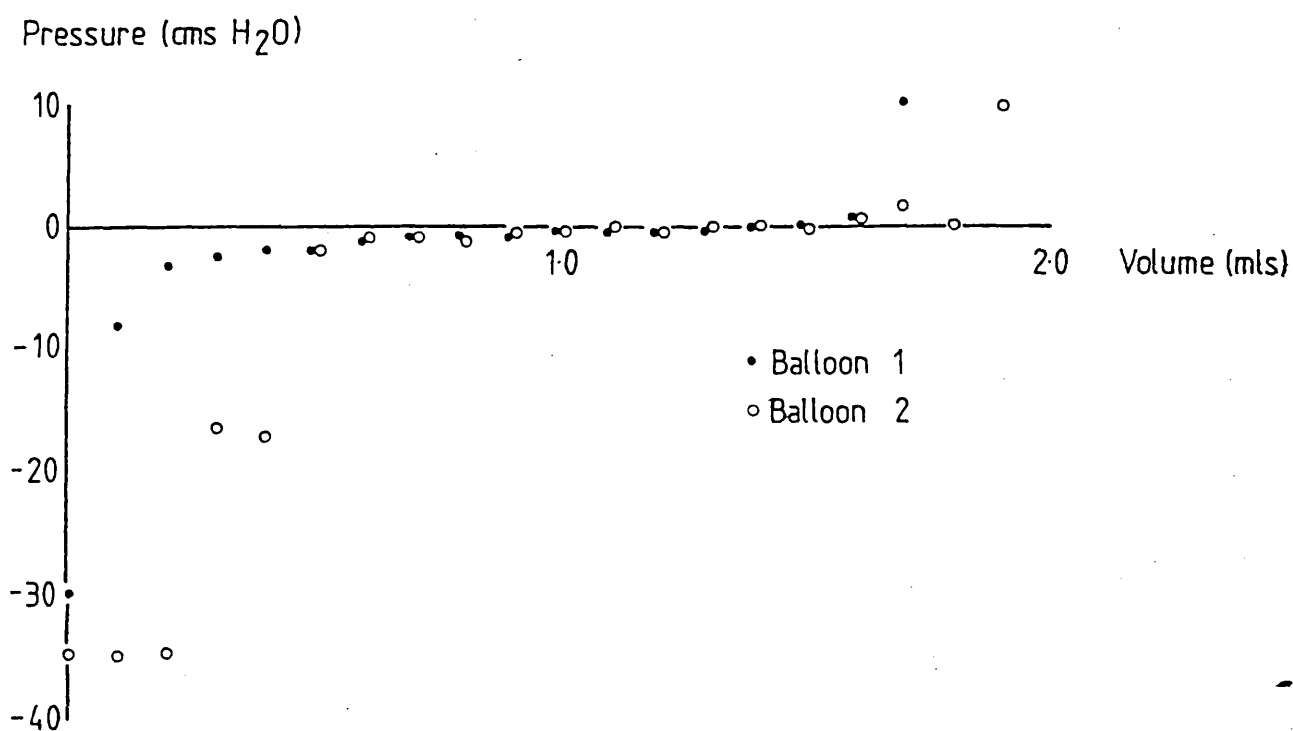
	Sex	PIa	PIb	PEa	PEb
1	M	117.5	130.0	195.0	200.0
2	F	92.0	88.0	96.0	152.0
3	M	166.0	177.6	196.0	228.0
4	F	65.0	50.0	55.0	65.0
5	M	135.2	42.0	152.0	196.0
6	M	144.0	168.0	164.8	230.4

