Net Acid Balance in Infants with Diarrhea and Carbohydrate Intolerance

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The most common acid–base disturbance in dehydrated infants with diarrhea is a hyperchloremic metabolic acidosis resulting from the loss of intestinal bicarbonate by two different mechanisms: (a) loss into the stool and (b) buffering by organic acids (OA) produced within the colonic lumen by bacterial fermentation of undigested food. The first mechanism is seen usually in secretory diarrhea, and the second in malabsorptive, fermentative, or osmotic diarrhea.

Malabsorptive diarrhea must be considered in those patients in whom diarrhea stops when the malabsorbed nutrient is eliminated from the diet. Watery, acid stools (pH < 5.5) and presence of carbohydrates in feces are observed in many of these patients, but even when carbohydrates are not detected in stools, shifts in blood pH concentration may occur. In fact, the amount of bicarbonate excreted and, consequently, the pH of the stools are determined by the amount of OA being produced into the colon. To the extent that intestinal bicarbonate is titrated by the OA, the corresponding organic anion (OA\textsuperscript{-}), rather than bicarbonate, is excreted with an acid or alkaline pH of the stools. Therefore, fecal pH is not a reliable test for the diagnosis of fermentation. Although fermentation must be considered whenever the stool pH is less than 5.5, it cannot be excluded if fecal pH is normal or elevated.

Several superimposed factors may be present in diarrheal illnesses (hyperventilation, vomiting, consequent electrolyte depletion, etc.) that may modify the usual acid–base picture commonly seen in infants dehydrated by diarrhea.

STUDY OF ACIDOSIS IN INFANTILE DIARRHEA

The study of acidosis in diarrheal disease of infancy was initiated by Howland and Marriot (1) and Schloss and Stetson (2). In independent work, they suggested that the failure of renal acid excretion secondary to dehydration was a major factor causing acidosis. Since then, other possible etiologies have been proposed.
Table 1 lists the principal theories as to the etiology of metabolic acidosis of infant diarrhea.

The first four causes of acidosis listed in Table 1 do not appear to play a major role in the genesis of the disorder in infant diarrhea (3). Those mechanisms can be observed in only a minority of infants with acidosis. Overproduction of lactic acid in dehydrated patients occurs only in relation to anaerobic situations, e.g., shock and tissue hypoxia. Shifts of hydrogen ion from intracellular to extracellular space were reported by Sotos and co-workers (4) as occurring in hypertonic status. Dilutional acidosis was suggested by Winters et al. (5) consequent to hyperosmotic infusions. Finally, increased production of ketoacids has been observed in fasting states, but their production in dehydration can be suppressed completely even when caloric intake is low (6).

Renal excretion of acid has been studied only during recovery from diarrheal dehydration (3,7–9). Defective renal excretion of acid obviously occurs during the transient period of renal failure as a result of reduction of glomerular filtration rate and renal plasma flow as a consequence of dehydration and hypovolemic status (9). Endogenous production of nonvolatile acids from neutral nutrient compounds and intestinal production of unabsorbed undetermined anions are discussed later in this chapter.

Excessive loss of bicarbonate in stools was found to be a major cause of acidosis in Asiatic cholera diarrhea (10) as well as in other noncholera secretory diarrheas but not in any common infantile diarrheas. The theory of bicarbonate loss into the stool as a cause of acidosis in common diarrhea is based on the classic observations of Darrow (11) and Chung (12). They observed an increased preponderance of fixed cations over anions in the stools of infants with diarrhea. This fact was demonstrated by Holt et al. in 1915 (13). Subsequently, Darrow suggested that such fecal losses would lead to the addition of acid to the body fluids. This predominant loss of inorganic cations over anions was taken as evidence of loss of bicarbonate into the stool. However, in 1965, Teree and co-workers (14) carried out fecal analyses and reported that the pH of the stool water in infant diarrhea was frequently acidic and that bicarbonate was very low or absent. They suggested that the presence of a high concentration of OA, based on the differences between (Na\(^+\) + K\(^+\) and Cl\(^-\)), was responsible for the low stool pH. In addition, they speculated that the OA production was consequent to sugar fermentation by colonic bacteria. Such a mechanism had already been

