PHYSIOLOGICAL BASIS OF VENTILATORY SUPPORT

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Muscle Function

Basic Concepts

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I. Introduction

Along with the heart, the respiratory muscles are the only muscles that have to work continuously, although intermittently, to sustain life. They have to move repetitively a rather complex elastic structure, the thorax, to achieve the entry of air into the lung and thence the gas exchange. Because of their great number, they must interact properly to perform their task despite their different anatomical location, geometrical orientation, and motor innervation. They must also be able to adapt to a variety of working conditions and respond to many different chemical and neural stimuli. Given their vital role, it is very fortune that machines, that is, ventilators, have been invented to substitute for the work of the respiratory muscles whenever they fail; and this marvellous achievement, that is, mechanical ventilation, is the subject of this book.

It would have been impossible, of course, to describe in a single chapter the function of the respiratory muscles. It is also very difficult, and subject to debate, to define the "basic concept" of the function so that it could be included in this chapter. We will present, therefore, some aspects of the respiratory muscles' function that are relevant to the understanding of what, in fact, the ventilator has to sub-

stitute for and when it becomes necessary. Accordingly, we will first discuss the functional anatomy of the respiratory muscles and their action. We will subsequently deal with the statics of breathing and give a description of the elastic properties of the thorax that the muscles, or ventilator, have to move to achieve ventilation. Next, the energetic aspects of the muscles' function will be presented: that is, the energy supplies (blood flow being the most important) and the energy demands, along with the factors that could lead to an imbalance between the supply and demand and, thus, to fatigue. Fatigue will be discussed afterwards. Finally, as an illustrative clinical example, the role of fatigue in the patient who fails to wean will be presented.

II. Functional Anatomy

A. Intercostal Muscles

The intercostal muscles are two thin layers of muscle fibers occupying each of the intercostal spaces. They are termed *external* and *internal* because of their surface relations, with the external being superficial to the internal (Fig. 1). The muscle fibers of the two layers run approximately at right angles to each other, with both layers being thicker behind than in front (1).

External Intercostals

The external intercostals extend from the tubercles of the ribs dorsally to the costochondral junctions ventrally, and their fibers are oriented obliquely, downward and forward, from the rib above to the rib below. Near the costochondral junctions, the external intercostals are replaced by a fibrous aponeurosis, the *anterior intercostal membrane* which extends to the anterior end of the intercostal space.

Internal Intercostals

The internal intercostals begin posteriorly as the *posterior intercostal membrane* on the inner aspect of the external intercostal muscles. From approximately the angle of the rib, the internal intercostal muscles run obliquely, upward and forward, from the superior border of the rib and costal cartilage below to the floor of the subcostal groove of the rib and the edge of the costal cartilage above, ending at the sternocostal junctions.

Although the intercostal spaces contain two layers of intercostal muscle fibers in their lateral portion, they contain a single muscle layer in their ventral and dorsal portion. Ventrally, between the sternum and the costochondral junctions, the only fibers are those of the internal intercostal muscles; these are particularly thick in this region of the rib cage, where they are conventionally called the *parasternal intercostals*. Dorsally, from the angles of the ribs to the vertebrae, the only fibers come from the external intercostal muscles. These latter, however, are

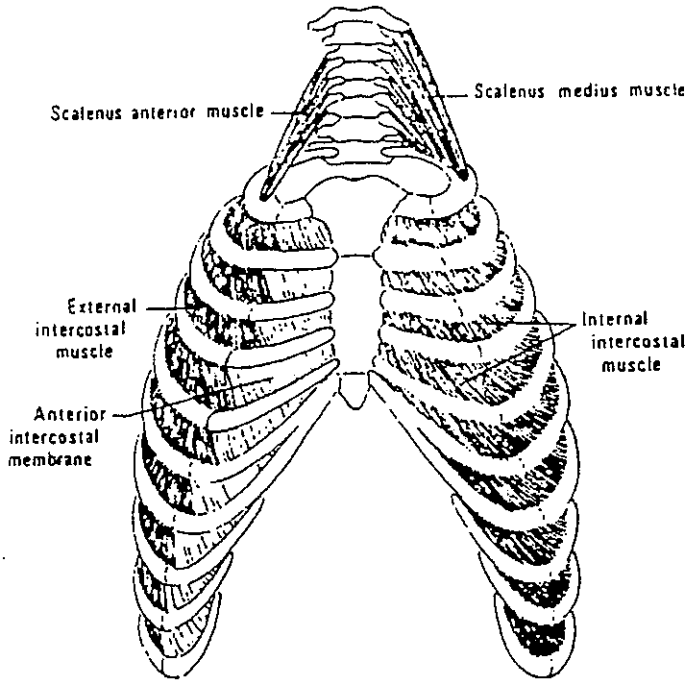

Figure 1 Intercostal and scalene muscles. On the left side of the chest, the external intercostal muscle and anterior intercostal membrane have been removed to reveal the internal intercostal muscle, whereas the left scalenus anterior has been removed to display the scalenus medius. (From Ref. 1.)

duplicated by a spindle-shaped muscle that runs in each interspace from the tip of the transverse process of the vertebra to the angle of the rib below; this muscle is the *levator costae*. All the intercostal muscles are innervated by the intercostal nerves.

Hamberger Model of the Respiratory Action of the Internal Intercostals

The respiratory action of the intercostal muscles has been a matter of controversy throughout medical history. The most influential of the theories proposed to explain this action was that of Hamberger (1749)(2), which was based on geometrical considerations (Fig. 2): When an intercostal muscle contracts in one interspace, it pulls the upper rib down and the lower rib up. The actual movement of the ribs depends on the relative amount of torque around the center of rotation (the vertebral articulations) acting on the two points of attachment of the muscle to the respective ribs: The external intercostals run obliquely downward and forward so that their insertion to the lower rib is more distant from the center of rotation than their insertion to the upper rib. Hence, when these muscles contract, the torque acting on the lower rib is greater than that acting on the upper rib and its net effect is to raise the ribs. The reverse is true for the internal intercostals, which run upward and forward so that their action is to lower the ribs to which they are attached. The parasternal intercostals are part of the internal intercostal layer, but

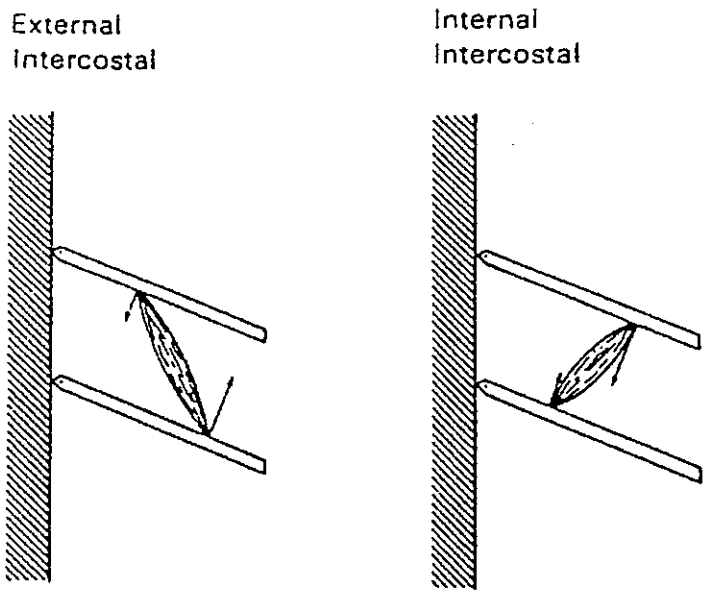

Figure 2 Diagram illustrating Hamberger's theory. In each panel, the hatched area represents the spine and the two bars oriented obliquely represent two adjacent ribs. The intercostal muscles are depicted as single bundles, and the torques acting on the ribs during contraction of these muscles are represented by arrows. See text for further explanation. (From Ref. 3.)

their action is referred to the sternum rather than to the vertebral column (i.e., the center of rotation is the sternocostal junctions); therefore by similar arguments, their contraction should raise the ribs (3).

