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CRITICAL REVIEW

Respiratory Muscle Function in Health and Disease*

John M. Luce, M.D., F.C.C.P.; and Bruce H. Culver, M.D.

The muscles of respiration comprise three groups: the diaphragm, the intercostal and accessory muscles, and the muscles of the abdomen (Fig 1). All three groups have inspiratory and expiratory function and work together in intricate ways. This article reviews respiratory muscle action and interaction. We also discuss respiratory muscle dysfunction and its treatment in several disease states, including chronic obstructive pulmonary disease, asthma, chest wall deformity, obesity, generalized neuromuscular disorders, cervical cord injury, and unilateral and bilateral diaphragmatic paralysis. We conclude with a discussion of how training may influence respiratory muscle fatigue. Other issues, including central nervous system control of the respiratory muscles, are covered by Derenne and colleagues. Their article contains an extensive bibliography.

THE DIAPHRAGM

In their comprehensive review of the respiratory muscles, Derenne and associates note that the diaphragm is inserted onto the ribs and that at the periphery its fibers are directed upwards, parallel to the rib cage. When the diaphragm contracts, it pushes down on the abdominal viscera, displaces the abdominal wall outward, and increases abdominal pressure (Pab). At the same time, the diaphragm lifts the rib cage upward, causing an outward displacement because of its rib articulation, and generates a negative pleural pressure (Ppl) that inflates the lungs (Fig 2). The increased abdominal pressure, applied to the lower rib cage below the diaphragm, also contributes to the outward displacement. The amount of respiratory work performed by the diaphragm during inspiration is reflected in the pressure gradient across the diaphragm, Pdi, which is the difference between Pab and Ppl. These values can be obtained by simultaneously recording pressures in esophageal and gastric balloons. In normal persons, Pdi ranges from 10 to 20 cm H2O during quiet breathing.

Although the diaphragm is primarily an inspiratory muscle, it has an expiratory action on the rib cage when its dome is flattened and its peripheral fibers are directed centrally rather than towards the head. This happens normally at high lung volumes, but it also can occur during tidal breathing in hyperinflated patients with an increased functional residual capacity (FRC). In such persons, the negative Ppl generated by the diaphragm sucks in the lower part of the chest, and the rib cage actually may decrease in its lateral dimension. The expiratory action of the diaphragm at high lung volumes...
explains Hoover’s sign, an inspiratory indrawing of the lateral costal margins seen in some patients with chronic obstructive pulmonary disease (COPD).

**Intercostal and Accessory Muscles**

The intercostal muscles include the internal and external intercostals, whose fibers run in an anterior-posterior direction. The accessory muscles include the scalenes, the sternomastoids, and the trapezoids. The external intercostal and the accessory muscles serve primarily an inspiratory function and are responsible for increasing the anterior-posterior diameter of the thorax. Inspiratory activity can be observed in the external intercostals in the upper few intercostal spaces during quiet breathing, with the lower intercostals becoming active with increased ventilation. The scalenes, sternomastoids, and trapezoids are recruited at high levels of inspiratory activity, at which point other back muscles that support the chest cage also become involved.

**Abdominal Muscles**

The abdominal respiratory muscles include the rectus and transverse abdominis and the external and internal obliques. These generally are regarded as expiratory muscles that augment the passive recoil of the lungs, especially during deep and forceful breathing. Yet, the abdominal muscles also play a facilitatory role in inspiration in that their contraction tends to lengthen the diaphragm and diminish its radius of curvature, allowing it to generate a greater tension as well as greater Pdi for a given tension. This improvement in the diaphragm’s mechanical advantage is significant in the upright posture, particularly during exercise.

**Respiratory Muscle Interaction**

Goldman and Mead\(^2\) believe that the diaphragm performs all the body’s respiratory muscle work during quiet breathing in the upright posture and have demonstrated that the rib cage is driven along its relaxation curve in experimental subjects trying to breathe with the diaphragm alone. In contrast to this viewpoint, Macklem et al\(^3\) have argued that the intercostal and accessory muscles are never electrically silent and that their contribution is necessary to properly displace the chest wall. Danon and colleagues\(^4\) studied three quadriplegic patients with lesions at C\(_1\), who for the purposes of the experiment breathed either with only their accessory muscles, with electrically-paced diaphragms, or with a combination of the two groups. They determined rib cage movement by means of magnetometry, in which magnets are placed on opposite sides of the chest and their displacement is recorded. The investigators demonstrated that the diaphragm functioning alone did not drive the rib cage along its relaxation curve, but instead caused rib cage distortion when the patients were semi-upright. Paradoxic movements in the upper rib cage due to the absence of accessory muscle activity also occurred in this position. These findings suggest that the other respiratory muscles stabilize the chest wall and convert diaphragmatic contraction into intrathoracic pressure and volume changes.