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TABLE 1. Genesis of acidosis in diarrhea

1. Shock and tissue hypoxia
2. Shifts of H\(^+\) from intracellular to extracellular compartment
3. Dilutional acidosis
4. Increased production of ketoacids in starvation
5. Endogenous production of nonvolatile acids from catabolism of neutral compounds
6. Excessive losses of bicarbonate into stools
7. Increased intestinal production of unabsorbed undetermined anions
8. Defective renal excretion of acid
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postulated for infants with fermentative diarrhea by Weijers and Van De Kamer in 1963 (15). Teree et al. concluded that organic anion lost in stool, regardless of the stool pH, contributed acid to the body fluids. When organic anions are lost in stool (as salts), their H⁺ remain behind, consume body buffer, and require urinary excretion for acid–base homeostasis. Teree and co-workers proposed that stool volume is an important and prominent factor in dictating the quantitative effect of stool loss on acid balance.

To test the hypothesis of Teree et al., Torres-Pinedo and co-workers (16) attempted to reproduce the conditions of systemic acidosis that occur in acute diarrhea. They studied the influence of milk intake on the composition of the stool and on the acid–base equilibrium during fasting and intravenous rehydration. The experimental design is shown in Fig. 1. Evaporated or cow’s milk was given to six diarrheal infants. Diarrhea ensued with stool volumes greater than 300 ml in the first 12 hr and a concomitant decrease in urine volume. Consequent to dehydration and low renal acid excretion, metabolic acidosis developed in all patients. The investigators also observed that the effect of milk feeding was apparent in both the volume and acidity of the stools. The low stool pH (pH = 5.34) was caused by the presence of high concentrations of organic acids, of which one-half the total was lactate. In the second period, after discontinuation of milk and starting of i.v. fluids, the reverse effect was observed. Normalization of acid–base balance in blood was seen during the last 12 hr of treatment.

The contribution of milk carbohydrate to the fecal alterations was still a question, and so a subsequent experiment was done in which four infants with diarrhea were challenged orally with glucose, lactose, sucrose, and fructose. The fecal sugar concentration increased and was accompanied by a fall in stool pH; concentrations of lactic and organic acids were increased. The changes induced in stool composition were quantitatively similar to those observed with milk ingestion in diarrhea. It was suggested that the organic acid in the stool was the consequence of carbohydrate ingestion and malabsorption. Carbohydrate reaching the colon caused overproduction of organic acids as a consequence of bacterial anaerobic metabolism. Rubenstein et al. (17), who studied the organic anion component by in vivo dialysis of feces as a method of stool analysis, have demonstrated a positive correlation between hydrogen ion activity and organic anion concentration in fecal dialysate. This striking relationship suggests that the generation of both is closely linked and probably derived from organic acids, which themselves arise from neutral precursors. Torres-Pinedo et al. (16) concluded that increased fecal excretion of endogenously produced organic anions as neutralized dissociated salts play an important role in the genesis of the acidosis in this type of infant diarrhea. In addition, they speculated that failure of renal excretion of increased acid loads was the precipitating factor of the acidosis.

