Supplementary Tables and Figures

Table S1. Association of Net Endogenous Acid Production with Serum Bicarbonate in Participants with Estimated Glomerular Filtration Rate ≥ 60 mL/min/1.73m^2

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Figure S1. Association of estimated animal protein-derived endogenous acid production (ADEAP, mEq/day) with age in 9,781 participants of NHANES 1999-2004.

Table S1. Association of Net Endogenous Acid Production with Serum Bicarbonate in 8,909 Participants with Estimated Glomerular Filtration Rate ≥ 60 mL/min/1.73m^2

	Coefficient (95% CI)		
	Model 1	Model 2	Model 3
NEAP			
Continuous*	**-0.22 (-0.28 to -0.16)**	**-0.20 (-0.27 to -0.14)**	**-0.15 (-0.21 to -0.10)**
< 39.3 mEq/d	[Ref]	[Ref]	[Ref]
39.3 – 52.9 mEq/d	-0.14 (-0.29 to 0.02)	**-0.17 (-0.32 to -0.02)**	-0.13 (-0.28 to 0.01)
53.0 – 69.9 mEq/d	**-0.39 (-0.59 to -0.19)**	**-0.38 (-0.58 to -0.18)**	**-0.29 (-0.47 to -0.10)**
≥ 70.0 mEq/d	**-0.60 (-0.77 to -0.43)**	**-0.55 (-0.72 to -0.38)**	**-0.43 (-0.57 to -0.28)**
P for trend	<0.001	<0.001	<0.001

Abbreviations: CI, confidence interval. NEAP, Net Endogenous Acid Production, **Bold** values indicate p<0.05.
Model 1: unadjusted
Model 2: adjusted for age, sex, and race/ethnicity
Model 3: Model 2 + adjusted for body mass index, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
*Per standard deviation higher NEAP (SD = 26.5 mEq/d)

Table S2. Odds Ratio of Acidosis by Net Endogenous Acid Production in 8,909 Participants with Estimated Glomerular Filtration Rate ≥ 60 mL/min/1.73m^2

	OR (95% CI)		
	Model 1	Model 2	Model 3
NEAP			
Continuous*	**1.18 (1.08 – 1.29)**	**1.15 (1.05 – 1.27)**	1.10 (1.00 – 1.22)
< 39.3 mEq/d	[Ref]	[Ref]	[Ref]
39.3 – 52.9 mEq/d	1.14 (0.93 – 1.40)	1.16 (0.95 – 1.42)	1.13 (0.92 – 1.40)
53.0 – 69.9 mEq/d	**1.46 (1.14 – 1.87)**	**1.43 (1.11 – 1.83)**	**1.30 (1.02 – 1.66)**
≥ 70.0 mEq/d	**1.66 (1.29 – 2.13)**	**1.54 (1.19 – 2.01)**	**1.36 (1.05 – 1.75)**
P for trend	<0.001	0.002	0.02

Abbreviations: OR, odds ratio; CI, confidence interval. **Bold** values indicate p<0.05.
Acidosis defined as serum bicarbonate <23 mEq/L.
Model 1: unadjusted
Model 2: adjusted for age, sex, and race/ethnicity
Model 3: Model 2 + adjusted for body mass index, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
*Per standard deviation higher NEAP (SD = 26.5 mEq/d)

Table S3a. Odds Ratio of Acidosis by Net Endogenous Acid Production in 9,781 Participants of NHANES 1999-2004[†]

	OR (95% CI)		
	Model 1	Model 2	Model 3
NEAP			
Continuous*	**1.19 (1.07 – 1.32)**	**1.18 (1.05 – 1.34)**	**1.15 (1.01 – 1.31)**
< 39.3 mEq/d	[Ref]	[Ref]	[Ref]
39.3 – 52.9 mEq/d	0.92 (0.68 – 1.29)	0.95 (0.69 – 1.29)	0.95 (0.70 – 1.30)
53.0 – 69.9 mEq/d	1.32 (0.95 – 1.82)	1.31 (0.94 – 1.81)	1.24 (0.90 – 1.70)
≥ 70.0 mEq/d	**1.45 (1.10 – 1.90)**	**1.39 (1.02 – 1.89)**	1.28 (0.94 – 1.74)
P for trend	0.002	0.02	0.07

