Interaction between the canine diaphragm and intercostal muscles in lung expansion

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Submitted 21 June 2004; accepted in final form 8 November 2004

De Troyer, André. Interaction between the canine diaphragm and intercostal muscles in lung expansion. J Appl Physiol 98: 795–803, 2005. First published November 12, 2004; doi:10.1152/japplphysiol.00632.2004.—Changes in intrathoracic pressure produced by the various inspiratory intercostals are essentially additive, but the interaction between these muscles and the diaphragm remains uncertain. In the present study, this interaction was assessed by measuring the changes in airway opening (ΔPao) or transpulmonary pressure (ΔPtp) in vagotomized, phrenicotomized dogs during spontaneous inspiration (isolated intercostal contraction), during isolated rectangular or ramp stimulation of the peripheral ends of the transected C5 phrenic nerve roots (isolated diaphragm contraction), and during spontaneous inspiration with superimposed phrenic nerve stimulation (combined diaphragm-intercostal contraction). With the endotracheal tube occluded at functional residual capacity, ΔPao during combined diaphragm-intercostal contraction was nearly equal to the sum of the ΔPao produced by the two muscle groups contracting individually. However, when the endotracheal tube was kept open, ΔPtp during combined contraction was 123% of the sum of the individual ΔPtp (P < 0.001). The increase in lung volume during combined contraction was also 109% of the sum of the individual volume increases (P < 0.02). Abdominal pressure during combined contraction was invariably lower than during isolated diaphragm contraction. It is concluded, therefore, that the canine diaphragm and intercostal muscles act synergistically during lung expansion and that this synergism is primarily due to the fact that the intercostal muscles reduce shortening of the diaphragm. When the lung is maintained at functional residual capacity, however, the synergism is obscured because the greater stiffness of the rib cage during diaphragm contraction enhances the ΔPao produced by the isolated diaphragm and reduces the ΔPao produced by the intercostal muscles.

mechanics of breathing; respiratory muscles

IT IS NOW WELL ESTABLISHED that the parasternal and external intercostal muscles contract during the inspiratory phase of the breathing cycle and that the changes in intrathoracic pressure generated by these muscles are essentially additive (2, 29). Thus, when the endotracheal tube in dogs is occluded at resting end expiration [functional residual capacity (FRC)] and the parasternal intercostals or the external intercostals are selectively activated by electrical stimulation, the change (Δ) in airway opening pressure (Pao) produced by the simultaneous, bilateral contraction of the muscles in two interspaces is nearly equal to the sum of the ΔPao observed during bilateral contraction of the muscles in each individual interspace (29). The ΔPao produced by the simultaneous contraction of the parasternal or external intercostals in one or two interspaces on the left and right sides of the sternum is also nearly equal to the sum of the ΔPao produced by separate left and right contraction (2). On the other hand, Di Marco et al. (18) have previously reported that the ΔPao obtained during simultaneous contraction of the canine diaphragm and intercostal muscles at FRC was 17% greater than the sum of the ΔPao resulting from their separate contraction. In addition, although the diaphragm and the parasternal intercostals were observed to shorten during both simultaneous and separate stimulation, both muscles shortened less in the first instance than in the second. Di Marco et al. (18) concluded, therefore, that the interaction between the diaphragm and the inspiratory intercostals is synergistic, and they further concluded that this synergism is largely related to the length-tension characteristics of the muscles, an intercostal muscle contraction in particular leading to an increase in diaphragmatic muscle length and, hence, to an increase in diaphragmatic force.

The technique used by these investigators to activate the inspiratory intercostal muscles and to obtain a quantitative assessment of the diaphragm-intercostal interaction, however, was not optimal. Indeed, the intercostal muscles were stimulated by applying rectangular trains of square pulses through an electrode positioned in the epidural space, and the diaphragm was stimulated by applying trains of similar pulses to the phrenic nerves in the neck. The precise mechanism of muscle activation by an epidural electrode remains uncertain, so the intensity and extent of intercostal activation during isolated stimulation may be different from that during simultaneous intercostal-diaphragm stimulation. More importantly, the epidural electrode does not reproduce the topographic gradients of parasternal and external intercostal activity that occur during spontaneous breathing (15, 21, 25, 27, 28). Instead, it induces a forceful and uniform activation of the muscles over a very large fraction of the rib cage. This technique also elicits strong contraction of all the expiratory muscles of the rib cage, including the triangularis sterni, as well as a number of muscles that, in the dog, are not involved in the act of breathing, such as the internal intercostals in the cranial interspaces, the serrati, the pectoralis, the scalenes and the sternomastoids.

