Effects of Isoflurane Anesthesia and Muscle Paralysis on Respiratory Mechanics in Normal Man

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Donald R. Krabill, M.D.,‡ Alan D. Sessler, M.D.§

In five healthy adult male volunteers in the supine position, respiratory mechanics and functional residual capacity (FRC) were studied in the awake state (control) and with muscle paralysis and mechanical ventilation during isoflurane anesthesia (inspired concentrations, 1 and 2 per cent). In eight of nine instances, FRC was less during isoflurane anesthesia compared with control. Static compliance of the total respiratory system (Ctot) decreased consistently during anesthesia and that of the lung (Clt) decreased in eight of nine instances; static compliance of the chest wall (Ccw) did not change. Average pulmonary resistance (Rlt) was significantly higher during anesthesia. The decrease in FRC and increase in Rlt appear to be somewhat less than those reported for other anesthetics. Increasing the inspired isoflurane concentration to 2 per cent had no further significant effect on FRC, Ctot, Clt, Ccw, and Rlt. Arterial blood pressure was decreased significantly and heart rate remained unchanged during anesthesia with 1 per cent isoflurane; with 2 per cent isoflurane, blood pressure was further significantly decreased and heart rate did not change significantly. (Key words: Anesthetics, volatile; isoflurane; Lung, respiratory mechanics; Ventilation, isoflurane.

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ISOFLURANE (Forane®; 1-chloro-2,2,2-trifluoroethyl difluoromethyl ether), a new nonflammable inhalation anesthetic agent, produces marked respiratory depression, but the effects of isoflurane on pulmonary mechanics and functional residual capacity (FRC) in man have not been reported.

FRC has been reported 2-9 to be decreased when patients in the supine position are anesthetized with most of the commonly used anesthetic agents, and these decreases may be associated with changes in static lung compliance, airway resistance, and “airway closure” in dependent lung regions.10 The last may lead to disturbances in pulmonary gas exchange.11 An ideal anesthetic agent would have none of these adverse effects. Knowledge of the effect of isoflurane on pulmonary resistance (airway plus lung tissue viscous) is important in deciding on its suitability for use in patients with chronic obstructive pulmonary disease.

In the present study the effects of isoflurane on blood pressure and heart rate also were examined, since isoflurane has been reported 12 to produce an increase in heart rate which is said to sustain the cardiac output despite decreased stroke volume.

Methods

Five healthy male nurse anesthetists†† (ages 23 to 28 years), untrained in performing relaxation pressure-volume maneuvers, were studied in the supine position, first awake and then again during isoflurane anest-

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†† The subjects were accepted into the study only after they had a careful explanation of the protocol and the associated risks and adequate time for consideration.

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thaesthesia and muscle paralysis at inspired concentrations of 1 and 2 per cent (henceforth referred to as 1 and 2 per cent isoflurane). For each of these three conditions, the sequence of measurements was: FRC, compliances, and average pulmonary resistance. All procedures in the awake and in the anesthetized subjects were similar, except for the volume history of the lung prior to the measurement of compliances. Mean (±SE) tidal volume was 0.57 ± 0.07 liter during the awake state, 0.67 ± 0.03 liter during 1 per cent isoflurane, and 0.65 ± 0.02 liter during 2 per cent isoflurane.

Total lung capacity (TLC) and its subdivisions were determined by nitrogen clearance and spirometry while the subjects were awake. Closing volume (CV, the lung volume above residual volume at which “airway closure” occurs) was determined in the awake subjects (one to five times) in the supine position by the modified single-breath oxygen technique in an expiratory flow rate of 0.5 l/s and the mean value was calculated. Closing capacity (CC) was calculated by adding closing volume to residual volume (RV): 

\[ CC = CV + RV. \]

Functional residual capacity (FRC) was determined by the nitrogen clearance technique after the subjects had breathed room air for 30 minutes. Expired gas was collected in a neoprene bag during a 7-minute clearance period and the volume was determined (gasometer); mean expired oxygen concentration was measured by a paramagnetic oxygen analyzer (Beckman, model E2) after passing a sample of the mixed expired gas through soda lime and silica gel. Mean expired carbon dioxide and isoflurane concentrations were measured by infrared analyzers (Beckman, medical gas analyzers LB-1 and LB-2). Mean expired nitrogen concentration was determined by difference. Alveolar nitrogen concentration at the end of the nitrogen clearance period was assumed to be 1 per cent. Mean expired nitrogen concentration was corrected for inspired nitrogen (duplicate Haldane analyses) and for the nitrogen eliminated from blood and tissue (see Appendix 1).