Table S3b. Odds Ratio of Acidosis by Net Endogenous Acid Production in 8,909 Participants with estimated Glomerular Filtration Rate ≥ 60 mL/min/1.73m^{2†}

	OR (95% CI)		
	Model 1	Model 2	Model 3
NEAP			
Continuous*	**1.22 (1.09 – 1.37)**	**1.20 (1.05 – 1.37)**	**1.17 (1.02 – 1.34)**
< 39.3 mEq/d	[Ref]	[Ref]	[Ref]
39.3 – 52.9 mEq/d	0.99 (0.70 – 1.41)	1.01 (0.70 – 1.46)	1.00 (0.69 – 1.43)
53.0 – 69.9 mEq/d	**1.49 (1.03 – 2.14)**	**1.46 (1.01 – 2.12)**	1.36 (0.95 – 1.94)
≥ 70.0 mEq/d	**1.61 (1.18 – 2.19)**	**1.50 (1.06 – 2.13)**	1.37 (0.98 – 1.92)
P for trend	0.001	0.01	0.03

Abbreviations: OR, odds ratio; CI, confidence interval. **Bold** values indicate p<0.05.
[†]**Acidosis defined as serum bicarbonate <22 mEq/L.**
Model 1: unadjusted
Model 2: adjusted for age, sex, and race/ethnicity
Model 3: Model 2 + adjusted for body mass index, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
*Per standard deviation higher NEAP (SD for Table S3a = 26.4 mEq/d; Table S3b = 26.5 mEq/d)

Table S4. Association of Animal Protein-Derived Endogenous Acid Production with Serum Bicarbonate in 9,781 Participants of NHANES 1999-2004

	Coefficient (95% CI)		
	Model 1	Model 2	Model 3
ADEAP			
Continuous*	**-0.12 (-0.20 to -0.04)**	**-0.14 (-0.23 to -0.06)**	**-0.11 (-0.18 to -0.03)**
< 1.6 mEq/d	[Ref]	[Ref]	[Ref]
1.6 – 15.5 mEq/d	-0.03 (-0.21 to 0.26)	-0.03 (-0.25 to 0.19)	-0.05 (-0.26 to 0.19)
15.6 – 32.9 mEq/d	-0.02 (-0.26 to 0.22)	-0.09 (-0.32 to 0.14)	-0.09 (-0.30 to 0.12)
> 32.9 mEq/d	**-0.31 (-0.56 to -0.07)**	**-0.38 (-0.62 to -0.14)**	**-0.28 (-0.50 to -0.05)**
P for trend	0.01	0.01	0.02

Abbreviation: CI, confidence interval; ADEAP, Animal Protein Derived-Endogenous Acid Production. **Bold** values indicate p<0.05.
Model 1: unadjusted
Model 2: adjusted for age, sex, and race/ethnicity
Model 3: Model 2 + adjusted for body mass index, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
*Per standard deviation higher ADEAP (SD = 26.2 mEq/d)

Table S5. Association of Animal Protein-Derived Endogenous Acid Production with Serum Bicarbonate within Age Categories

Age 20 to 39 years	Coefficient (95% CI)		
	Model 1	Model 2	Model 3
ADEAP (n = 3299)			
Continuous*	0.02 (-0.10 to 0.13)	-0.06 (-0.18 to 0.05)	-0.04 (-0.14 to 0.07)
< 1.6 mEq/d	[Ref]	[Ref]	[Ref]
1.6 – 15.5 mEq/d	0.04 (-0.34 to 0.42)	-0.03 (-0.39 to 0.32)	-0.03 (-0.35 to 0.28)
15.6 – 32.9 mEq/d	0.13 (-0.24 to 0.49)	-0.05 (-0.39 to 0.28)	-0.02 (-0.31 to 0.27)
> 32.9 mEq/d	-0.05 (-0.39 to 0.29)	-0.27 (-0.60 to 0.05)	-0.17 (-0.46 to 0.11)
P for trend	0.83	0.12	0.24

