The respiratory muscles

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Introduction

The respiratory muscles provide the motive power for breathing. Despite this 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. However, in the last decade, there has been considerable increase in interest, and a number of new concepts have arisen [1-3].

It is now appreciated that the translation of central nervous output into ventilation requires a sophisticated integration of the respiratory muscles, which have to subserve the requirements of posture and body movement, simultaneously with breathing. The importance of the shape (configuration) of the respiratory system to muscle action has been emphasized. Analysis has shown that the functions of the diaphragm are complex: it is anatomically and embryologically derived from two muscles, and these parts may have different physiological actions. The abdominal muscles appear to be not only powerful muscles of expiration, but also facilitate inspiration. Both internal and external intercostal muscles now seem to be inspiratory at low lung volumes and expiratory at high lung volumes. Like all skeletal muscles the respiratory muscles are capable of fatigue after heavy loads. It is increasingly believed that respiratory muscle fatigue may play an important part in the pathogenesis of respiratory failure, and part of the value of artificial ventilation may lie in resting the respiratory muscles.

The respiratory muscles comprise the diaphragm, the intercostal muscles, the abdominal muscles, and the so-called 'accessory' muscles including the sternomastoid and scalene muscles. However, probably all of the muscles of the trunk and neck can be recruited as respiratory muscles under heavy loads.

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Structure

The respiratory muscles are all skeletal ('voluntary') muscles, consisting of motor units innervated by α-motor neurones derived from anterior horn cells in the spinal column down to L2. The accessory, intercostal and abdominal muscles are well supplied with muscle spindles, tendon organs and Pacinian corpuscles, providing an anatomical basis for sensory input from these muscles [1]. The diaphragm contains relatively fewer sensory end-organs, and there appear to be more tendon organs than muscle spindles [4]. 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 organs are necessary to sample accurately its functions [5]. The main purpose of the diaphragm is to generate pressure differences, and the relatively greater number of tendon organs may reflect this, since tendon organs can sensitively reflect physiological contraction of muscle fibres [5].

The respiratory muscles contain a mixture of type 1 (slow twitch, oxygen dependent, fatigue resistant fibres) and type 2 (fast twitch fibres, most of which fatigue quickly, using glycolytic energy stores) in approximately the same proportion as limb skeletal muscles. In man the diaphragm contains about 55% of type 1 and 45% of type 2 fibres, although the number of studies is small and there appears to be variability between subjects [6]. The physiological attributes and size of fibres can be altered by suitable training and detraining programmes in animals [7].

Physiology

The respiratory muscles including the diaphragm appear to have physiological properties similar to the other skeletal muscles; they generate maximum force at resting length, and the force falls off as length diminishes: the length-tension relation-
ship. The diaphragm shows the same property studied both in vitro [8] and in vivo [9, 10]. It also tends to become less curved as it shortens, thus generating less pressure across it, by the Laplace relation [11]. This is probably a small effect in normal subjects but may become significant in hyperinflation. The most important consequence is that lung volume influences the pressures the diaphragm can generate, being maximal when it is longest, and most curved, at low lung volumes.

The force developed by skeletal muscles also falls off as the speed of shortening increases. It has been confirmed that the respiratory muscles also show this force-velocity relationship [12]. Thus as respiratory rate and depth increases the velocity of muscle shortening increases, and force generated for a given neural output falls. The respiratory muscles have similar time courses of pressure development [13, 14] and of relaxation [15] as do limb muscles.

The diaphragm

Anatomically the diaphragm consists of two main parts, inserted into the central tendinous dome. The larger (costal) part originates over the inner surfaces of the six lowest ribs and cartilages. These fibres initially 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, but diminishes during inspiration [16]. Both the origins and insertions of these costal fibres are mobile, and potentially move with respiration. By contrast the lumbar (crural) portion has its origins on the second to fourth lumbar vertebrae and associated ligaments, which do not move with respiration.

Contraction of the diaphragm has several effects [2, 16-19] (Fig. 1).

