Impact of diaphragmatic contraction on the stiffness of the canine mediastinum

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De Troyer A. Impact of diaphragmatic contraction on the stiffness of the canine mediastinum. J Appl Physiol 105: 887–893, 2008. First published July 17, 2008; doi:10.1152/japplphysiol.00198.2008.—To assess the coupling between a particular hemidiaphragm and the individual lungs, the left and right phrenic nerves were separately stimulated in anesthetized dogs, and the mean changes in pleural pressure over the two lungs were evaluated by measuring the changes in airway opening pressure (ΔPao) in the two bronchial trees. Stimulation induced a fall in Pao in both lungs. However, ΔPao in the contralateral lung was only 65% of that in the ipsilateral lung. Thus, although the canine ventral mediastinum is a delicate structure, it sustained a significant pressure gradient. The hypothesis was then considered that this gradient was allowed to develop through the stretching and stiffening of the mediastinum caused by the descent of the diaphragm, and it was tested by measuring ΔPao in the two lungs during isolated, unilateral contraction of the inspiratory intercostal muscles. In this condition, ΔPao in the contralateral lung was 92% of that in the ipsilateral lung. A model analysis of the respiratory system led to the estimate that mediastinal elastance was ~25 times greater during diaphragmatic contraction than during unilateral intercostal contraction. These observations indicate that 1) a particular hemidiaphragm has an expanding action on both lungs and 2) during contraction, however, it makes the mediastinum stiffer so that the pressure transmission from the ipsilateral to the contralateral pleural cavity is reduced. These observations imply that the mediastinum may play a significant role in determining the pressure-generating ability of the diaphragm.

chest wall mechanics; respiratory muscles; mediastinal elastance

IT IS WELL ESTABLISHED that, in cats, dogs, and humans, the right and left halves of the diaphragm receive separate motor supply from the right and left phrenic nerves, respectively (1, 13, 14, 20, 25), and indeed hemidiaphragmatic paralysis is a familiar condition in respiratory medicine (10, 11, 19). Several lines of evidence have been provided, however, indicating that a particular hemidiaphragm has an expanding action on both lungs. Specifically, radiographic studies of diaphragm silhouette in dogs have shown that isolated stimulation of one phrenic nerve causes both a large caudal displacement of the active hemidiaphragm and a smaller caudal displacement of the contralateral, inactive hemidiaphragm (4, 5). Also, the active hemidiaphragm pulls the central tendon laterally and induces a shift of the mediastinum away from the inactive side (4). Such a mediastinal displacement, combined with the caudal displacement of the inactive hemidiaphragm, implies that the pleural cavity opposed to the inactive hemidiaphragm expands. In addition, pressure measurements in dogs have shown that, during unilateral phrenic nerve stimulation, pleural surface pressure over the contralateral lung falls, in particular at the apex of the lung (2). However, the magnitude of the expanding action of the active hemidiaphragm on the contralateral vs. the ipsilateral lung is unknown.

The initial objective of the present study was to assess the mechanical coupling between a particular hemidiaphragm and the individual lungs. The right and left phrenic nerves were thus separately stimulated in anesthetized dogs, and the mean changes in pleural pressure (ΔPpl) over the two lungs were evaluated by measuring the changes in airway opening pressure (ΔPao) in the two bronchial trees. Stimulation did cause a fall in Pao in both lungs, but the pressure fall in the contralateral lung was substantially smaller than that in the ipsilateral lung. Thus, although the ventral part of the canine mediastinum consists only of a thin transparent sheet of connective tissue (9), it sustained a significant pressure gradient. The hypothesis was then considered that this gradient was allowed to develop through the stiffening of the mediastinum induced by diaphragmatic contraction, and this hypothesis was tested by measuring ΔPao in the two lungs during unilateral contraction of the intercostal muscles with the diaphragm inactive.