The Hamberger theory is incomplete, however, and cannot entirely explain the actions of the intercostal muscles on the ribs for two reasons (4,5). First, the Hamberger model is planar, whereas in reality the ribs are curved. As a result, the changes in the length of the intercostal muscles during a given rotation of the ribs (hence their mechanical advantage and action on the ribs) vary as a function of the position of the muscle fibers along the rib. Thus, during cranial rotation of the ribs, their curvature causes changes in muscle length that are greater in the dorsal region, decrease progressively as one moves around the rib cage, and are reversed as one approaches the sternum. This is in contrast to the Hamberger model, which predicts equal shortening of all external intercostals and equal lengthening of all internal intercostals during cranial rotation of two adjacent ribs. Second, the Hamberger model states that all the ribs rotate by equal amounts around parallel axes so that the distance between adjacent ribs remains constant. In fact, the radii of curvature of different ribs are different, increasing from the top downward so that their rotations are similarly different. Consequently, there is a change in intercostal muscle length owing to the changes in the distance between the ribs from the top downward.

Despite the inaccuracies included in the Hamberger model, its predictions

seem valid, since experimental data suggest that the external intercostals, the parasternal intercostals, and the levator costae have an inspiratory action on the rib cage, whereas the internal intercostals are expiratory. During breathing at rest, normal humans have inspiratory activity in the parasternal intercostals (6,7). This suggests that, in humans, the contribution of the parasternal intercostals to resting breathing is greater than that of the external intercostals. During loaded breathing, the activation of the external intercostals and levator costae increases, although the mechanical effectiveness of this reserve "load-compensating" system is relatively small (8).

B. Diaphragm

The floor of the thoracic cavity is closed by a thin musculotendinous sheet of complex structure and development, the diaphragm, which is anatomically unique among the skeletal muscles in that its fibers radiate from a central tendinous structure (the central tendon) to insert peripherally into skeletal structures.

The *central tendon* of the diaphragm is thin, strong, and roughly trilobed (Fig. 3). It has the shape of a boomerang, with its two ends pointing posterolaterally (9). The central part is fused above with the fibrous pericardial sac, with both structures at this point being derived from the embryonic septum transversum.

The muscle of the diaphragm, all which inserts into the central tendon, falls

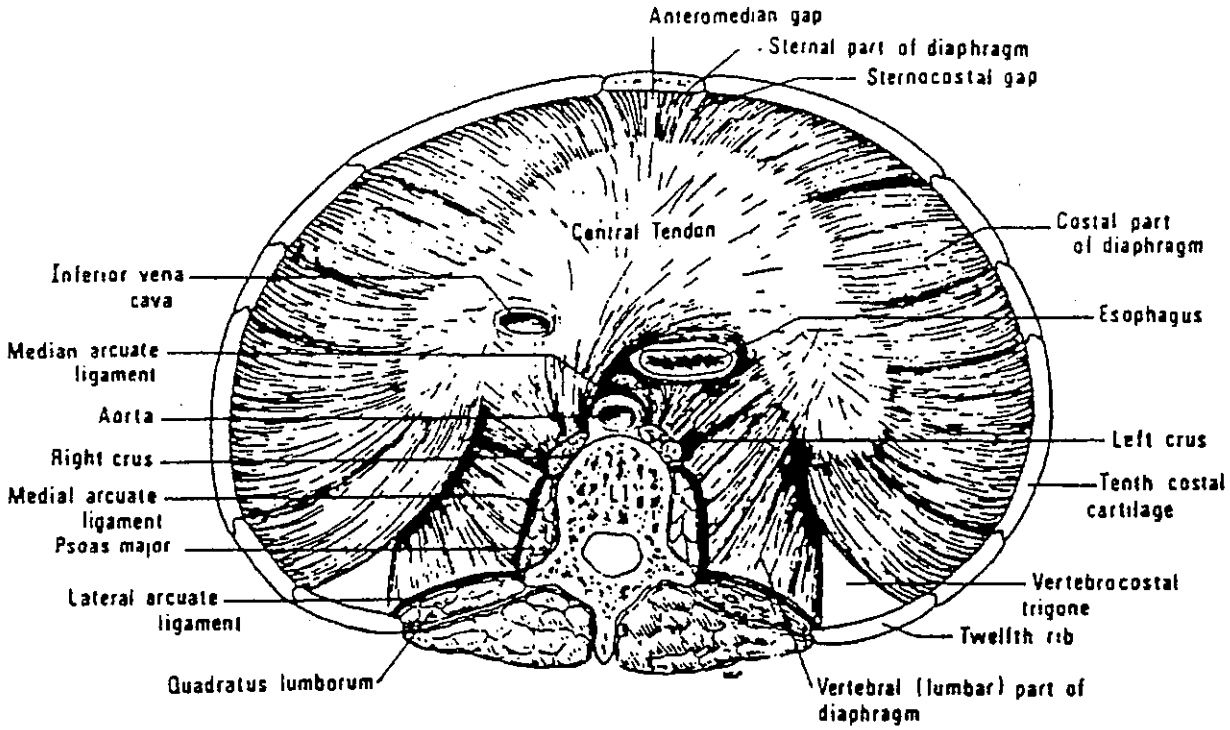

Figure 3 Inferior thoracic outlet from below, showing the attachments and form of the diaphragm. (From Ref. 1.)

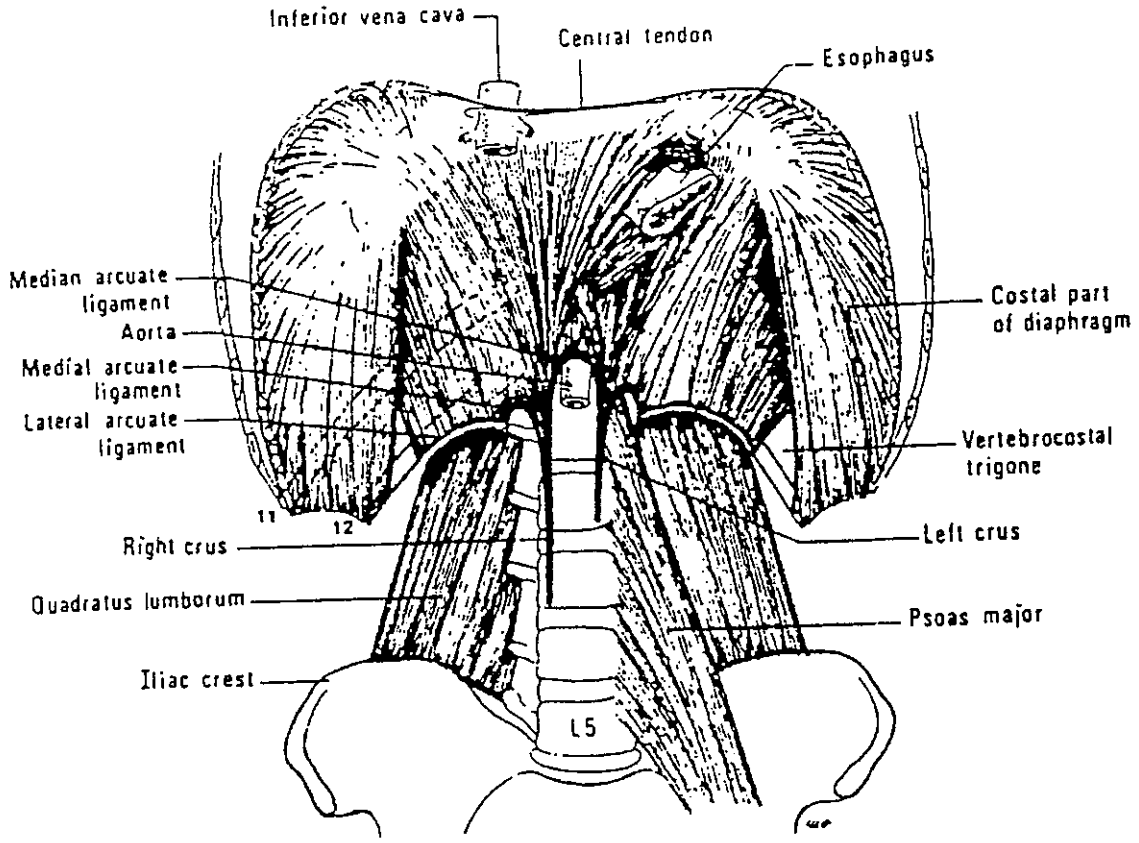

Figure 4 Origin of the diaphragm from the lumbar vertebrae and arcuate ligaments: quadratus lumborum muscle. The diaphragm is shown in schematic coronal section. The positions of the 11th and 12th ribs are indicated in broken outline. (From Ref. 1.)

into two main components according to its point of origin: the *crural (vertebral) part* and the *costal (sternocostal) part*. The *crural (vertebral) part* of the diaphragm arises from the crura and the three aponeurotic arcuate ligaments (Figs. 3 and 4). The crura are strong, tapering tendons attached vertically to the anterolateral aspects of the bodies and intervertebral disks of the first three lumbar vertebrae on the right and two on the left (Fig. 4). An ill-defined, fibrous thickening arch between the two crura forms the *median arcuate ligament*. A tendinous *medial arcuate ligament* passes from the crus on each side across the psoas major muscle to the tip of the transverse process of the first lumbar vertebra. From this point, a *lateral arcuate ligament* then runs to the 12th rib crossing the quadratus lumborum muscle. The medial and lateral arcuate ligaments are firmly adherent to the posterior body wall fused to the sheath and fascia of psoas and quadratus lumborum muscles, respectively (Fig. 4). Muscle fibers arising rom the crura and the arcuate ligaments pass upward to insert into the posterior border of the central tendon, overlapping to some extent and passing behind the fibers ascending from the 12th rib.