**Respiratory Muscle Fatigue**

In keeping with its prominent role in respiration, the diaphragm is well equipped for sustained activity, containing muscle fibers and mitochondrial enzymes that favor aerobic metabolism.\(^5\) Rochester and Bettini,\(^6\) who studied dogs breathing an
increased carbon dioxide (CO₂) mixture through inspiratory resistances, found that the diaphragm's increased oxygen (O₂) requirements were met by a combination of blood flow and O₂ extraction at high levels of work, at which point diaphragmatic blood flow continued to increase while oxygen extraction plateaued. Robertson et al² confirmed these findings in experimental animals and determined that conditions of extreme diaphragmatic work were associated with no limitation in diaphragmatic blood flow.

In spite of these studies, clinical experience suggests that respiratory muscle fatigue does occur at high levels of exertion, presumably because the diaphragm outstrips its blood supply. How this might occur was suggested in a recent study by Aubier and colleagues,⁴ who measured the diaphragmatic electromyogram (EMGdi), Pdi, and diaphragmatic lactate production in dogs whose cardiac output was markedly reduced by tamponade. One group of animals was mechanically ventilated during this period; another breathed spontaneously. The investigators found that whereas they could breathe indefinitely if their minute ventilation was 55 percent or less of the MVV.

Robertson et al⁷ confirmed these findings in experimental animals and determined that at any one moment the less active group supported the chest wall to enhance the function of the other group. Thus, the apparent discoordination of the chest wall. Andersen and associates¹⁴ have observed similar EMG patterns in patients with respiratory failure receiving mechanical ventilation; magnetometry revealed that many of these patients display thoracoabdominal discoordination during weaning from mechanical ventilation as well.

These findings suggest that discoordinate breathing is maladaptive, if not abnormal. However, Roussos and Macklem¹⁵ measured the elevated activity of the diaphragmatic and intercostal and accessory muscles in five normal seated subjects breathing through inspiratory resistance until exhaustion and found that the subjects alternated their use of the two muscle groups. Since neither muscle group was entirely inactive, the investigators felt that at any one moment the less active group supported the chest wall to enhance the function of the other group. Thus, the apparent discoordination activity was a coordinated effort that served to protect both muscle groups from total exhaustion by alternating their contribution to the breathing task.

Respiratory Muscle Dysfunction in Chronic Obstructive Pulmonary Disease

Patients with COPD must breathe at high lung volumes to maintain patency of their narrowed airways. The major abnormality of respiratory muscle function in patients with COPD is thought to be the mechanical disadvantage caused by this hyperinflation, which depresses the dome of the diaphragm, shortens its fibers, and forces it to work on an ineffective portion of its length-tension curve.
This explanation is supported by a study by Rousos et al. in which subjects breathing at FRC plus one-half of their inspiratory capacity generated an average mouth pressure of only −27 cm H2O breath after breath compared with −80 cm H2O in subjects inspirating at a normal FRC.

Sharp and associates studied 17 patients with COPD, seven of whom reported that their dyspnea was reduced when they leaned forward while sitting or when they lay down. All seven patients had paradoxical inward abdominal motion in the standing and erect seating postures, suggesting diaphragmatic dysfunction; this disappeared when they assumed their preferred position. These seven patients had significantly greater lung volumes than the other ten patients. They also used their accessory muscles more than the other patients while standing or sitting erect and also generated a smaller Pdi. This suggested that extremely hyperinflated individuals relieve dyspnea through postures that enhance function of the diaphragm by improving its length-tension relationship.

A correlation between diaphragmatic dysfunction and the degree of airflow obstruction is suggested by the finding of Sharp et al. that asynchronous breathing is common in patients with severe COPD. Many of these patients show minimal abdominal movement coincident with outward rib cage motion during inspiration; a small number of them even manifest complete asynchrony of abdomen and rib cage. Braun and Rochester measured maximum inspiratory and expiratory mouth pressure (Pimax and Pemin) in normal subjects and patients with moderate and severe COPD. They found that Pimax was reduced in both the moderately and the severely obstructed patients, who presumably had inspiratory muscle weakness; patients who could develop a Pimax of greater than −50 cm H2O generally had normal arterial carbon dioxide (CO2) levels, while patients whose Pimax was less retained CO2.

**Asthma**

Sternomastoid and intercostal muscle retraction frequently are observed in patients during severe asthma attacks. An explanation for why inspiratory muscles would be called upon in a disease that affects expiration was sought by Martin and coworkers, who studied the lung and chest wall mechanics of subjects in whom bronchoconstriction was induced by progressively larger doses of inhaled histamine. An increase in airflow resistance was associated with a linear increase in FRC up to 75 percent of TLC in these subjects. At each level of hyperinflation the most positive expiratory pleural pressures recorded during spontaneous breathing were less than the predicted chest wall relaxation pressure, suggesting persistent inspiratory muscle activity during expiration. The investigators concluded that this activity resulted in a chest wall configuration that decreased airway resistance and optimized the function of the diaphragm.