METHODS

The studies were carried out on 12 adult cross-breed dogs (14–34 kg) anesthetized with pentobarbital sodium (initial dose, 30 mg/kg iv), as approved by the Animal Ethics and Welfare Committee of the Brussels School of Medicine. The animals were placed in the supine position, intubated with a cuffed endotracheal tube, and connected to a mechanical ventilator (Harvard pump, Chicago, IL). A venous cannula was inserted in the forelimb to give maintenance doses of anesthetic, and the C5 and C6 phrenic nerve roots were isolated bilaterally through a midline incision of the neck, after which a tracheostomy was performed to insert two endobronchial tubes (n° 5–7) in the right and left main stem bronchi. The tubes were positioned under endoscopic guidance to ensure patency of all lobar bronchi, and they were tethered to the tracheal rings below and above the site of tracheostomy to avoid any inadvertent displacement later. A differential pressure transducer (Validyne, Northridge, CA) was then connected to a side port of each endobronchial tube to measure ΔPao in each lung, after which two experimental protocols were followed.

Experiment 1. Six animals were studied first to assess the pressure changes produced in the two lungs by unilateral diaphragmatic contraction. The C5 and C6 phrenic nerve roots were laid over two pairs of insulated stainless steel stimulating electrodes, and the animal was made apneic by mechanical hyperventilation. After the ventilator was stopped, the two endobronchial tubes were occluded at resting end

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tion and to compare these changes with those produced by unilateral 
changes produced in the two lungs by unilateral intercostal contrac-
demonstrated by the suppression of inspiratory EMG activity. Post-
each animal.

Experiment 2. Six animals were studied next to assess the pressure changes produced in the two lungs by unilateral intercostal contraction and to compare these changes with those produced by unilateral diaphragmatic contraction. In each animal, after the phrenic nerve 
roots were isolated and the two main stem bronchi were intubated, the rib cage and intercostal muscles were exposed on both sides of the chest from the first to the tenth rib by reflection of the skin and the superficial muscle layers, including the scalenes, and \( \Delta P_{\text{ao}} \) in the two lungs were measured during separate, rectangular stimulation of the right and left C5–C6 phrenic nerve roots, as described in experiment 1. The C5, C6, and C7 phrenic nerve roots on both sides were then infiltrated with 2% lidocaine (lignocaine) and sectioned to induce a complete paralysis of the diaphragm. The internal intercostal nerves in all interspaces from the first to the eighth were also exposed at the chondrocostal junctions on either the right (4 animals) or the left (2 animals) side, and they were sectioned to induce paralysis of the parasternal intercostal muscles in one hemithorax. The external inter-
costal muscles in the same interspaces were also sectioned from the costochondral junctions to the spine; the section, therefore, included the levator costae muscles. Finally, the vasi were sectioned bilaterally so that breathing frequency remained low and the \( \Delta P_{\text{ao}} \) generated in the two lungs by the intercostal muscles could be accurately mea-
ured.

After surgery was completed, two pairs of silver hook electrodes spaced 3–4 mm apart were implanted in the parasternal and external intercostal muscles in the intact hemithorax. Each electrode pair was placed in parallel fibers and inserted in the muscle area known to receive the greatest inspiratory drive. Thus implantation of the parasternal intercostal electrodes was made in the third interspace in the muscle bundles situated near the sternum (7, 21, 23), and the external intercostal electrodes were implanted in the dorsal portion of the second interspace, immediately ventral to the rib angle (12, 18, 22). The two electromyographic (EMG) signals were processed with amplifiers (model 830/1, CWE, Ardmore, PA), band-pass filtered below 100 and above 2,000 Hz, and rectified before their passage through leaky integrators with a time constant of 0.2 s.

The animal was allowed to recover for 30 min after instrumenta-
tion, after which it was disconnected from the ventilator and sponta-
neous breathing was allowed to resume. The inspiratory effort thus increased progressively in magnitude from breath to breath, as shown by the gradual increase in the peak height of the integrated parasternal and external intercostal EMG signals, and every 5–10 breaths the two endotracheal tubes were occluded at end-expiration for a single inspiratory effort. Seven to fifteen occluded breaths of increasing sizes were recorded, after which the animal was reconnected to the venti-
lator and hyperventilated again. Three runs of spontaneous breathing corresponding to a total of 20–40 occluded breaths were recorded in each animal.