These problems prompted us to reevaluate the interaction between the canine diaphragm and inspiratory intercostal muscles. The phrenic nerves in each animal were sectioned in the neck to induce a complete paralysis of the diaphragm, and the animals were breathing spontaneously. Consequently, only the inspiratory intercostals were activated, and the normal topo-
graphic distribution of neural drive to these muscles was maintained. Also, the diaphragm in a first series of experiments was activated by applying rectangular pulses to the distal ends of the phrenic nerves, but in a second series of experiments the nerves were given ramp stimulations so as to reproduce more closely the pattern of diaphragmatic and inspiratory intercostal activation during breathing. With the endotracheal tube occluded at FRC, $\Delta P_{ao}$ during simultaneous diaphragm-intercostal contraction was found in both experiments to be nearly the same as the sum of the $\Delta P_{ao}$ generated by the two sets of muscles individually. It was concluded, therefore, that separate contraction of the two muscles involves one or several mechanisms that compensate for the beneficial effect of the intercostals on the pressure-generating ability of the diaphragm, and the hypothesis was raised that these mechanisms are related to alterations in rib cage compliance during airway occlusion. This hypothesis was finally tested by examining the diaphragm-intercostal interaction during unimpeded breathing.

**METHODS**

Twenty-five adult mongrel dogs (13–38 kg) anesthetized with pentobarbital sodium (initial dose, 30 mg/kg iv) were studied as approved by the Animal Ethics and Welfare Committee of the Brussels School of Medicine. The animals were placed in the supine posture and intubated with a cuffed endotracheal tube, and a venous catheter was inserted in the forelimb to give maintenance doses of anesthetic. The rib cage and intercostal muscles were exposed on the right side of the chest from the 1st to 10th rib by deflection of the skin and underlying muscle layers, and the abdomen was opened by a midline incision from the xiphistemum to the umbilicus to insert a balloon-catheter system between the liver and the stomach; the balloon-catheter system placed in the abdominal cavity; the abdominal wall was then tightly sealed in two layers, after which the vagi and the C3 and C7 phrenic nerve roots were isolated bilaterally in the neck, infiltrated with 2% lidocaine (lignocaine), and sectioned. The right and left C5 phrenic nerve roots were also isolated and sectioned, but their distal ends were laid over two pairs of insulated stainless steel stimulating electrodes so that the diaphragm could be activated later.

**Measurements**

$P_{ao}$ and abdominal pressure ($P_{ab}$) were measured in each animal with differential pressure transducers (Validyne, Northridge, CA) connected, respectively, to a side port of the endotracheal tube and to the balloon-catheter system placed in the abdominal cavity; the abdominal balloon was filled with 1.0 ml of air. The electromyograms of the parasternal and external intercostal muscles in the third interspace were recorded with pairs of silver hook electrodes spaced 3–4 mm apart. Each electrode pair was implanted in parallel fibers in the portion of muscle receiving the greatest neural inspiratory drive; implantation of the parasternal electrodes, therefore, was made in the muscle bundles near the sternum (15), and implantation of the external intercostal electrodes was made in the dorsal portion of the muscle, immediately ventral to the angle of the ribs (21, 25, 28). The two electromyographic (EMG) signals were processed with amplifiers (model 8301; 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.

Airflow at the endotracheal tube was also measured in each animal with a heated Fleisch pneumotachograph connected to a differential pressure transducer, and the flow signal was integrated to assess the changes in lung volume. In addition, in 21 animals, the craniocaudal (axial) motion of the fourth rib was measured by a linear displacement transducer (Schaevitz, Pennsauken, NJ), as previously described (13).

The animal was allowed to recover for 30 min after instrumentation, after which measurements of $P_{ao}$, $P_{ab}$, tidal volume, intercostal EMG activity, and axial rib motion were made. Three experimental protocols were then followed.

**Protocols**

**Experiment 1.** The interaction between the diaphragm and inspiratory intercostal muscles in the generation of $P_{ao}$ was first studied in 10 animals (13–38 kg). The animal was spontaneously breathing room air, and every 5–10 breaths the inspiratory line of a Hans-Rudolph valve attached to the tracheal tube was occluded during the expiratory pause for a single inspiratory effort. Because all phrenic nerve roots were sectioned, these breaths were due to the isolated contraction of the inspiratory intercostals. In one-half of these occluded breaths, however, electrical stimuli were applied to the distal ends of the transected right and left C5 phrenic roots. The stimuli were rectangular trains of square pulses of 0.1-ms duration and 20-Hz frequency with a voltage of 2 V. Indeed, although diaphragmatic compound muscle action potentials were not recorded in these animals, previous studies using the same stimulator (model S44, Grass, Quincy, MA) and the same electrodes have shown that this voltage was well above the threshold current necessary to produce a compound muscle action potential of maximal amplitude (10).