Naive

1	M	137.5	200.0	207.5	200.0
2	M	88.0	96.0	139.2	180.0
3	M	77.5	72.5	95.0	105.0
4	M	96.8	79.2	219.2	228.0
5	M	90.0	88.0	150.0	186.0
6	M	170.0	180.0	187.0	190.0
7	M	122.5	127.5	130.0	150.0
8	F	78.0	86.0	124.0	145.6
9	F	53.0	60.0	108.0	145.0
10	F	110.0	112.0	164.0	192.0
11	F	105.0	117.6	138.6	147.0
12	F	68.0	90.0	134.0	148.0
13	F	104.8	106.0	152.0	220.0
14	F	60.0	66.0	96.0	92.0
15	F	124.0	123.2	100.0	140.0

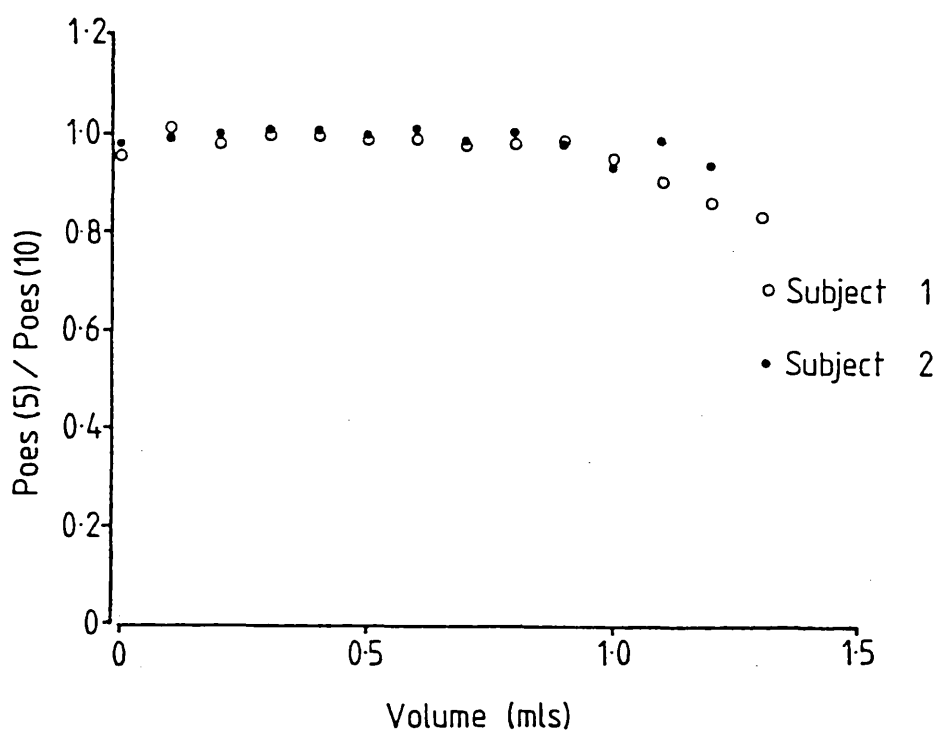
Appendix 2b
Maximum Static Mouth Pressures in normal (N)
and weak patients (L) with the flanged (a) and tube (b) mouthpiece
(cmH₂O, Best attempt data)