1. The central dome of the diaphragm descends with little change in its shape, peeling the muscular fibres from the inner surface of the rib cage along the area of apposition [10]. This tends to cause a fall in pleural pressure and an increase in lung volume (inspiration).

2. Contraction of the diaphragm causes an increase in abdominal pressure. In the absence of abdominal muscle contraction this causes the anterior abdominal wall to move outwards. There is also outward pressure exerted on the lower rib cage through the area of apposition. This force is inspiratory in direction and has been called the ‘appositional component’ [20].

3. The costal fibres of the diaphragm tend to lift the lower rib cage (insertional force). Because of the shape and articulations of the ribs, upward movement also tends to cause forwards (pump handle) and outward (bucket handle) motion, particularly at low lung volumes. Since these fibres of the diaphragm are mobile at both ends a fulcrum is necessary to prevent mere descent of the dome [(1) above]. This is provided by the abdominal contents and anterior abdominal wall. Removing the abdominal viscera in horses, dogs and rabbits changes the result of costal diaphragm contraction from expanding the lower rib cage to contracting it [17, 18, 21].

When the diaphragm acts in isolation it also tends to have some expiratory components. Patients with transection of the lower cervical cord but intact phrenic nerve and diaphragm function show paradoxical motion inwards of the upper rib cage during inspiration [22, 23]. This may also be seen during spinal anaesthesia [24] and diaphragm pacing [25].

Different physiological functions of the two parts of the diaphragm were proposed by Keith in 1904 [26] and subsequently by Briscoe in 1920 [27] but these suggestions have been ignored until recently. It has now been shown that the costal part of the diaphragm is active whilst the crural part is silent during vomiting, as might be expected [28]. De Troyer and colleagues have demonstrated in dogs that both parts of the diaphragm cause an increase in abdominal pressure and a fall in pleural pressure. However, only the costal part has a direct

![FIG. 1. Diagram to illustrate the actions of the diaphragm. On contraction the dome descends and abdominal pressure (P_{ab}) rises. This expands the lower rib cage via an 'appositional force' and simultaneously the costal diaphragm elevates the lower rib cage ('insertional force') with a resultant force R. These actions cause a fall in pleural pressure (P_{pl}), inspiration, and a tendency to indrawing of the upper rib cage.](image-url)
inspiratory action on the rib cage by lifting the lower ribs [18, 29]. There has been considerable debate as to the relative contribution of the direct effects of the diaphragm on the rib cage, and its indirect effects via the abdominal and pleural pressure [30-32]. Goldman & Mead [33] argued that the diaphragm expanded the rib cage along its relaxed pressure-volume characteristic. It now appears, however, that the rib cage deforms when intercostal activity is absent and that the pressures applied are complex, depending at least in part on the relative contributions of the two parts of the diaphragm [34].

Intercostal muscles

The importance of the intercostal muscles in stabilizing the rib cage and preventing paradoxical motion of its parts has been mentioned above. Even in quiet breathing in normal subjects they appear to play a necessary role in ensuring coordinated movement of the whole of the rib cage [34].

The parasternal intercostals elevate the ribs, but tend to lower the sternum [35], and are active during inspiration even in quiet breathing [36-38]. The external intercostal muscles run from the lower surface of each rib anteriorly and inferiorly to the upper surface of the rib below. The internal intercostals by contrast run inferiorly and posteriorly. On the basis of this anatomical arrangement Hamberger concluded in 1727 [39] that the external intercostal muscles were inspiratory since by their contraction each lower rib was pulled upwards and backwards towards the rib above it, thereby swinging outwards. Conversely the internal intercostal muscles pulled each upper rib posteriorly, downwards, and inwards, to cause expiration. Electromyographic studies have shown that the external intercostals are active during inspiration and internal intercostals during expiration [36, 37]. However, recently doubt has been cast on Hamberger's hypothesis by the studies of De Troyer and colleagues who have shown in dogs that the action of the intercostal muscles depends on lung volume [40]. At low lung volumes both external and internal intercostal muscles are inspiratory when they contract, and at high lung volumes both groups are expiratory. Since the uppermost and lowermost ribs are mobile, there must be stabilization of the rib cage for effective action by the intercostal muscles. The scalene and sternomastoid muscles stabilize the upper rib cage during inspiration, and the abdominal muscles help fixate the lower rib cage during expiration [35, 41].

