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# *Carbon Dioxide Absorption Is Not Linearly Related to Intraperitoneal Carbon Dioxide Insufflation Pressure in Pigs*

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***Background:*** **Carbon dioxide absorption into the blood during laparoscopic surgery using intraperitoneal carbon dioxide insufflation may lead to respiratory acidosis, increased ventilation requirements, and possible serious cardiovascular compromise. The relationship between increased carbon dioxide excretion ($\dot{V}_{CO_2}$) and intraperitoneal carbon dioxide insufflation pressure has not been well defined.**

***Methods:*** **In 12 anesthetized pigs instrumented for laparoscopic surgery, intraperitoneal carbon dioxide (n = 6) or helium (n = 6) insufflation pressure was increased in steps, and $\dot{V}_{CO_2}$ (metabolic cart), dead space, and hemodynamics were measured during constant minute ventilation.**

***Results:*** **$\dot{V}_{CO_2}$ increases rapidly as intraperitoneal insufflation pressure increases from 0 to 10 mmHg; but from 10 to 25 mmHg, $\dot{V}_{CO_2}$ does not increase much further. $Pa_{CO_2}$ increases continuously as intraperitoneal insufflation pressure increases from 0 to 25 mmHg. Hemodynamic parameters remained stable.**

***Conclusions:*** **By considering Fick's law of diffusion, the initial increase in $\dot{V}_{CO_2}$ is likely accounted for by increasing peritoneal surface area exposed during insufflation. The continued increase in $Pa_{CO_2}$ without a corresponding increase in $\dot{V}_{CO_2}$ is accounted for by increasing respiratory dead space. (Key words: Carbon dioxide. Deadspace. Hypercapnia. Laparoscopy. Peritoneal insufflation.)**

THERE has been a dramatic increase in laparoscopic surgery requiring intraperitoneal carbon dioxide insufflation during the past decade. Laparoscopic techniques are being applied for cholecystectomy, appendectomy, and pelvic lymphadenectomy, as well as other intra- and extraperitoneal operations. The patient population being exposed to intraperitoneal carbon dioxide insufflation is becoming older, with the potential for more underlying disease and more extensive surgical manipulation and trauma. In addition, the duration of intraperitoneal carbon dioxide insufflation required to perform procedures is increasing. Carbon dioxide is used as the insufflating gas because its high solubility is believed to reduce the occurrence and severity of embolic events and it does not support combustion.

It is known that carbon dioxide pneumoperitoneum can have significant effects on cardiovascular and respiratory function that may be deleterious[1–5] and that these effects appear to be more prominent in patients with preexisting cardiorespiratory disease.[6,7] There has been a resurgence of reports of episodes of life-threatening hypercapnia, respiratory acidosis, and cardiovascular collapse associated with laparoscopic cholecystectomy.[8–12] Cardiovascular morbidity and mortality associated with carbon dioxide pneumoperitoneum has been chronicled for at least 20 yr.[1,13] While it is known that there is significant carbon dioxide absorption from the peritoneal cavity[1,4] and that hemodynamic changes occur,[1–5] a complete description of carbon dioxide absorption and its subsequent systemic effects has not been fully elucidated.

Accordingly, the purpose of this study was to determine the relationship between changing intraperitoneal carbon dioxide insufflation pressures and carbon dioxide absorption, respiratory gas exchange, and hemo-

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dynamic changes over the range of clinically used pressures. This is important because, as we will show, the mechanism of increasing arterial $P_{CO_2}$ at low intraperitoneal carbon dioxide insufflation pressures differs from the mechanism of increasing arterial $P_{CO_2}$ at high intraperitoneal carbon dioxide insufflation pressures. These data help address the question of whether it is clinically desirable to keep intraperitoneal carbon dioxide pressures as low as possible to minimize carbon dioxide absorption, dead space, and hemodynamic changes.

Knowledge of the relationship between intraperitoneal carbon dioxide insufflation pressure and carbon dioxide absorption, dead space, and hemodynamic changes may help in anticipating ventilatory requirements and hemodynamic effects and in selecting appropriate monitoring for hypercapnia in different patient populations.

## Materials and Methods

The protocol was approved for study by the Animal Care Committee of the University of British Columbia.