After completion of the FRC determinations, the subjects were connected, via a mouthpiece, to a circuit incorporating a spirometer whose wheel was fitted with a potentiometer with linear response for electrical recording of volume changes. Airway pressure \( (P_{aw}) \) was detected just distal to the mouthpiece (Statham strain gauge, PM-131). Transpulmonary pressure \( (P_{t}) \) was estimated from the difference between \( P_{aw} \) and esophageal pressure \( (P_{ae}) \) (Statham strain gauge, PM-131) (see Appendix 2).

Static pressure–volume (PV) curves of the total respiratory system and of the lung were obtained, after a volume history consisting of three inspirations to TLC. The awake subjects were then asked to inspire maximally \( (P_{FIO2} = 0.60) \) and to relax their respiratory muscles (glottis open) with the airway occluded. The subjects then exhaled passively into the spirometer with 3- to 5-second periods of flow interruption interposed at several intervals during the exhalation. In the anesthetized subjects the lungs were inflated three times to an airway pressure of approximately 30 cm H\(_2\)O before the PV curves were obtained. Expiratory gas volume and \( P_{t} \) during the PV maneuver were recorded by a Honeywell 1912 oscillograph and the changes between the periods of flow interruption were measured. Two to five successful PV maneuvers were carried out, and the mean curve was drawn by visual approximation for each subject for each of the three experimental conditions.

Average pulmonary resistance \( (R_{p}) \) \( (P_{FIO2} = 0.60) \) was estimated from simultaneous recordings of \( P_{t} \) and inspiratory and expiratory flow rates (heated Fleisch pneumotachographs no. 1). \( R_{p} \) was determined for five breaths, and the mean value was calculated. Values determined in the anesthetized and intubated subjects were corrected by subtracting the measured resistance to gas flow of the 8.5-mm (inside diameter) endotracheal tube at corresponding flow rates (mean flow rates: awake subjects, 0.6 l/s; during anesthesia, 0.7 l/s). A final correction of 1.1 cm H\(_2\)O/l per second was added to correct for the resistance of the upper airway, which was excluded from the measurement in the intubated anesthetized subjects.

Arterial blood pressure (Statham strain...
ISOFLURANE, RESPIRATORY MECHANICS, AND FRC

TABLE I. Physical Characteristics and Lung Volumes (Total Capacity and Subdivisions)

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Height (m)</th>
<th>Weight (kg)</th>
<th>Total Lung Capacity (TLC)</th>
<th>Vital Capacity (VC)</th>
<th>Residual Volume (RV)</th>
<th>Closing Capacity (CC)</th>
<th>Functional Residual Capacity (FRC)</th>
<th>FRC 1 Per Cent Isoflurane</th>
<th>FRC 2 Per Cent Isoflurane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 1</td>
<td>23</td>
<td>1.78</td>
<td>71</td>
<td>7.46</td>
<td>5.88</td>
<td>1.58</td>
<td>1.98</td>
<td>2.41</td>
<td>2.69</td>
</tr>
<tr>
<td>Subject 2</td>
<td>23</td>
<td>1.80</td>
<td>75</td>
<td>6.78</td>
<td>4.91</td>
<td>1.87</td>
<td>2.39</td>
<td>2.61</td>
<td>2.29</td>
</tr>
<tr>
<td>Subject 3</td>
<td>26</td>
<td>1.87</td>
<td>79</td>
<td>6.49</td>
<td>5.08</td>
<td>1.41</td>
<td>1.97</td>
<td>2.54</td>
<td>2.56</td>
</tr>
<tr>
<td>Subject 4</td>
<td>26</td>
<td>1.89</td>
<td>75</td>
<td>7.23</td>
<td>5.67</td>
<td>1.56</td>
<td>1.85</td>
<td>3.05</td>
<td>2.92</td>
</tr>
<tr>
<td>Subject 5</td>
<td>26</td>
<td>1.76</td>
<td>80</td>
<td>6.22</td>
<td>5.12</td>
<td>1.10</td>
<td>2.10</td>
<td>2.23</td>
<td>1.97</td>
</tr>
<tr>
<td>Mean = SE</td>
<td></td>
<td></td>
<td></td>
<td>6.64 ± .23</td>
<td>5.23 ± .19</td>
<td>1.50 ± .13</td>
<td>2.06 ± .09</td>
<td>2.65 ± .14</td>
<td>2.45 ± .16</td>
</tr>
</tbody>
</table>

