

The Influence of Synthetic Amino Acid and Casein Hydrolysate on the Endogenous Production and Urinary Excretion of Acid in Total Intravenous Alimentation

JAMES, C. M. CHAN^[34]

Department of Pediatrics, University of Southern California School of Medicine, and the Renal Division, Childrens Hospital of Los Angeles, Los Angeles, California, USA

Extract

These investigations are designed to quantitate the acidogenic properties of several commonly used amino acid solutions. Infusion of amino acid solutions causes a rise in the sulfuric acid production ($H_{SO_4}^+$) to a rate of 26.8–93.1 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$, which is a 4- to 14-fold increase over the preinfusion rate of 6.6 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$. This is a reflection of the amount of sulfur-containing amino acids in the infusate; it is lower with the casein hydrolysate than with the synthetic amino acid. The increase in $H_{SO_4}^+$ is also significantly less with the 2.13% solutions than with the 4.25% solutions.

The rate of organic acid production (H_{OA}^+) tends to be higher with the 4.25% casein hydrolysate (48.1 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$) than with both the 2.13% and the 4.25% synthetic amino acid solutions (22.4–29.3 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$). The latter value is not significantly different from the preinfusion rate of H_{OA}^+ (20.4 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$). However, taken together, the results of these data are consistent with the view that the total amount of acid produced ($H_{SO_4}^+$ plus H_{OA}^+) in association with infusion of the synthetic amino acid solutions is proportionately higher than that associated with infusion of the casein hydrolysate.

The absolute values for the acid excretion during amino acid infusions also show differences from the preinfusion state of 23.7 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$. The net acid excretion increased nearly four times during the infusion of the 4.25% synthetic amino acid and casein hydrolysate solutions. The net acid excretion is shown to be linearly correlated with the net acid production ($r = 0.974$). On the other hand, only 65% of net acid production is excreted as net acid by the kidneys, and the extracellular buffering can account for only a fraction of the difference between the net acid production and excretion.

These studies also provide the first conclusive evidence that the rate of endogenous acid production during glucose-water infusion is 26.9 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$ or 2–3 mEq/kg/24 hr.

Speculation

The data presented suggest that the marked increase in endogenous acid production is related to the quantity and quality of amino acid-sulfur in the different types of

infusates used in total intravenous alimentation and further suggest a significant nonextracellular buffering mechanism (possibly the skeletal system).

Introduction

In 1967, Dudrick, Wilmore, and Vars [9] demonstrated that normal growth and development could be maintained on total parenteral alimentation, utilizing a protein hydrolysate-dextrose water solution as the sole source of nitrogen, calories, and minerals. This procedure has now been used extensively in malnutrition and in a variety of conditions in which bypassing the gastrointestinal tract was required for long periods [10, 12, 17, 24]. Septicemia and obstruction of major vessels were well known complications of intravenous alimentation [12, 17, 24]. But until recently, there have been virtually no studies on the biochemical and physiologic properties of these protein hydrolysates. Recently, Johnson *et al.* [16] reported the occurrence of hyperammonemia complicating parenteral nutrition in infants; Ghadimi *et al.* [13] confirmed the presence of inordinate amounts of ammonia in both fibrin hydrolysate [27] and casein hydrolysate [28], and Chan *et al.* [6] documented the high titratable acidity in casein hydrolysate as well as in synthetic amino acid [29] solutions.

These factors may have some bearing on the severe metabolic acidosis recently reported in small infants receiving parenteral alimentation [5, 15]. The pathophysiology of this acidosis is complex. It involves the endogenous production of acid from the intermediary metabolism of the amino acids, and organic acids as well as the titratable acidity of the infusates. In addition, it involves the acid produced from the metabolic processes involved with the growth and breakdown of body tissues, as well as the elimination of these metabolic end products either as carbon dioxide through the lungs or as nonvolatile (fixed) acids through the kidneys. The renal excretion of acid is easily determined and consists of the sum of urinary titratable acid (TA) plus ammonium (NH_4^+) minus bicarbonate (HCO_3^-) [21]. The quantitation of the net acidifying effects of the amino acid solutions is more difficult, on a conceptual as well as a technical basis. First, we are not dealing with a simple species of acid but with multiple sources of both external intake and endogenous production. Secondly, we are also dealing with internal metabolic processes, not easily accessible to external quantitative analysis. These conceptual and technical difficulties have proven to be a severe handi-