Two years later, Torres-Pinedo et al. (18) confirmed the generation of OA through compositional changes of the various constituents of saline and glucose–
saline solutions instilled into the colon of infants with acute diarrhea. The effects induced by the presence of glucose into the colon were (a) formation of poorly absorbable organic acid salts; (b) decrease of Na⁺ absorption; (c) increased K⁺ loss; and (d) net increase in volume of the colonic fluid and net gain of hydrogen ion by the body fluids. The last effect was based on the reaction shown in Fig. 2 and is quantitatively similar to the loss of an equivalent amount of bicarbonate in the colon. The constant neutralization of the HCO₃⁻ would preclude establishment of diffusion equilibrium maintaining a high rate of HCO₃⁻ facilitated by HCO₃⁻/Cl⁻ exchange. Other investigators arrived at these conclusions: Argenzio et al. (19) studied absorption of short-chain fatty acids (SCFA) in the large intestine of animals, and McNeil et al. (20) and Ruppin et al. (21) carried out the same studies in man. These studies showed that luminal hydration of
CO₂ occurs and allows protonation of the SCFA; their absorption (diffusion in the un-ionized form) would produce HCO₃⁻ accumulation and a fall in Pco₂. Lifshitz et al. (22) suggested that the organic acids were quickly absorbed by the colon, thus inducing metabolic acidosis, to explain the development of systemic acidosis in the premature infant.

In summary, pediatric gastroenterology studies have shown that fecal excretion of endogenously produced organic anions as neutralized dissociated salts is an important cause of metabolic acidosis in malabsorptive infant diarrhea.

**NUTRITION AND ACID–BASE STUDIES**

Another line of research that combined dietary and acid–base metabolism studies was carried out by Lennon et al. in 1966 (23). These authors also confirmed that the gastrointestinal tract plays a role in the acid balance in normal subjects. They emphasized that the excess organic anion excreted in the feces contributed hydrogen ion to the body and should be taken into account in net external acid balance studies.

A number of investigations were carried out to identify and clarify the components of endogenous production and fecal disposition of acid and base. Shohl and Sato (24) first studied acid–base balance and diet in 1923. They investigated the alterations in renal acid and fecal excretion in two infants when sodium bicarbonate and hydrochloric acid were administered with milk. The milk was considered to have a high net base concentration despite its low pH. Their balance data showed that a positive net base balance (cation retention greater
than anion) occurred with bicarbonate ingestion. The net base retention was associated with increased fecal base excretion and normal growth. These investigators believed that the effects of food on acid-base metabolism were related to the acidity or alkalinity of dietary ash. If the cations were in excess, the foodstuff was considered to provide an alkaline ash, which should give rise to an alkaline urine, as occurs in bicarbonate ingestion.

The effects of acidity or alkalinity of dietary ash were studied by Hunt (25). When diets with different alkaline ash (milk and vegetables) were administered to volunteers, no relationship was observed between an alkaline ash diet and urinary excretion of acid. He did find good correlation, however, between total net acid excretion and urinary sulfate excretion. This fact had been demonstrated earlier by Sherman (26). To test the influence of diets with a high sulfur content, one volunteer was persuaded to ingest a diet with 583 mEq of sulfur dl-methionine. He then observed that the net acid excretion matched the urinary sulfate excretion of this volunteer. But, in a further study, beef fillet was provided as the only source of food, and the relationship was not found.

To explain these discrepancies, Lemann and Relman (27) studied the influence of a sulfur-containing amino acid diet on net renal acid excretion. They concluded that in spite of observing a relationship between net acid excretion and urinary sulfate excretion, the latter was not sufficient to explain the total amount of renal acid excretion. Relman et al. (28) searched for a second component of endogenous acid production. They gave a special liquid-formula diet consisting of purified soy phosphoprotein, essentially free of mineral cations, to volunteers. They discovered that the discrepancies between sulfate production and net acid excretion in the steady state could be accounted for quantitatively by the sum of the total organic acids in the urine plus the acid derived from the cations neutralizing the phosphate groups in the protein ingested. They also found that hydrogen ion production, extrapolated from a combination of the two metabolic sources, accounted for the net acid excretion measured. Relman et al. proposed that endogenous acid production could be estimated by the sum of urinary inorganic sulfate and organic acid salts.