* RV = closing volume.
1 Anesthetized = anesthesia, muscle paralysis, and mechanical ventilation.
3 Mean of differences between FRC (awake) and FRC (1 per cent isoflurane) significant (P < 0.05).

gauge, P23 De) and lead II of the ECG were
recorded throughout the study. Arterial blood
gases were determined by electrodes
(Radiometer) and corrected for differences
between body temperature and that of the
water bath (37 C)16,19 and for the membrane
factor.

After completion of the awake study, the
subjects were anesthetized with 1 or 2 per
cent isoflurane in oxygen (calibrated Fluotec
vaporizers) delivered via a nonrebreathing
system. The larynx and trachea were sprayed
with 4 per cent lidocaine and the trachea was
intubated with a cuffed endotracheal tube
after muscle paralysis was achieved by intravenous injection of 100 mg succinyl-
choline chloride. Muscle paralysis was main-
tained by infusion of succinylcholine
chloride (average total dose, 15 mg/kg), and
the lungs were mechanically ventilated
(Bird, Mark 7–Mark 4). Adequacy of muscle
relaxation was confirmed by the absence of a
twitch response to a stimulus applied inter-
mittently to the ulnar nerve at the wrist
(Peripheral Nerve Stimulator, Burroughs
Wellcome Co.).

Thirty-minute equilibration periods
(FlO2 = 0.21) were used before the first meas-
urements (FRC) and after the inspired
isoflurane concentration was altered. In three
subjects, measurements were made first at 1
per cent and then at 2 per cent isoflurane; in
the two other subjects, the reverse order was
used. Anesthesia times ranged from 104 to
168 minutes, and the measurements were
begun 44 to 55 minutes after induction of
anesthesia.

Results

In eight of nine instances, FRC was less
during isoflurane anesthesia than in the
awake state, and the mean of differences
between FRC (awake) and FRC (1 per cent
isoflurane) was significant (P < 0.05) (table
1). The mean decrease in FRC was approxi-
mately 8 per cent. Increasing the inspired
isoflurane concentration from 1 to 2 per cent
did not result in a further significant change
of FRC. In two subjects, FRC decreased to
below control closing capacity (CC), but the
end-inspiratory level was above CC in all
subjects.

The mean of differences between Crs
(awake) and Crs (1 per cent isoflurane) was
significantly decreased; increasing the
isoflurane concentration from 1 to 2 per cent
resulted in no further consistent change in
Crs (table 2). The PV curves for the total
respiratory systems of four subjects shifted to
the right during anesthesia (fig. 1, upper),
indicating that less pressure at the airway
opening (Pao) was required to achieve a given
lung volume in the awake than in the anes-
thesitized state. For example, at 50 per cent
of control TLC, Pao was 7.4 ± 0.5 cm H2O
### TABLE 2. Mean Values of Compliances of Total Respiratory System, Lung, and Chest Wall

