The Acid-Base Vector of Open-Heart Surgery

By Francis A. Puyau, M.D., Richard E. L. Fowler, M.D., Rosalind Novick, M.D., Harold Albert, M.D., and Bert Glass, M.D.

The outstanding acid-base change associated with extracorporeal circulation in cardiac surgery has been demonstrated to be metabolic acidosis, which has been variously reported to occur during perfusion or in the postoperative period.1-4 Since thoracic operations other than cardiac are known to produce marked changes in acid-base balance,5-7 intensive serial study of patients during open-heart surgery might help to unravel some of the events influencing a patient’s acid-base status during these very complicated operative procedures. The present report presents the data derived from 14 patients studied in an attempt to relate acid-base changes to operative events.

The technic of plotting serial acid-base changes on the nomogram of Hastings and Steinhaus8 had long been used in our laboratory for following the course of patients with other acid-base disturbances, such as those produced by diarrhea or salicylate intoxication. This nomogram, shown in figure 1, is useful because a single point describes the relation of the three variables of the Henderson-Hasselbach equation; thus simultaneous values of pH, pCO2, and (HCO3)− can be plotted serially over an extended period. The changes that occur in these values can be identified as respiratory or metabolic in origin by the direction of the graphic pathway on the nomogram. Changes in relative concentrations of fixed cations and anions are displayed along, or in a direction parallel to, the metabolic axis; those representing primarily change in CO2 tension are displayed along or in a direction parallel to the respiratory axis.

Plan of Study—Methodology

Fourteen patients ranging in age from 3 to 35 years were submitted to open-heart surgery (table 1). Perfusion equipment consisted of a sigma motor pump and rotating disk oxygenator perfused with 100 per cent O2 at a flow of 12 to 15 liters per minute.

Oxygenation of perfusing blood was carried out in a large 98-disk chamber for all patients except nos. 2 and 11, in whom a 56-disk chamber was used. Blood passing through the oxygenator was warmed by means of an external wire-coil heater while the disks were rotated at 120 RPM. During perfusion the patient’s body temperature usually fell to 34-35 C, due to loss of heat from the perfusing blood during passage through the tubing between oxygenator and patient. An attempt was made to obtain flow rates approximating 2.2 L./M.2/minute; the problems of balancing perfusion sometimes caused some variation.

An indwelling arterial needle was placed in the radial artery of each patient prior to the induction of anesthesia when possible. Arterial blood was removed at intervals varying from as often as every 5 minutes during surgery to intervals of 1 to 2 hours in the postoperative period. The pH was measured immediately at 37 C. with a Coleman pH meter in the operative suite. Plasma was separated under mineral oil and refrigerated immediately, and CO2 content was measured later by the technic of Van Slyke and Neill. The pCO2 was calculated from the observed values. Plasma sodium and potassium were measured with a Weichselbaum-Vorney Universal Spectrophotometer. Plasma chlorides were measured by open curius digestion and Volhard titration. The pCO2 was calculated from observed pH, and pCO2 content according to the formula:

\[ \text{pCO}_2 = \frac{\text{serum CO}_2 \text{ content}}{\text{antilog (pH-6.11) + 1}} \times 0.0311. \]

The “R” fraction was calculated from the formula:

\[ R = \frac{\text{plasma [Na} - (\text{CO}_2 + \text{Cl}])}{.} \]

Results

After the data from patients had been plotted separately on the nomogram, it became apparent that the resultant curves
showed a similar pattern. The data were then grouped into 11 intervals, onset and termination of perfusion being used as points of chronologic identity in order to relate the curves. A composite curve was then developed by averaging values derived from samples drawn at comparable times as listed below.

The circled numbers refer to the same time periods discussed in the subsequent text, and were also used for serial plotting of plasma Na⁺, Cl⁻, CO₂ content, and the calculated R fraction.

Period 1 included samples drawn before anesthesia.

Periods 2, 3, and 4 included samples from 2 1/2 to 1 1/2 hours, 1 1/2 to 3/4 hours, 3/4 to 0 hours before perfusion, respectively. Period 2 usually included the samples obtained before the chest was opened and periods 3 and 4 included samples withdrawn after the chest had been opened.