### *Animal Preparation*

After a 12-h fast, 12 juvenile pigs (22–34 kg) were sedated using an intramuscular injection of 250 mg ketamine, and anesthesia was induced using a 250-mg intravenous thiopental bolus. Anesthesia was maintained using a ketamine infusion (125 mg/h) and inhalational halothane (0.5–1%). All animals received a bolus of normal saline of 20 $ml \cdot kg^{-1} \cdot h^{-1}$ for the duration of the experiment. Paralysis was maintained throughout the experimental period using pancuronium bromide.

The pigs' lungs were ventilated *via* a tracheostomy using a Harvard dual control respirator pump (Millis, MA) with a tidal volume of 17 ml/kg at a respiratory rate adjusted to maintain an arterial $P_{CO_2}$ of 35–45 mmHg at baseline. Ventilation parameters were held stable for the duration of the experiment. All expired gases were directed through a metabolic measurement cart (Sensormedics Deltratrac metabolic monitor, Anaheim, CA) for continuous measurements of carbon dioxide excretion ($\dot{V}_{CO_2}$) oxygen consumption ($\dot{V}_{O_2}$), and minute ventilation. Fraction of inspired oxygen was 0.4–0.5 for all cases.

A low compliance catheter was inserted in the left common carotid artery for arterial blood gas sampling and continuous recording of heart rate and blood pressure. Fluid and drugs were infused through a catheter inserted into the left external jugular vein. A flow-directed pulmonary artery catheter (Baxter 7F 1.5 cc 93A-095-75, American Edwards, Irvine, CA) was inserted through the right internal jugular vein for mixed venous blood sampling, temperature measurement, cardiac output determinations, and measurement of central venous pressure. The animals were instrumented as for laparoscopic surgery using the four-portal technique. Six pigs received carbon dioxide peritoneal insufflation and six pigs received helium peritoneal insufflation. Carbon dioxide or helium was insufflated through a Veress needle placed through a 2-cm abdominal midline incision (MP Video Medicam 900 insufflator, Hopkinton, MA). After insufflation to 12 mmHg intraperitoneal pressure, one 10-mm and three 5-mm surgical trocars (U.S. Surgical, Norwalk, CT) were introduced into the abdominal cavity percutaneously.

The peritoneal cavity was inspected for any signs of inadvertent surgical trauma (MP Video Medicam 800 MC + video camera and 800 M1 Light Source). Once completed, the peritoneal cavity was deflated and each animal was stabilized for 30 min at 0 mmHg baseline intraperitoneal insufflation pressure. For each incremental increase in intraperitoneal pressure, the pressure was maintained constant automatically by the insufflation machine.

Intraperitoneal insufflation used carbon dioxide (n = 6) or helium (n = 6). Intraperitoneal insufflation pressures were increased by 5-mmHg increments from 0 to 25 mmHg at 25-min intervals. After 20 min of stabilization at each new intraperitoneal pressure increment, $\dot{V}_{CO_2}$, dead space, and hemodynamic measurements were made over 5 min. This protocol occurred over 3–4 h, after which the animals were killed using a bolus infusion of potassium chloride.

### *Measurements*

Whole body $\dot{V}_{CO_2}$, $\dot{V}_{O_2}$, and minute ventilation were determined using the metabolic measurement cart which collected all expired gas. $\dot{V}_{CO_2}$, $\dot{V}_2$, and minute ventilation were calculated every 60 s based on a 60-s exhaled volume measurement and measurements of the concentration of inspired oxygen, expired oxygen, and expired carbon dioxide.[15] Values for $\dot{V}_{CO_2}$, $\dot{V}_2$, and expiratory minute ventilation were taken from the final 60 s of the 20-min equilibration period at each insufflation pressure.

Arterial blood gases, mixed venous blood gases, and mixed expired gas $P_{CO_2}$ were measured using an ABL 30 blood gas analyzer (Radiometer, Copenhagen, Denmark). Mixed expired gas samples were collected in a 40-l gas-impermeable collection bag over 3 min at the completion of each 20-min stabilization interval. After complete mixing, 60 ml of this gas sample was then aspirated into the blood gas analyzer for measurement of mixed expired gas $P_{CO_2}$ as described by the manufacturer (Radiometer). In addition, end-tidal carbon dioxide values were obtained using a Datex Normocap 200 capnometer (Instrumentarium, Helsinki, Finland).