The investigator received continuous feedback of parasternal intercostal activity via a loudspeaker, which allowed the investigator to initiate the stimuli together with or shortly after the onset of intercostal muscle contraction and to maintain the stimuli until the onset of the expiratory pause. At least 10 occluded breaths with phrenic nerve stimulation alternating with 10 occluded breaths without stimulation were recorded in every animal. When these measurements were completed, the animal was made apneic by mechanical hyperventilation (Harvard pump, Chicago, IL), the endotracheal tube was occluded at resting end expiration, and isolated stimulation of the C5 phrenic roots was performed in triplicate.

**Experiment 2.** We were concerned that the interaction between the diaphragm and inspiratory intercostals as assessed in experiment 1 might be affected by the difference between the rectangular patterns of diaphragmatic contraction and the natural, ramp-like pattern of intercostal muscle contraction. In seven animals (23–37 kg), therefore, the distal ends of the C5 phrenic nerve roots were isolated by using another commercially available stimulator (model MP 16; Physitech Elect, Marseille, France) that allowed the stimulus frequency to increase gradually from 10 to 20 Hz during the course of inspiration. As a result, the force generated by the diaphragm increased progressively and continuously in much the same way as the intercostal muscle force did. The experimental procedure was otherwise similar to that used in experiment 1.

**Experiment 3.** Eight animals (21–31 kg) were finally studied to assess the diaphragm-intercostal interaction in lung expansion. Two procedures were performed in each animal. The initial procedure was identical to that used in experiment 1 and involved measuring $\Delta P_{ao}$ during occluded breaths with the intercostal muscles alone, during occluded breaths with superimposed, rectangular stimulation of the C5 phrenic nerve roots, and during isolated stimulation of the phrenic nerve roots. After completion of this procedure, however, a balloon-catheter system filled with 0.5 ml of air was advanced into the midesophagus to measure pleural pressure, and transpulmonary pressure ($P_{tp}$) was obtained with a differential pressure transducer as the difference between Pao and pleural pressure ($P_{tp} = P_{ao} - P_{pleural}$). The position of the esophageal balloon was adjusted by using the occlusion technique (1). Measurements of $P_{tp}$, tidal volume, Pab, intercostal EMG activity, and rib motion were then made, and, as for the initial procedure, rectangular stimulation (20 Hz, 0.1 ms, 2 V) of the C5 phrenic nerve roots was superimposed on intercostal muscle contraction at intervals. In contrast to the initial procedure, however, the endotracheal tube was maintained open throughout. At least 10
breaths with superimposed phrenic nerve stimulation were obtained in each animal. When the measurements were completed, the animal was made apneic, and isolated phrenic nerve stimulation was repeated.

The animals were maintained at a constant, rather deep level of anesthesia throughout the study. Specifically, they had no pupillary light reflex and no movement other than those involved in the act of breathing, including during phrenic nerve stimulation. Rectal temperature was maintained constant between 36 and 38°C with infrared lamps. At the end of the study, the animal was given an overdose of anesthetic (30–40 mg/kg).

Data Analysis

In each animal, the changes in Pao and Pab and the axial rib motions obtained at the peak of the occluded breaths with the intercostal muscles alone (control breaths), during the occluded breaths with superimposed phrenic nerve stimulation (stimulated breaths), and during isolated phrenic nerve stimulation were averaged over all trials. The mean change in Pao obtained during the control breaths was then added to the change in Pao obtained during isolated phrenic nerve stimulation, and the value thus calculated (it will be referred to here as the predicted ΔPao) was compared with the ΔPao measured during the stimulated breathing. Similarly, in each animal of experiment 3, the changes in lung volume, Ptp, Pab, and the axial rib motions obtained during the breaths with superimposed phrenic nerve stimulation and during the immediately preceding nonstimulated (control) breaths were averaged over all trials, and the mean changes in lung volume and Ptp during the stimulated breaths were compared with the predicted values.

Phasic inspiratory EMG activity in the parasternal and external intercostal muscles during the control breaths and the stimulated breaths was quantified by measuring the peak height of the integrated EMG signal in arbitrary units; these measurements were also averaged over all trials. However, to allow comparison between the two muscles in the different animals, the inspiratory EMG activity recorded during the stimulated breaths was subsequently expressed as a percentage of the activity recorded during the control breaths.