Inactivation of the parasternal intercostals in one hemithorax was demonstrated by the suppression of inspiratory EMG activity. Post-
mortem examination of this hemithorax also confirmed that both the external intercostal and levator costae muscle in each interspace was entirely severed. However, eliminating the diaphragm and all the inspiratory intercostals in one hemithorax from the act of breathing might have elicited inspiratory contraction of several neck muscles, such as the sternohyoid, the sternothyroid, and the sternomastoid. These muscles are not used during breathing under normal circum-
stances (3), but by contracting in our animals they would generate a \( \Delta P_{\text{ao}} \) in both lungs such that the pressure developed by the active intercostal muscles in the contralateral (inactive) hemithorax would be overestimated. To evaluate this potential confounding factor, the electromyograms of these neck muscles were examined in each animal. And indeed, two of six animals did not have any EMG activity, but four animals showed consistent phasic inspiratory EMG activity during the larger breaths. In these animals, the three neck muscles were bilaterally severed. We can ensure, therefore, that in each animal the parasternal and external intercostal muscles on one side of the chest were the only muscles active during inspiration.

The animals in both experiments appeared to remain at a satisfac-
tory depth of anesthesia throughout. They did not react to painful stimuli and made no spontaneous movements other than respiratory movements both during surgery and during the measurements, includ-
ing during phrenic nerve stimulation. Also, they had no pupillary light reflex and no corneal reflex, thus indicating a deep level of anesthesia. Rectal temperature was kept constant between 36 and 38°C with infrared lamps. At the end of the experiment, the animals were given an overdose (30–40 mg/kg iv) of anesthetic.

Data analysis. For each stimulation frequency (rectangular trains) of the right C5–C6 phrenic nerve roots in each animal of experiment 1, the \( \Delta P_{\text{ao}} \) recorded in the two lungs were averaged over the two trials. The values obtained in the left lung for the different stimulation frequencies were then plotted against the values obtained in the right lung, and the relationship between these values was fitted by a linear regression equation (\( r \) value between 0.997 and 0.999). The \( \Delta P_{\text{ao}} \) recorded during rectangular stimulation of the left C5–C6 phrenic nerve roots and those recorded during ramp stimulations were ana-
yzed similarly, although the values recorded during ramp stimula-
tions were measured at 0.2-s intervals.

The \( \Delta P_{\text{ao}} \) recorded during phrenic nerve stimulation in experiment 2 were analyzed by using the same procedure. However, because there was no consistent difference between the data obtained during stimula-
tion of the right vs. the left phrenic nerve, the relationship for the two nerves between pressure in the contralateral lung and pressure in the ipsilateral lung was fitted by a single linear regression equation (\( r \) value between 0.970 and 0.997). In each animal, the \( \Delta P_{\text{ao}} \) values obtained in the two lungs during each occluded breath were also measured, and as for phrenic nerve stimulation, the values recorded in the inactive hemithorax were plotted against the values recorded in the active hemithorax. The relationship between these values was also fitted by a linear regression equation (\( r \) value between 0.993 and 0.999). It is worth pointing out that these \( \Delta P_{\text{ao}} \) values were measured relative to the onset of the parasternal and external intercostal inspiratory burst. Consequently, the values that were considered in the calculations resulted exclusively from the con-
traction of the inspiratory intercostals in the intact hemithorax and were not corrupted by the relaxation of the triangularis sterni and the internal intercostals in the lower interspaces at the end of expiration (8, 22).

The slopes of these relationships were finally averaged over the animal group, and they are presented as means ± SE. Statistical comparison between the slopes for unilateral intercostal contraction and those for unilateral phrenic nerve stimulation (experiment 2) was made by using a paired \( t \)-test. The criterion for statistical significance was taken as \( P < 0.05 \).
RESULTS