Age 40 to 59 years	Coefficient (95% CI)		
	Model 1	Model 2	Model 3
ADEAP (n = 3139)			
Continuous*	**-0.19 (-0.30 to -0.09)**	**-0.25 (-0.35 to -0.14)**	**-0.20 (-0.31 to -0.08)**
< 1.6 mEq/d	[Ref]	[Ref]	[Ref]
1.6 – 15.5 mEq/d	0.05 (-0.30 to 0.39)	0.01 (-0.35 to 0.31)	-0.001 (-0.33 to 0.33)
15.6 – 32.9 mEq/d	0.02 (-0.32 to 0.36)	-0.08 (-0.41 to 0.24)	-0.05 (-0.37 to 0.27)
> 32.9 mEq/d	**-0.37 (-0.73 to -0.01)**	-0.52 (-0.87 to 0.17)	**-0.41 (-0.77 to -0.05)**
P for trend	0.04	0.01	0.02

Age ≥ 60 years	Coefficient (95% CI)		
	Model 1	Model 2	Model 3
ADEAP (n = 3343)			
Continuous*	**-0.15 (-0.28 to -0.01)**	-0.14 (-0.28 to 0.003)	-0.10 (-0.24 to 0.03)
< 1.6 mEq/d	[Ref]	[Ref]	[Ref]
1.6 – 15.5 mEq/d	-0.08 (-0.33 to 0.18)	-0.07 (-0.32 to 0.18)	-0.09 (-0.32 to 0.13)
15.6 – 32.9 mEq/d	-0.22 (-0.46 to 0.03)	-0.19 (-0.44 to 0.06)	-0.19 (-0.42 to 0.03)
> 32.9 mEq/d	**-0.35 (-0.66 to -0.04)**	-0.33 (-0.65 to 0.001)	-0.22 (-0.54 to 0.09)
P for trend	0.02	0.04	0.10

Abbreviation: CI, confidence interval; ADEAP, Animal Protein Derived Endogenous Acid Production. **Bold** values indicate p<0.05.
P for interaction by age = 0.01
Model 1: unadjusted
Model 2: adjusted for age, sex, and race/ethnicity

Model 3: Model 2 + adjusted for body mass index, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
*Per standard deviation higher ADEAP (SD = 26.2 mEq/d)

Table S6. Association of Dietary Protein with Serum Bicarbonate in 9,781 Participants of NHANES 1999-2004

	Coefficient (95% CI)		
	Model 1	Model 2	Model 3
Dietary Protein			
Continuous*	-0.02 (-0.12 to 0.08)	-0.09 (-0.20 to 0.02)	-0.10 (-0.22 to 0.01)
≤54.5 g/day	[Ref]	[Ref]	[Ref]
54.5 – 76.6 g/day	-0.04 (-0.19 to 0.12)	-0.07 (-0.22 to 0.09)	-0.11 (-0.27 to 0.05)
76.7 – 103.7 g/day	-0.03 (-0.22 to 0.16)	-0.12 (-0.31 to 0.06)	-0.15 (-0.34 to 0.03)
≥103.7 g/day	-0.02 (-0.26 to 0.21)	-0.18 (-0.44 to 0.07)	**-0.23 (-0.50 to -0.04)**
P for trend	0.83	0.12	0.09

Abbreviation: CI, confidence interval, **Bold** values indicate p<0.05.
Model 1: adjusted for dietary energy
Model 2: adjusted for age, sex, race/ethnicity and dietary energy
Model 3: Model 2 + adjusted for body mass index, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
*Per standard deviation higher dietary protein (SD = 42.4 g/day)

Table S7. Association of Dietary Potassium with Serum Bicarbonate in 9,781 Participants of NHANES 1999-2004

	Coefficient (95% CI)		
	Model 1	Model 2	Model 3
Dietary Potassium			
Continuous*	**0.32 (0.23 to 0.42)**	**0.16 (0.08 to 0.25)**	**0.14 (0.05 to 0.24)**
<47.4 mEq/d	[Ref]	[Ref]	[Ref]
47.4 – 66.7 mEq/d	**0.31 (0.16 to 0.46)**	**0.19 (0.04 to 0.34)**	0.09 (-0.05 to 0.22)
66.8 – 89.4 mEq/d	**0.46 (0.29 to 0.62)**	**0.29 (0.13 to 0.45)**	**0.17 (0.01 to 0.33)**
≥ 89.5 mEq/d	**0.78 (0.51 to 1.04)**	**0.52 (0.24 to 0.79)**	**0.30 (0.05 to 0.55)**
P for trend	<0.001	0.001	0.01