Data were finally averaged for the animal group, and they are presented as means ± SE. Statistical comparisons between the measured and predicted values of ΔPao, ΔPtp and lung volume were made by using paired t-tests; moreover, the linear regression of ΔPtp on predicted ΔPtp across the animal group was calculated by using the least squares method. Statistical assessments of the differences in axial rib motion and intercostal EMG activity between the stimulated breaths and the control breaths and of the differences in Pab between the stimulated breaths and isolated phrenic nerve stimulation were also made by paired t-tests. The criterion for statistical significance was taken as P < 0.05.

RESULTS

Diaphragm-Intercostal Interaction in ΔPao During Rectangular Stimulation (Experiment 1)

A representative example of the traces obtained during an occluded control breath, during isolated stimulation of the C5 phrenic nerve roots with a rectangular train of square pulses, and during an occluded breath with superimposed phrenic nerve stimulation is shown in Fig. 1, and the changes in Pao and Pab measured in the 10 animals are summarized in Table 1. As anticipated (13), isolated contraction of the parasternal and external intercostals with the endotracheal tube occluded (Fig. 1A) elicited a cranial displacement of the ribs and a fall in Pao and Pab. At peak inspiration, the cranial rib motion amounted to 8.7 ± 2.0 mm, and ΔPao and ΔPab were −14.3 ± 1.7 and −5.3 ± 0.6 cmH2O, respectively. In contrast, during isolated stimulation of the phrenic nerves (Fig. 1B), the fall in Pao was associated with a rise in Pab and a 6.4 ± 0.6-mm caudal displacement of the ribs. On average, ΔPao during isolated phrenic nerve stimulation was similar to that recorded in the control breaths.

When stimulation of the C5 phrenic nerve roots was superimposed on occluded breaths (Fig. 1C), 8 of 10 animals showed an increase in the inspiratory EMG activity recorded from the external intercostals, and 6 animals had a decrease in the activity recorded from the parasternal EMG activity. Also, the cranial rib motion was markedly reduced in two of six animals and reversed into a caudal motion in the other four animals. For the animal group, the peak integrated EMG signal from the external intercostal during the stimulated breaths thus amounted to 120.7 ± 5.3% of that measured during the control breaths (P < 0.01), the peak parasternal EMG signal was 95.2 ± 2.3% (P = 0.06), and rib motion at peak inspiration was −1.6 ± 1.5 mm (P < 0.001).

The rise in Pab observed during the stimulated breaths was much smaller than that measured during isolated phrenic nerve stimulation in every animal (P < 0.001). However, as shown in Fig. 2, ΔPao values recorded during these breaths were nearly the same as the predicted values. In fact, the measured ΔPao was slightly greater than the predicted value in 7 of 10 animals, but it was similar to the predicted value in 1 animal and smaller than the predicted value in 2 animals. As a result, the difference between the measured ΔPao (−31.5 ± 2.6 cmH2O) and the predicted ΔPao (−30.5 ± 2.5 cmH2O) for the animal group was not statistically significant (P = 0.4).

Diaphragm-Intercostal Interaction in ΔPao During Ramp Stimulation (Experiment 2)

Figure 3 shows the records obtained during an occluded control breath, during isolated ramp stimulation of the C5 phrenic nerve roots, and during an occluded breath with superimposed ramp stimulation of the phrenic nerves in a representative animal. Isolated ramp stimulation of the phrenic nerves induced progressive, rather than abrupt, changes in Pao and Pab and caused progressive caudal rib motion (Fig. 3B). The changes in pressure recorded at peak stimulation, however, were nearly the same as those obtained with rectangular stimulation (Table 1), and the caudal rib motion similarly averaged 5.7 ± 1.5 mm.

Superimposing such stimulations to occluded breaths also produced essentially similar results as rectangular stimulations. Thus, relative to the control breaths, external intercostal EMG activity increased to 125.4 ± 15.0% (P = 0.14), parasternal intercostal activity decreased to 92.6 ± 2.4% (P < 0.05), and the cranial rib motion decreased markedly from 10.5 ± 0.9 to 1.9 ± 2.2 mm (P < 0.001). Also, ΔPab during the stimulated breaths was consistently smaller than during isolated phrenic nerve stimulation (P < 0.001), and the measured ΔPao was greater than the predicted value in only four of seven animals (Fig. 2). For the animal group, therefore, the difference between the measured ΔPao (−29.5 ± 3.3 cmH2O) and the predicted value (−27.7 ± 3.7 cmH2O) did not reach the level of statistical significance (P = 0.15).
Diaphragm-Intercostal Interaction in Lung Expansion
(Experiment 3)