Subject	Sex	LPIa	LPIb	LPEa	LPEb	Sex	NPIa	NPIb	NPEa	NPEb
1	F	20.0	37.50	77.5	82.50	M	75.0	95.0	142.5	160.0
2	M	55.0	42.50	70.0	80.00	M	85.0	102.5	210.0	242.5
3	F	45.0	52.50	90.0	67.50	F	55.0	65.0	80.0	87.5
4	M	42.5	50.00	160.0	187.50	M	75.0	70.0	105.0	92.5
5	M	20.0	37.50	115.0	97.50	F	75.0	70.0	150.0	160.0
6	M	40.0	20.00	52.5	75.00	M	80.0	75.0	120.0	130.0
7	M	47.5	30.00	67.5	82.50	M	125.0	145.0	185.0	185.0
8	M	50.0	55.00	127.5	155.00	M	147.5	137.0	152.5	172.5
9	F	32.5	55.00	100.0	105.00	M	102.5	110.0	127.5	187.5
10	M	35.0	30.00	100.0	80.00	F	65.0	57.5	92.5	132.5
11	M	35.0	32.50	45.0	92.50	F	75.0	87.5	75.0	125.0
12	M	62.5	70.00	147.5	150.00	F	47.5	77.5	147.5	190.0
13	M	45.0	55.00	70.0	85.00	F	52.5	67.5	52.5	67.5
14	F	50.0	50.00	80.0	117.50	F	107.5	122.5	162.5	160.0
15	M	65.0	70.00	107.5	122.50	F	60.0	67.5	72.5	105.0
16	F	42.5	42.50	55.0	67.50	F	57.5	62.5	82.5	107.5
17	M	37.5	45.00	80.0	87.50	F	56.0	60.0	76.0	80.0
18	F	22.5	27.50	87.5	97.50	M	144.0	152.0	108.0	128.0
19	F	50.2	53.37	25.1	26.16	F	67.5	87.5	72.5	125.0
20	M	16.0	16.00	24.0	36.00	M	135.0	150.0	137.5	212.5



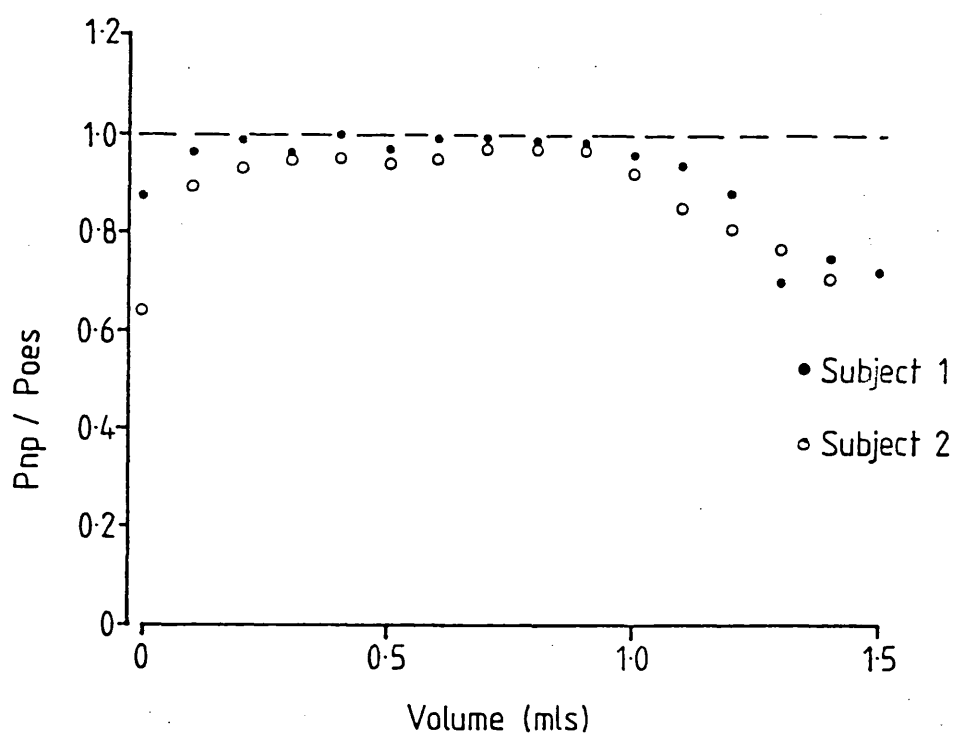
Appendix 3a

Pressure volume relationship of the 5 cm balloon.
Flat portion between 0.6-1.5 ml of air in two different
balloons tested.