Periods 5 and 6 included samples from 0 to 1/2 and 1/2 to 1 hour of perfusion.

Periods 7, 8, 9, 10, and 11 included samples from 0 to 1/2, 1/2 to 1, 1 to 2, 2 to 4, and 4 to 6 hours after perfusion. Period 9 included samples usually obtained during extubation when the patient was breathing without assistance. Periods 10 and 11 included samples obtained in the recovery unit.

Data on the 14 patients, including pH, CO₂ content, Na⁺, Cl⁻, and "R" fraction are shown in figures 2 to 5 as scatter graphs. Since mean plasma Na⁺ and Cl⁻ vary little from period to period, only pH, CO₂ content, and "R" will be further considered. Mean values for these measurements determined for each period are shown in Table 2. "R" value determined from 35 patients without acid-base disturbance previously studied in our laboratory averaged 13.8 ± 2.5 mEq./L. When mean pH and pCO₂ values were plotted in...
### Table 1

**Clinical Data in 14 Patients**

<table>
<thead>
<tr>
<th>No.</th>
<th>Patient</th>
<th>Age (yr.)</th>
<th>Weight (lb.)</th>
<th>Diagnosis</th>
<th>Perfusion Time in min.</th>
<th>Perfusion Rate L per min.</th>
<th>Surgical results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>L.W.</td>
<td>3</td>
<td>25</td>
<td>Endocardial cushion defect with pulmonary hypertension</td>
<td>53</td>
<td></td>
<td>Died 22 hours after perfusion from extensive intrathoracic bleeding and pulmonary atelectasis</td>
</tr>
<tr>
<td>3</td>
<td>T.L.</td>
<td>14</td>
<td>80</td>
<td>Ventricular septal defect, mitral stenosis, pulmonary hypertension</td>
<td>20 2.0</td>
<td></td>
<td>Died on 12th postoperative day from complete heart block when pacemaker wires pulled out of myocardium</td>
</tr>
<tr>
<td>4</td>
<td>R.M.</td>
<td>14</td>
<td>94½</td>
<td>Ventricular septal defect</td>
<td>18 4.0</td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>5</td>
<td>W.W.</td>
<td>18</td>
<td>109</td>
<td>Ventricular septal defect</td>
<td>30 2.9</td>
<td></td>
<td>Survived—defect recurred</td>
</tr>
<tr>
<td>6</td>
<td>W.B.</td>
<td>6</td>
<td>38½</td>
<td>Ventricular septal defect, severe pulmonary hypertension</td>
<td>27 2.8</td>
<td></td>
<td>Died 11 hours after perfusion; autopsy showed common ventricle, corrected transposition of great vessels</td>
</tr>
<tr>
<td>7</td>
<td>R.B.</td>
<td>13</td>
<td>104</td>
<td>Atrial and ventricular septal defects, pulmonary valvular stenosis, anomalous pulmonary vein</td>
<td>31 4.0</td>
<td></td>
<td>Died 14 days after surgery—2 days previously had median sternotomy evisceration. Autopsy showed tracheobronchitis, bronchopneumonia, hemotherax</td>
</tr>
<tr>
<td>8</td>
<td>E.C.</td>
<td>23</td>
<td>110</td>
<td>Atrial septal defect</td>
<td>15</td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>9</td>
<td>A.D.</td>
<td>29</td>
<td>99</td>
<td>Myxoma of left atrium</td>
<td>24 3.1</td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>10</td>
<td>M.W.</td>
<td>35</td>
<td>108</td>
<td>Mitral stenosis and insufficiency</td>
<td>57 2.6</td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>11</td>
<td>O.V.</td>
<td>4</td>
<td>32</td>
<td>Ventricular septal defect, previously banded pulmonary artery</td>
<td>44 1.75</td>
<td></td>
<td>Survived—defect recurred</td>
</tr>
<tr>
<td>12</td>
<td>R.C.</td>
<td>13</td>
<td>69</td>
<td>Ventricular septal defect with infundibular pulmonary stenosis; previous infundibulecctomy</td>
<td>50 3.2</td>
<td></td>
<td>Died 6 hours after perfusion; autopsy showed ventricular septum to be open and a torn aortic valve cusp from a penetrating suture</td>
</tr>
<tr>
<td>13</td>
<td>M.N.</td>
<td>26</td>
<td>119</td>
<td>Atrial septal defect with pulmonary stenosis</td>
<td>6 3.6</td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>14</td>
<td>J.J.</td>
<td>13</td>
<td>75</td>
<td>Atrial septal defect; anomalous pulmonary vein</td>
<td>18 3.3</td>
<td></td>
<td>Survived</td>
</tr>
<tr>
<td>15</td>
<td>B.L.</td>
<td>7</td>
<td>46</td>
<td>Atrial septal defect</td>
<td>16 2.2</td>
<td></td>
<td>Survived</td>
</tr>
</tbody>
</table>
mild respiratory alkalosis develops. "R" rises slightly (table 2).