<table>
<thead>
<tr>
<th></th>
<th>Compliance (l/cm H2O)*</th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td><strong>Anesthetized</strong></td>
<td><strong>Awake</strong></td>
<td><strong>Awake</strong></td>
<td><strong>Awake</strong></td>
</tr>
<tr>
<td></td>
<td>1 Per Cent Isoflurane</td>
<td>2 Per CentIsoflurane</td>
<td>1 Per Cent Isoflurane</td>
<td>2 Per Cent Isoflurane</td>
</tr>
<tr>
<td><strong>Cn (Total System)</strong></td>
<td>0.125</td>
<td>0.084</td>
<td>0.088</td>
<td>0.214</td>
</tr>
<tr>
<td>Subject 1</td>
<td>0.106</td>
<td>0.074</td>
<td>0.073</td>
<td>0.247</td>
</tr>
<tr>
<td>Subject 2</td>
<td>0.088</td>
<td>0.080</td>
<td>0.080</td>
<td>0.177</td>
</tr>
<tr>
<td>Subject 3</td>
<td>0.104</td>
<td>0.101</td>
<td>0.219</td>
<td>0.200</td>
</tr>
<tr>
<td>Subject 4</td>
<td>0.133</td>
<td>0.094</td>
<td>—</td>
<td>0.220</td>
</tr>
<tr>
<td>Mean</td>
<td>0.113</td>
<td>0.087</td>
<td>0.086</td>
<td>0.215</td>
</tr>
<tr>
<td>± SE</td>
<td>± 0.010</td>
<td>± 0.005</td>
<td>± 0.006</td>
<td>± 0.011</td>
</tr>
</tbody>
</table>

* Compliance was measured at lung volumes between functional residual capacity and FRC + 10 per cent total lung capacity.
† Mean of differences between Cn (awake) and Cn (1 per cent isoflurane) significant (P < 0.05).
1 Difference between mean Cn (awake) and mean Cn (1 per cent isoflurane) significant (P < 0.05).

### TABLE 3. Mean Values of Pressures of Respiratory System at 50 Per Cent of Control Total Lung Capacity

<table>
<thead>
<tr>
<th></th>
<th>Pressure (cm H2O)*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Anesthetized</strong></td>
<td><strong>Awake</strong></td>
<td><strong>Awake</strong></td>
<td><strong>Awake</strong></td>
</tr>
<tr>
<td></td>
<td>1 Per CentIsoflurane</td>
<td>2 Per CentIsoflurane</td>
<td>1 Per CentIsoflurane</td>
<td>2 Per CentIsoflurane</td>
</tr>
<tr>
<td><strong>Pn (Total System)</strong></td>
<td>7.9</td>
<td>11.8</td>
<td>12.0</td>
<td>5.2</td>
</tr>
<tr>
<td>Subject 1</td>
<td>7.5</td>
<td>13.2</td>
<td>9.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Subject 2</td>
<td>7.9</td>
<td>10.7</td>
<td>9.7</td>
<td>3.2</td>
</tr>
<tr>
<td>Subject 3</td>
<td>—</td>
<td>7.3</td>
<td>7.2</td>
<td>6.7</td>
</tr>
<tr>
<td>Subject 4</td>
<td>6.0</td>
<td>11.4</td>
<td>—</td>
<td>3.0</td>
</tr>
<tr>
<td>Mean</td>
<td>7.4</td>
<td>10.9</td>
<td>9.6</td>
<td>4.1</td>
</tr>
<tr>
<td>± SE</td>
<td>± 0.5</td>
<td>± 1.0</td>
<td>± 1.0</td>
<td>± 0.8</td>
</tr>
</tbody>
</table>

* Pn = pressure at airway opening; Pn = transpulmonary pressure; Pn = esophageal pressure.
† Mean of differences between Pn (awake) and Pn (1 and 2 per cent isoflurane) significant (P < 0.05).

(mean ± SE) in the awake subjects and 10.9 ± 1.0 and 9.6 ± 1.0 cm H2O, respectively, in the anesthetized subjects (table 3), a significant difference.

The major cause for the decrease in Cn appeared to be a decrease in the static compliance of the lung (Cn) (table 2, fig. 1, lower), which was higher in the awake state than during anesthesia in eight of nine instances. The difference between the mean values of Cn (awake) and Cn (1 per cent isoflurane) was significant (P < 0.05). Increasing the isoflurane concentration from 1 to 2 per cent resulted in no further consistent change in Cn. Static compliance of the chest wall (Cn) did not change significantly with isoflurane anesthesia at either concentration (table 2); the mean PV curve of the chest wall shifted to the right (fig. 2).