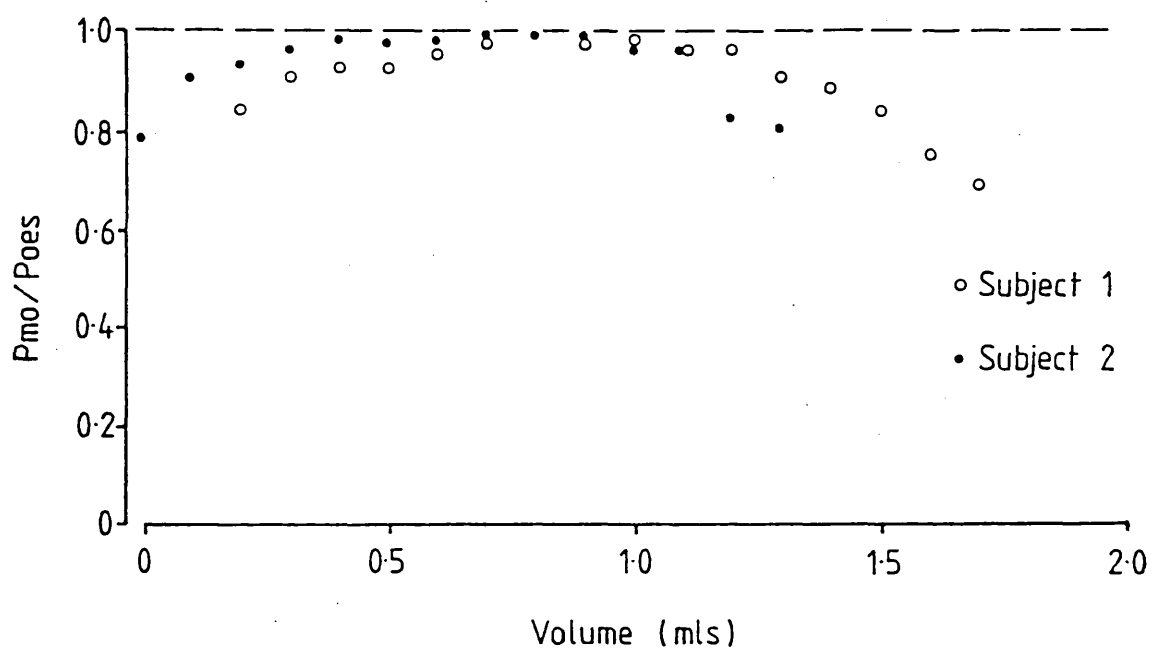
Appendix 3b

5 cm and 10 cm balloons placed in mid-oesophagus.
Ratio Poes (5)/Poes (10) = 1.0 when 5 cm balloon
contained from 0 - 0.9 mls of air and 10 cm balloon 0.5
mls, tested in two different normal subjects.