The *costal (sternocostal) part* of the diaphragm arises from the xiphoid process and the lower end of the sternum and the costal cartilages of the lower six ribs. From the back of the xiphoid process and the lower end of the sternum, mus-

cle fibers pass almost horizontally backward into the anterior border of the central tendon. Separated from the sternal portion by a small gap, the *sternocostal triangle*, muscle fibers arise from the inner aspects of each costal cartilage from the 7th to the tip of the 12th rib (see Figs. 3 and 4). These costal fibers run cranially so that they are directly apposed to the inner aspect of lower rib cage, creating a *zone of apposition*. Only at higher levels does an angle open up between them and the chest wall, and finally they horizontally converge onto the anterior, lateral, and, to some extent, posterior borders of the central tendon, increasing progressively in length around the chest and from front to back. Frequently, a triangular gap remains between the fibers from the 12th rib and the most lateral fibers from the lateral arcuate ligament, leaving a muscular deficiency, the vertebrocostal trigone (see Fig. 3).

The shape of the relaxed diaphragm at functional residual capacity (FRC) is that of two domes joined by a saddle that runs from the sternum to the anterior surface of the spinal column (10,11). The free surface curves to join the inside of the rib cage and then continues downward so that the diaphragm becomes cylindrical in the zone of apposition (Fig. 5). The height of this zone in the standing human at rest is about 6–7 cm in the midaxillary line and occupies 25–30% of the total internal surface area of the rib cage. The motor innervation of the diaphragm is from the phrenic nerves, which also provide a proprioceptive supply to the muscle. When tension develops within the diaphragmatic muscle fibers, a caudally oriented force is applied on the central tendon and the dome of the diaphragm descends. This descent has two effects. First, it expands the thoracic cavity along

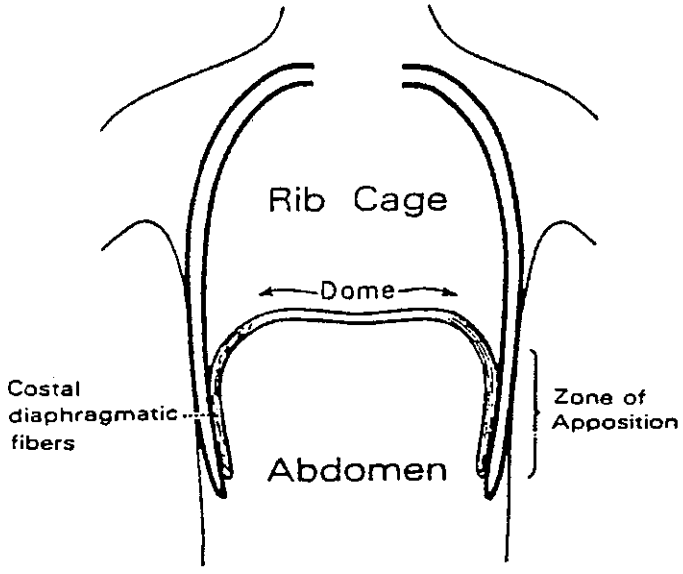

Figure 5 Frontal section of the chest wall at end-expiration, illustrating the functional anatomy of the diaphragm. Note the orientation of the costal diaphragmatic fibers at their insertion on the ribs; these fibers run cranially and are apposed directly to the inner aspect of the lower rib cage (zone of apposition). (From Ref. 3.)

its craniocaudal axis and consequently the pleural pressure falls. Depending on whether the airways are open or closed, lung volume increases or alveolar pressure falls. Second, it produces a caudal displacement of the abdominal visceral contents and an increase in the abdominal pressure which in turn results in an outward motion of the ventral abdominal wall. Furthermore, diaphragmatic contraction acts to displace the bony rib cage both directly through the insertions of the costal diaphragmatic fibers onto the ribs and indirectly through the effect of changing the pleural and abdominal pressures. Thus, when the diaphragm contracts, a cranially oriented force is applied by the costal diaphragmatic fibers to the upper margins of the lower six ribs that has the effect of lifting and rotating them outward (*insertional force*). The actions mediated by the changes in pleural and abdominal pressures are more complex: If one assumes that the diaphragm is the only muscle acting on the rib cage, it appears that it has two opposing effects when it contracts. On the upper rib cage, contraction of the diaphragm causes a decrease in the anteroposterior diameter, and this expiratory action is primarily due to the fall in pleural pressure (12). On the lower rib cage, contraction of the diaphragm causes an expansion that is more pronounced along its transverse diameter than along its anteroposterior diameter. This inspiratory action on the lower rib cage is caused by the concomitant action of two different forces—the "insertional" force already described and the "appositional" force. The zone of apposition makes the lower rib cage, in effect, part of the abdominal container, and measurements in dogs have established that during breathing, the changes in pressure in the pleural recess between the apposed diaphragm and the rib cage are almost equal to the changes in abdominal pressure (13). Pressure in this pleural recess rises rather than falls during inspiration, indicating that the rise in abdominal pressure is truly transmitted through the opposed diaphragm to expand the lower rib cage. This mechanism of diaphragmatic action has been termed the *appositional force*, and its magnitude depends directly on the size of the zone of apposition and on the rise in abdominal pressure and indirectly on the resistance provided by the abdominal contents to diaphragmatic descent. Clearly, for a given diaphragmatic contraction, the appositional force is greater when the rise in abdominal pressure and the zone of apposition are larger and when the resistance to diaphragmatic descent is higher, since in this case the dome of the diaphragm descends less, the zone of apposition remains significant throughout inspiration, and the rise in abdominal pressure is larger. An illustrative clinical example of this latter effect is provided by the tetraplegic patients: When the compliance of their abdomen decreases either by having them in the seated position or by means of a pneumatic cuff or an elastic binder around their abdomen, the expansion of their lower rib cage during inspiration is accentuated (14). The greater area of apposed diaphragm at the sides of the rib cage compared with that at the front presumably accounts for the fact that the diaphragm in humans has a greater expanding action on the transverse than on the anteroposterior diameter of the lower rib cage (12).

The balance between pleural pressure and the insertional and appositional

forces of the diaphragm is also markedly affected by changes in lung volume. As lung volume decreases below FRC, the zone of apposition increases in size (15) and the fraction of the rib cage exposed to pleural pressure decreases. As a result, the appositional force increases, whereas the effect of pleural pressure diminishes, so that the inspiratory action of the diaphragm on the rib cage is enhanced. Conversely, as lung volume increases, the zone of apposition decreases in size and a larger fraction of the rib cage becomes exposed to pleural pressure. Hence, the diaphragm's inspiratory action on the rib cage diminishes (15–17). When lung volume approaches total lung capacity, the zone of apposition all but disappears (15), and the diaphragmatic muscle fibers become oriented internally as well as cranially. As in the eviscerated animal, the insertional force of the diaphragm is then expiratory rather than inspiratory in direction. These two effects of increasing lung volume account for the inspiratory decrease in the transverse diameter of the lower rib cage in subjects with emphysema and severe hyperinflation (Hoover's sign). It is worth noting that the relationship between the lung volume and the mechanical effectiveness/advantage of the diaphragm is more pronounced whenever the lung volume acutely changes. When the lung volume chronically increases, some form of adaptation takes place to compensate partially for the mechanical disadvantage created for the diaphragm. In fact, it has been shown that in emphysematous hamsters the diaphragm drops out sarcomers, resulting in a leftward shift of the whole length-tension curve so that the muscle adapts to the shorter operating length (17a). The extent that this adaption occurs in humans remains unclear as yet.