5. In the initial period of perfusion the oxygenator causes marked respiratory alkalosis. Through this point the main changes in acid-base balance have occurred along the respiratory axis of the nomogram, although it should be noted that a significant increase in "R" occurs during this period (table 2).

6. At this point during prolonged perfusion, a basically different change occurs along the direction of the metabolic axis of the nomogram characterized by a fall in pH while pCO₂ remains constant. This change may be considered to be a decrease in alkali reserve or (HCO₃⁻)⁻ concentration while the pCO₂ level is kept relatively constant by the oxy-

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genator. This change in the curve hereafter will be referred to as the 'metabolic shift,' and occurs simultaneously with progression of "R" value to a peak level (table 2).

7. Immediately after perfusion pCO$_2$ rises to the pre-perfusion level while pH falls steadily. This period may be considered a transient mixed state between respiratory alkalosis with superimposed metabolic acidosis and a state of essentially pure metabolic acidosis, which remains after the hyperventilation effect of the oxygenator has disappeared. "R" falls slightly (table 2).

8 and 9. During the remainder of the operation pH continues to fall to a moderately acidic level, influenced mostly by persistence of the metabolic shift but compounded by increasing pCO$_2$ as the patient resumes his own respiration. This trend culminates at period 9, when hypoventilation occurs associated with the events at extubation. "R" continues to fall (table 2).

10 and 11. During these periods shortly after surgery (when the patient is in the recovery room) the vector begins to move toward normal values in a direction parallel to the metabolic axis. The secondary rise in "R" noted at this time results chiefly from the poor postoperative status of several patients.

Vectors from three individual patients are shown in figures 7 to 9. The pattern of the curves is similar, though the individual values and time periods vary widely. Patient no. 3 (fig. 7) showed the widest deviation along the metabolic axis of any of the patients of this series, despite the fact that the initial change during perfusion was the development of marked respiratory alkalosis. The initial flow rate in this patient was low, 1.5 L./M.$^2$; however, the rate was increased gradually during perfusion to 2.2 L./M.$^2$ after 18 minutes, then to 2.4 L./M.$^2$ after 50 minutes of perfusion. Despite a flow rate considered adequate during the last half hour of perfusion, this patient's pH fell into the acidotic range, while bicarbonate declined simultaneously. Patient no. 10 (fig. 8) developed marked respiratory acidosis during induction of anesthesia, but followed the usual pattern of respiratory alkalosis during the initial period of perfusion. Despite a long perfusion time (57 minutes) and a low flow rate, 1.8 L./M.$^2$, she did not demonstrate the metabolic shift commonly seen in other patients. Following perfusion, at the time of extubation pCO$_2$ again rose to a high level, in the range of respiratory acidosis, and showed gradual fall toward normal during recovery. Her respiratory acidosis may have been related to position during surgery (left side up), which has been reported as a significant factor.