Cardiac output was measured by the thermodilution technique using 5 ml of iced normal saline injectate and a cardiac output computer (model 9520, American Edwards). Concentrations of lactate in arterial blood were measured using a YSI 2300 stat glucose/L-lactate analyzer (Yellow Springs, OH). Heart rate and all pressures were measured with the pigs in the supine position and transducers zeroed to the midchest position using membrane transducers (DTX disposable pressure transducer, Viggo-Spectramed, Oxnard, CA). Peak inspiratory pressures were measured using a differential pressure transducer (model DP 45-32, Validyne, Northridge, CA) calibrated using a water manometer. Heart rate, blood pressure, central venous pressure, and peak inspiratory pressure were displayed and recorded using a multichannel computerized transducer recording system (DIREC Recording System, Raytech, Vancouver, British Columbia, Canada).

Dead space ventilation ($V_d/V_t$) was calculated using:

$$V_d/V_t = \frac{Pa_{CO_2} - P\bar{E}_{CO_2}}{Pa_{CO_2}}, \quad (1)$$

where $P\bar{E}_{CO_2}$ is the partial pressure of carbon dioxide in mixed expired gas.

*Analysis*

We tested the principle hypothesis that $\dot{V}_{CO_2}$ increases as intraperitoneal carbon dioxide insufflation pressure increases using a two-way repeated measures analysis of variance (Systat, Evanston, IL). When a significant F value was obtained ($P < 0.05$), we tested the first-order polynomial for a significant increase as intraperitoneal insufflation pressure increased. For illustrative purposes, we tested for differences between the carbon dioxide and helium groups at 0, 10, and 25 mmHg intraperitoneal insufflation pressures using unpaired *t* tests, and within each group using paired *t* tests corrected for multiple comparisons using a sequentially rejective Bonferroni test procedure.[16] We applied a similar analysis to other variables to illustrate differences. All values are expressed as mean ± SD.

## Results

$\dot{V}_{CO_2}$ increased from 139 ± 23 ml/min at baseline to 166 ± 25 ml/min as carbon dioxide intraperitoneal insufflation pressure increased from 0 to 25 mmHg (fig. 1). The increase in $\dot{V}_{CO_2}$ was nonlinear so that most of the increase in $\dot{V}_{CO_2}$ occurred as the intraperitoneal insufflation pressure increased from 0 mmHg ($\dot{V}_{CO_2}$ 139 ± 23 ml/min) to 10 mmHg ($\dot{V}_{CO_2}$ 172 ± 30 ml/min; $P < 0.001$; fig. 1). $\dot{V}_{CO_2}$ did not appear to increase any further ($P$ = NS) despite increasing intraperitoneal carbon dioxide insufflation pressure to 25 mmHg. This increase in $\dot{V}_{CO_2}$ was not seen in the group in which the peritoneal cavity was insufflated with helium (fig. 1). The difference in $\dot{V}_{CO_2}$ between groups was significant ($P < 0.02$).

$Pa_{CO_2}$ increased in both the carbon dioxide and helium insufflated groups as intraperitoneal insufflation pressure increased (fig. 2). This increase was greater for carbon dioxide insufflated animals compared to the helium insufflated animals ($P < 0.002$). To account for this, we found that dead space ventilation increased significantly with increasing intraperitoneal insufflation pressure in both groups from 0.42 at baseline to 0.52

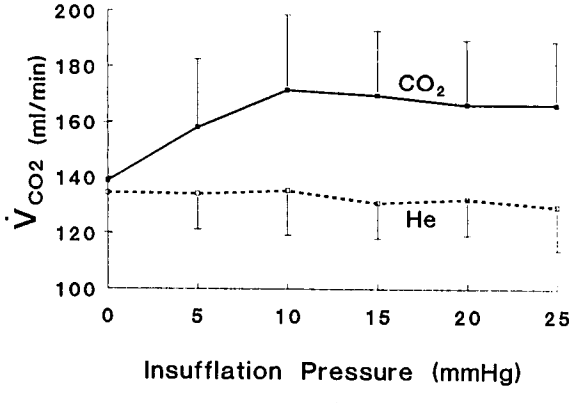


**Fig. 1. Carbon dioxide excretion ($\dot{V}_{CO_2}$) is plotted against increasing carbon dioxide (n = 6) or helium (n = 6) intraperitoneal insufflation pressure. Error bars indicate standard deviations. $\dot{V}_{CO_2}$ rises rapidly and then plateaus at an intraperitoneal insufflation pressure of 10 mmHg in the carbon dioxide group. The difference between the carbon dioxide and helium groups is significant by analysis of variance ($P < 0.05$). The increase in $\dot{V}_{CO_2}$ as intraperitoneal insufflation pressure rises is significant (first-order polynomial, $P < 0.05$) in the carbon dioxide group.**