The mean of differences between Rn (awake) and Rn (1 and 2 per cent isoflurane) was significantly increased (table 4), and Rn did not change.
when the isoflurane concentration was increased from 1 to 2 per cent.

Arterial systolic, diastolic, and mean blood pressures were significantly lower during anesthesia, at both isoflurane concentrations, than in the awake state. Increasing the isoflurane concentration from 1 to 2 per cent resulted in a further significant decrease of blood pressure (table 5). Heart rate did not change significantly with isoflurane anesthesia.

Adequate arterial oxygenation and normocarbia prevailed throughout the study; no significant change occurred in $P_{aO_2}$, $P_{aCO_2}$, or body temperature.

**Discussion**

This study demonstrated a decrease of approximately 8 per cent in FRC during anesthesia with 1 per cent isoflurane and muscle paralysis with succinylcholine chloride; increasing the isoflurane concentration to 2 per cent did not result in a further consistent change in FRC. In none of these subjects did FRC decrease to below control.
residual volume (RV), as occurred in three of five subjects anesthetized with thiopental and meperidine.

Although two theories have been advanced, the mechanism of the decrease in FRC under anesthesia remains unclear. Don and associates thought that the apparent decrease in FRC measured by helium dilution was caused in part by trapping of gas. If trapping of gas were involved, one might expect a relationship between CC and the decrease in FRC after induction of anesthesia. When we plotted the ratio, CC/FRC (measured awake) against the absolute decrease in FRC observed with isoflurane anesthesia for each subject, we noted a significant positive correlation \( r = 0.92; \ P < 0.05 \), suggesting that trapping of gas might have contributed to the decrease in FRC.

Westbrook and associates, whose data do not support the hypothesis of Don et al., suggested that anesthesia alters the mechanics of the chest wall so that the PV curve of the chest wall is displaced to the right. In agreement with the hypothesis of Westbrook et al., we observed a shift of the PV curve of the chest wall to the right in three subjects. Thus, it appears from our data that both trapping of gas and a change in mechanics of the chest wall contributed to the decrease in FRC with isoflurane anesthesia.

The decrease in lung compliance \( (C_L) \) with 1 per cent isoflurane appeared to be the main cause of the decreased compliance of the total respiratory system \( (C_T) \). Before discussing the possible mechanisms for the decrease in \( C_L \), we will consider potential errors involved in estimating transpulmonary pressure \( (P_t) \) from the difference between esophageal pressure \( (P_e) \) and airway pressure \( (P_{aw}) \) in anesthetized and paralyzed subjects in the supine position. The measurements obtained in the awake and anesthetized subjects should be comparable because the position and the volume of the balloon placed in the esophagus were kept constant. However, if the anesthetic agent or the muscle relaxant had a direct effect on the muscle tone of the esophagus, that is, on its elastance, the position of the PV curve and its slope, particularly at the extremes of the lung volume, could be changed. We cannot rule out this possibility.

Elastic recoil of the total respiratory system increased after induction of anesthesia and, in Subjects 1, 2, and 3, was associated with an increase in the calculated elastic recoil of the chest wall. The apparent shift to the right of the PV curve of the chest wall during anesthesia could be the result of incomplete muscle relaxation of the awake subjects. However, we think that failure to achieve complete relaxation was probably not the sole mechanism, because of the consistency of the data obtained during the awake state.
We therefore suspect this shift to be partially due to the effect of general anesthesia on the mechanics of the chest wall.

The average pulmonary resistance (airway plus tissue viscous) ($R_t$) was consistently and significantly smaller in the awake subjects than in the anesthetized subjects; it remained unchanged when the isoflurane concentration was changed to 2 per cent. The increase in $R_t$ during isoflurane anesthesia deserves comment. First, the resistance values for the anesthetized subjects were calculated by subtracting the resistance of the endotracheal tube to gas flow and then adding a constant value for the resistance of the upper airway to gas flow. Each of these two corrections amounted to approximately 25 per cent of the total value; the contribution of the upper airway to the total airway resistance can vary greatly among individuals, and the introduction of a constant correction factor may produce a significant error. Second, $R_t$ includes the tissue viscous resistance of the lung, which normally constitutes only about one sixth of the pulmonary resistance. Because a many-fold increase in tissue viscous resistance would be required, it is unlikely that tissue viscous resistance contributed significantly to the increase in $R_t$. Last, changes in the viscosity of the inspired gas mixture may influence the pulmonary resistance even though the airway dimensions remain unchanged. We were unable to demonstrate such a difference in the viscosity when 1 or 2 per cent isoflurane vapor was added to a mixture of 60 per cent oxygen in nitrogen.