cap in the study of acid-base metabolism in general, and in the study of the mechanism of the acidogenic properties of dietary components in particular. Recently, most of these difficulties have been alleviated by a series of elegant experiments, performed in the laboratories of Relmann, Lennon, and Lemann [14, 20, 22] and later extended by Kildeberg, Engels, and Winters for studies in rapidly growing premature infants [18]. Since the present study utilizes these new concepts to study endogenous acid production, it is necessary to present the following brief review on the general applicability and limitations of the net acid balance technique.

Net acid production is defined as the daily net gain of noncarbonic, nonmetabolizable acid from all extrarenal sources and consists of contributions from sulfuric acid production, organic anion excretion, and skeletal mineralization, each of which can be measured or approximated [7, 18]. The first major component of endogenous acid consists of sulfuric acid production from metabolism of amino acids and is based on the oxidative pathway of amino acid-sulfur proposed by Lemann and Relman [19]. This is illustrated in Figure 1, where two hydrogen ions (H^+) are produced as the consequence of biologic oxidation of methionine-sulfur to sulfate in an aqueous medium. Therefore, by measuring the urinary concentrations of sulfate, one could extrapolate the amount of hydrogen ions (H^+) stranded inside the body, obligating the kidneys as the only route of elimination [7, 18]. The second major component of endogenous acid production is generated through the metabolism of neutral carbohydrate, fat, and protein and may be dissociated into organic

BODY INTERMEDIARY METABOLISM	URINE
<p>SULFUR-CONTAINING</p> <p>AMINO ACIDS e.g. METHIONINE</p> <p>$\text{HS-R (NH}_2\text{) COOH}$</p> <p>$\longrightarrow \text{mCO}_2 + \text{n H}_2\text{O} + \text{urea} + \text{2H}^+ + \text{SO}_4^{--} \text{ ---}$</p> <p>ORGANIC ACIDS</p> <p>$\text{RCOOH} \longrightarrow \text{H}^+ + \text{RCOO}^- \text{ ---}$</p>	<p>SO_4^{--}</p> <p>RCOO^-</p>

Fig. 1. The components of endogenous acid production from intermediary metabolism [18].

anions with the release of equivalent quantities of H^+ . In the event that these organic anions are completely metabolized to CO_2 and H_2O , these H^+ are in effect "recaptured" and therefore do not affect the net acid balance. The organic acid which simply dissociates into organic anion and H^+ and which subsequently never is oxidized but is excreted in the urine as organic anions would leave behind an equivalent amount of H^+ stranded in the body fluids with the kidney as the only route of excretion. It is this quantity of organic acid which contributes to endogenous net acid production. Therefore, by measuring the urinary organic anions one can extrapolate the amount of H^+ produced as a result of this metabolic process (Fig. 1). These two processes constitute the major components of endogenous production of acid in the adult. In the rapidly growing premature infants there are complexities due to the release of H^+ through the deposition of hydroxyapatite in the growing bone [18] and in the absorption of potential base through the gastrointestinal tract [7, 18]. In the present study the last two components of the net acid balance were not examined because the gastrointestinal tract was bypassed by the total intravenous alimentation. However, it must be pointed out that an error could occur because of stooling, but with the short period of study in our patients and no stooling in almost all cases, the error would be small. Another potential source of underestimation of the total endogenous acid production could be the exclusion of the hydrogen ions produced from new bone formation; however, since our balance collections lasted only a few days, it would certainly be invalid to consider any data from such short term calcium balances. It should be recognized that this criticism of short term balance studies applies only to cal-

cium balances which require a long control period. It does not apply to the present study because the production of sulfuric acids and nonvolatile organic acids is very rapid and responsive to changes in cellular metabolism as well as the composition of the amino acid infusates and is not subject to the same inherent limitations of calcium balance studies.