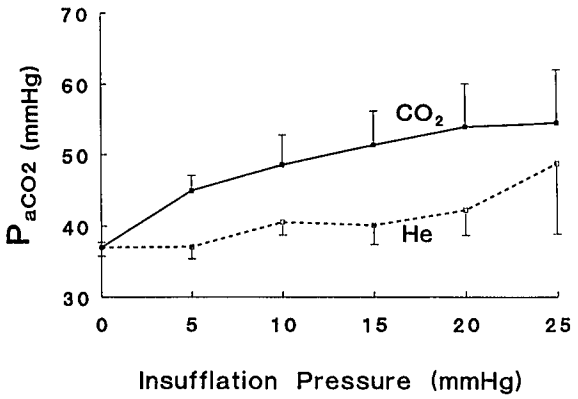


**Fig. 2. Arterial partial pressure of carbon dioxide ($Pa_{CO_2}$) is plotted against increasing carbon dioxide (n = 6) or helium (n = 6) intraperitoneal insufflation pressure. Error bars indicate standard deviations. The difference between the carbon dioxide and helium groups is significant by analysis of variance ($P < 0.05$). $Pa_{CO_2}$ increases in both carbon dioxide and helium groups (first-order polynomial, $P < 0.05$) even when the corresponding $\dot{V}_{CO_2}$ does not increase.**

at 25 mmHg intraperitoneal insufflation pressure, an increase of about 24% (fig. 3). Though $\dot{V}_{CO_2}$ did not increase significantly as intraperitoneal insufflation pressure increased above 10 mmHg, dead space continued to increase at high intraperitoneal insufflation pressure. Therefore, the increase in $Pa_{CO_2}$ as intraperitoneal insufflation pressure increased from 0 to 10 mmHg largely is accounted for by the increase in $\dot{V}_{CO_2}$, whereas the increase in $Pa_{CO_2}$ as insufflation pressure increased from 10 to 25 mmHg largely is accounted for by the increase in dead space.

End-tidal carbon dioxide also increased continuously in both groups with increasing intraperitoneal insufflation pressure. The end-tidal carbon dioxide levels were greater for the carbon dioxide insufflated group compared to the helium insufflated group at intraperitoneal insufflation pressures of 10 mmHg ($CO_2$ 41 ± 4 mmHg *vs.* helium 34 ± 2 mmHg; $P < 0.05$) and 25 mmHg ($CO_2$ 43 ± 6 mmHg *vs.* helium 36 ± 2 mmHg; $P < 0.05$) but not at baseline ($CO_2$ 33 ± 2 mmHg *vs.* helium 33 ± 1 mmHg; $P$ = NS). Additionally, the increase in end-tidal carbon dioxide for the carbon dioxide insufflated group occurred both over increases in insufflation pressure from 0 to 10 mmHg (33 ± 2 mmHg to 41 ± 4 mmHg; $P < 0.001$) and over increasing insufflation pressure from 10 to 25 mmHg (41 ± 4 mmHg to 43 ± 6 mmHg; $P < 0.05$). For the helium insufflated group, the increase in end-tidal carbon dioxide was relatively small over intraperitoneal insufflation pressure increases from 0 to 10 mmHg (33 ± 1 mmHg to 34 ± 2 mmHg; $P = 0.462$) and was slightly larger over intraperitoneal insufflation pressure increases from 10 to 25 mmHg (34 ± 2 mmHg to 36 ± 2 mmHg; $P < 0.05$).

Peak inspiratory pressures increased in both groups from 19.2 ± 3.1 $cmH_2O$ at 0 mmHg intraperitoneal insufflation pressure to 47.5 ± 6.1 $cmH_2O$ at 25 mmHg intraperitoneal insufflation pressure. There was no significant difference between the two groups in the change in peak inspiratory pressure ($CO_2$ 19.8 ± 2.7 to 46.3 ± 6.9 $cmH_2O$, helium 18.5 ± 3.5 to 48.6 ± 5.4 $cmH_2O$).