Although the diaphragm contracting alone causes distortion of the rib cage at all lung volumes, normal humans breathing at rest expand the rib cage without distortion (Fig. 6). Thus, during inspiration, the anteroposterior and transverse diameter of the lower rib cage increase proportionately and synchronously and the anteroposterior diameter of the upper rib cage increases as well. This implies that, even during resting breathing, normal humans contract other muscles that expand the upper rib cage and increase the anteroposterior diameter of the lower rib cage.

C. The Neck Muscles

Sternocleidomastoids

The sternocleidomastoids arise from the mastoid process and descend to the ventral surface of the manubrium sterni and the medial third of the clavicle. Their neural supply is from the accessory nerve. The action of the sternocleidomastoids is to displace the sternum cranially during inspiration, to expand the upper rib cage more in its anteroposterior diameter than in its transverse one, and to decrease the transverse diameter of the lower rib cage. This is inferred from the measurements of chest wall motion in subjects with transection of the upper cervical cord (18) in which the sternocleidomastoids are the only muscles spared. In essence, their isolated action counteracts the isolated action of the diaphragm on the upper rib cage.

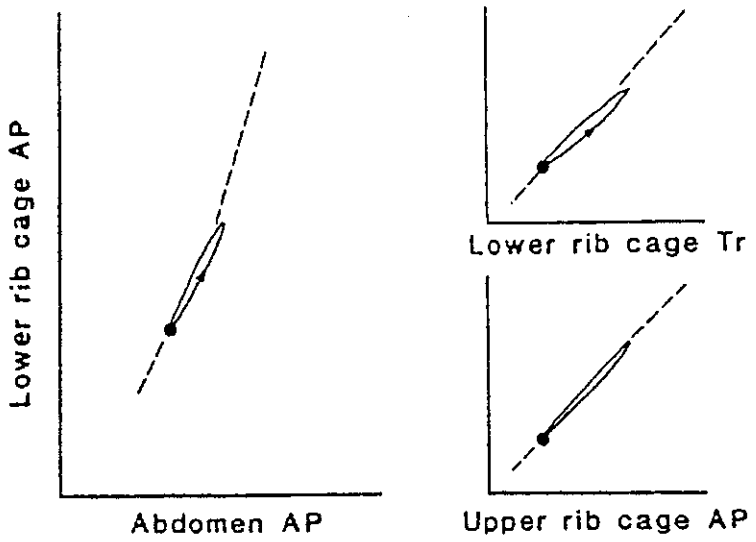

Figure 6 Pattern of chest wall motion in a normal subject breathing at rest in the seated position. Note that the chest wall, including the entire rib cage, moves on its relaxed configuration. AP, anteroposterior diameter; Tr, transverse diameter. (Adapted from Ref. 12.)

In normal subjects breathing at rest, however, the sternocleidomastoids are inactive, being recruited only when the inspiratory muscle pump is abnormally loaded or when ventilation increases substantially (19,20). Therefore, they should be considered as accessory muscles of inspiration.

Scalenes

The scalenes comprise three muscle bundles that run from the transverse processes of the lower five cervical vertebrae to the upper surface of the first two ribs. They receive their neural supply mainly from the lower five cervical segments. Their action is to increase (slightly) the anteroposterior diameter of the upper rib cage (21). Although earlier studies (19) had suggested that the scalenes function as accessory muscles of inspiration, more recent data (22) provide convincing evidence that they are invariably active during inspiration. In fact, seated normal subjects cannot breathe without contracting the scalenes even when they reduce the required inspiratory effort by reducing tidal volume considerably (22). Therefore, the scalenes in humans are primary muscles of inspiration and their contraction is an important determinant of the expansion of the upper rib cage during breathing.

III. Statics of Breathing

The respiratory system is an elastic structure; that is, if a force is applied to it, it changes volume, and when the force is released, it returns to its resting configura-

tion. Rohrer (23) proposed in 1916 that movement of the respiratory system is caused by pressure differences across the system to overcome the elastic resistance to volume change (elastic load), the frictional resistance to flow (resistive load), and the inertial resistance to mass acceleration (inertial load). The main function of the respiratory muscles is to provide the required pressure across the respiratory system to achieve its movement and, thus, the entry of air into the thorax. Although the act of breathing incorporates all the components initially described by Rohrer, it is really didactic to isolate each one and determine the pressure required to overcome each of the elastic, resistive, and inertial loads.

The term *statics of breathing* refers to the pressure-volume relationship of the respiratory system. As the origin of the word *static* (Greek, "with no movement") denotes, this relationship has to be determined with no movement of air (no resistive pressure losses) and no acceleration of tissues (no inertial pressure losses) to reflect the elastic behavior of the respiratory system (elastic load).

One of the first experimental descriptions of the static properties of the respiratory system was that of Rahn et al. (24) in 1946. Normal subjects were asked to inspire a volume of air from a spirometer and then to relax against an occluded airway with an open glottis for a few seconds. This was repeated at various lung volumes. The pressure at the mouth was measured together with the lung volume and recorded on ah X - Y plot. Since under these conditions there is no flow of air within the airways, the pressure at the mouth equals the pressure in the airways and that of the alveoli. Consequently, the difference between the pressure in the mouth and the atmospheric pressure (i.e., body surface pressure) represents the distending pressure of the respiratory system. The volume at zero pressure is the resting volume of the respiratory system where mouth pressure equals zero and is called functional residual capacity (FRC). The horizontal distance from the solid line to the zero-pressure ordinate indicates total respiratory system distending (elastic) pressure ($P_{el.rs}$) and is negative (subatmospheric) below FRC and positive above FRC. Although Rahn et al. (24) reasoned that total pressure at the mouth is the sum of the pressures exerted by the elastic recoil properties of the chest wall ($P_{el.W}$) and the lung ($P_{el.L}$), that is, $P_{el.rs} = P_{el.L} + P_{el.W}$, they were unable to measure them directly. The best they could do was to use published values of the lung's in vitro pressure-volume relationship and plot them on the P-V diagram; then by subtracting $P_{el.L}$ from $P_{el.rs}$ at any volume, they calculated $P_{el.W}$ (Fig. 7). This diagram illustrates that lung recoil is positive at all lung volumes above residual volume (RV). On the contrary, the chest wall exhibits a more complex behavior: from RV to about 60% of VC, the chest wall exerts an outward elastic pressure (i.e., tends to expand). At FRC (about 40% of vital capacity [VC]), there is an equilibrium between the inward pressure of the lungs and the outward pressure exerted by the rib cage; hence, alveolar and mouth pressures are zero. From 60% of VC to total lung capacity (TLC), the chest wall recoil is inward and is additive to that of the lungs.

The next major advance in the study of the statics of breathing came with the

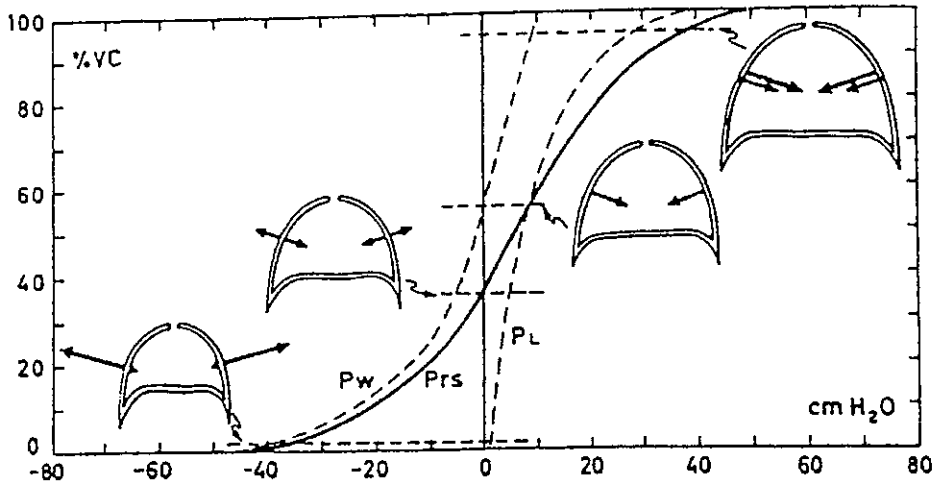

Figure 7 Static volume-pressure curves of the lung (P_L), chest wall (P_W), and total respiratory system (P_{rs}) during relaxation in the sitting posture. The static forces of the lung and the chest wall are pictured by the arrows in the side drawings. The dimensions of the arrows are not to scale; the volume corresponding to each drawing is indicated by the horizontal broken lines. (From Ref. 24, as modified in Ref. 26.)