Until recently, there have been few studies describing the relationship between infusions of synthetic amino acids and protein hydrolysate solutions and the development of severe metabolic acidosis [9, 10]. At the present time there is no quantitative information on the components of endogenous production of acid from total intravenous alimentation. The present work was therefore designed to clarify this problem by applying the net acid balance technique to: (1) isolate and compare the components of endogenous acid production; (2) delineate the differences and similarities of net acid production and excretion of different types of amino acid solutions; and (3) determine how the premature infants differ from the child with respect to quantity of net acid production and urinary excretion of acid.

Material and Methods

One 10-year-old child and four 1- to 2-week-old premature infants were studied (Table I). All patients were receiving either casein hydrolysate or synthetic amino acid (concentrations of either 4.25 or 2.13%) therapeutically through a central venous catheter placed in the subclavian vein [1, 17]. These solutions were supplemented with 20% glucose, potassium phosphate, and multiple vitamins to meet the minimal caloric, mineral, and vitamin requirements as previously reported [1, 5, 6, 17].

Table I. Clinical data on patients

Patient	Age	Sex	Weight, kg	Surface area, m ²	Presenting disorder	Specific procedures
FM	10 yrs	M	30.90	1.07	Perforated appendix with intraperitoneal abscesses and intestinal fistulae	Appendectomy, drainage of pelvic abscess, drainage of subphrenic abscess, repair of enterocutaneous and coloenteric fistulae
MG	2 wks	M	2.55	0.19	Tracheoesophageal fistula, imperforate anus, ileal atresia, prematurity	Gastrostomy, ligation of tracheoesophageal fistula, laparotomy and lysis of adhesions for jejunal volvulus, double barreled ileostomy, sigmoid colostomy
RJ	1 wk	F	2.72	0.20	Gastroschisis	Duodenoduodenostomy, gastrostomy
RG	1 wk	F	1.68	0.14	Duodenal atresia, esophageal atresia, Down's syndrome	Repairs of gastroschisis with silon sac technique, ileostomy
AL	2 wks	M	1.70	0.14	Tracheoesophageal fistula, imperforate anus, ileal atresia, prematurity	Gastrostomy, ligation of tracheoesophageal fistula, laparotomy and lysis of adhesions for jejunal volvulus, double barreled ileostomy, sigmoid colostomy

Table II. Representative study of 10-year-old male patient FM (weight, 30.9 kg; surface area, 1.07 m²)¹