There were no differences between the two groups in the hemodynamic variables examined. Heart rate was quite stable for intraperitoneal insufflation pressures from 0–15 mmHg for both groups (averaging 93 beats/min), then increased only slightly for high insufflation pressures at 25 mmHg (table 1). Mean arterial pressure also remained quite constant over the range of intraperitoneal insufflation pressure; increasing for both groups by 24% from baseline to 25 mmHg intraperitoneal insufflation pressure (table 1). There was no statistically significant difference in cardiac output between the carbon dioxide and helium groups at any set, and there was no significant change of cardiac output in either group (table 1).

Oxygen consumption ($\dot{V}_{O2}$) did not change greatly with increasing intraperitoneal insufflation pressure in either group (table 2). Mixed venous $P_{O_2}$ also remained

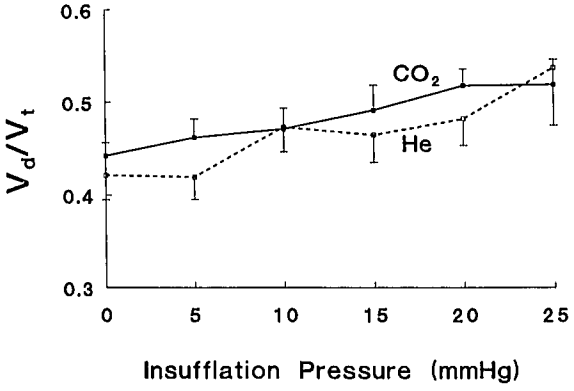


**Fig. 3. Dead space ventilation ($V_d/V_t$) is plotted against increasing carbon dioxide (n = 6) or helium (n = 6) intraperitoneal insufflation pressure. Error bars indicate standard deviations. There is no significant difference between the carbon dioxide and helium groups by analysis of variance. The rise in ($V_d/V_t$) is significant (first-order polynomial, $P < 0.05$) in both groups and accounts for increasing $Pa_{CO_2}$, even when $\dot{V}_{CO_2}$ is not increasing.**

**Table 1. Effect of Increased Intraperitoneal Pressure on Hemodynamics**

| Hemodynamic Variable | Insufflation Gas | Intraperitoneal Insufflation Pressure (mmHg) 0 | 5 | 10 | 15 | 20 | 25 |
|---|---|---|---|---|---|---|---|
| Heart rate (beats/min) | $CO_2$ | 96 ± 12 | 93 ± 7 | 94 ± 10 | 91 ± 5 | 97 ± 7 | 102 ± 6 |
| | He | 95 ± 13 | 93 ± 9 | 92 ± 6 | 93 ± 9 | 90 ± 8 | 97 ± 15 |
| Mean arterial pressure (mmHg) | $CO_2$ | 77 ± 13 | 86 ± 15 | 94 ± 16 | 91 ± 14 | 91 ± 13 | 94 ± 10 |
| | He | 75 ± 15 | 78 ± 16 | 84 ± 12 | 87 ± 10 | 89 ± 12 | 95 ± 14 |
| Cardiac output (l/min) | $CO_2$ | 3.9 ± 1.4 | 3.9 ± 1.0 | 3.6 ± 1.1 | 3.4 ± 0.8 | 3.4 ± 1.0 | 3.5 ± 1.2 |
| | He | 3.1 ± 0.7 | 3.3 ± 0.8 | 3.4 ± 0.9 | 3.1 ± 0.8 | 3.0 ± 0.7 | 3.1 ± 0.8 |

Values expressed as the mean ± standard deviation of six animals in each group.

reasonably stable within each group (table 2). There was no statistically significant difference between the two groups. Arterial lactate concentrations did not change significantly (table 2). Again, there was no significant difference between the two groups.

## Discussion

We found that $\dot{V}_{CO_2}$ increases as intraperitoneal carbon dioxide insufflation pressure increases but plateaus at 10 mmHg intraperitoneal carbon dioxide insufflation pressure (fig. 1). Continuing increases in $Pa_{CO_2}$ beyond this point are due to increases in ventilatory dead space associated with further increase in intraperitoneal pressure and peak airway pressure (figs. 2 and 3). The helium control group demonstrates that the differences seen in $\dot{V}_{CO_2}$ with varying intraperitoneal insufflation pressure are due to carbon dioxide absorption from the peritoneal cavity and not differences in hemodynamics, ventilation, or metabolic carbon dioxide production (fig. 1, tables 1 and 2). Hemodynamic parameters did not change significantly in either group over the experimental range of intraperitoneal insufflation pressures (table 1).