The technique developed by Relman et al. required the use of a special diet that was unpalatable and nutritionally poor. Lennon and associates (23) modified this technique by measuring endogenous acid production utilizing three different types of diets: two consisted of whole foods, and one was a new liquid-formula diet. When studies were done using these diets, no correlation was found between renal acid excretion and the sum of urinary sulfate and organic acid salts. However, when gains of potential alkali from the diet (undetermined anions) were subtracted (Fig. 3, middle graph) from total effective acid production, a good correlation between acid production and renal acid excretion was found. Better correlation was achieved by taking the undetermined anion in the stool into consideration (Fig. 3, bottom graph). With this refinement, Lennon et al. accounted for the contribution of the gastrointestinal tract (GIT), closing the circle with the clinical studies of Torres-Pinedo.
NET EXTERNAL ACID BALANCE TECHNIQUE

Figure 4 is a schematic diagram of net acid balance (NAB) and its components of acid production and excretion. The NAB is defined as the difference between acid production (AP) and urinary acid excretion (AE).

Acid Production

Acid production is the consequence of the metabolic reactions listed in Table 2.

Metabolism of Neutral Compounds Ingested or Produced in the Body

Normally, urine contains a mixture of organic anions ingested or produced as a result of incomplete metabolism of carbohydrates and lipids (e.g., lactate, citrate, ketoacetate) or end products of metabolism such as uric acid.
Other compounds include inorganic sulfate, associated with sulfuric acid production by the oxidation of the sulfur-containing amino acids methionine and cystine.

The two components mentioned can be estimated by measuring the amounts of inorganic sulfate ($SO_4^{2-}$) and titrating the organic acid salts ($OA_s$) excreted in the urine. Only OA fractions that are excreted in the urine as salts contribute to the AP. If they are excreted as acids (with $H^+$), they do not contribute to AP.

**Ingestion of Preformed or Potential Base**

Foods (fruits, vegetables, milk) that contain an excess of inorganic cations over anions represent potential base because of the presence of citrate, lactate, etc. that are being metabolized to bicarbonate.
<table>
<thead>
<tr>
<th>Source of net acid</th>
<th>Metabolic reactions</th>
<th>Estimated by</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metabolism of neutral compounds</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>Glucose $\rightarrow 2$ lactate$^-^2 + 2$ H$^+$</td>
<td>Urinary excretion of organic salt</td>
</tr>
<tr>
<td>Lipids</td>
<td>Triglycerides $\rightarrow$ acetoacetate$^-^2 +$ H$^+$</td>
<td></td>
</tr>
<tr>
<td>Nucleoproteins</td>
<td>Nucleic acids $\rightarrow$ urate$^-^2 +$ H$^+$</td>
<td></td>
</tr>
<tr>
<td>Sulfur-containing amino acids</td>
<td>Methionine $\rightarrow$ urea + CO$_2$ + H$_2$O + SO$_4^{2-}$ + 2 H$^+$</td>
<td>Urinary excretion of SO$_4$</td>
</tr>
<tr>
<td><strong>Ingestion of preformed or potential base or acid</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphoproteins</td>
<td>Phosphoserine $\xrightarrow{H_2O \text{ at pH 7.4}}$ ROH + $\frac{0.8 \text{ HPO}_4^{2-} + 1.8 \text{ H}^+}{0.2 \text{ H}_2\text{PO}_4}$</td>
<td></td>
</tr>
<tr>
<td>Phospholipids</td>
<td>Lechitin $\xrightarrow{H_2O \text{ at pH 7.4}}$ ROH + $\frac{0.8 \text{ HPO}_4^{2-} + 1.8 \text{ H}^+}{0.2 \text{ H}_2\text{PO}_4}$</td>
<td>(Na + K + Ca + Mg) - (Cl + 1.8P) in diet</td>
</tr>
<tr>
<td>&quot;Combustible&quot; cations (NH$_4$Cl, arginine Cl etc.)</td>
<td>R$-NH_3^+ \rightarrow$ urea + CO$_2$ + Cl$^- +$ H$^+$</td>
<td></td>
</tr>
<tr>
<td>&quot;Combustible&quot; anions Na (citrate, lactate etc.)</td>
<td>R$-\text{COO}^- \rightarrow$ K$^+$ urea + CO$_2$ + K$^+$ + HCO$_3^-$</td>
<td></td>
</tr>
<tr>
<td>Fecal losses of preformed or potential base</td>
<td>Fecal loss of K$^+$ HCO$_3^-$ or of K$^+$ acetate$^-$, propionate$^-$, butyrate$^-$, etc.</td>
<td>(Na + K + Ca + Mg) - (Cl + 1.8P) in stool</td>
</tr>
</tbody>
</table>