Days	Whole blood							Endogenous acid production, μEq/min/1.73 m ²			Urine volume, ml/24 hr	Urinary acid excretion				Infusion of casein hydrolysate (CH) and synthetic amino acid (SAA), ml/24 hr		
	pH	pCO ₂	tCO ₂	BE	Na ⁺	K ⁺	Cl ⁻	H ₂ SO ₄ ⁺	H ₂ OA ⁺	Total		pH	TA	NH ₄ ⁺	Total			
		mm Hg	mEq/liter				μEq/min/1.73 m ²											
Period A																		
1-2	7.41	35.0	23.0	-2.0	140	4.4	96	7.7	19.4	27.1	825	5.89	9.3	20.5	29.7			
Period B																		
3	7.38	28.5	17.3	-7.0												1800	SAA	4.25%
4								73.5	26.2	99.8	950	5.58	13.2	64.8	78.0	1800	SAA	4.25%
5								44.4	25.5	114.5	900	5.50	8.2	69.4	77.6	1800	SAA	4.25%
6								165.5	44.0	209.6	1350	5.90	12.5	140.0	146.5	1800	SAA	4.25%
7	7.41	36.0	23.6	-1.5	144	4.5	101	105.5	25.2	130.7	695	5.58	8.8	83.0	91.8	1800	SAA	4.25%
8								80.3	24.4	104.7	650	5.50	9.4	62.7	72.1	1600	SAA	4.25%
9								89.2	26.2	115.4	770	5.42	11.6	60.9	72.5	1800	SAA	4.25%
Mean								93.1	28.6	129.1	881		10.6	80.1	89.8	1766	SAA	4.25%
Period C																		
10	7.38	40.0	24.5	-1.5	140	5.0	99	41.0	29.2	70.3	850	5.60	19.9	39.3	59.1	1800	CH	4.25%
11								60.9	39.5	100.4	1150	5.26	32.1	44.8	76.9	2250	CH	4.25%
12								23.6	21.6	45.2	1500	6.08	8.8	15.0	23.8	2400	CH	4.25%
13								75.9	49.1	125.0	1000	5.22	31.3	45.2	76.5	2400	CH	4.25%
14	7.38	33.5	20.4	-4.2	141	4.7	98	108.1	64.2	172.3	1450	5.40	45.6	66.3	111.8	2400	CH	4.25%
15								116.1	70.7	186.9	1700	5.20	51.2	72.4	123.6	2400	CH	4.25%
16								107.6	62.7	170.3	1500	5.09	49.1	60.4	109.4	2400	CH	4.25%
17	7.43	46.0	32.0	+5.0	141	4.4	93									2400	CH	4.25%
Mean								76.2	48.1	124.3	1307		34.0	49.1	83.0	2306	CH	4.25%
Period D																		
18																1800	SAA	2.13%
19	7.42	36.5	24.2	-1.0	143	5.3	104	71.0	25.9	96.9	1000		22.3	31.1	53.5	1800	SAA	2.13%

¹ H₂SO₄⁺: sulfuric acid production; H₂OA⁺: organic acid production; TA: titratable acid; NH₄⁺: ammonium.

In order to quantitate and compare the endogenous production of acid unaugmented by the exogenous amino acid infusions, four of the patients were sustained on 20% glucose-water intravenously for 2 days without the addition of casein hydrolysate or synthetic amino acid solutions but with the same supplements of mineral and vitamins [6]. During this period the caloric intake was 80 kcal/kg/24 hr and should be sufficient to prevent any rise in endogenous acid production secondary to increased catabolism.

Twenty-four-hour urine specimens were collected for 2 to 19 consecutive days and frozen until measured. The volumes of casein hydrolysate or synthetic amino acid solutions infused were recorded and accurately timed. Blood samples were taken every 2nd to 5th day for determinations of acid-base status by the equilibration method of Astrup [2]; sodium and potassium by flame photometry; chloride by the Buchler-Cotlove technique [8]. Urinary sulfate was determined by the method of Yatzidis *et al.* [26]. Urinary organic anion concentration and urinary net acid excretion (TA + NH₄⁺ - HCO₃⁻) were determined by previously described methods from this laboratory [3, 4].

Results

Complete analytical data from one subject who received both concentrations of synthetic amino acid solutions (4.25 and 2.13%) as well as casein hydrolysate (4.25%) are shown in Table II. Days 3, 17, and 18 were equilibration periods, and no urine collection was obtained. The four collection periods correspond to (A) no infusion; (B) 4.25% synthetic amino acid infusion; (C) 4.25% casein hydrolysate infusion; and (D) 2.13% synthetic amino acid infusion.

Table III presents the mean endogenous production of acid for subjects receiving the different types of synthetic amino acid or casein hydrolysate solution and compares this with the mean endogenous acid production during periods of no amino acid infusion. In addition, the urinary excretion of acid is shown. Each component of acid production and excretion is also presented.

Figure 2 compares the net acid production with the net acid excretion, showing a linear relationship between them ($r = 0.974$).