The records obtained in a representative animal with the endotracheal tube open are shown in Fig. 4, and the pressure changes measured in the eight animals both with the tube open and the tube occluded are summarized in Table 2. Opening the endotracheal tube attenuated the response of parasternal and external intercostal muscles (Fig. 1). Traces of airway opening pressure (Pao), abdominal pressure (Pab), and electromyographic (EMG) activity of the parasternal and external intercostal muscles (3rd interspace) obtained in a representative animal during an occluded breath with the intercostal muscles alone (A), during isolated rectangular stimulation (20 Hz) of the C5 phrenic nerve roots in the neck (B), and during an occluded breath with superimposed stimulation (stimul.) of the C5 phrenic nerve roots (C). The horizontal dashed line in C corresponds to the Pao that would be obtained at peak inspiration if the effects of the inspiratory intercostals and diaphragm were perfectly additive. Note that Pab during the occluded breath with superimposed phrenic nerve stimulation is lower than that during isolated stimulation. Note also that external intercostal EMG activity is greater during the occluded breath with superimposed stimulation than during the occluded breath without stimulation.

Table 1. Pressure changes produced by the intercostal muscles and the diaphragm during isolated and combined contraction

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<th>Intercostal Muscles</th>
<th>Diaphragm</th>
<th>Intercostal Muscles + Diaphragm</th>
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<tr>
<td>Rectangular stimulation of phrenic nerves (experiment 1)</td>
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<tr>
<td>ΔPao, cmH2O</td>
<td>-14.3±1.7</td>
<td>-16.2±2.2</td>
<td>-31.5±2.6</td>
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<tr>
<td>ΔPab, cmH2O</td>
<td>-9.3±0.6</td>
<td>+3.7±0.5</td>
<td>+1.4±0.7</td>
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<tr>
<td>Ramp stimulation of phrenic nerves (experiment 2)</td>
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<tr>
<td>ΔPao, cmH2O</td>
<td>-14.8±2.1</td>
<td>-12.9±2.6</td>
<td>-29.5±3.3</td>
</tr>
<tr>
<td>ΔPab, cmH2O</td>
<td>-5.3±0.6</td>
<td>+3.9±0.6</td>
<td>+0.6±0.7</td>
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Data are means ± SE values obtained in the 10 animals of experiment 1 and the 7 animals of experiment 2. ΔPao, change in airway opening pressure; ΔPab, change in abdominal pressure.

Fig. 2. Comparison between the change (Δ) in Pao measured during combined diaphragm-intercostal contraction and the sum of the ΔPao measured during isolated contraction of the 2 sets of muscles (predicted ΔPao). Individual data was obtained in the 10 animals of experiment 1, in which the phrenic nerves were given rectangular stimulation (●), and in the 7 animals of experiment 2, in which the nerves were given ramp stimulation (○). The solid line is the line of identity.
external intercostals to phrenic stimulation but did not fundamentally alter it. Thus, with the airway occluded, parasternal and external intercostal inspiratory activity during the stimulated breaths was, respectively, 94.6 ± 2.0 and 126.8 ± 10.8% of the activity measured during the control breaths ($P < 0.05$ for both); similarly, with the airway open, parasternal and external intercostal activity during the stimulated breaths was 97.9 ± 1.2 and 117.4 ± 12.1%, respectively ($P = \text{not significant}$). Also, whether the airway was open or occluded, the rise in Pab during the stimulated breaths was significantly smaller ($P < 0.01$) than that during isolated phrenic nerve stimulation (Table 2).

However, although the ribs moved caudally during isolated phrenic nerve stimulation both with the airway open and with the airway occluded, this motion was much smaller with the airway open ($-1.5 \pm 0.4 \text{ vs. } -4.7 \pm 1.3 \text{ mm}; P < 0.02$). Consequently, whereas the ribs moved 1.6 ± 1.4 mm caudally during the stimulated breaths with the airway occluded, with the airway open they moved 7.0 ± 1.4 mm cranially ($P < 0.01$). In addition, whereas the measured $\Delta$Pao (airway occluded) was similar to the predicted value in two of the eight animals and smaller than the predicted value in two animals, the measured $\Delta$Ptp (airway open) was greater than the predicted value in every animal (Fig. 5). As a result, the measured $\Delta$Pao for the animal group was only 103.9 ± 2.6% of the predicted value ($P = \text{not significant}$), but the measured $\Delta$Ptp amounted to 122.7 ± 4.2% of the predicted value ($P < 0.001$). The measured $\Delta$Ptp was closely related to the predicted $\Delta$Ptp ($r = 0.946; P < 0.001$), and the slope of the linear relationship was 1.23. The increase in lung volume during the stimulated breaths (692 ± 81 ml) was also greater than the predicted value (635 ± 68 ml; $P < 0.05$).