Pressure changes during phrenic nerve stimulation (experiment 1). The records of $P_{ao}$ in the right and left lungs obtained during isolated, rectangular stimulation of the right C5–C6 phrenic nerve roots in a representative animal are shown in Fig. 1A, and the values of $\Delta P_{ao}$ measured in the left lung for the different stimulation frequencies are plotted against the values of $\Delta P_{ao}$ measured in the left lung in Fig. 1B. The values of $\Delta P_{ao}$ measured in the right lung during stimulation of the left C5–C6 phrenic nerve roots in the same animal are also plotted against the values of $\Delta P_{ao}$ measured in the left lung in this figure. Stimulating the right or the left phrenic nerve induced a fall in $P_{ao}$ in both lungs. For any stimulation frequency, however, $\Delta P_{ao}$ in the contralateral lung was smaller than $\Delta P_{ao}$ in the ipsilateral lung. In this particular animal, therefore, the slope of the linear relationship between $\Delta P_{ao}$ in the contralateral lung and $\Delta P_{ao}$ in the ipsilateral lung during stimulation of the right phrenic nerve was 0.53, and the slope of the corresponding relationship for the left phrenic nerve was 0.69. Similar results were obtained in all animals (Table 1). For the right phrenic nerve in the six animals, the slope of the linear relationship between $\Delta P_{ao}$ in the left vs. the right lung ranged from 0.47 to 0.83 and was, on average, 0.66 ± 0.05. For the left phrenic nerve, the slope of the relationship similarly ranged from 0.56 to 0.69 and averaged 0.62 ± 0.02.

Similar results were also obtained during ramp stimulation of the phrenic nerves, as shown for one representative animal in Fig. 2. In any particular animal, the slopes of the relationships between $\Delta P_{ao}$ in the contralateral lung vs. $\Delta P_{ao}$ in the ipsilateral lung during such stimulations were, in fact, nearly identical to those obtained during rectangular stimulations (Table 1).

Pressure changes during unilateral intercostal contraction (experiment 2). The records of $P_{ao}$ in the right and left lungs obtained in a representative animal during an occluded breath performed by the parasternal and external intercostal muscles in the left hemithorax are shown in Fig. 3; the electromyograms of these muscles are also shown as the time reference. An additional procedure was performed in this study. Thus, during unilateral contraction of the inspiratory intercostals, the

Table 1. Ratios of the pressure changes in the contralateral vs. the ipsilateral lung during unilateral phrenic nerve stimulation

<table>
<thead>
<tr>
<th>Dog</th>
<th>Rectangular Stimulation</th>
<th>Ramp Stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>1</td>
<td>0.68</td>
<td>0.61</td>
</tr>
<tr>
<td>2</td>
<td>0.73</td>
<td>0.56</td>
</tr>
<tr>
<td>3</td>
<td>0.47</td>
<td>0.58</td>
</tr>
<tr>
<td>4</td>
<td>0.53</td>
<td>0.69</td>
</tr>
<tr>
<td>5</td>
<td>0.83</td>
<td>0.66</td>
</tr>
<tr>
<td>6</td>
<td>0.74</td>
<td>0.63</td>
</tr>
<tr>
<td>Mean</td>
<td>0.66</td>
<td>0.62</td>
</tr>
<tr>
<td>SE</td>
<td>0.05</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Note that these values are the slopes of the relationship between change in airway opening pressure ($\Delta P_{ao}$) in the contralateral lung and $\Delta P_{ao}$ in the ipsilateral lung during separate rectangular or ramp stimulation of the right and left C5–C6 phrenic nerve roots. Differences between stimulation of the right and left phrenic nerves did not reach the level of statistical significance. At peak inspiration, $\Delta P_{ao}$ in the left and the right lung was $-6.75$ and $-6.15$ cmH$_2$O, respectively, and this small inter-pulmonary difference was observed in all occluded breaths whatever their size (Fig. 4A). As a result, the linear relationship between $\Delta P_{ao}$ in the right vs. the left lung for all the breaths had a slope of 0.88. In contrast, the relationship between $\Delta P_{ao}$ in the contralateral vs. the ipsilateral lung obtained during unilateral stimulation of the phrenic nerves in this animal had a slope of 0.63 (Fig. 4B).

All animals of the study showed a similar difference between unilateral intercostal contraction and unilateral phrenic nerve stimulation (Table 2). For the animal group, although the largest $\Delta P_{ao}$ values recorded during intercostal contraction varied among the six animals from $-6.75$ to $-12.00$ cmH$_2$O, the slope of the relationship between $\Delta P_{ao}$ in the contralateral vs. the ipsilateral lung was $0.92 \pm 0.01$. In agreement with the results of experiment 1, however, the slope of the corresponding relationship during phrenic nerve stimulation was only $0.67 \pm 0.02$ ($P < 0.001$).