Table IV compares the mean values of net acid production and excretion in the subjects during the con-

Table III. Mean values of components of endogenous acid production and renal acid excretion during steady acid-base status in patients on synthetic amino acid (SAA) or casein hydrolysate (CH) alimentation and off infusion¹

Subject	Age	Days of study	Surface area, m ²	Endogenous acid production ¹				Urine volume, ml/24 hr	Urinary acid excretion, $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$			Infusion, ml/24 hr		
				H ⁺ SO ₄	H ⁺ O _A	Total	H ⁺ SO ₄ total, %		TA	NH ₄ ⁺	Total			
				$\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$										
<i>Group I</i>														
FM	10 yrs	2	1.07	7.7	19.4	27.1	28	825	9.3	20.5	29.7	No infusion		
MG	2 wks	2	0.19	13.1	13.6	26.6	49	143	2.4	21.8	24.2	No infusion		
RJ	1 wk	2	0.22	3.3	26.4	29.7	11	334	4.7	16.4	21.1	No infusion		
RG	1 wk	2	0.14	2.4	22.1	24.5	10	116	-0.2	19.9	19.7	No infusion		
Average				6.6	20.4	26.9	25		4.1	19.7	23.7			
<i>Group II</i>														
FM	10 yrs	6	1.07	93.1	28.6	129.1	72	881	10.6	80.1	89.8	1766	SAA	4.25%
MG	2 wks	2	0.19	80.6	24.7	105.3	77	220	8.5	73.0	81.5	360	SAA	4.25%
<i>Group III</i>														
FM	10 yrs	7	1.07	76.2	48.1	124.3	61	1307	34.0	49.1	83.0	2306	CH	4.25%
<i>Group IV</i>														
FM	10 yrs	2	1.07	71.0	25.9	96.9	73	1000	20.3	31.1	53.5	1800	SAA	2.13%
MG	2 wks	4	0.19	39.7	22.4	62.1	64	180	2.2	34.6	36.8	324	SAA	2.13%
AL	1 wk	4	0.14	26.8	29.3	56.1	48	140	4.8	40.3	45.1	240	SAA	2.13%
<i>Group V</i>														
RG	1 wk	3	0.14	29.4	28.9	58.3	50	197	4.4	18.7	23.1	265	CH	2.13%

¹ H₂SO₄⁺, sulfuric acid production; H₂OA⁺, organic acid production; TA, titratable acid; NH₄⁺, ammonium.

trol period with only glucose-water administration (group I) and during the infusions of the two different concentrations (4.25 and 2.13%) of synthetic amino acid and casein hydrolysate solutions (groups II–V). The net acid excretion accounts for only 40–88% (average 65%) of the net acid production.

Discussion

The experimental data presented above indicate that in the absence of amino acid infusion, the endogenous acid production in premature infants and the child varied from 24.5 to 29.7 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$ with a mean of 26.9 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$ (Table III, group I). This confirmed our earlier assumption [5] that the rate of endogenous acid production in a steady state for infants and children was 29 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$. These data substantiated the previous theoretical assumption [15, 23] that the endogenous acid production in infants and children was about 2–3 mEq/kg/24 hr. There were no differences between the rates of endogenous acid production in premature infants and the child on a body surface basis, although on a weight basis it was less in the child than in the infant (1.4 versus 2.8 mEq/kg/24 hr [30]. It is, however, difficult to draw general conclusions for children of his age group from this single observation.

Analysis of the urinary acid excretion in the prein-

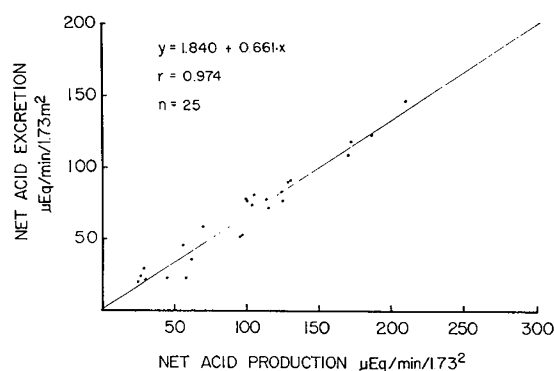


Fig. 2. Regression of net acid excretion (NAE) on net acid production (NAP), by the method of least squares: $\text{NAE} = 1.840 + 0.661 \cdot \text{NAP}$; $S_{y \cdot x}$ 8.064; SD_b 0.031.