introduction of the esophageal balloon technique (25) that allowed the measurement of esophageal pressure as an estimate of pleural pressure (P_{pl}) and consequently the partitioning of the respiratory system into its two components: lungs and chest wall. Because both share the same volume change, pressure partitioning is all that is necessary. Accordingly, Heaf and Prime (27) and Campbell (28) modified the Rahn diagram by plotting lung volume against pleural pressure (P_{pl}) under two conditions (Fig. 8): during breath-holding with the glottis open (which is achieved by the coordinated action of the inspiratory muscles) and during relaxation of the respiratory muscles with the airway occluded. Under the first condition, since there is no movement of air and the airway (glottis) remains open, the pressure in the mouth (that is the same with the atmospheric pressure) equals the pressure in the alveoli; that is, $P_m = P_{atm} = P_{alv}$. The difference between this pressure and the P_{pl}, that is, $P_{alv} - P_{pl}$, represents the distending pressure of the lung ($P_{el,L}$). Since pressures are measured relative to P_{atm}, that is, P_{atm} is considered to be zero, under this condition $P_{el,L} = -P_p \Rightarrow P_{pl} = -P_{el,L}$. Accordingly, if lung volumes were plotted against P_{pl}, the pressure-volume relationship of the lung would be obtained (left curve in Fig. 8). Under the second condition, the respiratory muscles are relaxed and so the difference between P_{pl} and body surface pressure, that is, P_{atm}, represents the distending pressure of the chest wall: $P_{el,w} = P_{pl} - P_{atm}$. Since $P_{atm} = 0$, $P_{el,w} = P_{pl}$, and if lung volume were plotted against P_{pl}, the pressure-volume relationship of the chest wall would be obtained (right curve in Fig. 8). This is identical to the chest wall P-V curve in the Rahn diagram. The two curves intersect at about -5 cmH_2O, which is the P_{pl} value at resting FRC. The horizontal distance between the two curves gives the elastic pressure that must be developed (by

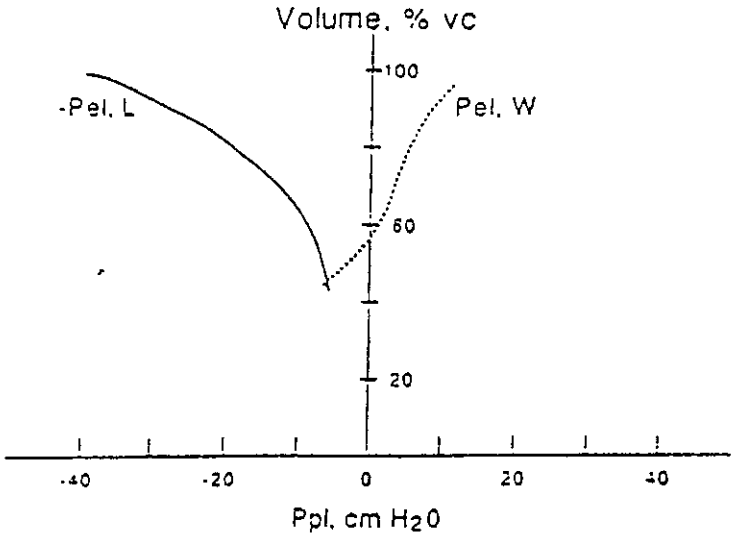

Figure 8 Pressure-volume curves of lung and chest wall. Esophageal pressure as estimate of pleural pressure (P_{pl}) on the horizontal axis is plotted against volume on the vertical axis expressed as percentage of vital capacity (%VC). Data were obtained from normal young men under two conditions. Left curve: $-P_{el}$ is pressure-volume relationship when lung is held by inflated by respiratory muscles with glottis open and, thus, is negative of transpulmonary pressure (alveolar minus pleural pressure). Right curve: $P_{el,W}$ is pressure-volume curve during muscular relaxation against occluded airway. Curve defines transthoracic pressure (pleural minus atmospheric pressure)–volume relationship. (From Ref. 29.)

either the respiratory muscles or the ventilator) to displace the system above or below its equilibrium volume (where the two curves intersect) and, thus, corresponds to the pressure-volume relationship of the entire respiratory system.

Neglecting dynamic considerations, the left-hand curve of the Rahn diagram shows the pleural pressure-volume relationship during spontaneous breathing when airway pressure is near zero. The right-hand curve shows the pleural pressure-volume relationships during mechanical ventilation (when the respiratory muscles are relaxed) and the distance between the curves approximates alveolar pressure during mechanical ventilation (29).

Note that this analysis considers the chest wall as a single compartment model; that is, as having a single degree of freedom. This means that it is possible to measure the change in a single dimension of the chest wall and solve for changes in all other dimensions. Of course, the contribution of the abdomen, diaphragm, or rib cage to the volume displacements cannot be differentiated. Before this volume partitioning could be attempted, one had to know the pressures acting on these different compartments. This became possible after the work of Agostoni and Rahn (30), who developed the method of measuring transdiaphragmatic pressure as the difference between gastric and esophageal pressure. By measuring gastric pressure as an index of abdominal pressure (P_{ab}) and esophageal

pressure as an index of pleural pressure, they accomplished the pressure partitioning necessary to determine the pressures displacing the abdomen (P_{ab}) as well as those acting on the inner surface of the rib cage (P_{pl}). This set the stage for partitioning of the chest wall elastic properties into those of the abdomen and the rib cage. Although several techniques and models for this partitioning have been proposed (31–33), the one introduced by Konno and Mead (34) has gained wide acceptance and will be further analyzed. These investigators measured the surface motions-displacements of the rib cage and abdomen and used them to represent the corresponding volume changes in both sitting and supine normal subjects keeping a fixed body position. They hypothesized that the chest wall has two degrees of freedom (i.e., can accommodate lung volume by displacing the rib cage or diaphragm-abdomen independently as parallel pathways). The sum of both displacements was monotonically related to changes in lung volume. Anteroposterior (A-P) displacements of the rib cage and abdominal wall were initially measured on many different chest wall surface points by means of linear differential transducers. Displacement of loci on the middle sternum and above the umbilicus were found to be those which best represent the volume displacement relationship of the rib cage and abdomen, respectively. The investigators recognized that in the boundary between the rib cage and the abdomen there were more degrees of freedom. Even more degrees of freedom emerged by considering the cranial movement of rib cage (35) and by allowing flexion of the spine. Konno and Mead (34) expressed chest wall configuration by plotting rib cage versus abdominal A-P wall dimensions (Fig. 9) (36). Each point in the diagram (i.e., each pair of A-P dimensions) would represent a unique configuration of the chest wall at volumes from TLC to RV. The dashed line encircling the data points represents the limits of possible configurations. The continuous line from RV to TLC represents the chest wall configurations (i.e., pairs of A-P dimensions) obtained when the corresponding lung volumes were held by relaxing against a closed airway. This relaxation curve represents the minimum energy configuration at each lung volume and distortion away from this configuration requires energy. If at any point along the relaxation line the subject closes the airway and shifts volume between the abdominal and rib cage compartments while lung volume remains constant (isovolume maneuver), the A-P diameters of the rib cage and the abdomen will follow a line with a negative slope; that is the A-P diameter of the abdomen becomes smaller when the A-P diameter of the rib cage becomes bigger and vice versa. In reality, these isovolume isopleths are flat loops showing hysteresis rather than lines. The A-P diameter can be derived not only by linear pressure transducers as originally describe, but also with the use of magnetometers or *Respitrace* [respiratory inductive plethysmography bands; AMI (Ambulatory Monitoring Inc., New York)] that in fact measure cross-sectional area which is less susceptible to local distortion than are magnetometers (37). Calibration of chest wall dimensions can be achieved by doing isovolume maneuvers at different lung volumes, for example,