To understand why $\dot{V}_{CO_2}$ plateaus at relatively low intraperitoneal insufflation pressures, we considered each term in Fick's law of diffusion for carbon dioxide in this setting:

$$\Phi_{CO_2} = D \frac{A}{d} (Pp_{CO_2} - PB_{CO_2}). \quad (2$$

$\Phi_{CO_2}$ is carbon dioxide flux, D is diffusivity of carbon dioxide between the peritoneal cavity and the blood, A is the area of peritoneum exposed to carbon dioxide, d is distance between peritoneal surface and blood, $Pp_{CO_2}$ is the partial pressure of carbon dioxide in the peritoneum, and $PB_{CO_2}$ is the partial pressure of carbon dioxide in the blood.

We cannot think of a reason why the first term, D, would change as intraperitoneal insufflation pressure increases because D represents a physical property. At low intraperitoneal insufflation pressures, we observed *via* the laparoscope that the exposed peritoneal area increases as intraperitoneal insufflation pressure increases. At intraperitoneal insufflation pressures of 10 mmHg, the porcine abdomens appeared, through the laparoscope, to be fully distended. Therefore, it is conceivable that the second term, A, increases substantially at low intraperitoneal insufflation pressures, but above about 10 mmHg pressure, any further increases in in-

**Table 2. Effect of Increasing Intraperitoneal Insufflation on Oxygen Transport**

| Variable | Insufflation Gas | Intraperitoneal Insufflation Pressure (mmHg) 0 | 5 | 10 | 15 | 20 | 25 |
|---|---|---|---|---|---|---|---|
| Oxygen consumption (ml $O_2$/min) | $CO_2$ | 191 ± 39 | 192 ± 51 | 190 ± 34 | 182 ± 29 | 189 ± 33 | 184 ± 29 |
| | He | 197 ± 15 | 196 ± 19 | 193 ± 16 | 191 ± 15 | 194 ± 20 | 196 ± 23 |
| Mixed venous oxygen tension (mmHg) | $CO_2$ | 40.0 ± 6.2 | 44.5 ± 4.6 | 46.3 ± 4.5 | 45.6 ± 3.3 | 47.7 ± 5.1 | 49.1 ± 3.0 |
| | He | 34.0 ± 6.8 | 37.1 ± 6.5 | 36.6 ± 4.4 | 37.5 ± 5.4 | 38.9 ± 4.6 | 40.1 ± 3.5 |
| Arterial lactate (mM) | $CO_2$ | 1.1 ± 0.5 | 0.8 ± 0.2 | 0.6 ± 0.1 | 0.5 ± 0.2 | 0.5 ± 0.1 | 0.5 ± 0.1 |
| | He | 1.3 ± 0.4 | 0.8 ± 0.3 | 0.7 ± 0.2 | 0.6 ± 0.1 | 0.6 ± 0.1 | 0.8 ± 0.3 |

Values expressed as the mean ± standard deviation of six animals in each group.

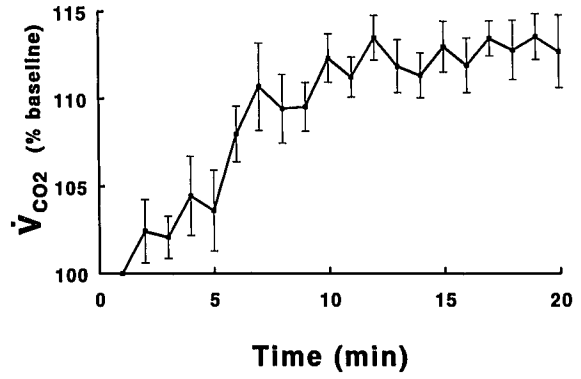


**Fig. 4. Average minute-by-minute carbon dioxide excretion ($\dot{V}_{CO_2}$) is illustrated following an increase in intraperitoneal carbon dioxide insufflation pressure from 0 to 5 mmHg (n = 6). The increase in $\dot{V}_{CO_2}$ appears to plateau and the rise in $\dot{V}_{CO_2}$ toward the plateau value occurs, to a large extent, before 10 min.**