Table IV. Percentage of net acid production excreted in the urine by subjects on synthetic amino acid (SAA) and casein hydrolysate (CH) of different concentrations

Group	Net acid production (NAP)	Net acid excretion (NAE)	$\frac{\text{NAE}}{\text{NAP}} \times 100, \%$
	$\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$		
<i>I. No infusion</i>	26.9	23.7	88
<i>II. SAA, 4.25%</i>	132.2	85.7	65
<i>III. CH, 4.25%</i>	124.3	83.0	67
<i>IV. SAA, 2.13%</i>	71.7	45.1	63
<i>V. CH, 2.13%</i>	58.3	23.1	40
Average			65

fusion period (Table III, *group I*) showed that the net acid excretion varied between 19.7 and 29.7 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$, with a mean of 23.7 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$, which closely approximated the endogenous acid production. This zero net acid balance was reflected in the normal blood acid-base status as illustrated by *patient FM* in Table II (*period A*).

Sulfuric acid production ($\text{H}_{\text{SO}_4}^+$) increased 4 to 14 times after the infusions of both synthetic amino acid and casein hydrolysate. A more than 10-fold increase (Table III, *groups II* and *III*) occurred with the 4.25% concentration of either casein hydrolysate or synthetic amino acid. A mean increment of fourfold increase was obtained with the 2.13% concentration of either solution (Table III, *groups IV* and *V*). This probably reflected the larger amount of sulfur-containing amino acids at the 4.25% concentration. The $\text{H}_{\text{SO}_4}^+$ with the casein hydrolysate tended to be lower than that produced by synthetic amino acid. In contrast, net organic acid production (H_{OA}^+) with the 4.25% casein hydrolysate (*group III*) tended to be higher than that produced by the 4.25% synthetic amino acid (*group II*). This probably reflected the quality and quantity of protein in the different amino acid solutions although the total amount of net acid generated was approximately identical for both.

It was of interest to note that in the preinfusion period (Table III, *group I*) the sulfuric acid production ($\text{H}_{\text{SO}_4}^+$) accounted for 10–49% of the total acid production, with an average of 25%. With the infusion of 4.25% synthetic amino acid (Table III, *group II*), sulfuric acid production varied between 72 and 77% of the total acid production, and with the 4.25% casein hydrolysate it was 61%. Analysis of the data from the subjects receiving 2.13% solutions also showed similar differences.

These data indicate that the amount of acid produced when infusing synthetic amino acid solutions was proportionately higher than with casein hydrolysate. This was probably a reflection of the high concentration of sulfur-containing amino acids (*e.g.*, methionine, casein, etc.) in the synthetic amino acid solutions.

The absolute values for the acid excretion during amino acid infusion also differed from the preinfusion state. The total urinary acid excretion for the four subjects during the preinfusion period in *group I* (Table III) varied between 19.7 and 29.7 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$ (mean 23.7 $\mu\text{Eq}/\text{min}/1.73 \text{ m}^2$). This net acid excretion increased approximately fourfold in *groups II* and *III* during the period of 4.25% synthetic amino acid and casein hydrolysate infusions. Such a marked

increase did not result from infusions of the 2.13% solutions.

A linear relationship between the net acid excretion and the net acid production was depicted in Figure 2 (correlation coefficient $r = 0.974$). However, the net acidifying effect of the alimentation solutions cannot be completely accounted for by the increased net acid excretion. Table IV showed that the kidneys excreted only 65% of the net acid production. This suggested either that the other 35% of released acid was partially neutralized by extracellular buffers or that considerable nonextracellular buffers were involved. These data supported our previous observation that nonextracellular buffers during development or recovery from metabolic acidosis were significant [25]. The decreased serum bicarbonate and base excess could account for only a fraction of the difference between the net acid production and excretion (Table II).