Abdominal muscles

Contraction of these powerful muscles tends to pull the rib cage inwards and downwards and to push the abdominal contents upwards, elevating the diaphragm. Both these actions cause expiration and these muscles have generally been viewed as purely expiratory [42]. However, their actions now appear to have additional complexities [20, 43]. Thus contraction of the abdominal muscles increases abdominal pressure. This, as seen above (Fig. 1), tends to expand the lower rib cage through the area of apposition, an inspiratory motion. Furthermore upward motion of the dome of the diaphragm tends to stretch its costal fibres, and thus to lift the lower rib cage, which is also in an inspiratory direction. Theoretically, the net effect of contraction of abdominal muscles would depend on the relative importance of these factors, and studies in dogs have shown a significant inspiratory tendency, particularly of the external oblique muscles [43].

The abdominal muscles also ensure that the diaphragm returns to its resting length at end-expiration, so that it is best placed on its length-tension characteristic for subsequent contraction during inspiration [10, 22, 44]. The maintenance of abdominal pressure by abdominal muscle contraction during inspiration serves as a fulcrum for the costal diaphragm to elevate the lower ribs, so that the abdominal muscles can be considered as 'accessory muscles of inspiration' [20].

The abdominal muscles are electrically silent during quiet breathing when supine, but when erect there is tonic activity which is greatest in the lower abdomen [45]. This has been conceived as entirely postural [37, 46]. However, active contraction of the abdominal muscles during both inspiration and expiration may play a role in both phases of breathing, suggesting that this activity may be partly ventilatory.

Accessory muscles

The most important of these are the scalene muscles and the sternomastoids. Studies of the scalenes using needle electrodes show that they have inspiratory electrical activity even during quiet breathing, so that they should probably be viewed as muscles of normal inspiration rather than 'accessory muscles' [41], acting to elevate, or to prevent downward displacement of, the upper rib cage during inspiration [35]. These muscles have increased activity during stimulated ventilation, in patients with lesions of the upper cervical cord and in chronic airways obstruction [23, 47].
Configuration and lung volume

During inspiration the mechanical difficulty of producing a negative pressure pump using only contractile elements has been overcome by the complex geometry and interactions of the respiratory muscles. The shape of the system has been termed its configuration, and this importantly determines the efficiency of ventilation. Configuration is closely, but not uniquely, related to lung volume. As lung volume increases the respiratory muscles become less advantageously placed for inspiration and more advantageously placed for expiration. In normal subjects this appears to be an important mechanism for maximizing the efficient use of the muscles. However, it can have disadvantages in disease: airways obstruction leads to hyperinflation, putting the inspiratory muscles at a less advantageous configuration. By contrast fibrotic lung diseases, causing a reduction of lung size, tend to put the inspiratory muscles at a more advantageous configuration so that they are better placed to overcome the increased mechanical load provided by the stiff lungs [48].

Modelling the respiratory muscles

A number of attempts have been made to model the function of the respiratory muscles using mechanical, electrical or pneumatic analogies [34]. A mechanical model, modified from these by permission, is shown in Fig. 2.

Respiratory muscle fatigue

Patients with severe lung disease and hyperinflation have reduced force generating capacity of the respiratory muscles. In contrast their ventilatory requirements are increased. The muscles, particularly the inspiratory muscles, are subject to large loads with every breath for prolonged periods and with little opportunity for rest. Patients with severe chronic airways obstruction have a high neural output to the respiratory muscles [49] comparable with that required to sustain near maximum ventilation in normal subjects. This combination of high drive and large loads for long periods has led to the suggestion, by analogy with limb muscles, that fatigue could develop in the respiratory muscles and contribute to hypercapnic ventilatory failure [50].