**Chest Wall Deformity**

Decreased chest wall compliance is found in ankylosing spondylitis, kyphoscoliosis, and other processes that distort the normal configuration of the chest wall. The chests of patients with ankylosing spondylitis also are held in an inspiratory position throughout the respiratory cycle; these patients make more use of their abdominal muscles than do other individuals, perhaps because their intercostal and accessory muscles fatigue more readily. The diaphragm functions normally in patients with ankylosing spondylitis, and they can maintain normal lung volumes, MVV, and arterial blood gases unless their abdominal muscles cannot function properly, as might occur after abdominal surgery. By contrast, kyphoscoliosis is characterized by small lung volumes, especially the expiratory reserve volume (ERV) and FRC; a low MVV; and hypoxemia and hypercapnia in many patients. Although the contribution of respiratory muscle dysfunction to the CO2 retention of patients with severe kyphoscoliosis had not been quantitated, their hypercapnea might be attendant in part to fatigue related to the stiff chest wall.

**Obesity**

Massive obesity also causes a decrease in chest wall compliance that is associated with a reduced ERV, FRC, and vital capacity (VC); a low MVV; hypoxemia; and hypercapnia in certain patients with the obesity-hypoventilation syndrome. Rochester and Enson have noted that VC and MVV are significantly lower in patients with the obesity-hypoventilation syndrome than in simple obesity, either because they have greater mass loading of the respiratory muscles or their muscles cannot handle a ventilatory load. To test this latter hypothesis, Arora and Rochester measured MVV and Pimax and Pemin in obese patients with and without CO2 retention and expressed them as percent predicted; respiratory muscle strength was calculated as Pimax%/ + Pemin%/2. These parameters were reduced more in the hypercapnic patients than in those without CO2 retention, suggesting that impaired strength and endurance of the respiratory muscles is characteristic of the obesity-hypoventilation syndrome.

Respiratory muscle dysfunction also may con-
FIGURE 3. Diaphragmatic function is maintained in quadriplegics with cervical cord injury, but these patients lack lower intercostal and abdominal muscle activity. Inspiration to total lung capacity, therefore, is complicated by paradoxical inward motion of the upper thorax, whereas normal residual volume cannot be achieved in expiration due to abdominal muscle dysfunction. Quadriplegic patients are more comfortable in the supine position, where the abdominal viscera push up on the diaphragm and enhance its activity.
results from involvement of the phrenic nerve by primary or metastatic tumor. It also may result from trauma, surgery, neurologic disease, and infection, as well as unknown causes. Few patients report symptoms referable to unilateral diaphragmatic paralysis, and most cases are picked up on routine chest x-ray examination. Although unilateral diaphragmatic paralysis usually induces immobility of the ipsilateral anterior abdominal wall and a lag in the upward and outward movement of the costal margin in deep inspiration, this frequently is obscured by the proper function of the contralateral hemidiaphragm (Fig 4). Paradoxic upward movement of the paralyzed diaphragm usually can be detected during a “sniff” test under fluoroscopy, however.

Arborelius and co-workers studied regional lung function by means of radioactive $^{133}$Xe scans in patients with unilateral diaphragmatic paralysis and showed a reduction in perfusion of 19 percent, in ventilation of 20 percent, and in volume of 7 percent in the affected side. Arterial Po$_2$ was reduced from 83 mm Hg to 75 mm Hg when these patients went from an upright to a supine position and fell slightly more when they laid on the affected side. Although this relatively small drop in
$PO_2$ should not be clinically significant in most adults, respiratory failure has been described in infants with unilateral diaphragmatic paralysis as a sequela of cardiac surgery, several of whom required surgical plication of the hemidiaphragm.

**Bilateral Diaphragmatic Paralysis**

If one breathes only with the intercostal and accessory muscles, as is the case in patients with bilateral diaphragmatic paralysis, $P_{di}$ equals zero and $P_{ab}$ equals $P_{pl}$. As a result, with each inspiration, the decrease in $P_{pl}$ not only expands the lung, but also sucks in the abdomen and the diaphragm (Fig 5). This paradoxical inward motion of the abdomen may not be apparent in the upright position if the abdominal muscles have contracted and elevated the diaphragm to aid expiration, for in this situation the diaphragm may descend passively in early inspiration as the previously-tensed abdominal muscles relax. Nevertheless, paradox should be apparent if the patient is supine because in this position the diaphragm cannot fall passively. The upward motion of the diaphragm in inspiration is expiratory in direction and opposes lung inflation. Thus, breathing with only the intercostal and accessory muscles is quite inefficient, and the work of breathing is inordinately high.

