**Laboratory and animal investigations**

**Gastric Intramural Pco₂ During Peritonitis and Shock**

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**Objective:** To define whether increases in gastric intramural tissue CO₂ and H⁺ increase during experimentally induced peritonitis with circulatory shock as they do under conditions of hemorrhagic shock and cardiac arrest.

**Design and setting:** Peritonitis was induced in Sprague-Dawley rats by cecal ligation and fecal spillage.

**Measurements and results:** Over an interval of 260 ± 20 min in 5 animals, there was a progressive reduction in mean aortic pressure from 153 ± 12 to 40 ± 20 mm Hg and a decline in cardiac index from 429 ± 135 to 178 ± 7 ml/min. This was associated with increases in gastric intramural [H⁺] from 34.5 ± 2 to 217.9 ± 93 mmol/L (p = 0.001). Arterial blood lactate content concurrently increased from 0.9 ± 0.1 to 4.6 ± 0.7 mmol/L (p = 0.001). Only a late increase in gastric intramural Pco₂ from 45 ± 5 to 128 ± 38 mm Hg (p = 0.01) was observed.

**Conclusion:** In contrast to the gastric acid base changes that accompany hemorrhagic shock, in which there is an early and prominent increase in both Pco₂ and [H⁺] in close relationship to decreases in cardiac output and arterial pressure, there was a prominent increase in gastric [H⁺] but only a delayed rise in gastric intramural Pco₂. Arterial blood lactate and central venous oxygen saturation were earlier indicators of perfusion failure. Since the bicarbonate concentration in the stomach wall was substantially greater than that of simultaneously measured arterial blood, this has bearing on the current clinical method of gastric tonometry which assumes that arterial blood bicarbonate is equivalent to gastric wall bicarbonate.

(Chest 1993; 104:1254-58)

**SVO₂ = mixed venous oxygen saturation**

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In ischemia, associated with circulatory failure due to cardiac arrest and resuscitation, hemorrhagic shock and cardiogenic shock has in each instance been associated with increases in the venoarterial Pco₂ gradient and usually with venous hypercarbia. The extent to which these conditions apply to septic shock and whether the high Pco₂ levels in splanchnic venous blood observed by Paluch et al during canine endotoxemia reflect the circulatory condition of the regional circuits and tissues have not as yet been firmly established. In undertaking the present study, it was our hypothesis that during shock induced by fecal peritonitis, like other low flow states, increases in tissue Pco₂ exceed those of mixed venous blood and that this applies especially to the viscera and specifically to the stomach wall. Accordingly, studies were undertaken to relate gastric intramural Pco₂ and pH to hemodynamic blood gas, and metabolic changes that characterized lethal progression of peritonitis in a rat model.

**Methods**

**Animal Preparation**

The experiments were performed in a previously described rat model of septic peritonitis utilizing methods noted by Rackow et al and Wichterman et al. Experiments were conducted under aseptic conditions. Sprague-Dawley rats, weighing between 450 and 550 g, were housed in groups of two in standard cages and the animals had free access to chow (Purina) and tap water. Animals were anesthetized by intraperitoneal injection of pentobarbital sodium, 45 mg/kg. Additional doses of 10 mg/kg were administered by intraperitoneal injection when there was spontaneous movement. No changes in hemodynamic parameters followed injection of pentobarbital. The animals were then placed on a surgical board in a supine position with the front and hind limbs immobilized in full abduction. Groin, neck, and abdominal areas were cleansed with a povidone iodine solution. Through a median incision, the trachea was exposed, incised, and cannulated with a 14-gauge catheter (Quick cath., Vicra Division, Travenol Labs, Inc., Dallas). The left carotid artery and right jugular vein were surgically exposed and cannulated with a polyethylene catheter (PE 50, Intramedic, New York). The external jugular catheter was advanced into the right atrium. Through the surgically exposed right carotid artery, a thermistor probe (No. 1F, Columbus Instruments, Columbus, Ohio) was advanced into the ascending aorta to a site approximately 7.5 mm proximal to the aortic valve. Cather position were confirmed in each animal at autopsy. The dead space of each catheter was filled with 0.9 percent physiologic salt solution which contained 2.5 U/ml of crystalline bovine heparin. The arterial and right atrial pressures were measured with high sensitivity pressure transducers (P23Gb, Gould Instruments, Oxnard, Calif) and recorded on a multichannel amplifier and strip chart recording system (89A Amplifier, Hewlett-Packard).
Heart rate was measured from the arterial pressure pulses. All pressures were recorded with the rats in the supine position and with reference to midchest. A conventional lead 2 ECG was recorded with the aid of subcutaneous needles for monitoring cardiac rhythm. Rectal temperature was measured continuously with a rectal thermistor.