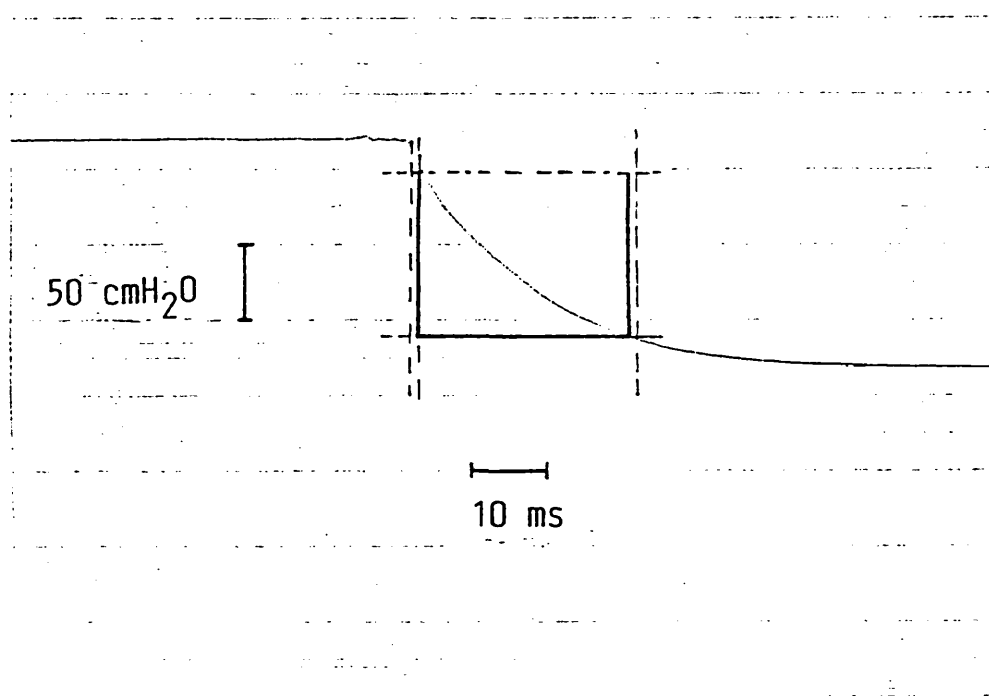
Appendix 3c

5 cm balloon withdrawn into the nasopharynx. The ratio P_{np}/P_{oes} was close to unity in subject (1) with 0.3 - 0.9 ml of air in 5 cm balloon and 0.7 - 0.9 ml in subject (2). The 10 cm Poes balloon was always filled with 0.5 ml air.



Appendix 3d

The 5 cm balloon placed in the oral cavity (P_{mo}).
The ratio $P_{mo}/P_{oes} = 1.0$ when the 5 cm balloon contained
0.7 - 0.9 mls of air in 2 subject Poes balloon 0.5 ml.