In all groups (Table III), the urinary ammonium (NH_4^+) excretion was the largest single component, and there seemed to be little difference in the response of the infants compared with the child (*FM*). Of particular interest was the relatively small response in urinary titratable acidity (TA) in the infants compared with that of the child (*FM*). This was contrary to the pattern of hydrogen ion excretion in normal infants, where there was a higher rate of TA excretion and a lower rate of excretion of NH_4^+ [11]. A possible explanation of these differences was suggested by the low phosphate excretion secondary to the relatively small phosphate supplements in the amino acid solutions [6]. A previous study from this laboratory had shown that the total net acid excretion ($\text{TA} + \text{NH}_4^+ - \text{HCO}_3^-$) in these infants was not impaired. The higher rate of NH_4^+ excretion adequately compensated for the lower rate of TA excretion [5].

In view of the complexities presented above on the acidogenic effects of amino acid solutions, a previous report on the high titratable acidity of the casein hydrolysate and synthetic amino acid solutions [5, 6] as an explanation for the pathophysiology of the severe metabolic acidosis encountered in total intravenous alimentation may be too simplistic. The high titratable acidity of the infusates may represent volatile acid, metabolizable to carbon dioxide and eliminated in the lungs without obligating renal excretion; conversely, prolonged administration of casein hydrolysate and synthetic amino acid may present such an excessive exogenous acid intake as to overwhelm the extracellular buffering capacity and renal acid excretion so that

metabolic acidosis develops [5, 15]. Further studies are necessary to clarify this point.

The present study gives further experimental confirmation of our previous recommendation for the use of the 2.13% solutions instead of the 4.25% solutions [5] because the acidifying effects are shown to be significantly less with the former (Table III). The daily minimal amino acid requirements are still fulfilled at the lower concentration.

Summary

The acidogenic potential of the commonly used casein hydrolysate and synthetic amino acid solutions were tested by independent measurements of the urinary sulfate and organic anions to assess the quality and quantity of endogenous sulfuric acid and organic acid production. In all five patients studied, both solutions were found to be highly acidogenic, resulting in total endogenous acid production ($58.3\text{--}129.1\ \mu\text{Eq}/\text{min}/1.73\ \text{m}^2$) several times higher than that during the control periods ($26.9\ \mu\text{Eq}/\text{min}/1.73\ \text{m}^2$).

It was also shown that sulfuric acid production is proportionately higher with synthetic amino acid infusions, which seems likely to be related to the higher quantity of amino acid-sulfur. The increased acid production correlates well with kidneys' response to increased net acid excretion ($r = 0.974$). However, the data indicate that the renal net acid excretion could account for 65% of the net acid production and the extracellular buffers could account for only a fraction of the other 35%, thereby suggesting a heretofore unrecognized mechanism of nonextracellular buffering.

The net effect of this imbalance of endogenous production over renal excretion of acid results in accumulation of acid, which probably contributes to the development of metabolic acidosis seen in the patients receiving total intravenous alimentation.

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27. Aminosol, Abbott Laboratories, Chicago, Ill.
28. Hyprotigen, McGaw Laboratories, Glendale, Calif.
29. FreAmine, McGaw Laboratories, Glendale, Calif.
30. For example, in the 10-year-old child (*FM*) who weighed 30.9 kg (surface area, 1.07 m²), the endogenous acid production of 27.1 μ Eq/min/1.73 m² (Table III, *group 1*) is equivalent to 1.4 mEq/kg/24 hr, *i.e.*, $[27.1 \mu\text{Eq/min/1.73 m}^2 \times (1440 \text{ min/1000}) \times 1.07 \text{ m}^2] \div 30.9 \text{ kg} = 1.4 \text{ mEq/kg/24 hr}$. Similarly for the 2-week-old infant (*MG*) with body weight of 2.59 kg (surface area, 0.19 m²), the endogenous acid production at a rate of 26.6 μ Eq/min/1.73 m² is equivalent to 2.8 mEq/kg/24 hr.
31. This study was performed within the spirit of the Declaration of Helsinki.
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34. Requests for reprints should be addressed to: JAMES C. M. CHAN, M.D., Childrens Hospital of Los Angeles, P. O. Box 54700 Terminal Annex, Los Angeles, Calif. 90054 (USA).
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