* Adapted from ref. 6.
Fecal Losses of Preformed Base or Potential Base

The excess of cations in feces results from the presence of organic anions (OA\textsuperscript{−}) as acetate, butyrate, propionate, and other volatile fatty acids (VFA). The excretion of OA\textsuperscript{−}, which could have been metabolized to bicarbonate, represents potential base loss by the organism. Normally, the fecal excretion of OA\textsuperscript{−} depends on the amount ingested. In diarrhea, however, large amounts of VFA are produced by colonic fermentation of carbohydrates; thus, variable amounts of OA\textsuperscript{−} are excreted.

The undetermined anion (UA) in the diet or in stool is the difference between the cations and the anions, calculated as the sum of Na\textsuperscript{+} + K\textsuperscript{+} + Ca\textsuperscript{2+} + Mg\textsuperscript{2+} minus the sum of Cl\textsuperscript{−} + 1.8P (1.8 corresponds to the mean valence of phosphorus at pH 7.4).

The difference between UA of diet (UA\textsubscript{d}) and UA of stool (UA\textsubscript{s}) constitutes the amount of absorbed UA.

Acid Excretion

Acid excretion is measured by the urinary excretion of titratable acidity (TA) plus the excretion of ammonium (NH\textsubscript{4}) less the excretion of HCO\textsubscript{3}\textsuperscript{−}. Because TA, measured by titration, includes not only the fraction of phosphate but also the fraction associated with the OA excreted as acid, a calculation of TA is required.

Titratable acidity is calculated using the Henderson–Hasselbalch equation to estimate the urinary excretion of inorganic phosphorus fraction (pK\textsuperscript′ = 6.8) plus the creatinine fraction (pK\textsuperscript′ = 4.92).

\[ cTA = TA_{phosphorus} + TA_{creatinine} \]

Calculations

\[ NAB = AP - AE \]
\[ AP = u(SO_4) + (OA_s) - Abs\ UA \]
\[ Abs\ UA = UA_d - UA_s \]
\[ AE = cTA + NH_4^+ - HCO_3^- \]

Kildberg and co-workers (29) introduced the concept of net acid balance in pediatrics while studying healthy premature infants. They suggested the contribution of the gastrointestinal tract in maintaining acid–base homeostasis and the growth associated with negative NAB as a result of base deposition in skeleton. When the contribution of growth is included, the AP is calculated as follows:

\[ AP = u(SO_4) + u(OA_s) - Abs\ UA + 0.4\ Ca\ balance. \]
ACID–BASE BALANCES IN INFANTS WITH ACIDOSIS AND CARBOHYDRATE MALABSORPTION

Chronic Diarrhea Patients

Four patients, 2 to 5 months old, with chronic diarrhea (CD) consequent to acquired monosaccharide intolerance (AMI) were studied for 3 to 4 days according to the external acid balance technique described by Lennon et al. (23). These patients were shown to have a typical clinical course of CD associated with failure to thrive and recurrent metabolic acidosis. None of the infants were breast fed. After i.v. or oral rehydration, most of them received long-term total parenteral nutrition (TPN), which improved their nutritional status; TPN was indicated when the infants were unable to absorb 3 to 5% glucose in electrolyte solution or formula. They usually were fed with a soy-based, carbohydrate-free formula to which a gradually increasing concentration of glucose or glucose polymers can be added. An excess concentration of glucose caused CD patients to spill glucose into the stools, which were watery and acid (pH less than 5.5). Dehydration and severe metabolic acidosis ensued. After the carbohydrate was discontinued in the formula, diarrhea and acidosis subsided within a few days. Although episodes of acidosis recurred during the course of recovery in these patients, they were studied during one episode only. Small bowel biopsies done on these patients showed moderate to severe villus atrophy.