An additional procedure was performed in this study. Thus, during unilateral contraction of the inspiratory intercostals, the

![Fig. 1](http://jap.physiology.org/)

Fig. 1. A: traces of airway opening pressure ($P_{ao}$) in the right and left lungs obtained during isolated 15- and 30-Hz stimulation of the right C5–C6 phrenic nerve roots in a representative animal with the airways closed. B: relationship between $\Delta P_{ao}$ in the left (contralateral) lung and $\Delta P_{ao}$ in the right (ipsilateral) lung during stimulation of the right phrenic nerve at different frequencies from 10 to 30 Hz (● and broken line). The relationship between $\Delta P_{ao}$ in the right (contralateral) lung and $\Delta P_{ao}$ in the left (ipsilateral) lung during isolated stimulation of the left phrenic nerve in the same animal is also shown (○ and dashed line). The solid line is the line of identity.

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ribs in the active hemithorax moved cranially and, at the same
time, the sternum was displaced laterally toward the inactive
side. We were concerned that such a lateral sternal displace-
ment might induce a cranial displacement of the ribs in the
inactive hemithorax and thereby contribute to the fall in Pao in
the contralateral lung. To evaluate the role of this confounding
factor, we periodically applied in every animal external forces
to the sternum to prevent it from moving laterally during
inspiration. As shown by the open circles in Fig. 4A, the
interpulmonary difference in Pao during these breaths was
not larger than that seen during the unimpeded breaths.

DISCUSSION

The results of the study confirmed, in agreement with
previous radiographic observations (4, 5) and measurements of
local pleural pressure (2), that isolated contraction of a hemi-
diaphragm causes bilateral lung expansion. The results also
showed, however, during both rectangular and ramp contrac-
tion, that the fall in Pao in the lung apposed to the inactive
hemidiaphragm is consistently smaller than that in the lung
apposed to the active hemidiaphragm (Figs. 1 and 2); for a
stimulation frequency of 30 Hz, the interpulmonary difference
amounted, on average, to 7.0 ± 0.5 cmH2O. Because these
Pao values were obtained with no airflow, they also represent
the mean Ppl over the two lungs separately. Such interpul-
monary differences in Pao therefore imply that, during he-
midiaphragmatic contraction, there is a significant transmural
pressure across the mediastinum.

Although the ventral mediastinal pleura in the dog only
consists of a thin transparent sheet of connective tissue (9),

Fig. 2. A: traces of ΔPao in the right and left lungs obtained during isolated ramp stimulation of the right C5–C6 phrenic nerve roots in a representative animal
with the airways closed (same animal as in Fig. 1). The stimulation involved a gradual increase in frequency from 10 to 30 Hz over 2.0 s. B: relationship between
ΔPao in the left (contralateral) lung and ΔPao in the right (ipsilateral) lung during the stimulation (● and dashed line). The solid line is the identity line.

Fig. 3. Records of Pao in the right and left lungs obtained during two unimpeded breaths and an occluded breath (arrows) in an animal with complete paralysis
of both the diaphragm and the inspiratory intercostal muscles on the right side of the chest. The parasternal intercostals and external intercostals on the left side,
therefore, were the only muscles active during inspiration; the traces of EMG activity in these two muscles are also shown. Note that, during the occluded breath,
ΔPao in the right lung was only slightly smaller than ΔPao in the left lung.
pressure gradients across the canine mediastinum have been previously reported. Thus, in their studies of the distribution of pleural pressure during passive, single-lung inflation, Hubmayr and Margulies (15) noted that, with inflation, $\Delta P_{pl}$ over the inflated lung increased slightly more than that over the contralateral, noninflated lung. More recently, De Troyer and Leduc (6) recorded $\Delta P_{ao}$ in the two lungs in dogs performing occluded inspiratory efforts before and after single-lung inflation. The $\Delta P_{ao}$ values recorded in the two lungs were equal when the effort was performed with both lungs at FRC, but when the occluded breath occurred after one lung had been inflated, $\Delta P_{ao}$ in the inflated lung was consistently smaller than that in the noninflated lung. Moreover, the interpulmonary difference in $\Delta P_{ao}$ (and $\Delta P_{pl}$) increased gradually with increasing lung volume. To the extent that single-lung inflation stretches the mediastinum, it is reasonable to believe that it would also make it stiffer. The present study did not involve any lung inflation. However, it involved unilateral phrenic nerve stimulation and, with it, a caudal displacement of the diaphragm and a lateral displacement of the central tendon (4). This led us to consider the hypothesis that hemidiaphragmatic contraction would also stretch and stiffen the mediastinum.