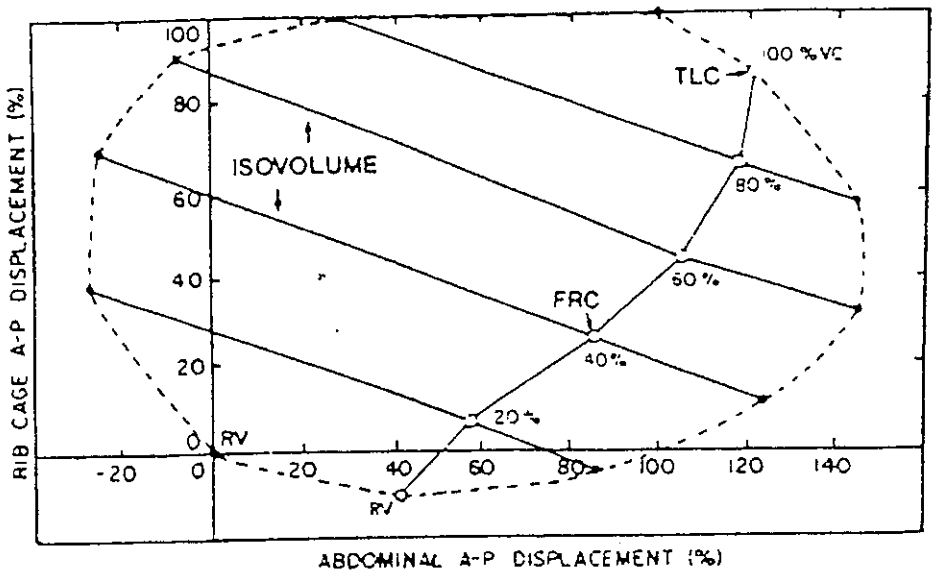

Figure 9 The Konno-Mead diagram. The rib cage anteroposterior (A-P) dimensions are plotted against abdominal A-P dimensions. The displacements are expressed as a percentage of total over the vital capacity (VC) relative to values at active residual volume (RV). The solid line with open points indicates the configurations in relaxed states from total lung capacity (TLC) (100%) isovolume obtained by shifting volume from abdomen to chest and vice versa and keeping a closed glottis (isovolume maneuvers). The area enclosed by the dashed line illustrates a range of possible configurations produced by submaximal contraction of rib-cage and abdominal muscles. (From Ref. 36.)

at 20% intervals of the VC as indicated in Figure 9, thus providing a quantitative link between configuration and lung volume. The measurement of chest wall displacements has become a useful method to monitor ventilation noninvasively, giving a precision to within approximately 10% of spirometric measurements.

By combining the pressure partitioning of Agostoni and Rahn with the volume partitioning already presented, one can measure the elastic properties of the rib cage and abdomen separately (38). In the upright, standing position, the abdomen is considerably less compliant than the rib cage, because the action of gravity causes the abdominal contents to stretch the anterior abdominal wall; in the supine position, however, abdominal compliance increases markedly (Fig. 10) (39). As a result, abdominal motion during breathing is more prominent in the supine position than in the upright position (40).

The Konno-Mead method does not measure displacement of the diaphragm. The actual lung volume displaced by the diaphragm is included in both rib cage expansion and abdominal displacement, and the exact contribution of the diaphragm to the two compartments remains a matter of controversy despite thorough investigation and ingenious theoretical analysis. This stems from the complex actions of the diaphragm and the fact that the rib cage and the diaphragm-abdomen rather than being two independent pathways seem to be mechanically

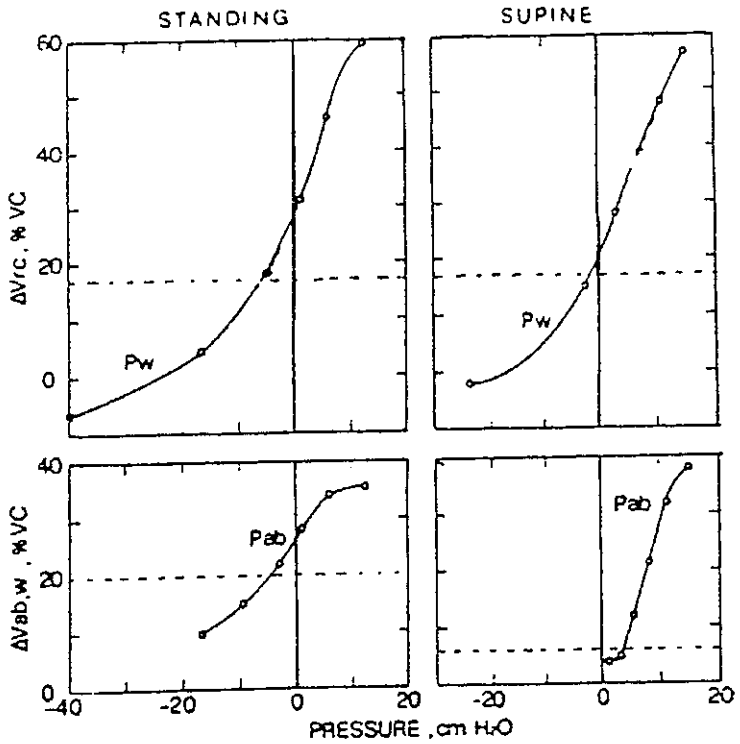

Figure 10 Static volume-pressure curves of the rib cage (upper diaphragms) and of the abdominal wall (lower diagrams) during relaxation in the standing (left diagrams) and supine posture (right diagrams). Data of volume contribution of the rib cage ($\Delta V_{ab,w}$), as well as of pressure of the chest wall (P_w) and abdomen (P_{ab}) are from Konno and Mead (38). In the standing position, the slope of the abdominal V-P curve (i.e., the compliance) is lower than the one of the rib cage, whereas exactly the opposite occurs in the supine position. (Modified from Ref. 39.)

coupled in ways that are not well understood. Detailed presentation of this challenging area of controversy is, however, beyond the scope of this chapter and the interested reader should consult recent, excellent reviews (39–41).

IV. Energetics and Blood Flow

For humans to take a spontaneous breath, the inspiratory muscles must generate sufficient force to overcome the elastance of the lungs and chest wall (lung and chest wall elastic loads) as well as the airway and tissue resistance (resistive load). This requires an adequate output of the centers controlling the muscles, anatomical and functional nerve integrity, unimpaired neuromuscular transmission, an intact chest wall, and adequate muscle strength. This can be schematically represented by considering the ability to take a breath as a balance between inspiratory load and neuromuscular competence (Fig. 11). Under normal conditions, this system is polarized in favor of neuromuscular competence; that is, there are reserves that permit considerable increases in load. However, for a person to breathe spon-

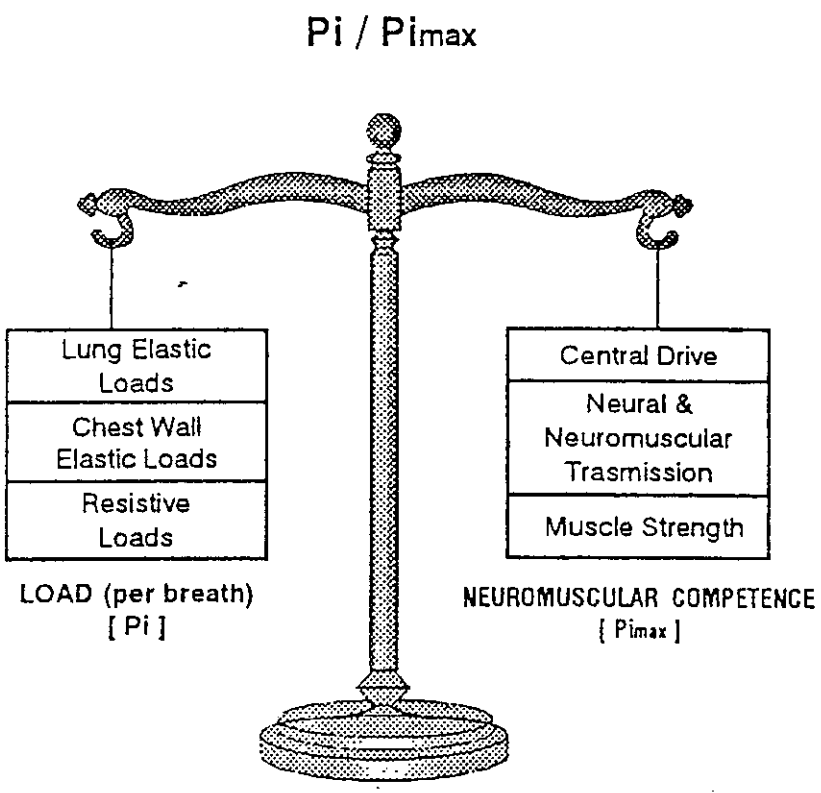

Figure 11 The ability to take a spontaneous breath is determined by the balance between the load imposed upon the respiratory system (P_I) and the neuromuscular competence of the ventilatory pump ($P_I$max). Normally this balance weighs in favor of competence permitting significant increases in load. However, if the competence is, for whatever reason, reduced below a critical point (e.g., drug overdose, myasthenia gravis), the balance may then weigh in favor of load rendering the ventilatory pump insufficient to inflate the lungs and chest wall. (From Ref. 126.)

