PROFOUND ACIDOSIS IN AN ANESTHETIZED HUMAN: REPORT OF A CASE

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Standard physiological, biochemical and medical texts state that the lower limit of arterial plasma pH compatible with human life is 7.00 \textsuperscript{1,2} or 6.80.\textsuperscript{3} The increased use of the glass electrode pH meter as a clinical and research instrument has revealed that such figures must be revised, since instances of acidosis with arterial pH values of less than 6.8 are being reported.\textsuperscript{4-7} It is our purpose to report such a case occurring during general anesthesia, to discuss its management and ultimate outcome. Further, the occurrence enabled us to extend some previous studies\textsuperscript{8} on electrolyte metabolism related to acidosis in the human and these will be reported and discussed.

CASE REPORT

An eighteen year old female was readmitted to the hospital for an elective subtotal gastric resection. Apart from a history of peptic ulcer with perforation and uneventful closure three months earlier, she had been in good health all her life. Her blood pressure was 120/75 mm. of mercury, pulse 90/minute, and, except for the scar from her previous laparotomy, her physical examination was negative. Laboratory investigation revealed 93 degrees of free acid in the stomach. All routine preoperative laboratory tests (hemoglobin, white and differential counts, bleeding, clotting and prothrombin times, and urinalysis) were normal.

On the day of operation she received 100 mg. of secobarbital intramuscularly and was taken to the operating room. After intravenous administration of 0.6 mg. of atropine, anesthesia was induced with thiopental-succinylcholine. During induction the patient's lungs were ventilated with oxygen after which her trachea was intubated with a cuffed endotracheal tube. Anesthesia was continued with a diethyl ether oxygen mixture administered via a closed circle system. The immediate preinduction pulse rate was 120/minute and the systolic blood pressure (oscillometric reading) was 110 mm. of mercury. During the next three hours her systolic blood pressure varied between 110 and 130 mm. of mercury and her pulse rate ranged between 120 and 140/minute. On two occasions the anesthetic was intentionally deepened because it was believed respirations were too vigorous and were interfering with the surgical procedure. Apart from this the anesthetic course appeared uneventful.

Three hours after induction of anesthesia a check of the anesthetic machine revealed that the directional valves were absent from the rebreathing circuit. In the gas machine being used, the directional valves of the circle system had been contained in the face piece of the anesthetic mask. In changing from face mask to endotracheal tube, the anesthesiologist had unwittingly removed the valve-containing face piece after tracheal intubation, and had connected the endotracheal tube to the rebreathing tubes with a nonvalved fitting. As a consequence, the patient had been rebreathing and carbon dioxide had been accumulating over a period of three hours. Physical examination at the time of discovery revealed a systolic blood pressure of 120 mm. of mercury, a regular pulse of 130/minute, dilated pupils, tachypnea, a marked flush of the face and a bright red color of the lips. Profuse perspiration was observed on the forehead and upper trunk of the patient.

Another machine with proper directional valves was substituted for the defective apparatus, end-tidal CO\(_2\) monitoring was begun and arterial blood samples were drawn (see Methods). The anesthesiologist then began gradually to return the patient's alveolar CO\(_2\) to normal over the period of an hour by slowly incorporating the gas machine soda lime cannister into the breathing circuit. During this period end-tidal CO\(_2\) was monitored continuously and blood samples were drawn intermittently.

During the first five minutes of CO\(_2\) washout a few extrasystoles were noted, and the systolic pressure declined from 120 to 110 mm. of mercury. The systolic pressure and pulse rate then stabilized at 130 mm. Hg and 125/minute respectively. The remainder of the washout period was without incident, the flush disappearing in about twenty minutes. The alveolar CO\(_2\) returned to normal about one hour after beginning washout.

The operation was completed five hours and fifty-five minutes after anesthesia was induced. ACD blood, 1,800 ml., was administered to the patient during this time. Her systolic blood pressure on discharge from the operating room was 130 mm. of mercury and pulse rate 125/minute.

The patient was admitted to the postanesthesia recovery room unconscious but breathing spontaneously and apparently adequately, with the
endotracheal tube in situ. Her pulse rate was 140/minute and systolic blood pressure 90 mm. of mercury. Final blood samples were withdrawn.

Forty five minutes later her pulse abruptly rose to 160/minute, and she became rigid and began to exhibit convulsive-like movements with an arched back. These movements abated upon intravenous administration of 1.0 Gm. of calcium gluconate. The endotracheal tube was removed, her pulse gradually declined to 100/minute and systolic pressure rose to 130 mm. of mercury. Two and one-half hours postoperatively the patient was fully conscious, asking questions, and moving all extremities. She was discharged to the ward one and one-half hours later when her systolic blood pressure was 130 mm. of mercury and pulse rate 95/minute. She had an uneventful convalescence and was discharged from the hospital on her eighth postoperative day. She has been well since discharge.