traperitoneal pressure may cause only increasing tension in the abdominal wall without increasing A. This is one potential mechanism for the plateau in $\dot{V}_{CO_2}$ as intraperitoneal insufflation pressure rises. The third term, d, is the anatomic distance between the peritoneal surface and the adjacent capillary beds. It is conceivable that the capillaries just below the peritoneal surface collapse as intraperitoneal insufflation pressure rises above peritoneal capillary hydrostatic pressure, diverting blood flow away from the peritoneal surface. This would increase d and therefore limit further increases in carbon dioxide absorption and $\dot{V}_{CO_2}$.[17] Therefore, this is a second potential mechanism for the plateau in $\dot{V}_{CO_2}$ as intraperitoneal insufflation pressure rises. The fourth term, $PP_{CO_2}$, is approximately atmospheric pressure, or about 760 mmHg at sea level. Further increases by 5–25 mmHg in $PP_{CO_2}$ by increasing intraperitoneal carbon dioxide insufflation pressures represent a small fraction of the initial carbon dioxide partial pressure and, therefore, probably do not significantly contribute to the rise in $\dot{V}_{CO_2}$ or blood $P_{CO_2}$. Likewise, changes in the fifth term, $P_{BCO2}$, are small compared to atmospheric pressure and do not likely account for our results. Thus, consideration of each component of Fick's law of diffusion for carbon dioxide suggests that a rapid increase in area for diffusion at low intraperitoneal insufflation pressures most likely accounts for the rapid rise in $\dot{V}_{CO_2}$. Marginal further area recruitment and compression of capillaries below the peritoneal surface probably limit further increases in $\dot{V}_{CO_2}$ as intraperitoneal carbon dioxide insufflation pressure increases above 10 mmHg.

To the extent that an increase in area for diffusion accounts for the rapid increase in $\dot{V}_{CO_2}$ at low intraperitoneal insufflation pressures, a potentially important corollary follows. That is, if carbon dioxide dissects further into tissues, as it does when subcutaneous emphysema occurs,[12] the area for diffusion increases and $\dot{V}_{CO_2}$ may increase substantially. Interestingly, a number of recent reports have been made of uncontrollable hypercapnia and respiratory acidosis occurring in patients undergoing laparoscopic procedures in the presence of extensive, presumably carbon dioxide, subcutaneous emphysema.[9–12] It has been recognized that the large area for diffusion of carbon dioxide into the bloodstream created by the subcutaneous emphysema probably leads to the observed severe hypercapnia and acidosis.[12]

Others examining carbon dioxide uptake and excretion using constant intraperitoneal carbon dioxide insufflation pressure have found time-related plateaus in end-tidal carbon dioxide values[18] and $\dot{V}_{CO_2}$[14,18] occurring 15–30 min from the time of initiation of carbon dioxide pneumoperitoneum. The plateau in $\dot{V}_{CO_2}$ in our experiment at 10 mmHg insufflation pressure also coincides with a time of approximately 50 min from first insufflation. However, we believe that the plateau in $\dot{V}_{CO_2}$ is not simply a time-related plateau because we took care to avoid this potential problem. A step change in carbon dioxide flux due to a step change in intraperitoneal carbon dioxide insufflation pressure would, as a first-order approximation, result in an exponential rise in $\dot{V}_{CO_2}$ described by:

$$\dot{V}_{CO_2}(t) = \Delta\dot{V}_{CO_2}(1 - e^{-t/\tau}) + \dot{V}_{CO_{2baseline}}, \qquad (3)$$

where $\Delta\dot{V}_{CO_2}$ is the increment in $\dot{V}_{CO_2}$ at steady state above the $\dot{V}_{CO_2}$ at baseline, and $\tau$ is the exponential time constant for this rise.