**DISCUSSION**

Studies of the mechanics of the diaphragm in animals (23, 24, 31–33) and in humans (7, 34) have clearly established that the pressure obtained in response to a given stimulation of the phrenic nerves decreases rapidly as lung volume is passively increased above functional residual capacity. Conversely, pressure increases as lung volume decreases toward residual volume. This influence of lung volume on the pressure-generating
ability of the diaphragm is primarily determined by muscle length, an increase in lung volume leading to a decrease in muscle length, and vice versa. Although we did not measure diaphragmatic muscle length in the present study, our animals invariably had a smaller rise in Pab when phrenic nerve stimulation was superimposed on intercostal muscle contraction than when stimulation was performed in isolation. This suggests, in agreement with the measurements of Di Marco et al. (18), that the diaphragm in our animals was longer in the first instance than in the second. Consequently, it would be expected that its pressure-generating ability would be greater. In addition, although the effect of diaphragmatic contraction on the pressure-generating ability of the inspiratory intercostals is unknown, it would also be expected that the change in intrathoracic pressure during combined diaphragm-intercostal contraction would be greater than the sum of the pressure changes produced by the two sets of muscles contracting individually.

In agreement with this prediction, the \[ \Delta P_{\text{Ptp}} \] measured during combined diaphragm-intercostal contraction was 109% of the sum of the \[ \Delta P_{\text{Ptp}} \] produced by the muscles during separate contraction (Fig. 5B). The measured \[ \Delta P_{\text{Ptp}} \] was also closely related to the predicted value across the animal group, and the slope of the linear relationship was 1.23, thus confirming that the average increase was 23%. In addition, because of the sigmoid shape of the pressure-volume curve of the lung, such that, at high lung volumes, large changes in pressure produce only small changes in volume, the increase in lung volume during combined diaphragm-intercostal contraction would be expected to be hardly greater or to be smaller than the sum of the increases in lung volume produced by the two muscles contracting separately. To the extent that our animals had complete paralysis of the diaphragm and so breathed most of the time with the intercostal muscles alone, lung expansion could be further limited. Indeed, there is ample evidence, beginning with the work in dogs by Mead and Collier (30), that breathing at a small constant tidal volume is associated with an increase in the surface tension of the alveolar lining layer and with the development of atelectasis, and thereby leads to a decrease in pulmonary compliance (35, 37). Yet, despite these confounding factors, the increase in lung volume during combined diaphragm-intercostal contraction was 109% of the sum of the individual increases in lung volume. The conclusion must be drawn, therefore, that the diaphragm and inspiratory intercostals do act synergistically on the lung during breathing.

However, when the airway was occluded at FRC, \[ \Delta P_{\text{Pao}} \] during combined diaphragm-intercostal contraction was nearly equal to the sum of the \[ \Delta P_{\text{Pao}} \] produced by the two muscles during separate contraction (Figs. 2 and 5A). This result was obtained with both rectangular and ramp stimulation of the phrenic nerves, thus indicating that the pattern of diaphragmatic contraction was not a determining factor. If the diaphragm and inspiratory intercostals were activated equally

<p>| Table 2. Pressure and volume changes produced by the intercostal muscles and the diaphragm during isolated and combined contraction with the airway occluded and open |
|---------------------------------|-----------------|-----------------|-----------------|</p>
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<th>Intercostal Muscles</th>
<th>Diaphragm</th>
<th>Intercostal Muscles + Diaphragm</th>
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<tr>
<td>Airway occluded</td>
<td>[ \Delta P_{\text{Pao}}, \text{cmH}_2\text{O} ]</td>
<td>[-11.1 \pm 1.5 ]</td>
<td>[-12.4 \pm 2.0 ]</td>
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<tr>
<td></td>
<td>[ \Delta P_{\text{Pab}}, \text{cmH}_2\text{O} ]</td>
<td>[-5.6 \pm 0.7 ]</td>
<td>[+4.3 \pm 0.4 ]</td>
</tr>
<tr>
<td>Airway open</td>
<td>[ \Delta P_{\text{Ptp}}, \text{cmH}_2\text{O} ]</td>
<td>[+4.0 \pm 0.7 ]</td>
<td>[+4.0 \pm 0.3 ]</td>
</tr>
<tr>
<td></td>
<td>[ \Delta P_{\text{Pab}}, \text{cmH}_2\text{O} ]</td>
<td>[-3.8 \pm 0.5 ]</td>
<td>[+4.8 \pm 0.4 ]</td>
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<tr>
<td>[ \Delta \text{Lung volume, ml} ]</td>
<td>[322 \pm 36 ]</td>
<td>[313 \pm 59 ]</td>
<td>[692 \pm 81 ]</td>
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Data are means \( \pm \) SE values obtained from the 8 animals of experiment 3. \[ \Delta P_{\text{Ptp}} \] change in transpulmonary pressure.