To test this hypothesis, we eliminated from the act of breathing both the diaphragm and the intercostal muscles on one side of the chest, such that the entire inspiratory effort was produced by the intercostal muscles in one hemithorax. It was expected that, in this condition, since there was no lung inflation and no diaphragmatic contraction, there would be little or no mediastinal stretching and, therefore, that the $\Delta P_{pl}$ in the two pleural cavities would be equal or nearly equal. And indeed, as shown in Figs. 3 and 4, the interpulmonary differences in $\Delta P_{ao}$ in this condition were very small. Specifically, whereas in hemidiaphragmatic contraction the slope of the relationship between $\Delta P_{ao}$ in the contralateral lung and $\Delta P_{ao}$ in the ipsilateral lung was, on average, 0.65, during isolated unilateral intercostal contraction the slope of the relationship was 0.92. Furthermore, the slope of this relationship remained unchanged when external forces were applied to maintain the sternum in the midline, thus indicating that the connections between the left and right ribs via the sternum played no role in determining the pressure transmission from the active to the inactive hemithorax. On the basis of these observations, the conclusion can therefore be drawn that the canine mediastinum indeed is very flaccid during relaxation and becomes stiffer during diaphragmatic contraction.

A quantitative analysis of the effects of the diaphragm and intercostal muscles on mediastinal stiffness can be made by using a simple model of the respiratory system, as shown in Fig. 5. The muscle and piston at the left of the cylinder represent either the active hemidiaphragm (and passive rib cage) or the active inspiratory intercostals (and passive diaphragm) on the ipsilateral side of the thorax, the two spaces in the cylinder represent the two pleural cavities separated by the mediastinum, and the boundary at the right end of the cylinder represents the contralateral, inactive part of the chest wall. When the muscle on the left contracts, it generates a pressure fall in the ipsilateral pleural cavity, and this pressure fall causes a volume displacement of the mediastinum that, in turn, induces a pressure fall in the contralateral pleural cavity and a volume displacement of the contralateral chest wall. If the pressure falls in the ipsilateral and contralateral pleural cavities are denoted $P_1$ and $P_2$, respectively, the volume displacements of the mediastinum and the contralateral chest wall are denoted

Table 2. Ratios of the pressure changes in the contralateral vs. the ipsilateral lung during unilateral diaphragmatic and intercostal contraction

<table>
<thead>
<tr>
<th>Dog</th>
<th>Diaphragm</th>
<th>Intercostal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1'</td>
<td>0.62</td>
<td>0.88</td>
</tr>
<tr>
<td>2'</td>
<td>0.63</td>
<td>0.92</td>
</tr>
<tr>
<td>3'</td>
<td>0.66</td>
<td>0.90</td>
</tr>
<tr>
<td>4'</td>
<td>0.74</td>
<td>0.97</td>
</tr>
<tr>
<td>5'</td>
<td>0.71</td>
<td>0.94</td>
</tr>
<tr>
<td>6'</td>
<td>0.63</td>
<td>0.88</td>
</tr>
<tr>
<td>Mean</td>
<td>0.67</td>
<td>0.92</td>
</tr>
<tr>
<td>SE</td>
<td>0.02</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Note that these values are the slopes of the relationship between $\Delta P_{ao}$ in the contralateral lung and $\Delta P_{ao}$ in the ipsilateral lung during 1) separate stimulation of the right and left C5–C6 phrenic nerve roots (Diaphragm) and 2) contraction of the inspiratory intercostal muscles on one side of the chest (Intercostal). The slope during unilateral diaphragmatic contraction was consistently smaller than that during unilateral intercostal contraction.
Fig. 5. Diagram of the respiratory system during inspiratory muscle contraction on one side of the chest. The muscle and piston at the left of the cylinder represent the active hemidiaphragm or the active inspiratory intercostals on the ipsilateral side of the thorax, the two spaces in the cylinder represent the two halves of the pleural cavity separated by the mediastinum, and the boundary at the right end of the cylinder represents the contralateral, inactive part of the chest wall. When the muscle on the left contracts, it generates a pressure fall (P1) in the ipsilateral pleural cavity, and this pressure fall induces a volume displacement of the mediastinum (hatched area; ΔVms). This volume displacement causes, in turn, a pressure fall (P2) in the contralateral pleural cavity and, with it, a volume displacement of the contralateral chest wall (ΔVcwc).