All patients were malnourished at the time of the study, and ages varied between 2 and 5 months. Serum electrolytes, creatinine, and alkaline phosphatase were within normal range. Mean acid–base values (arterial blood gases) at the beginning and at the end of the study are shown in Table 3.

Acute Diarrhea Patients

Five well-nourished infants between 2 and 7 months of age and seven marasmic infants between 2 and 24 months of age, dehydrated by acute diarrhea, were

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>pH</th>
<th>Pco₂ (mm Hg)</th>
<th>HCO₃⁻ (mEq/liter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic diarrhea</td>
<td>4</td>
<td>7.38 ± 0.06*</td>
<td>26.2 ± 3.3</td>
<td>12.1 ± 2.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.35 ± 0.08b</td>
<td>26.9 ± 5.7</td>
<td>15.0 ± 3.7</td>
</tr>
<tr>
<td>Acute diarrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well-nourished</td>
<td>5</td>
<td>7.30 ± 0.06*</td>
<td>28.0 ± 6.7</td>
<td>12.8 ± 4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.40 ± 0.03b</td>
<td>34.2 ± 5.8</td>
<td>20.0 ± 2.6</td>
</tr>
<tr>
<td>Marasmic</td>
<td>7</td>
<td>7.32 ± 0.06*</td>
<td>23.1 ± 6.1</td>
<td>11.7 ± 3.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.42 ± 0.03b</td>
<td>32.9 ± 5.1</td>
<td>20.9 ± 4.4</td>
</tr>
</tbody>
</table>

* Admission.  
** End of study.
studied during recovery for 6 or more days with the acid balance technique. All of them were fed diluted cow's milk after 24 hr of treatment. For purposes of comparison, only the first 3 days of the study are described in this report. Acidosis was recognized in infants from both groups at admission (Table 3). Without bicarbonate infusions, blood pH was normal on the following day in both groups. Plasma bicarbonate was normal after the second day in the marasmic infants and after the fourth day in the well-nourished patients (Table 3).

Net Acid Balance: Comparison Among the Groups

The methods and techniques have been described previously (30). Figure 5 depicts the mean daily net acid balance in milliequivalents per kilogram body weight. Table 4 summarizes the components of acid balance in the three groups of patients. The data are averaged for 3 days of the study.

![Graph showing mean plasma bicarbonate and net acid balance](image)

**FIG. 5.** Comparison of plasma bicarbonate concentration and net acid balance in three groups of infants with diarrhea. CD, chronic diarrhea; AD, acute diarrhea; N, well-nourished infants with acute diarrhea; M, marasmic infants with acute diarrhea; NAB, net acid balance. Endogenous acid production (EAP) (uSO₄ + uOA₄ - Abs.UA) was below base line, and renal acid excretion (TA + NH₄⁺ - HCO₃⁻) was above. **Shaded area** represents H⁺ retention below base line; H⁺ excretion is represented above base line. Mean plasma bicarbonate concentration is depicted in the upper part of the chart for each group.
Acid Production

Mean daily AP was higher in patients with CD than in either group of patients with acute diarrhea. These patients had higher AP only on the first day as a result of increased excretion of OA and the unabsorbed organic anion. Increased endogenous production of organic acids occurred only on the first day of the study when the patients with acute diarrhea were severely dehydrated and hypovolemic because of tissue hypoxia. Torres-Pinedo et al. (16) and Lifshitz et al. (22) reported that moderate lactic acidemia occurred shortly after lactose-induced diarrhea. With hydration, renal function improved, and all catabolic intermediary products retained were excreted by the kidneys. Acid production was higher in patients with acute diarrhea because of unabsorbed organic anion during the first 3 days of the study. With improvement of diarrhea, organic anions were absorbed, and acid production was diminished.