For measurement of gastric intramural \( \text{PCO}_2 \), an ion-sensitive field effect transistor sensor was utilized. For measurement of gastric intramural pH, a miniature glass electrode was used together with a thermistor for simultaneous measurement of gastric intramural temperature. The methods and validity of these measurements have been previously reported.

For placement of \( \text{PCO}_2 \), pH, and a gastric wall temperature probe, a midline abdominal incision was made after the skin was aseptically prepared and anesthetized with 1 percent lidocaine. The stomach was exposed and the \( \text{PCO}_2 \), pH, and temperature sensors were advanced into the submucosa of the anterior wall to a depth of 5 mm at distances of approximately 4 mm from each other (Fig 1). A potassium chloride reference electrode was inserted in a subcutaneous pocket which was surgically created in the proximal area of the posterior portion of the left leg.

In the experimental group, the cecum was then isolated. After milking stool back from the ascending colon into the cecum, the cecum was ligated immediately distal to the ileocecal valve with a 3-0 silk ligature. A 1-cm incision was then made on the antimesenteric surface of the isolated cecum, and feces were expressed into the abdominal cavity. Though the bacterial inoculum was unmeasured, this procedure produced a lethal injury. The abdominal contents were then returned to the peritoneal cavity and the abdomen was closed in two layers. Control animals were identically treated except that the abdominal contents were returned to the peritoneal cavity after placement of gastric \( \text{PCO}_2 \), pH, and temperature probes such that the cecum was neither mobilized nor incised. The control animals were euthanized by central venous injection of saturated potassium chloride. Correct position of the catheters was confirmed at autopsy in each animal.

### Procedures

Arterial blood was sampled in amounts of 1.2 ml and right atrial blood was sampled in amounts of 0.5 ml after 0.1 ml was aspirated to clear the dead space of the catheter system. Immediately after blood removal, a 2.0 ml transfusion of donor blood containing 2.5 U/ml of heparin was injected into the right atrium. This donor blood had been withdrawn from the carotid artery of an identically anesthetized rat from the same colony immediately prior to the transfusion.

Oxygen tension, pH, carbon dioxide tension, and hemoglobin levels were measured in aortic and right atrial blood with the aid of a conventional blood gas analyzer and cooximeter system (IL-813 Instrumentation Lab., Waltham, Mass.). Lactic acid was measured by electrode technique (23L Lactate Analyzer, Yellow Springs Instruments, Yellow Springs, Ohio). Cardiac output was measured by the aortic thermodilution method following bolus injection of 200 \( \mu \)l of isotonic saline solution indicator at room temperature (20°C) into the right atrium. Cardiac output measurements were obtained with a Cardiomax II computer (Columbus Instruments, Columbus, Ohio), and measurement in this experimental setting was previously validated in our laboratory.

### Measurements

Baseline measurements of heart rate, respiratory frequency, mean arterial pressure, central venous pressure, cardiac index per kilogram of animal weight, arterial and central venous blood gas levels, arterial lactate, tissue pH, and \( \text{CO}_2 \) tensions obtained prior to cecal ligation and repeated at 1-h intervals thereafter. The gastric intramural and the blood [HCO\(_3^-\)] were computed with the Henderson-Hasselbach equation.

### Statistical Analyses

Experimental and control groups were compared by the unpaired Student’s t test. Comparison between time-based measurements within groups was performed by analysis of variance repeated measures. Measurements were reported as mean ± SD. A probability value of less than 0.05 was considered significant.

**EXPERIMENTAL METHOD**

**Figure 1.** Experimental method. \( \text{PETCO}_2 \), end-tidal \( \text{CO}_2 \). The pH, \( \text{PCO}_2 \), and temperature CT are all gastric values.
Table 1—Hemodynamic and Laboratory Data in Control and Septic Rats*