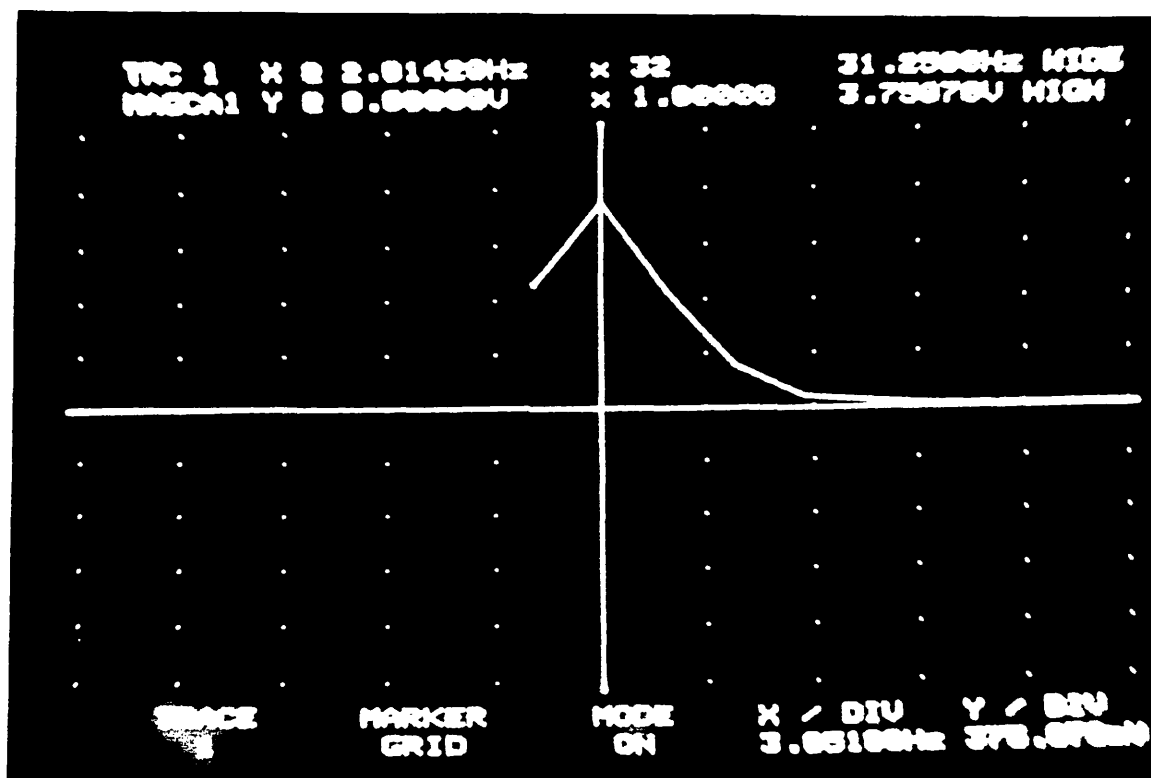


Appendix 3e

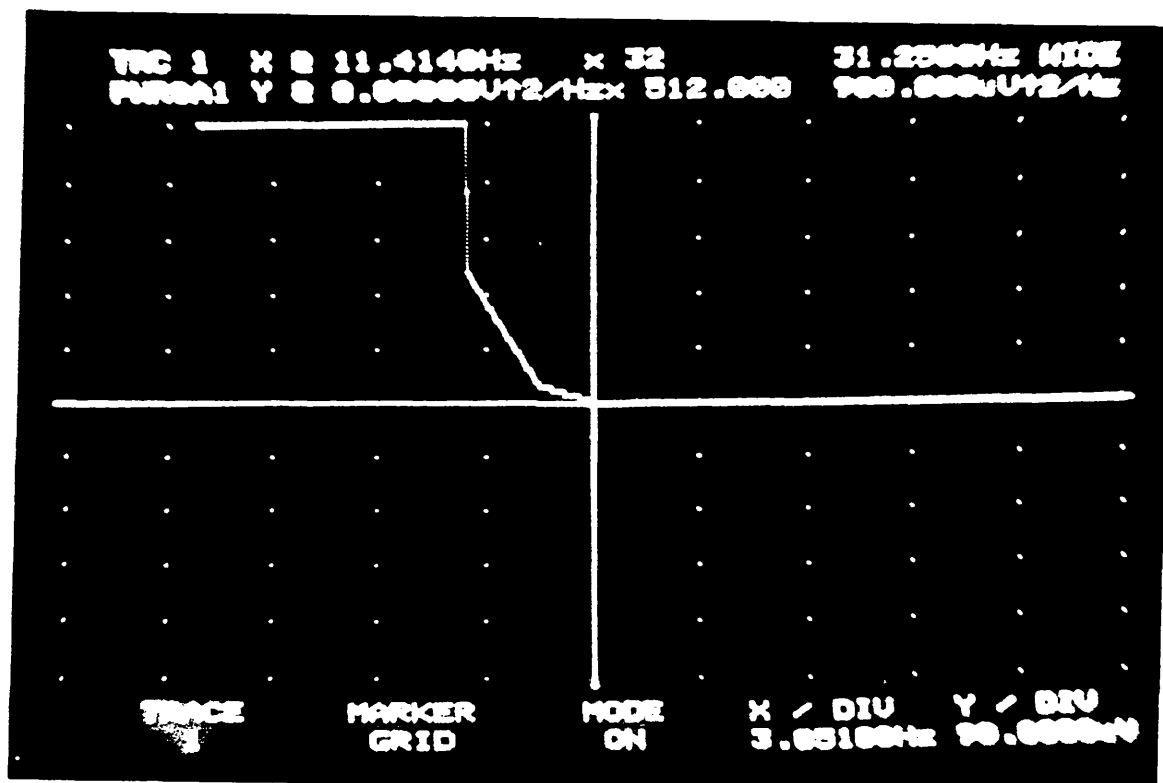
Frequency response of the 5 cm balloon. $Tr =$
 $0.027s$, $f_{3db} = 1/3Tr = 12.3 \text{ Hz}$

Appendix 3f

Power spectral analysis of a sniff pressure wave. Maximum power is at 2Hz (Fig. a), with harmonics up to 12 Hz (Fig. b) in a normal subject. Similar results were obtained from another normal individual.



a.



b.