taneously, the inspiratory muscles should be able to sustain the above-mentioned load over time and also adjust the minute ventilation in such a way that there is adequate gas exchange. The ability of the respiratory muscles to sustain this load without the appearance of fatigue is called *endurance* and is determined by the balance between energy supplies (U_s) and energy demands (U_d) (Fig. 12).

Energy supplies depend on the inspiratory muscle blood flow, the blood substrate (fuel) concentration and arterial oxygen content, the muscle's ability to extract and utilize energy sources, and the muscle's energy stores (42,43). Under normal circumstances, energy supplies are adequate to meet the demands and a large recruitable reserve exists (see Fig. 12). Energy demands increase proportionally with the mean tidal pressure developed by the inspiratory muscles (P_I) expressed as a fraction of maximum (P_I/P_Imax), the minute ventilation ($\dot{V}_E$), the inspiratory duty cycle (T_I/Ttot), and the mean inspiratory flow rate (V_T/T_I) and are inversely related to the efficiency of the muscles (42,43). *Fatigue* develops when

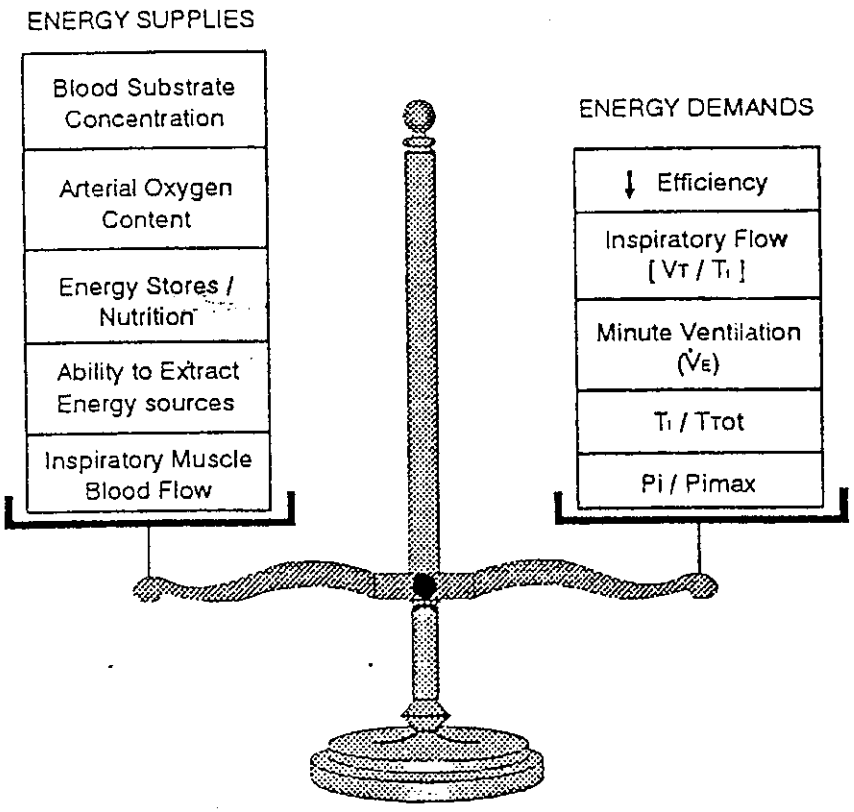

Figure 12 Respiratory muscle endurance is determined by the balance between energy supplies and demands. Normally, the supplies meet the demands and a large reserve does exists. Whenever this balance weighs in favor of demands, the respiratory muscles ultimately become fatigued, leading to inability to sustain spontaneous breathing. (From Ref. 126.)

the mean rate of energy demands (U_d) exceeds the mean rate of energy supply (U_s) (44) (i.e., when the balance is polarized in favor of demands)

$$U_d > U_s \Rightarrow \frac{\dot{W}}{E} > U_s \qquad (1)$$

where $\dot{W}$ is the mean muscle power and E is efficiency.

Bellemare and Grassino (45) have suggested that the product of T_I/Ttot and the mean transdiaphragmatic pressure expressed as a fraction of maximal (Pdi/Pdi max) defines a useful "tension-time index" (TTIdi) that is related to the endurance time (i.e., the time that the diaphragm can sustain the load imposed on it). Whenever TTIdi is smaller than the critical value of 0.15, the load can be sustained indefinitely; but when TTIdi exceeds the critical zone of 0.15–0.18, the load can be sustained only for a limited time period; in other words, the endurance time. This was found to be inversely related to TTIdi. By analogy, a tension time index was calculated for the rib cage muscles:

$$\text{TTIrc} = \text{mean value } \frac{P_{pI}}{P_{pI}\text{max}} \cdot \frac{T_I}{T_T} \qquad (2)$$

where P_{pl} is the pleural pressure and the critical value was found to be 0.30 (46). The TTI concept is assumed to be applicable not only to the diaphragm but to the respiratory muscles as a whole (47):

$$TTI = \frac{P_I}{P_I max} \cdot \frac{T_I}{Ttot} \tag{3}$$

where P_I = mean inspiratory pressure per breath and $P_I max$ = maximal inspiratory pressure. Since we have stated that endurance is determined by the balance between energy supply and demand, TTI of the inspiratory muscles has to be in accordance with the energy balance view. In fact, as Figure 12 demonstrates, $P_I/P_I max$ and $T_I/Ttot$, which constitute the TTI, are among the determinants of energy demands; an increase in either that will increase the TTI value will also increase the demands. The energy balance may then weigh in favor of demands leading to fatigue. Furthermore, Roussos et al. (48) have directly related $P_I/P_I max$ with the endurance time. The critical value of $P_I/P_I max$ that could be generated indefinitely at FRC was around 0.60. Greater values of $P_I/P_I max$ ratio were inversely related to the endurance time in a curvilinear fashion. When lung volume was increased from FRC to FRC + 0.5 inspiratory capacity, the critical value of $P_I/P_I max$ and the endurance time were diminished to very low values (20–25% of $P_I max$).

But what determines the ratio $P_I/P_I max$? The nominator, the mean inspiratory pressure, is determined by the elastic and resistive loads imposed on the inspiratory muscles. The denominator, the maximum inspiratory pressure, is determined by the neuromuscular competence; that is, the maximum inspiratory muscle activation that can be achieved. It follows, then, that the value of $P_I/P_I max$ is determined by the balance between load and competence (see Fig. 11). But $P_I/P_I max$ is also one of the determinants of energy demands (see Fig. 12); therefore the two balances, that is, between load and competence and energy supply and demand, are in essence linked, creating a system. Schematically, when the central hinge of the system moves upward, or is at least at the horizontal level, spontaneous ventilation can be sustained indefinitely (Fig. 13). One can easily see that the ability of a subject to breathe spontaneously depends on the fine interplay of many different factors. Normally this interplay moves the central hinge far upward and creates a great ventilatory reserve for the healthy individual. When the central hinge of the system, for whatever reason, moves downward, spontaneous ventilation cannot be sustained and ventilatory failure ensues, ultimately necessitating mechanical ventilation.