METHODS AND ANALYSES

The sampling tube of a mobile gas mass spectrometer was connected to the endotracheal tube of the patient and a continuous analysis of carbon dioxide concentration was recorded throughout the washout period. The limitations and accuracy of this instrument have been described elsewhere.5,10 End-tidal measurement of CO₂ was taken as alveolar concentration. Samples of arterial blood were drawn for estimation of pH, total plasma carbon dioxide, plasma potassium, and inorganic phosphate before the washout of carbon dioxide was begun. During the washout, arterial samples for plasma potassium and inorganic phosphate were withdrawn intermittently, and final samples, together with arterial pH were withdrawn in the postanesthesia recovery room two hours after completion of the washout period. Venous samples for the estimation of plasma 17-hydroxycorticosteroids were drawn during the washout period and in the postanesthesia recovery room.

All analyses were done in duplicate. Blood samples for pH and total plasma CO₂ were drawn in oiled heparinized syringes which were capped and immediately iced. Arterial pH was measured within five minutes of sampling with a Beckman Model G pH meter and a Beckman anaerobic glass electrode assembly immersed in a constant temperature water bath at 37.5 C. CO₂ content of plasma was determined within three hours by the manometric method of Van Slyke and Neill,11 with re-extraction for ether in plasma.12 Plasma potassium was determined by flame photometry. Plasma inorganic phosphate was analysed by the method of Fiske and Subbarow.13 Plasma hydroxycorticosteroids * were determined by the method of Silber and Porter.14 Arterial CO₂ tension (PₐCO₂) was calculated from pH and total plasma CO₂ by the Henderson-Hasselbalch equation, with pK’ = 6.10 and the solubility coefficient = 0.0301 mM./L./mm. Hg CO₂ tension.

In an attempt to separate the effects of anesthesia and surgery from the effects of

* We are grateful to Dr. Richard P. Doe, Veterans Hospital, Minneapolis, for determination of plasma hydroxycorticosteroids.
acidosis, studies were undertaken subsequently in patients undergoing operations during uncomplicated diethyl ether anesthesia. In these patients samples of blood taken immediately before operation were compared with those taken during anesthesia and surgery. The phenomena studied were similar to those in the acidotic patient.

RESULTS

The data are shown in tables 1, 2 and 3.

The arterial pH of the acidotic patient at the beginning of the study period was 6.71 and the total plasma CO₂ was 35.79 mM/L. The arterial PCO₂ at this time was 234 mm. of mercury. The pH taken in the postanesthesia recovery room three hours later was 7.31. The initial alveolar PCO₂ was 238 mm. of mercury, and this was reduced over the period of an hour to 41 mm. of mercury. The plasma potassium level prior to CO₂ washout was 4.8 mEq./L. (The amount of hemolysis observed in this sample probably contributed less than 0.2 mEq./L. to the measured value.) The plasma potassium declined during the washout period and showed a further fall two hours after the washout period was completed. Plasma inorganic phosphate was high (three times normal) at the beginning of the washout period and remained high during the washout. Two hours after the washout the phosphate had declined to approximately 50 per cent of the initial value. Plasma 17-hydroxycorticosteroids were high at the beginning of the washout period and remained at high levels two hours after the washout was completed.

Control patients exhibited no significant change in serum potassium levels as a consequence of anesthesia and operation (P = .12), and no control patient exhibited levels as high

<table>
<thead>
<tr>
<th>TABLE 2</th>
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<tr>
<td>PLASMA POTASSIUM AND PHOSPHORUS DURING UNCOMPlicated DIETHYL Ether ANESTHESIA AND Operation</td>
</tr>
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<table>
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<tr>
<th>Patient Age and Sex</th>
<th>Operation</th>
<th>Time (minutes)</th>
<th>pH</th>
<th>(CO₂)ₚ mM/L</th>
<th>PCO₂ mm Hg</th>
<th>K mEq/L</th>
<th>P mg %</th>
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<td>(1) 63, F</td>
<td>Gastrectomy</td>
<td>Preanest.</td>
<td>7.51</td>
<td>24.7</td>
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<td>130</td>
<td>7.45</td>
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<td>35.6</td>
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<td></td>
<td>350*</td>
<td>7.42</td>
<td>20.1</td>
<td>31.2</td>
<td>3.8</td>
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<td>(2) 18, M</td>
<td>Revision of colostomy</td>
<td>Preanest.</td>
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<td>—</td>
<td>—</td>
<td>3.4</td>
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<td></td>
<td></td>
<td>120</td>
<td>7.49†</td>
<td>23.4</td>
<td>30.4</td>
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<td></td>
<td>210</td>
<td>7.48</td>
<td>21.4</td>
<td>28.4</td>
<td>3.1</td>
<td>4.6</td>
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<td>250</td>
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<td>(4) 42, M</td>
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<td>32.2</td>
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<td>Splenectomy, transverse colostomy and subtotal gastrectomy</td>
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<td>37.0</td>
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<td>Mean</td>
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<td>33.6</td>
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<td>25.9</td>
<td>33.5</td>
<td>3.8</td>
<td>5.4#</td>
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</tbody>
</table>