After reviewing the earlier literature, Nunn concluded that, during anesthesia, resistance to gas flow in the lower airways is about double that in the whole respiratory tract of an awake subject. The increases in $R_t$ that we observed with isoflurane, while somewhat lower, appeared to be consistent with this conclusion. Our data suggest that isoflurane is as suitable as other anesthetic agents for use in patients with chronic obstructive pulmonary disease.

The subjects in this study were mechanically ventilated because of the respiratory depressant effect of isoflurane. We therefore cannot separate the effect of succinylcholine from that of isoflurane. In previous studies, we were unable to demonstrate any significant change in FRC and lung elastic properties or in intrapulmonary inspired gas

### Table 4. Average Pulmonary Resistance

<table>
<thead>
<tr>
<th></th>
<th>Anesthetized</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Awake</td>
<td>1 Per Cent</td>
<td>2 Per Cent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Isoflurane</td>
<td>Isoflurane</td>
</tr>
<tr>
<td>Subject 1</td>
<td>2.2</td>
<td>4.4</td>
<td>4.3</td>
</tr>
<tr>
<td>Subject 2</td>
<td>1.8</td>
<td>3.3</td>
<td>3.3</td>
</tr>
<tr>
<td>Subject 3</td>
<td>2.7</td>
<td>3.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Subject 4</td>
<td>3.0</td>
<td>3.1</td>
<td>3.6</td>
</tr>
<tr>
<td>Subject 5</td>
<td>4.3</td>
<td>5.4</td>
<td>—</td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>2.8 ± .4</td>
<td>3.9 ± .5</td>
<td>3.7 ± .2</td>
</tr>
</tbody>
</table>

* Values obtained by subtracting the resistance to gas flow of the endotracheal tube and adding a constant value for the resistance of the upper airway (1.1 cm H$_2$O/L per second) which had to be excluded from the measurements in the intubated subjects.

† Mean of differences between $R_t$ (awake) and $R_t$ (1 and 2 per cent isoflurane) significant ($P < 0.05$).

### Table 5. Arterial Blood Pressure and Heart Rate (Mean ± SE)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Blood Pressure (mm Hg)*</th>
<th>Heart Rate (Beats/Min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
</tr>
<tr>
<td>Awake</td>
<td>148 ± 10</td>
<td>74 ± 3</td>
</tr>
<tr>
<td>Anesthetized, 1 per cent isoflurane</td>
<td>103 ± 6</td>
<td>59 ± 2</td>
</tr>
<tr>
<td>Anesthetized, 2 per cent isoflurane</td>
<td>77 ± 8</td>
<td>48 ± 3</td>
</tr>
</tbody>
</table>

* Systolic, diastolic, and mean blood pressures were significantly different: 1) between the awake and anesthetized states, and 2) between anesthesia with 1 per cent isoflurane and anesthesia with 2 per cent isoflurane.
distribution as a consequence of muscle paralysis during thiopental–meperidine anesthesia. Similarly, Bergman found no change in FRC with muscle paralysis during thiopental anesthesia. These studies suggest that muscle paralysis may have little effect on FRC and pulmonary compliance, but further studies are needed to examine the effect of isoflurane without muscle paralysis.

Stevens et al. reported no change in cardiac output with increasing alveolar isoflurane concentrations, and attributed this to a significant increase in heart rate that compensated for a decrease in stroke volume. In agreement with the data of Stevens et al., we also observed a significant decrease in arterial blood pressure with isoflurane anesthesia, but we were unable to demonstrate a significant increase in heart rate. Both studies showed progressive decreases in blood pressure with increasing isoflurane concentrations. The concentration-dependent effect on blood pressure is in contrast to the phenomenon that the decreases in compliances and FRC and the increase in pulmonary resistance were not dose-dependent in the examined range of inspiratory isoflurane concentrations. This, however, does not exclude a concentration-dependent effect on these variables at lower inspiratory isoflurane concentrations.