ΔVms and ΔVcwc, and the elastance of the mediastinum and the contralateral chest wall is denoted Kms and Kcwc, then the equations of static equilibrium of the system are

\[ P_1 - P_2 = K_{ms} \cdot \Delta V_{ms} \]  

(1)

and

\[ P_2 = K_{cwc} \cdot \Delta V_{cwc} \]  

(2)

Because the volume of each lung in our animals was maintained constant, \( \Delta V_{ms} = \Delta V_{cwc} \). Therefore, dividing Eq. 1 by Eq. 2 yields

\[ (P_1 - P_2)/P_2 = K_{ms}/K_{cwc} \]  

(3)

The values of \( \Delta P_{ao} \) in the two lungs were measured in the animals of experiment 2 for both hemidiaphragmatic contraction and unilateral intercostal contraction, and although the values obtained in the first instance covered a much wider range than those obtained in the second instance, the relationship between pressure in the contralateral cavity and that in the ipsilateral cavity was linear in both instances (Figs. 1 and 4). In addition, the \( \Delta P_{ao} \) values obtained during hemidiaphragmatic contraction at low stimulation frequencies (i.e., 10 to 12 Hz) were similar in magnitude to the highest \( \Delta P_{ao} \) recorded during intercostal contraction. For each individual animal, therefore, these \( \Delta P_{ao} \) values were substituted for \( P_1 \) and \( P_2 \) in Eq. 3, and the values thus calculated for Kms/Kcwc in the two conditions are shown in Table 3. If one assumes that Kcwc is similar for hemidiaphragmatic contraction and unilateral intercostal contraction, it appears that, for the animal group, Kms was 6.5 times greater in the first instance than in the second.

This quantitative result, however, should be taken as a minimal value for two reasons. First, during isolated hemidiaphragmatic contraction, the contralateral (relaxed) hemidiaphragm is stretched (4, 5). Consequently, it should develop passive tension. Also, hemidiaphragmatic contraction causes a rise in Pab, and it would be expected that this pressure rise would be transmitted to the zone of apposition of the contralateral hemidiaphragm. As a result, the lower portion of the contralateral rib cage would expand and reduce the deflation of the upper portion in response to \( \Delta P_{pl} \). Compared with unilateral intercostal contraction, therefore, Kcwc during hemidiaphragmatic contraction should be greater, and Kms should be increased in proportion.

Second, the model analysis rests on the assumption that \( P_2 \) exclusively results from the displacement of the mediastinum, and although this assumption appears reasonable in the case of intercostal contraction, it is incorrect in the case of hemidiaphragmatic contraction. Thus, as we have pointed out above (see INTRODUCTION), isolated contraction of a canine hemidiaphragm at FRC causes not only a lateral displacement of the mediastinum but also a caudal displacement of the inactive hemidiaphragm (4, 5). Both of these displacements should provide a significant contribution to \( \Delta P_{pl} \) in the contralateral pleural cavity. In fact, because the caudal displacement of the inactive hemidiaphragm is, on average, approximately one-third of the displacement of the active hemidiaphragm (4, 5), the \( \Delta P_{pl} \) resulting from this displacement would, as a first approximation, be one-third of the \( \Delta P_{pl} \) in the ipsilateral pleural cavity or one-half of the total \( \Delta P_{pl} \) measured in the contralateral pleural cavity. In other words, if \( \Delta P_{pl} \) in the contralateral cavity were entirely the result of the displacement of the mediastinum, \( P_2 \) in Eq. 3 would be decreased by a factor of 2 and \( (P_1 - P_2) \) would be increased by a similar factor, so that Kms/Kcwc would be increased by a factor of 4. Even if the difference in Kcwc between hemidiaphragmatic and unilateral intercostal contraction were ignored, therefore, the ratio of Kms during hemidiaphragmatic to intercostal contraction would amount to ~25.