Bilateral diaphragmatic paralysis may occur either in association with generalized neuromuscular disease, as noted above, or as an isolated phenomenon. Patients with this disorder characteristically complain of orthopnea, disturbed sleep, daytime fatigue, and morning headaches, and they may be misdiagnosed as having left ventricular dysfunction, idiopathic hypoventilation, or sleep apnea. According to McCredie and colleagues, bilateral diaphragmatic paralysis causes hypoxemia, hypercapnea, and decreases in $VC$, $RV$, and $TLC$ that are accentuated in the supine position, when the abdominal viscera push the inactive diaphragm into the chest and limit the effectiveness of the other respiratory muscles, and when paradoxical inward movement of the abdomen is most apparent during inspiration. Bilateral diaphragmatic paralysis should be suspected in the presence of such paradox; it is suggested by fluoroscopy and confirmed by trans-diaphragmatic pressure recordings.

Newsom-Davis and associates studied eight patients with bilateral diaphragmatic paralysis and neuromuscular disease, all of whom demonstrated paradoxical abdominal motion during inspiration in the supine position. None of these patients could generate a $P_{di}$ greater than 6 cm $H_2O$, and all had an elevated arterial $PCO_2$ that climbed during sleep but could be normalized by voluntary hyperventilation. These authors speculated that their patients’ blood gases worsened during sleep because they had a central insensitivity to hypoxia and hypercapnea that could only be overcome by the stimulus of wakefulness. Another explanation recently was provided by Skatrud and colleagues who described a patient with muscular dystrophy, bilateral diaphragmatic paralysis, chronic $CO_2$ retention, and hypersomnolence. Awake hypoventilation was associated with a weak inspiratory effort that could be overcome by forced hyperventilation only until the patient tired; during sleep, his hypoventilation worsened during REM-induced intercostal and accessory muscle inhibition.

Treatment of patients with bilateral diaphragmatic paralysis involves attention to underlying disorders, if present, and relief of respiratory failure. Although some patients require continuous ventilatory support with positive or negative pressure respirators, others can be assisted, particularly at night, with such devices as the rocking bed, which imparts motion to the abdominal contents in time with the respiratory cycle; the chest cuirass, a negative pressure device that is affixed to the front of the chest; and the pneumobelt, which intermittently compresses the abdomen and pushes the diaphragm into the thorax. Diaphragmatic pacing by radiofrequency stimulation has been used in patients with idiopathic hypoventilation and cervical cord injuries, in addition to those with COPD, kyphoscoliosis, and the obesity-hypoventilation syndrome; it may be suitable in some patients with bilateral diaphragmatic paralysis and intact phrenic nerves.

**Respiratory Muscle Training**

Patients with bilateral diaphragmatic paralysis and other disorders characterized by respiratory muscle fatigue also may be helped by respiratory muscle training, a technique introduced by Leith and Bradley. Their study involved four “strength trainers” who performed repeated static maximum inspiratory and expiratory pressure maneuvers while breathing through an obstructed mouthpiece for fifteen minutes a day over a three-month period. At the same time, four “endurance trainers” performed repeated runs of normocapnic hyperpnea to exhaustion while breathing through a rebreathing system that allowed them to try to meet a preset maximum sustainable ventilatory capacity (MSVC) based on their MVV. The strength trainers increased their peak inspiratory and expiratory mouth pressure by 55 percent, but did not change their lung volumes or MSVC. By contrast, the endurance trainers increased their MSVC from 81 to 96 percent without affecting peak mouth pressures. The
improvement in strength and endurance fell off as the subjects stopped exercising; their values returned to pre-study levels after one year.

The improvement in respiratory muscle function after endurance training is these and other patients that such training may help mechanically-ventilated patients, especially those in whom asynchronous breathing indicates respiratory muscle fatigue. In the study cited above, Andersen et al\(^1\) found that the thoracoabdominal discoordination after endurance training is these and other patients while providing respiratory muscle exercise. Downs and co-workers\(^2\) believe that IMV reinforces the proper sequence of muscular efforts necessary for effective ventilation while providing respiratory muscle exercise.

At the same time, some patients who are ventilated at a low IMV rate complain of extreme dyspnea. Rochester and associates\(^3\) have demonstrated that diaphragmatic contraction can be reduced to zero in patients with severe COPD who are treated with negative pressure ventilation; coincident with this is a loss of dyspnea independent of improvement in arterial blood gases. These investigators feel that resting overburdened muscles with negative pressure breathing may aid patients with chronic respiratory failure. It appears that respiratory muscle relaxation is preferable to aggressive training in certain persons, and that not all patients with respiratory failure profit from the increased work of breathing associated with IMV.

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