Table 2

<table>
<thead>
<tr>
<th>Period</th>
<th>pH</th>
<th>pCO$_2$ mm.Hg</th>
<th>CO$_2$ content mM/L.</th>
<th>&quot;R&quot; mEq./L.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preanesthesia</td>
<td>1</td>
<td>7.42</td>
<td>36.0</td>
<td>23.4</td>
</tr>
<tr>
<td>Induction of anesthesia</td>
<td>2</td>
<td>7.31</td>
<td>49.1</td>
<td>23.3</td>
</tr>
<tr>
<td>After thoracotomy</td>
<td>3</td>
<td>7.43</td>
<td>32.7</td>
<td>22.6</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>7.43</td>
<td>31.2</td>
<td>20.1</td>
</tr>
<tr>
<td>Perfusion</td>
<td>5</td>
<td>7.50</td>
<td>19.5</td>
<td>15.5</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>7.45</td>
<td>18.8</td>
<td>13.2</td>
</tr>
<tr>
<td>After perfusion</td>
<td>7</td>
<td>7.37</td>
<td>28.7</td>
<td>16.7</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>7.30</td>
<td>36.7</td>
<td>18.6</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>7.28</td>
<td>41.3</td>
<td>20.5</td>
</tr>
<tr>
<td>Recovery</td>
<td>10</td>
<td>7.32</td>
<td>38.3</td>
<td>21.4</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>7.33</td>
<td>37.4</td>
<td>20.9</td>
</tr>
</tbody>
</table>
Figure 6

Mean acid-base vector in 14 patients undergoing open-heart surgery, the double line representing perfusion.

Patient no. 11 (fig. 9) has a fairly typical vector, showing respiratory acidosis initially, mild respiratory alkalosis during thoracotomy, marked respiratory alkalosis initially during perfusion followed by a metabolic shift, then passage through metabolic acidosis, and finally mixed metabolic and respiratory acidosis before returning toward normal. He was perfused for 10 minutes at a flow rate of 2.0 L/min., then for 34 minutes at a rate of 2.9 L/min. The metabolic shift occurred in this patient also during the period of the higher perfusion rate. All three of these patients survived the acidosis of the postoperative period without administration of alkali.

Discussion

Although an enormous amount of data concerning the effects of pump oxygenators on acid-base balance has appeared in the recent literature, the results have not always been in agreement, in part because of a diversity of equipment and methods. Thus, type of oxygenator, rate of blood flow, rate of gaseous perfusion, type of perfusing gas, status of acid-base balance of pump-priming blood, length of perfusion, and many other factors affect the nature of the observed data. Metabolic acidosis has frequently been reported during perfusion or in the postoperative period and thought due to pre-existing
respiratory alkalosis, rising lactic acid levels, hypoxia, or low flow rates. It would seem that in a situation in which rapid change of the patient’s status is inevitable and anticipated, occasional cross-sectional sampling may produce results which, while valid, throw little light on the developmental pathophysiology of abnormalities of acid-base balance. The hazards of interpretation of such data must not be overlooked, since a single point in a curve gives no information of the direction in which the disturbance is moving. The therapeutic implications of such gaps in knowledge are obvious.

The present report represents an attempt to delineate the serial acid-base disturbances encountered by patients submitted to such surgery under conditions which, while possibly not ideal, were at least relatively uniform. A clearer understanding of the meaning of such data can be obtained by plotting the patients’ consecutive states of acid-base balance on a nomogram such as the one used in this report. Such a depiction demonstrates that metabolic acidosis concealed by sustained hyperventilation (respiratory alkalosis) is uncovered only in the post-perfusion state after respiratory alkalosis has subsided but should be considered a phenomenon of the perfusion rather than the post-perfusion phase. The developed curve also appears to indicate that ordinarily in the immediate postoperative period, when attention is usually first focused on the patient’s acid-base status, the disturbance has already begun to subside spontaneously as demonstrated by declining “R” values. Our data indicate that unidentified anions begin to accumulate in the “R” fraction before perfusion but reach a maximum level during perfusion. We have
Figure 8
Acid-base vector of patient no. 10, the double line representing perfusion.

not measured lactic and pyruvic acid in these patients though their accumulation during extracorporeal circulation and during periods of hypotension or poor tissue perfusion have been emphasized by other workers. There is good evidence that lactic acid accumulates during respiratory alkalosis as a buffering mechanism. Recent authors have emphasized the occurrence of "excess" lactic acid during anaerobic metabolism as a result of perfusion at inadequate flow rates as an explanation of metabolic acidosis.