On the other hand, it should be acknowledged that the model analysis also assumes that isolated hemidiaphragmatic contraction causes uniform pleural pressure changes over the ipsilateral lung and that these pressure changes are equal to \( \Delta P_{ao} \). The studies by D’Angelo et al. (2) in dogs have shown, however, that bilateral diaphragmatic contraction leads to larger \( \Delta P_{pl} \) over the base of the lung than over the apex. In our animals, therefore, the mean \( \Delta P_{pl} \) produced by the active hemidiaphragm over the ipsilateral side of the mediastinum could well be smaller than the \( \Delta P_{ao} \) values measured in the ipsilateral lung. If so, the actual pressure gradients across the mediastinum could be smaller than the interpulmonary differences in \( \Delta P_{ao} \), and the computed value of Kms for hemidiaphragmatic contraction could be smaller than anticipated on the basis of the increase in Kcwc and the displacement of the inactive hemidiaphragm.

Irrespective of these approximations, the finding that diaphragmatic contraction stiffens the mediastinum implies that the mediastinum, in turn, exerts a cranially oriented force on

Table 3. Computed values for mediastinal elastance during unilateral diaphragmatic contraction and unilateral intercostal contraction relative to the elastance of the contralateral, inactive side of the chest wall

<table>
<thead>
<tr>
<th>Dog</th>
<th>Diaphragm</th>
<th>Intercostal</th>
<th>Diaphragm/Intercostal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1'</td>
<td>0.61</td>
<td>0.13</td>
<td>4.7</td>
</tr>
<tr>
<td>2'</td>
<td>0.59</td>
<td>0.09</td>
<td>6.6</td>
</tr>
<tr>
<td>3'</td>
<td>0.52</td>
<td>0.10</td>
<td>5.2</td>
</tr>
<tr>
<td>4'</td>
<td>0.35</td>
<td>0.03</td>
<td>11.7</td>
</tr>
<tr>
<td>5'</td>
<td>0.41</td>
<td>0.06</td>
<td>6.8</td>
</tr>
<tr>
<td>6'</td>
<td>0.59</td>
<td>0.14</td>
<td>4.2</td>
</tr>
<tr>
<td>Mean</td>
<td>0.51</td>
<td>0.09</td>
<td>5.6</td>
</tr>
<tr>
<td>SE</td>
<td>0.04</td>
<td>0.02</td>
<td>1.1</td>
</tr>
</tbody>
</table>


the diaphragm, and such a force, if large enough, might have significant effects on the mechanics of the muscle. First, it might prevent the muscle from descending excessively, in which case it would limit its lung-expanding action. Second, by opposing muscle shortening, it might also impact on the lung volume dependence of the muscle pressure-generating ability. Although the conventional wisdom maintains that the detrimental effect of increasing lung volume on this ability is exclusively or primarily the result of the decrease in active muscle length (17, 24), it is worth emphasizing that Hubmayr et al. (16) previously reported that, during bilateral phrenic nerve stimulation at different lung volumes in dogs, the decrease in transdiaphragmatic pressure with increasing lung volume was much greater than anticipated on the basis of the decrease in diaphragm length alone. Finally, an axial force exerted by the mediastinum might oppose transmission of tension from one-half of the diaphragm to the other. Although tension in the muscle fibers cannot be assessed directly, this mechanism might account in part for the asymmetrical configuration of the diaphragm during unilateral phrenic nerve stimulation (4, 5).

The extent to which the present observations apply to humans can only be a matter of speculation at this stage. It should be pointed out, however, that the ventral part of the mediastinum in humans is considerably thicker than that in the dog. Therefore, it would be expected that the human mediastinum would be stiffer and that both hemidiaphragmatic contraction and unilateral intercostal contraction would elicit larger pressure gradients across it. Furthermore, and perhaps more important, the central tendon in humans is more firmly attached to the mediastinal structures, in particular the pericardium, than in the dog. On this basis, the speculation could also be offered that, in humans, the descent of the diaphragm during contraction would have a greater effect on the stiffness of the mediastinum and that the mediastinum, in turn, might have a more prominent influence on the action of the muscle.

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