Muscle fatigue can usefully be defined as the inability to sustain the required force with continued contractions. This is a characteristic of limb muscles and recent studies have demonstrated that the respiratory muscles can also fatigue. Normal subjects can sustain large respiratory loads for only short periods. Thus the diaphragm cannot maintain greater than 40% of its maximum pressure with each breath indefinitely [51]. The overall respiratory pressures that can be sustained indefinitely are further reduced (i) by high lung volumes when the muscles are shortened, (ii) as mean inspiratory flow rates increase when there is increased velocity of shortening, (iii) as breathing frequency increases, (iv) as the proportion of the time devoted to inspiration during each breath rises with longer contraction of the inspiratory muscles [52,53].

In spite of much research over recent years, the precise cause of skeletal muscle fatigue is not clear; indeed it is unlikely that a single cause is responsible and it is probable that under different circumstances a variety of factors can become relevant. Reduced central neural drive, especially
during sustained maximum voluntary effort, may be important [54]. However, for many contractions including the repetitive submaximal ones of ventilation, an important aspect of fatigue is likely to be reduced muscle contractility [55]. As fatiguing exercise continues and contractility falls, so central firing frequency increases to counteract force loss, but eventually central frequency itself falls despite the reduction in muscle tension. This fall in firing frequency may represent an adaptation to peripheral fatigue that avoids excessive ATP depletion and the onset of rigor.

The situation may be rather different when a muscle is acutely subjected to an overwhelming load. In this case there is likely to be a rapid fall in local chemical energy supplies and a failure of muscle excitation, an energy consuming process, thereby causing a 'catastrophic' loss of force but no further energy consumption [56]. During respiratory failure both these patterns of fatigue may operate. In patients with longstanding respiratory disease, due to chronic airways obstruction or scoliosis, the central nervous system may modify respiration in response to muscle fatigue by changing the respiratory rate, inspiratory time and mean inspiratory flow, thereby avoiding critical depletion of chemical energy stores but only at the expense of allowing hypoventilation and hypercapnia. By contrast in severe acute disease, as in life-threatening asthma, the overwhelming load on the respiratory muscles may precipitate catastrophic force loss and acute ventilatory failure.

Detection of fatigue

Detection of fatigue in the respiratory muscles is difficult because there is no simple technique for measuring their force generation. Therefore, less direct techniques have been employed. Muscle fatigue has been investigated by measuring the frequency spectrum of the electromyogram (EMG) [57]. When skeletal muscle generates a tension that cannot be sustained there is an early alteration in the EMG with reduction in high frequency and increase in low frequency activity, resulting in reduction in the EMG 'high/low' ratio. This has been used as a marker of muscle fatigue and has been applied to the muscles of respiration, particularly the diaphragm [58]. However, the cause of the shift in the power spectrum is not known, nor is the relation of the EMG change to force loss understood; for example, after diaphragm and quadriceps fatigue the high/low ratio returns to normal at a time when force generation is still abnormal [59].

With fatigue the speed of muscle characteristically slows. Recent work on the respiratory muscles has examined the relaxation of the human diaphragm measured from transdiaphragmatic pressure during a maximal sniff. In normal subjects the relaxation rate for the non-fatigued diaphragm is similar to that of limb muscles and after prolonged inspiratory loading relaxation is slowed [15]. The investigation of respiratory muscle relaxation rates may be possible in patients and allow identification of fatigue clinically.