* Received 500 ml. blood.
† Assisted respiration.
‡ Received 250 ml. blood.
§ Received 1,100 ml. blood.
# Change is statistically significant (P < 0.001).
as the initially observed value in the acidic patient. A two to three hour period of operation under uncomplicated diethyl ether anesthesia was associated with a significant progressive rise in the plasma inorganic phosphate level (P < .001), but the absolute values observed were much lower than those in the acidic case. A three-hour period of surgery under uncomplicated diethyl ether anesthesia raised plasma 17-hydroxycorticosteroids to the values found in the acidic patient.

**DISCUSSION**

The degree of acidosis observed in this patient is one of the most severe we have found reported. Four patients have been reported having plasma pH values less than 6.8. Three of these 4-6 have expired within forty-eight hours of sampling, after pH values of 6.67, 6.73 (venous) 5 and 6.7, 6 Stephen, Bourgeois-Gavardin and Dent 7 have reported recovery after an arterial pH value of 6.80 in a patient following general anesthesia.

The similarity between the alveolar and arterial CO₂ tensions in the patient reported here, each obtained by different methods, attests to the validity of the pH value. While the nature of the disturbance is predominantly respiratory, a metabolic component doubtless contributed in part to the low pH. Diethyl ether anesthesia is associated with a varying degree of fixed acid accumulation 15, 16 and hypercapnea itself will evoke a metabolic acidosis. 17, 18 The acidosis in this patient is largely a consequence of the large instrumental dead space of the defective apparatus and the resulting hypoventilation. Increasing the external dead space has been utilized occasionally to raise the alveolar and arterial carbon dioxide levels. Rahn and Otis 19 employed such a method when plotting alveolar pathways during voluntary hypoventilation in conscious humans. Our measurements indicate that in the patient reported here the external dead space was between 700 and 1,000 ml. Stannard and Russ 20 have shown that in the resting conscious subject alveolar CO₂ will rise if the external dead space exceeds 600 ml. This critical value of dead space for CO₂ accumulation will of course be lowered in the anesthetized individual. The rate of CO₂ elimination undoubtedly was uneven because of changing depths of anesthesia and occasional emptying of the rebreathing bag, but it is probable that a steady state of carbon dioxide elimination with an alveolar CO₂ of about 30 per cent existed at least twenty minutes and possibly as long as two and one-half hours. Oxygenation was not a problem in this case because of the high concentrations of oxygen in the inspired gas mixture (in excess of 70 per cent). Under such conditions the saturation of arterial blood will remain normal even though alveolar ventilation is reduced to low levels. 20-23

Clinically one of the most striking aspects of this case is the relative lack of signs indicative of hypercapnea and acidosis. The discovery of the absent directional valves was fortuitous and in no way did the anesthesiologist believe the patient in jeopardy immediately before the discovery.

A rise in blood pressure, which has classically been associated with hypercapnea 24, 25 was not observed in this patient. However, Dripps 26 was unable to elicit a pressor response with hypercapnea in a patient under ether anesthesia, and it is possible that the diethyl ether in this patient similarly prevented the pressor response. In retrospect, the two
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transient periods of hyperpnea were probably a consequence of hypercapnea and acidosis, but were misinterpreted as signs of light anesthesia. In time, however, the hydrogen ion stimulus for ventilation probably became ineffective and the narcotic effects of high CO₂ and deep ether anesthesia began to act on the respiratory center to suppress ventilatory drive. The vasodilation seen in the face and lips of the patient at the time of discovery probably reflects the direct dilatory actions of carbon dioxide on the peripheral vessels. The rest of the clinical picture at this time is best explained by the release of epinephrine and norepinephrine evoked by hypercapnea and ether anesthesia.

The gradual reduction of alveolar carbon dioxide was deliberate in this case, since rapid carbon dioxide washout after hypercapnea is associated with arrhythmias, hypotension and ventricular fibrillation in animals and humans. The pH of 7.31 two hours after the alveolar CO₂ had been returned to normal levels again suggests the presence of a metabolic component to the acidotic picture.