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>2 h</th>
<th>4 h</th>
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<tr>
<td>Heart rate, min '</td>
<td>Control rats</td>
<td>323 ± 15</td>
<td>311 ± 3</td>
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<td></td>
<td>Septic rats</td>
<td>303 ± 11</td>
<td>378 ± 25</td>
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<tr>
<td>Respiratory rate, min '</td>
<td>Control rats</td>
<td>78 ± 4</td>
<td>73 ± 9</td>
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<td></td>
<td>Septic rats</td>
<td>74 ± 4</td>
<td>96 ± 9†</td>
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<td>Mean arterial pressure, mm Hg</td>
<td>Control rats</td>
<td>154 ± 12</td>
<td>152 ± 3</td>
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<td></td>
<td>Septic rats</td>
<td>153 ± 12</td>
<td>107 ± 22</td>
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<tr>
<td>Gastric intramural Pco2, mm Hg</td>
<td>Control rats</td>
<td>44 ± 3</td>
<td>47 ± 3</td>
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<td></td>
<td>Septic rats</td>
<td>45 ± 5</td>
<td>55 ± 22</td>
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<td>Lactate, mmol/L</td>
<td>Control rats</td>
<td>0.8 ± 0.1</td>
<td>0.9 ± 0.1</td>
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<td></td>
<td>Septic rats</td>
<td>0.9 ± 0.1</td>
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<td>Cardiac index, ml·kg '·min '</td>
<td>Control rats</td>
<td>480 ± 150</td>
<td>399 ± 63</td>
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<td></td>
<td>Septic rats</td>
<td>429 ± 135</td>
<td>338 ± 14</td>
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<td>Hemoglobin, g/dl</td>
<td>Control rats</td>
<td>16.1 ± 0.5</td>
<td>16 ± 0.6</td>
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<td>Septic rats</td>
<td>16.1 ± 0.5</td>
<td>16 ± 0.5</td>
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<td>Arterial oxygen saturation, %</td>
<td>Control rats</td>
<td>90 ± 2</td>
<td>89 ± 2</td>
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<td>Septic rats</td>
<td>92 ± 2</td>
<td>95 ± 2</td>
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<td>SvO2, %</td>
<td>Control rats</td>
<td>62 ± 2</td>
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<td>Septic rats</td>
<td>63 ± 3</td>
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<td>Arterial pH, U</td>
<td>Control rats</td>
<td>7.41 ± 0.01</td>
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<td>Septic rats</td>
<td>7.41 ± 0.01</td>
<td>7.49 ± 0.01§</td>
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<td>Right atrial pH, U</td>
<td>Control rats</td>
<td>7.39 ± 0.01</td>
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<td>7.40 ± 0.01</td>
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<td>PacO2, mm Hg</td>
<td>Control rats</td>
<td>40 ± 1</td>
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<td>Septic rats</td>
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<td>Right atrial Paco2, mm Hg</td>
<td>Control rats</td>
<td>43 ± 1</td>
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<td>Septic rats</td>
<td>42 ± 1</td>
<td>34 ± 2‡</td>
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*Values are expressed as mean ± SD.
†p<0.02 compared with control rats.
‡p<0.001 compared with baseline values.
§p<0.05 compared with control rats.
||p<0.05 compared with baseline values.

RESULTS

Animals died within an average interval of 260 ± 20 min after peritoneal soilage. No cardiac arrhythmias were observed. No significant differences were observed between baseline measurements of control and septic animals (Table 1). In septic animals, heart rate progressively increased from 303 ± 11 to 413 ± 41 beats per minute (p = 0.0001) with concurrent and progressive decline in mean arterial pressure from 153 ± 12 to 40 ± 20 mm Hg (p = 0.0001). Respiratory rate increased from 74 ± 4 to 96 ± 9 breaths per minute (p = 0.001) in the initial 120-min interval following peritoneal spillage. It subsequently decreased to 67 ± 10 over the following 120 min. Cardiac index decreased from 429 ± 129 to 178 ± 7 ml/min (p = 0.04) (Table 1). The decreases in cardiac index were highly correlated with decreases in aortic pressure (r = 0.99), and these were accompanied by decreases in the mixed venous oxygen saturation ([SvO2]) from 63 ± 3 to 36 ± 2 (p = 0.001). Gastric wall [H+] increased from 34 ± 5 to 217 ± 93 mmol/L (p = 0.001 [Fig 2]). Arterial blood lactate content concurrently increased from 0.9 ± 0.1 to 4.6 ± 0.7 mmol/L with the upper limit of normal being 1.5 mmol/L (p = 0.001 [Fig 3]). A high negative correlation between cardiac index and arterial lactate content was observed (r = 0.98). The venoarterial Paco2 gradient increased from 3 ± 1 to 10 ± 1 mm Hg (p = 0.001) (Fig 3). Gastric intramural Paco2 increased after peritoneal spillage from 45 ± 5 to a maximum of 96 ± 31 mm Hg (p = 0.04) at the end of 240 min. One animal died between 240 and 260 min.