Our results indicate that the concentration of unidentified anions associated with an increase in "R" begins to fall just after perfusion. The level in the second half hour after perfusion, 16.6 mEq./L, is not significantly different from the level of 16.2 mEq./L observed immediately before perfusion. These two positions on the vectors 7 and 4, however, represent mild metabolic acidosis and mild respiratory alkalosis, respectively. These significantly different pH and CO₂ content values are not accounted for by observed differences in unidentified anion levels. A more precise evaluation of the influence of the "R" factor would have been provided by measurement of lactate and pyruvate values not carried out in this study.

The reasons for the metabolic shift during perfusion are not completely clear. Prolonged perfusion appears to be a factor, though the shift did not occur in one patient (no. 10) perfused for 57 minutes. Inadequate flow with systemic hypotension appeared to be a factor in one patient (no. 12), who developed a marked metabolic shift associated chronologically with this complication. Accumulation of organic acids in the priming blood before beginning perfusion might play a role...
in producing the fall in bicarbonate during perfusion. This factor, not evaluated in this study, would not seem to be involved in these patients in whom the metabolic shift seemed to occur late in perfusion. The significance of the shift is unclear, since the patient with the greatest change during perfusion (no. 3) did very well in the immediate postoperative period without specific treatment for acidosis, though she died 12 days after as a result of complete heart block.

One patient, whose data were not included in this series, underwent three separate periods of perfusion over a period of 1½ hours: 9 minutes at a flow of 1.75 L./M.², 18 minutes at 2.2 L./M.², and 9 minutes at 1.75 L./M.². Each period of perfusion was associated with development of respiratory alkalosis and a small metabolic shift. The largest metabolic shift occurred during the second perfusion at the time of the highest flow rate. Subsequently, after the third perfusion, metabolic acidosis developed.

Comparison of low with high flow rates in animals by several authors has shown that acidosis usually occurs with “normal” or high flow rates, as well as low flow rates, though it is not so severe. Additional factors may be presumed to be involved or possibly “high flows” may still be inadequate.

Finally, it is apparent that respiratory acidosis is a frequent occurrence early in surgery, due to inadequate ventilation during induction of anesthesia. A period of mixed respiratory and metabolic acidosis occurs in a similar manner during closure of the chest when the anesthesiologist decreases the level of anesthesia and allows the patient to assume spontaneous respiration. These changes during surgery, while predictable on the basis of...
ACID-BASE VECTOR

previous reports, are again demonstrated and emphasized by the serial sampling technic followed in this study.

Summary

Fourteen patients submitted to open-heart surgery were studied by serial acid-base and electrolyte determinations in order to demonstrate the sequence and magnitude of disturbances associated with the procedure. Under conditions of the study, including the use of 100 per cent oxygen as the perfusing gas for the oxygenator, respiratory alkalosis develops as the initial change during perfusion but is followed by a "metabolic shift" characterized by falling pH and CO₂ content, while a stable, moderately low pCO₂ is maintained by the oxygenator. The resulting state of mixed respiratory alkalosis and metabolic acidosis changes into a state of relatively pure metabolic acidosis as the bicarbonate content rise while pH falls after perfusion. The factors involved in the "metabolic shift" responsible for development of metabolic acidosis are not identified by this study although length of perfusion, perfusion pressure, and rate of flow are considered as possible factors. Acidosis persists through the early phases of the recovery period but ordinarily resolves without administration of alkali. Serial sampling technics as used in this study may aid in the interpretation of postoperative acidosis, distinguishing between patients who are deteriorating and those who are passing through a transient phase in the process of recovery.

References


On coming to Harvard College I was suddenly plunged into the new experience of listening to lectures and being required to take notes. At the first lecture I attended, I happened to sit beside a rather badly battered and very ponderous member of the football team. In my ignorance I turned to him for advice, asking him what to put down in my notebook. He growled back *sotto voce*, "Wait till he says something loud. Put that down." It was not long before I learned that, in spite of such expert testimony, there was a great difference between sound and sense.—WALTER B. CANNON, M.D. The Way of An Investigator. New York, W. W. Norton & Company, Inc., 1945, p. 17.
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