From the literature,[14,18,19] we estimated $\tau$ to be less than 10 min. Spacing the measurement sets by 25 min would mean that 90% ($1\text{-}e^{-25/10} > 90\%$) of the change in $\dot{V}_{CO_2}$ had occurred by the next measurement set. To test that this assumption was true in our data, we fit the rise in minute-by-minute $\dot{V}_{CO_2}$ measurements from baseline to the first set of data for each carbon dioxide insufflated pig with equation 3 using a Newton-Raphson nonlinear least-squares technique (Systat). We found that the mean $\tau$ was 8 ± 6 min. Since this is less than our prior estimate, we conclude that the interval between our sets was sufficient for $\dot{V}_{CO_2}$ to be within 5% of steady state. The average minute-by-minute $\dot{V}_{CO_2}$ data after intraperitoneal insufflation pressure was increased

from 0 to 5 mmHg is shown in figure 4 and illustrates that a plateau in $\dot{V}_{CO_2}$ had been reached. Even if a time-related plateau in $\dot{V}_{CO_2}$ had not been reached, we would have arrived at the same conclusion from our data. That is, if $\dot{V}_{CO_2}$ were linearly related to intraperitoneal carbon dioxide insufflation pressure, then we would not have found a plateau in the relationship between these two variables (fig. 1). Therefore, the plateau that we observed indicates that carbon dioxide absorption is not linearly related to intraperitoneal carbon dioxide insufflation pressure.

The physiologic dead space measured by the Bohr equation (equation 1) is an indication of ineffective or wasted ventilation[20] and either an increase in dead space or a decrease in alveolar ventilation could account for the continuing increases in $Pa_{CO_2}$ beyond the point where $\dot{V}_{CO_2}$ plateaus (10 mmHg insufflation pressure). Increased intraperitoneal pressure will cause a decrease in functional residual capacity, thus it is difficult to imagine a mechanism by which increased intraperitoneal pressure would result in an increase in dead space. However, one conceivable explanation is that increased intrathoracic pressures shifted more of the lung to a West's "zone 1" condition, resulting in increased physiologic dead space. An alternative explanation is that alveolar ventilation decreased as a result of a decrease in delivered tidal volume. The inspiratory limb of our ventilator circuit plus the lung volume of the pigs was approximately 2 l. This compressible volume would have lost approximately 50 ml at a peak inspiratory pressure of 25 $cmH_2O$ given that the compliance of air is about 1 $ml \cdot cmH_2O^{-1} \cdot l^{-1}$. This represents 10–15% of the delivered tidal volume and therefore accounts for a substantial proportion of the approximately 20% drop in tidal volume that would be required to increase $V_d/V_t$ from 0.42 to 0.52.

Since $\dot{V}_{CO_2}$ did not change in the control helium insufflated group (fig. 1), the differences in $\dot{V}_{CO_2}$ observed with varying intraperitoneal carbon dioxide insufflation pressures (fig. 1) are due to changes in carbon dioxide absorption from the peritoneal cavity and not to differences in metabolic carbon dioxide production. There were no differences between the two groups in terms of indicators of changes in metabolism that might lead to increased carbon dioxide from metabolic sources. $\dot{V}_{O_2}$, mixed venous oxygen saturation, and lactate were relatively stable in both groups throughout the experimental period (table 2).

Our data also support the conclusion that hemodynamic factors were not responsible for the observed changes in $\dot{V}_{CO_2}$. Heart rate, mean arterial pressure, and cardiac output were similar between the control helium group and the carbon dioxide group and remained stable in both groups (table 1). This finding is in contrast to other studies both in human subjects and animal models[1–6,18] that have found significant changes in hemodynamic parameters with intraperitoneal carbon dioxide insufflation. Various studies[1–6,18] have reported increased and decreased cardiac output, increased and unchanged heart rate, increased and decreased central venous pressure, and increased mean arterial pressure and systemic vascular resistance depending on insufflation pressures, subject positioning, and other variables. Thus, the hemodynamic results of carbon dioxide insufflation appear to be quite variable. One possible explanation is that different animal species respond differently to intraperitoneal insufflation; for example, abdominal compliances may differ. Another possibility is that many of the differences in the literature are accounted for by differences in fluid resuscitation. In our fluid-resuscitated model, we are not surprised that the hemodynamic changes are small, although in relatively hypovolemic models, the hemodynamic changes could be quite large.

In summary, we have found that carbon dioxide absorption from the peritoneal cavity is not linearly related to intraperitoneal insufflation pressures in pigs. Carbon dioxide absorption seems to reach a maximum at relatively low intraperitoneal carbon dioxide insufflation pressures and does not increase significantly beyond this despite further increases in intraperitoneal carbon dioxide insufflation pressure. However, it is important to note that further increases in $Pa_{CO_2}$ may occur after carbon dioxide absorption has plateaued. These increases appear to be related to increasing dead space ventilation associated with increasing intraperitoneal pressure.

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