Abbreviation: CI, confidence interval, **Bold** values indicate p<0.05.
Model 1: adjusted for dietary energy
Model 2: adjusted for age, sex, race/ethnicity and dietary energy
Model 3: Model 2 + adjusted for body mass index, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
*Per standard deviation higher dietary potassium (SD = 32.9 mEq/d)

Table S8. Association of Net Endogenous Acid Production with Serum Bicarbonate After Adjustment for Total Body Fat in 9,499 Participants of NHANES 1999-2004 Who Underwent Dual Energy X-ray Absorptiometry

	Coefficient (95% CI)		
	Model 1	Model 2	Model 3
NEAP			
Continuous*	**-0.15 (-0.21 to -0.10)**	**-0.15 (-0.21 to -0.10)**	**-0.15 (-0.21 to -0.09)**
< 39.3 mEq/d	[Ref]	[Ref]	[Ref]
39.3 – 52.9 mEq/d	-0.10 (-0.25 to 0.04)	-0.12 (-0.27 to 0.02)	-0.11 (-0.26 to 0.04)
53.0 – 69.9 mEq/d	**-0.25 (-0.44 to -0.07)**	**-0.26 (-0.45 to -0.08)**	**-0.25 (-0.44 to -0.06)**
≥ 70.0 mEq/d	**-0.42 (-0.57 to -0.28)**	**-0.43 (-0.58 to -0.28)**	**-0.42 (-0.56 to -0.27)**
P for trend	<0.001	<0.001	<0.001

Abbreviation: CI, confidence interval. NEAP, Net Endogenous Acid Production,
Bold values indicate p<0.05.
Model 1: adjusted for age, sex, race/ethnicity, **body mass index**, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
Model 2: adjusted for age, sex, race/ethnicity, **% total body fat**, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.
Model 3: Model 1 + adjusted for **% total body fat**
*Per standard deviation higher NEAP (SD =26.5 mEq/d)

Table S9. Association of Net Endogenous Acid Production with Serum Bicarbonate within Age Categories After Adjustment for Total Body Fat in 9,499 Participants of NHANES 1999-2004 Who Underwent Dual Energy X-ray Absorptiometry

	Coefficient (95% CI)		
	20 to 39 years (n=3211)	40 to 59 years (n=3060)	≥ 60 years (n=3228)
NEAP			
Continuous*	-0.07 (-0.15 to 0.02)	**-0.28 (-0.39 to -0.18)**	**-0.17 (-0.30 to -0.04)**
< 39.3 mEq/d	[Ref]	[Ref]	[Ref]
39.3 – 52.9 mEq/d	-0.10 (-0.41 to 0.20)	-0.13 (-0.42 to 0.16)	-0.13 (-0.42 to 0.15)
53.0 – 69.9 mEq/d	-0.14 (-0.42 to 0.14)	**-0.38 (-0.66 to -0.09**)	-0.18 (-0.44 to 0.07)
≥ 70.0 mEq/d	-0.24 (-0.49 to 0.001)	**-0.67 (-0.99 to -0.35)**	**-0.50 (-0.85 to -0.16)**
P for trend	0.05	<0.001	0.01

Abbreviation: CI, confidence interval. NEAP, Net Endogenous Acid Production, **Bold** values indicate p<0.05.

P for interaction by age = 0.004

Models adjusted for age, sex, race/ethnicity, **% total body fat**, poverty, education, smoking status, diuretic use, diagnosis of diabetes mellitus, hypertension, cardiovascular disease, estimated glomerular filtration rate, log-transformed urine albumin-creatinine ratio, serum albumin and log-transformed C-reactive protein.

*Per standard deviation higher NEAP (SD = 26.5 mEq/d)

Figure S1. Association of estimated animal protein-derived endogenous acid production (ADEAP, mEq/day) with age in 9,781 participants of NHANES 1999-2004. Each bar represents an ADEAP quartile. Error bars represent standard errors.