The convulsive episode observed one hour postoperatively and two and a half hour after return to normal alveolar CO₂ levels has never been observed as a posthypercapneic phenomenon by us, and is possibly related to the low ultrafiltrable calcium levels in the posthypercapnic state. The response of this patient to intravenous calcium gluconate tends to support this assumption.

The initially observed plasma potassium level in the acidotic patient is greater than the mean value observed in the control group of nonacidotic patients. The initial level in the acidotic patient is greater than any individual values observed in the control group, although two values in the control group approach the initial acidotic value. We are, of course, unable to determine whether the initial potassium value in the acidotic patient indicates a real increase as a consequence of hypercapnea or an unchanged high random value. We believe, however, that the figure probably represents a value which is elevated above the unknown preanesthetic level. Brown observed a mean plasma potassium level of 4.4 mEq./l. in dogs after ½ hour of 30 per cent CO₂ inhalation, and a mean level of 5.0 mEq./l. after one hour of CO₂ inhalation. The value observed in this patient appears to be consistent with the levels observed in Brown's animals after a similar period of CO₂ inhalation. Plasma potassium estimation in this patient showed a twenty-four hours after the insult was found to be 3.9 mEq./l. A similar mean figure for plasma potassium was observed in the preanesthetic controls in this series and in the group previously reported from this department. Lurie et al. were unable to find any striking relationship between plasma potassium and carbon dioxide tension in the anesthetized human. Elkin and co-workers failed to show any change in the plasma potassium of conscious humans exposed to concentrations of 7.5 per cent CO₂ for short periods of time. Similarly, a one-hour inhalation of 10 per cent CO₂ by anesthetized humans produced no alterations in plasma potassium although elevations have been observed in the dog and rat when breathing concentrations in excess of 10 per cent. On the basis of the observations in this one patient, it seems possible that a critical concentration of inspired CO₂ must be exceeded if a rise in plasma potassium is to be evoked in the human. This critical concentration probably lies between 10 and 30 per cent. Fenn and Asano have found such a threshold in the cat.

The elevated serum inorganic phosphate in the presence of hypercapnea is consistent with the finding of other observers. Haldane, Wigglesworth and Woodrow reported slight rises in blood inorganic phosphate in the human during the inhalation of carbon dioxide mixtures, and rises have been noted in the dog and cat. The levels observed in the patient are comparable to those observed in dogs after four hours of 30–40 per cent CO₂ inhalation and are much greater than values observed under uncomplicated diethyl ether anesthesia. Tulin et al. have observed a direct relationship between plasma phosphate and hydrogen ion concentration in vitro. These workers suggest that the increased phosphorus is derived from the breakdown of organic phosphate esters. The plasma phosphate level in this patient twenty-four hours later was 4.2 mg. per cent.

Richards and Stein have reported that
anesthetized dogs exposed to 20% carbon dioxide display an early persistent manifestation of maximal adrenocortical stimulation. Since we observed a rise in 17-hydroxycorticosteroids in a control patient (table 3) we believe that the elevated levels in the acidoic patient are more likely a consequence of the anesthesia and surgery. Rises in 17-hydroxycorticosteroids during ether anesthesia and surgery have been reported by Virtue, Helmreich and Gainza and Hammond et al. We assume that diethyl ether anesthesia and surgery evoked a maximal adrenal cortical response and that the additional hypercapneic challenge therefore failed to increase adrenocortical activity.

The decline in plasma potassium during the carbon dioxide washout period has been observed in the dog and cat. If the carbon dioxide washout is slow, as it was by intent in this case, the potassium decline is not preceded by an initial abrupt rise at the beginning of the washout period. The persistence of the hyperphosphatemia during the washout period is consistent with what has been observed in animals.

Since submission of this manuscript, Frumin, Epstein and Cohen have reported changes associated with apneic oxygenation in eight anesthetized humans. In their study one patient exhibited an arterial pH of 6.72. Plasma potassium levels were measured in three patients, and in each patient were elevated above control values. Data relating to pH and CO₂ concentration at the time of potassium elevation are tabulated for one of these three patients and these data appear consistent with our assumption concerning the critical concentrations of CO₂ necessary to evoke the potassium response in man.

**Summary**

A case of severe acidosis in an anesthetized human is described. Determination of plasma electrolytes in this patient suggests that both potassium and inorganic phosphate will rise as a consequence of carbon dioxide inhalation. The critical concentration of carbon dioxide necessary to evoke the potassium response is in excess of 10 per cent, but probably less than 30 per cent. Slow return from the acidoic state is associated with a decline in plasma potassium but the hyperphosphatemia tends to persist.

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**REFERENCES**


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