Some of the techniques used to study limb muscle fatigue can also be applied to the respiratory muscles. Studies in resting hand and leg muscles of the force produced by electrical stimulation show a characteristic relationship of stimulation frequency to force, described by the frequency-force curve [60]. With fatigue the shape of the curve is altered with a reduction in the forces generated at high stimulation frequencies ('high frequency fatigue') [61] and/or reduction in the forces at low stimulation frequencies, less than 30 Hz ('low frequency fatigue') [62]. In high frequency fatigue there is defective muscular excitation due either to neuromuscular junction failure or to impaired depolarization of the muscle cell membrane. This excitatory failure is associated with a reduced EMG and is rapidly restored to normal by rest. In low frequency fatigue excitation of the muscle cell membrane is normal and the EMG is not diminished, but the force per membrane action potential is reduced implying impaired contractility of the muscle fibre itself. This type of fatigue can be long lasting, sometimes persisting for many hours. After prolonged muscular activity, force generation at low frequencies may also be reduced by changes in tendons which become more extensible [63]. Furthermore muscle shortening due to hyper-inflation reduces forces at low frequencies to a greater extent than at high frequencies [64]. Thus, a number of factors can shift the frequency-force curve to the right and may be of particular physiological importance because the firing frequency of motor neurones during everyday activities is low (5-30 Hz) [65]. Even during a maximum voluntary contraction the motor neurone firing frequency falls to below 30 Hz within a few seconds [66].

Electrical stimulation has been used to investigate the contractile properties of the respiratory muscles and to detect fatigue. Crucially the frequency-force curve of the sternomastoid and the frequency-transdiaphragmatic pressure curve of the diaphragm have the same shape as the curves of other skeletal muscles [67, 68]. In normal subjects, inspiratory loading and sustained
maximum voluntary ventilation produces low frequency fatigue both in the sternomastoid and also in the diaphragm (Fig. 3). Furthermore, patients with chronic airways obstruction who voluntarily breathe maximally develop low frequency fatigue of the sternomastoid [69]. To date it has not been possible to evaluate low frequency fatigue of the diaphragm in these patients.

Although it is likely that low frequency fatigue of the respiratory muscles is of clinical importance, the detection of such fatigue in patients with respiratory failure presents great difficulties. During very brief maximum voluntary efforts lasting less than 2 or 3 s motor neurone firing frequencies are high so that force generation is little affected by low frequency fatigue, probably due to saturation of the interior of muscle fibres with calcium ions [70]. Thus maximum respiratory pressures, peak expiratory flow rates and forced vital capacity are not reduced [71]. Resting ventilation is associated with lower neural firing frequencies. Experimental data for the cat suggest that during tidal breathing phrenic motor neurone firing frequency is 10-15 Hz rising to 20-30 Hz with CO₂ stimulation [72]. Low frequency fatigue might therefore cause an important fall in respiratory muscle force production not revealed by tests of maximum effort. Consistent with this suggestion is the observation that respiratory muscle fatigue may cause a reduction in the ventilatory response to carbon dioxide of normal subjects [71].

In limb muscles, fatigue is most likely to develop when contractions are each a large proportion of maximum force. During high force contractions many limb muscles become ischaemic [73] and metabolism is therefore anaerobic. However, the blood supply of the diaphragm is excellent and continues to rise with hyperventilation [74]. Despite this there could be poor oxygen delivery at a cellular level, particularly when the respiratory muscles contract throughout the respiratory cycle, as may be the case in severe asthma. The importance of oxygen delivery appears to be supported by the observation that during loaded breathing the endurance of the inspiratory muscles of normal subjects is decreased by hypoxia [51]. However, the mechanism of this effect is not clear and could be mediated via the central nervous system or through a direct action on peripheral muscle.

**Therapy**

Treatment of patients with respiratory disease should take account of factors that can affect respiratory muscle function. Adequate nutrition is important to maintain muscle mass since wasting causes weakness and predisposes to fatigue. In wasting diseases the respiratory muscles atrophy and pressure generation is impaired [75]. High dose steroids commonly used in chest medicine and known to cause skeletal muscle wasting could produce respiratory muscle weakness in addition to hypokalaemia.

It is possible to increase the strength and endurance of muscle by appropriate training. It is not known whether training renders muscle less susceptible to low frequency fatigue, but training for strength may raise the threshold for fatigue and endurance training increases capillaries, mitochondria and oxidative enzymes. Maximum respiratory pressures can be increased in normal subjects by training [76] and specific training of the respiratory muscles can improve ventilatory performance of patients with cystic fibrosis, quadriplegia and chronic airways obstruction [77-79]. However, respiratory muscle training is difficult, the increases in strength may be only small [80] and whether such training schedules produce long term benefit remains uncertain.