In summary, we conclude that isoflurane anesthesia produces a decrease in static compliance of the total respiratory system (Crs) and lung (Ct) and a small decrease in FRC. In addition, the average pulmonary resistance (Rl) increases during isoflurane anesthesia. Increasing the inspired isoflurane concentration from 1 to 2 per cent did not produce further changes in FRC, Crs, Ct, or Rl. The directional changes were similar to those observed with other commonly used anesthetic agents. Finally, we found isoflurane to have a marked hypotensive effect, and heart rate did not increase significantly. The hypotensive effect was increased when the inspired isoflurane concentration was increased.

References
17. Hyatt RE, Wilcox RE: Extrathoracic airway

APPENDIX 1

The accuracy and precision of determining nitrogen concentration in the presence of isoflurane were assessed by using the nitrogen clearance technique for the measurement of a known volume (1.05 liters). With the methods described in the text, the following mean (±SE) values were obtained: for air with no isoflurane, 1.11 ± 0.02 liters; for air with 0.7 per cent isoflurane, 1.11 ± 0.05 liters; and for air with 1.6 per cent isoflurane, 1.13 ± 0.02 liters. Although these values were significantly higher than the known gas volume, they did not vary significantly from each other. Hence, the nitrogen concentration could be measured with equal degrees of precision with or without isoflurane in the gas mixture.

As an additional check of our method of gas analysis, in the awake subjects mean expired nitro-
gen concentration was also determined by duplicate Haldane analyses. The values for the FRC calculated from expired nitrogen determined by the Haldane method and the above methods were not significantly different (mean ± SE: 2.71 ± 0.13 liters and 2.65 ± 0.14 liters, respectively).

APPENDIX 2

Esophageal pressure was measured with a 12-cm latex balloon with a 3.3-cm perimeter and a wall thickness of 0.06 mm. The balloon was tied onto the distal end of a catheter (inside diameter [ID], 1.4 mm) so that it covered several small holes just proximal to the tip; it was positioned in the middle third of the esophagus, and 0.4 ml of air was introduced into it.* The position was kept constant during the study and the volume of air contained in the balloon was checked repeatedly. To detect an artifact that might distort the record of P02, the awake subjects were asked to suck and blow against a temporarily occluded airway. If no artifact was present, P02 changes reflected only the small alterations in lung volume due to the compression of gas. In the anesthetized, paralyzed subjects who were unable to suck and blow, the chest was manually compressed for detection of recording artifacts. A small catheter (6F, 1.4 mm) was inserted into the esophagus and secured with its tip resting approximately 1.0 cm above the upper end of the balloon. Before each measurement, suction was applied to this catheter to aspirate esophageal contents; virtually no secretions were obtained.


Endoclines

PARATHYROID RESPONSE TO INFUSED PHOSPHATE Acute parathyroid response was evaluated in eight cows, during constant infusion of 0.5 M sodium phosphate for 16 minutes. A significant increase in serum inorganic phosphorus [P] was associated with a decrease in Ca ++ and a multiphasic parathyroid hormone (PTH) response. [Ca] remained unchanged during the first 4 minutes, while PTH reached its peak level at that time. Although Ca ++ decreased, PTH reached a plateau at 4 to 12 minutes and decreased thereafter, while C ++ increased. Previous data from the literature have indicated that PTH response is to a change in [Ca ++], not to P [simultaneous infusion of P and Ca]. The experiments suggest that the immediate response to a decrease in [Ca ++] is an increase in PTH which is not sustained despite a further fall in [Ca ++], probably due to inadequate PTH synthesis. (Fisher, J.A.,Binswanger, U., and Blum, J.W.: Acute Parathyroid Hormone Response to Changes in Ionized Calcium during Phosphate Infusion in the Cow. Eur J Clin Invest 3: 151–155, 1973.)