Fig. 4. A: traces of lung volume, transpulmonary pressure (Ptp), Pab, axial rib motion, and EMG activity of the parasternal and external intercostal muscles obtained in a representative animal during 2 breaths with the intercostal muscles alone and a breath with superimposed, rectangular stimulation of the C5 phrenic nerve roots. The horizontal dashed lines correspond to the Ptp and the lung volume that would be obtained if the effects of the inspiratory intercostals and diaphragm on the lung were perfectly additive. B: traces obtained during isolated stimulation of the C5 phrenic nerve roots are also shown. The endotracheal tube was open throughout.
during combined and separate contraction, one would therefore conclude that one or several mechanisms act to reduce or eliminate the synergism when lung volume is held constant at FRC.

Activating the diaphragm through electrical stimulation of the phrenic nerves ensured that the neural input to the muscles during combined diaphragm-intercostal contraction was exactly the same as that during isolated contraction. In the dog, however, phrenic nerve afferents originating from diaphragmatic tension receptors are known to elicit powerful reflex inhibition of the inspiratory intercostals, in particular the external intercostals (10, 11). To avoid this reflex inhibition in our animals, we thus sectioned all phrenic afferent fibers and so the diaphragm and inspiratory intercostals in this condition. Indeed, previous studies in dogs have shown that external intercostal activity shows a reflex increase. To the extent that the fall in Pao induced by a given diaphragmatic contraction is the result of a reduction in spindle afferent inputs, but mechanoreceptors in the costovertebral joints, as described by Godwin-Austen (20) in the cat, could also be involved (9). Conversely, when the normal inspiratory cranial displacement of the ribs is reduced by an external, caudally oriented force, external intercostal activity shows a reflex increase. To the extent that the stimulated breaths with the airway occluded caused a marked reduction in the inspiratory cranial displacement of the ribs (Fig. 3) or reversed this cranial displacement into a caudal displacement, the increase in external intercostal activity can therefore be understood. This increase, however, cannot account for the lack of synergism between the diaphragm and inspiratory intercostals in this condition. Indeed, should this alteration have a mechanical effect, it would induce an increase rather than a decrease in the measured ΔPao relative to the predicted value.

On the other hand, the stimulated breaths with the airway occluded were commonly associated with a decrease in parasternal intercostal activity, and this might cause a reduction in the measured ΔPao relative to the predicted value. It seems unlikely, however, that the decrease in parasternal intercostal activity played any significant role for two reasons. First, the decrease amounted, on average, to only 5–7% of the activity recorded in the control breaths, and 10 of the 25 animals of the study showed no decrease at all. In these animals, parasternal EMG activity during the stimulated breaths thus averaged 100.1 ± 0.8% of control and external intercostal activity was 111.2 ± 5.6%; yet, as for the entire animal group, the measured ΔPao was also nearly identical to the predicted value (−25.3 ± 1.8 vs. −24.8 ± 2.1 cmH2O). Second, a small decrease in parasternal activity also occurred during the stimulated breaths with the airway open, but the measured ΔPtp was invariably and substantially higher than the predicted value. This suggests that the mechanism responsible for the lack of synergism during airway occlusion at FRC does not result from alterations in the activation of the muscles but rather is not associated to the mechanical properties of the respiratory system. Moreover, the fact that the animals of the study had a bilateral cervical vagotomy and that the airway was occluded also suggests that the mechanism lies in the mechanical properties of the chest wall rather than in the lung.

In humans, the abdomen becomes less compliant when it expands and the abdominal muscles are stretched (5, 22). To the extent that the rise in Pab in our animals was much greater during isolated diaphragmatic contraction than during combined diaphragm-intercostal contraction, abdominal compliance might therefore be smaller in the first instance than in the second. However, a similar difference in Pab between isolated diaphragmatic contraction and combined diaphragm-intercostal contraction was seen when the airway was open (Table 2), yet a clear-cut synergism was present. Furthermore, the analysis of a two-compartment model of the chest wall indicates that a stiffening of the abdomen reduces, rather than increases, the fall in Pao induced by a given diaphragmatic contraction (see Appendix). If the abdomen were stiffer during isolated...
diaphragmatic contraction than during combined diaphragm-intercostal contraction, our predicted values for ΔPao would therefore be low and the ratio of the measured to the predicted ΔPao would be increased.