Therapy directed at the underlying respiratory disorder may reduce the load on the respiratory

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**FIG. 3.** Frequency-pressure curves of the diaphragm. The phrenic nerve of a normal subject was stimulated in the neck at increasing frequencies (abscissa) and the resultant transdiaphragmatic pressure (▲) was measured with oesophageal and gastric balloons and expressed as a percentage of the maximum Pdi (ordinate). The subject then fatigued his diaphragm by breathing through an inspiratory resistance to exhaustion. After fatigue (△) there was a characteristic shift of the curve to the right.
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muscles to a level that will not precipitate or perpetuate fatigue. Delivery of oxygen to the working muscle can be optimized by attention to arterial oxygen tensions, haemoglobin levels and cardiac output. Metabolic acidosis should be corrected as well as other metabolic disturbances known to cause muscle weakness such as hypophosphataemia, hypokalaemia and disorders of calcium metabolism. Therapy that reduces over-phosphataemia, hypokalaemia and disorders of cardiac output. Metabolic acidosis should be offset by an increase in motor neurone firing frequency; thus respiratory stimulants may have a short term therapeutic role. Conversely drugs causing depression of the respiratory centre may substantially impair ventilation.

Drugs that increase muscle twitch tension would be particularly helpful, shifting the frequency-force curve to the left and improving force generation at physiological firing frequencies (Fig. 3). Furthermore, such a shift would diminish the effect of low frequency fatigue and muscle shortening. Xanthine-related drugs can improve the contractile performance of skeletal muscle studied in vitro [81] and aminophylline has been reported to improve the force-generating properties of the diaphragm in man [82]. However, studies in vivo of the effect of aminophylline on the adductor pollicis muscle of the hand show that twitch-tension, the frequency-force curve and low frequency fatigue are not affected by this drug at therapeutic concentrations [83]. Similarly the transdiaphragmatic twitch pressure from stimulation of the phrenic nerve of normal subjects is not affected by intravenous aminophylline [84]. Thus, while the usefulness of aminophylline in respiratory disease is not in doubt, a direct beneficial action on respiratory muscle contractility remains unproven. β-Receptor agonists such as terbutaline and salbutamol may enhance respiratory muscle contractility [85]. The effect of terbutaline appears to be greater on fatigued than fresh muscle. This may be due to the slowing of muscle contraction and relaxation with fatigue since terbutaline has a greater potentiating effect on slow twitch than on fast twitch fibres.

In patients with progressive respiratory failure, assisted ventilation may become necessary. If fatigue is present, one benefit may be the total resting of the respiratory muscles for sufficient time for fatigue to resolve. It is also conceivable that carefully selected patients can be helped by patient-triggered positive pressure ventilators to assist inspiration and reduce the workload of the respiratory muscles, protect against fatigue and thereby avoid the necessity of intubation and mandatory ventilation. In patients with neuromuscular weakness, intermittent support by tank and cuirass ventilation can be beneficial. Scoliosis patients and those who have had thoracoplasties in the past can be similarly helped by intermittent assisted ventilation [86]. The mechanism whereby such patients derive benefit is not certain but resting the respiratory muscles may be an important factor serving to avoid or reverse fatigue. If this is so, efforts to rest the respiratory muscles intermittently by using techniques that do not require intubation may deserve careful reappraisal in patients with severe chronic airways obstruction.

The clinical importance of respiratory muscle fatigue is not yet clear and further progress must depend on developing suitable techniques for its detection. Only then will the relative contributions of, for example, inadequate respiratory centre output or reduced muscle contractility become apparent. The many stages from central nervous system output via respiratory muscle force generation to the production of appropriate ventilation are of bewildering complexity. The process is one of integration, both when functioning normally and during ventilatory failure. Biological feedback serves to modify overall function in response to failure at any given level. Thus, in most cases of respiratory failure to identify any single step as the crucial weak link may be neither sensible nor possible.

References


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