We will subsequently take a more in-depth look at the determinants of this system from the point of view of energetics. We will discuss how the energy supplies are controlled under normal and stressed conditions and when they can become inadequate to meet the demands. We will also analyze how the energy demands are determined based on theoretical calculations and present the methods used for their measurement in clinical practice along with the experimental data available.

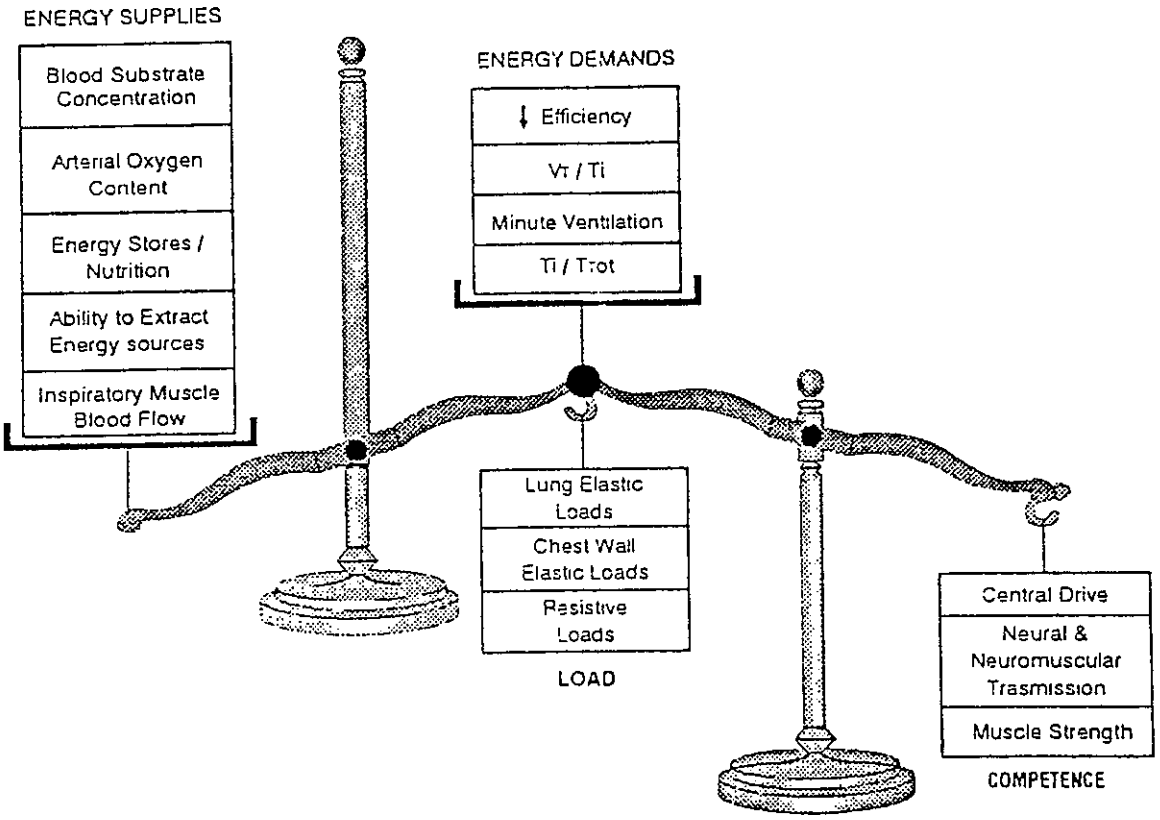

Figure 13 The system of two balances incorporating the various determinants of load, competence, energy supplies, and demands is represented schematically. The $P_I/P_I max$ that was one of the determinants of energy demands (see Fig. 12) is replaced by its equivalent: the balance between load and neuromuscular competence (see Fig. 11). In fact, this is the reason why the two balances are linked. When the central hinge of the system moves upward or is at least at the horizontal level, an appropriate relationship between ventilatory needs and neurorespiratory capacity exists and spontaneous ventilation can be sustained. In healthy persons, the hinge moves far upwards creating a large reserve. (From Ref. 126.)

A. Energy Supplies

Substrate Metabolism

The respiratory muscles are not qualitatively different from other skeletal muscles in terms of *substrate* metabolism; that is, they can use glucose, fatty acids, acetoacetate, D-3-hydroxybutyrate, L-lactate, and amino acids (49–51). However, the important feature of the respiratory muscles (particularly the diaphragm) is that because they receive their energy supply in "real time" through their abundant blood flow, the *fuel storage* in these muscles is of little importance under most working conditions. Normally the respiratory muscles derive half of their energy requirement from the oxidation of carbohydrates and the rest from the combustion of free fatty acids (52,53) much like other skeletal muscles.

Most studies indicate that the diaphragm, and perhaps the other respiratory muscles, are resistant to anaerobic metabolism (53–60) suggesting that glycolytic pyruvate production is adjusted to its rate of aerobic oxidation. In fact, Rochester

and Briscoe (53) have shown that diaphragmatic lactate production becomes prominent only when diaphragmatic venous P_{O_2} fall below 10–20 mmHg. However, when the respiratory muscles are subjected to a very high-power output, they employ anaerobic metabolism to maintain adequate ventilation before becoming exhausted, and under this circumstance, the muscles' energy stores (mainly in the form of glycogen) become important. Accordingly Hollanders (61) has demonstrated that the excised perfused diaphragm can produce lactate for a prolonged period. Normal humans breathing 15% O_2 who hyperventilate through inspiratory resistances increase their blood lactate by 0.4 mM (62). Similarly, normal subjects breathing against very high inspiratory resistances and inhaling either room air or 13% O_2 increase their blood lactate by ≈1 mM (57). Although the exact origin of lactate and the rate of lactate removal by the liver have not been established, it is reasonable to suppose that strenuous work by the respiratory muscles may be partly responsible for the elevated blood lactate levels. The most convincing evidence for this comes from the work of Aubier et al. (62), who subjected two groups of dogs to the same degree of low cardiac output by pericardial tamponade and found that the blood lactate concentration in the spontaneously breathing animals reached 9 mM, a value twice as high as that of the paralyzed and mechanically ventilated dogs (Fig. 14).

Under most circumstances, energy supplies do not become limited owing to the lack of blood substrate or energy stores. Low blood substrate concentration, as in extreme inanition, and depletion of glycogen and other energy stores, as observed in catabolic states and malnutrition, nevertheless may decrease the

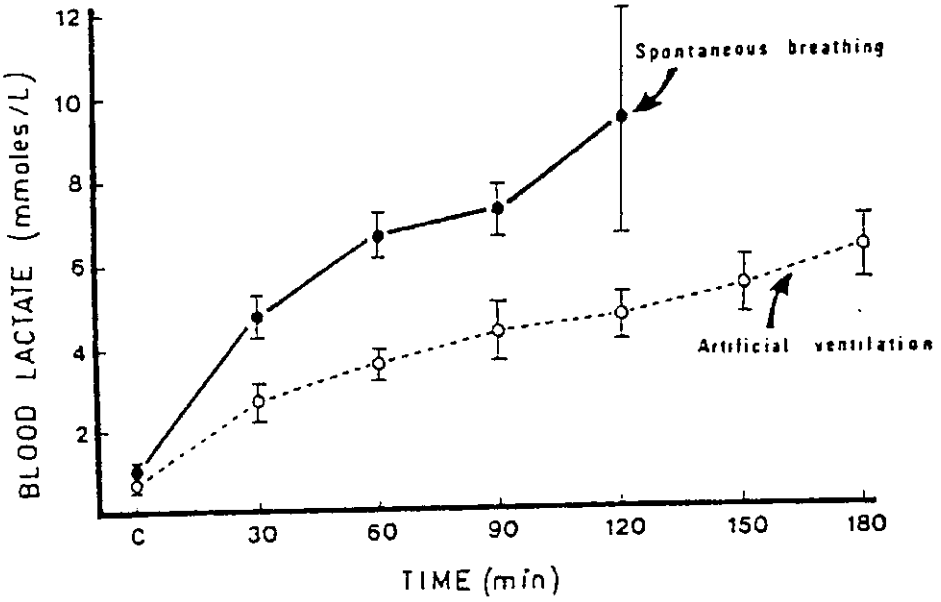

Figure 14 Blood lactate levels in two groups of dogs submitted to low cardiac output. Spontaneously breathing dogs had greater blood lactate concentration than the paralyzed and mechanically ventilated dogs. (From Ref. 62.)