On the other hand, isolated diaphragmatic contraction with the airway occluded induced a large caudal displacement of the ribs in every animal of the study, and it is well known that the canine rib cage becomes less compliant when it contracts below its resting, end-expiratory volume (6, 12). Thus, when the airway was occluded in our animals, the rib cage was stiffer during isolated diaphragmatic contraction than during combined diaphragm-intercostal contraction, and such a change in compliance should have a dual effect on the mechanics of the diaphragm. First, a stiffening of the rib cage enhances the fall in Pao produced by isolated diaphragmatic contraction (Ref. 12; also see APPENDIX). Second, a stiffening of the rib cage also in supine dogs at resting end expiration, a given force applied to the ribs in the caudal direction causes a smaller rib displacement than the same force applied in the cranial direction (14, 17). As a corollary, a given cranially oriented force applied to the ribs below resting end expiration should produce a smaller cranial rib displacement and, with it, a smaller fall in Pao than if the same force were applied at resting end expiration. The caudal displacement of the ribs observed during the stimulated breaths in many animals suggests, therefore, that the ΔPao produced by the parasternal and external intercostals may be lower during combined diaphragm-intercostal contraction than during isolated contraction. The observation that the diaphragm and intercostal muscles have a synergistic interaction when the airway is kept open, i.e., when isolated diaphragmatic contraction causes only a small caudal displacement of the ribs and when combined diaphragm-intercostal contraction is associated with a clear-cut cranial rib displacement (Fig. 4), is fully consistent with the idea that the decrease in rib cage compliance plays a major role during airway occlusion.

**APPENDIX**

The effects of a decrease in abdominal or rib cage compliance on the ΔPao produced by the diaphragm were evaluated with a simple, two-compartment model of the chest wall. This model was recently developed to analyze the action of the abdominal muscles (3) and is shown in a simplified form in Fig. 6. The rib cage and abdominal compartments are represented by the pistons, springs, and muscles shown at the top and the bottom of the cylinder, respectively, and the lung is represented by the spring between the two pistons. If the volume displacements of the rib cage and abdominal compartments are denoted VR and VA, the elastances of the compartments are denoted KR and KA, the volume displacement and the elastance of the lung spring are denoted VL and KL, and the effective pressures exerted by the rib cage inspiratory muscles and the diaphragm are denoted PR and PA, the equations of static equilibrium for the two pistons are

\[ P_{ao} + P_R = K_R V_R + K_A V_A \]  \hspace{1cm} (1)

and

\[ P_{ao} + P_A = K_A V_A + K_L V_L \]  \hspace{1cm} (2)

The volume displacement of the lung is the sum of the compartmental volume displacements, so that

\[ V_L = V_R + V_A \]  \hspace{1cm} (3)

and substituting for VR and VA from Eqs. 1 and 2 yields the following relation

\[ V_L = [P_{ao}(K_R + K_A) + P_R K_R + P_A K_A + K_r V_L (K_R + K_A)]/K_R K_A \]  \hspace{1cm} (4)

When the endotracheal tube is occluded, VL = 0 and Eq. 4 yields

\[ P_{ao} = -(P_R K_R + P_A K_A)/(K_R + K_A) \]  \hspace{1cm} (5)

So, when rib cage inspiratory muscles such as the parasternal and external intercostals contract alone (PR = 0),

\[ P_{ao} = -[K_A/(K_R + K_A)]P_A \]  \hspace{1cm} (6)

and when the diaphragm contracts alone (PA = 0),

\[ P_{ao} = -[K_A/(K_R + K_A)]P_R \]  \hspace{1cm} (7)

If, for the sake of simplicity, K_A in the intact respiratory system is assumed to be equal to K_A, an isolated contraction of the diaphragm would yield P_{ao} = -P_A/3. However, if the abdomen were stiffer, such that K_A = 2K_R, Pao during isolated contraction of the diaphragm would be only -P_A/3. On the other hand, if the rib cage stiffened such as...
that $K_R = 2K_A$. Pao during isolated diaphragm contraction would amount to $-2P_{al}$. Thus a reduction in abdominal compliance tends to reduce the $\Delta P_{ao}$ induced by isolated diaphragmatic contraction, and a reduction in rib cage compliance tends to enhance it.

ACKNOWLEDGMENTS

The author gratefully acknowledges T. A. Wilson for helpful discussions.

GRANTS

The Fonds National de la Recherche Scientifique provided financial support (grant no. 3.4509.04).

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