Gastric Intramural Paco2 during Peritonitis and Shock (Desai et al)
RAT : SEPTIC SHOCK

GASTRIC INTRAMURAL [H⁺] and Pco₂

![Graph showing changes in gastric intramural [H⁺] and Pco₂ over time.](image)

**Figure 2.** Progressive increases in gastric intramural [H⁺] and Pco₂ during experimentally induced peritonitis.

In the survivors, there were additional increases in gastric intramural Pco₂ to 128 ± 38 mm Hg over the ensuing 40-min interval (p = 0.01). The computed gastric intramural HCO₃⁻ exceeded arterial HCO₃ prior to and during the first 120 min that followed onset of peritonitis (Fig 4). Rectal temperature increased from 36.5 ± 0.3 to 37.1 ± 0.8 °C (p = 0.05), and PaO₂ increased from 95 ± 2 to 116 ± 6 mm Hg, along with a gradual decrease in venous HCO₃ from 26.6 ± 1.1 to 17.3 ± 2.1 mEq/L (p = 0.03).

**Discussion**

Kivilaakso et al measured gastric Pco₂ and PaO₂ in the setting of hemorrhagic shock in piglets by two Silastic tubes filled with hypoxic saline solution and implanted into the stomach wall. After hemorrhage, the gastric blood flow was reduced to 20 percent of control values. The Pco₂ of fluid sampled from the gastric wall increased approximately twofold. Our group reported on studies of hemorrhagic shock in rats in which directly measured gastric intramural Pco₂ increased approximately threefold. These observations indicated that hemorrhagic shock was accompanied by gastric intramural hypercarbia. The present studies document comparable changes but only during the late stages of experimentally induced peritonitis with circulatory shock. Striking increases in gastric intramural Pco₂ from 49 to 160 mm Hg also were demonstrated during nonfatal cardiac arrest. These were reversed within 30 min after successful resuscitation.

Current evidence points, in part, to decreased CO₂ clearance by the viscera when blood flow is critically reduced. Both aerobic and anaerobic CO₂ production of [H⁺] are implicated. Excesses of [H⁺] are explained by the intracellular breakdown of high-energy phosphate compounds and by the anaerobic generation of lactic acid with bicarbonate buffering of these excesses of [H⁺]. Although substantial increases in gastric intramural Pco₂ were demonstrated in this study, they represented a late indicator of critical perfusion failure in comparison with the earlier decline in cardiac index, arterial pressure, arterial blood lactate levels, and intramural [H⁺]. Accordingly, we identified differences in the severity of gastric hypercarbic acidosis in various circulatory shock states. In the setting of peritonitis and septic shock in the rat, arterial blood lactate levels and SvO₂ values were earlier indicators of systemic perfusion failure, the gastric intramural [H⁺] was an intermediate indicator, and gastric intramural Pco₂ was a late indicator of outcome.

**Figure 3.** Relationships between arterial pressure, venousarterial Pco₂ gradient (Pv-aCO₂) arterial blood lactate, and SvO₂ during the course of experimentally induced peritonitis.
The present experiments, like those of Tang et al in hemorrhagic shock, do not fully support the assumption that gastric bicarbonate is quantitatively equivalent to arterial blood bicarbonate. More recently, Fiddian-Green and colleagues have advocated H+ receptor blockade to minimize differences potentially stemming from secretion of gastric acid during clinical tonometry. The effects of this additional intervention are not addressed by the present studies.

We conclude that acid-base measurements on the stomach wall are indicative of the severity of visceral ischemia and therefore of perfusion failure. However, the prognostic value of intramural H+ was better than that of Pco2. The rate of change of these parameters differs contingent on the mechanism underlying the low visceral blood flow state. Predictability of intramural [H+] and Pco2 measurements with respect to outcome were earlier with hemorrhagic than with septic shock. During peritonitis, arterial pressure and arterial blood lactate levels were earlier indicators of the severity and outcome than the gastric intramural acid-base measurements.

REFERENCES
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5 Mathias DW, Clifford PS, Klopotenstein HS. Mixed venous gases are superior to arterial blood gases in assessing acid-base status and oxygenation during acute cardiac tamponade in dogs. J Clin Invest 1986; 82:533-38