The acid production in patients with chronic diarrhea was caused by the endogenous production of organic acid (estimated by the excretion in the urine as salts) and by the increase in unabsorbed fecal organic anion consequent to diarrhea. The origin of the organic anion excreted into the urine is uncertain, because these patients were not hypovolemic, were not in shock, and did not present any symptoms of tissue hypoxia.

Net Acid Excretion

Mean NAE was similar in the three groups but markedly inadequate based on the degree of metabolic acidosis in the CD patients. Urinary pH was abnormally high in all patients except those with acute diarrhea. Net acid excretion in AD patients decreased after the first day of the study with subsequent improvement of acidosis and normalization of acidemia.

The NAE in CD patients was less than the degree of AP, which was the precipitating cause of acidosis in these patients. Titratable acidity was markedly reduced, accounting for only 13% of NAE. At a mean plasma bicarbonate level of 14 mEq/liter, significant amounts of bicarbonate were detected in the urine. Bicarbonate reabsorption in the nephron may be defective in these malnourished patients. Reduced renal acid excretion was reported in similar patients with chronic diarrhea and acidosis by Kohaut et al. (31) as a result of phosphate...
depletion. Human potassium depletion also was a cause of inadequate acidification of urine in response to an acid load (32,33). These studies suggest that potassium depletion induced a state of acquired renal tubular acidosis. Similarly, potassium deficiency acidosis in dogs resulted from an impaired ability to lower urinary pH (34).

Net Acid Balance

Mean NAB in CD patients was positive during the study, which indicates that part of hydrogen ion produced endogenously by the body was being retained. This explains the clinical findings of chronic acidosis and the maintenance of low bicarbonate levels. On the average, the CD patients retained 0.86 mEq/day per kg body weight. The reverse situation was found in the AD patients, who had a negative balance during the study, which means that they were excreting the H\(^+\) from the body. The average values for the AD patients were \(-0.56\) and \(-2.81\) mEq/kg body weight per day for the well-nourished and malnourished infants, respectively.

The NABs of the three groups were compatible with their respective blood acid–base parameters, especially with the plasma bicarbonate concentrations. Figure 5 shows the relationship between the means of NAB and plasma bicarbonate concentrations for the three groups.

Implications

From the analysis of the preceding data, the NAB was found to be compatible with the measurements of blood acid–base metabolism in acidotic infants with acute and chronic diarrhea. The method, therefore, allows the valid study of acid–base balance in infants with metabolic acidosis. Metabolic acidosis in these infants was accounted for largely by overproduction of H\(^+\) in the gastrointestinal tract and by a decrease in renal excretion. Acid production into the gastrointestinal tract, related to increased fecal organic acid salts, was a consequence of carbohydrate malabsorption. This condition was seen in patients with chronic diarrhea and in the first few days of management in patients with acute diarrhea.

Net acid excretion was lower than acid production in CD patients and was responsible for an increase in the H\(^+\) body pool and maintenance of metabolic acidosis. In AD patients, renal acid excretion was greater than acid production, even during the first day of treatment. Consequently, routine administration of bicarbonate solutions for the treatment of diarrheal dehydration is not required. The kidney is capable of coping with the acid load generated during and following acute diarrheal dehydration. Therefore, the administration of bicarbonate solutions becomes mandatory only in cases of severe acidosis and/or acidemia. Sperotto et al. (6) suggested that the following blood criteria be observed in acute diarrhea patients: blood pH lower than 7.10 and/or a plasma HCO\(_3\) lower than 8 mEq/liter. Chronic diarrhea patients must be evaluated carefully.
Potassium and phosphate deficiencies may also contribute to impairment in renal net acid excretion. Although bicarbonate is important in the correction of acidosis, phosphate or potassium may be required to complement the treatment of these patients.

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