How does acid production from the foods we eat drive metabolic disease?

- DAL- dietary acid load
- PRAL- potential renal acid load
- NEAP- net endogenous acid production

Table 1 Best predictive formulas for DAL. Table adjusted from Parmenter et al. [110]

Equation	Formula
$NEAP_R$ [87]	([0.488 × protein in g/d] + [0.0366 × phosphorus in mg/d]) − ([0.0205 × potassium in mg/d] + [0.0263 × magnesium in mg/d] + [0.0125 × calcium in mg/d]) + body surface area × 41 / 1.73
$NEAP_L$ [65]	([0.488 × protein in g/d] + [0.0366 × phosphorus in mg/d]) − ([0.0205 × potassium in mg/d] + [0.0263 × magnesium in mg/d] + [0.0125 × calcium in mg/d]) + 32.9 + (0.15 × [{potassium} + {calcium × 2} + {magnesium × 2} − {phosphorus × 1.8}]) (all in mmol/d)
$PRAL_S$ [96]	([0.75 × sulfate] + [0.63 × phosphorus]) − ([0.80 × potassium] + [0.25 × calcium] + [0.32 × magnesium]) (all in mEq/d)

European Journal of Physiology (2024) 476:427–443

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•**Average PRAL Range:** Contemporary Western diets typically produce a total dietary acid load ranging from **50 to 80 mEq per day**. In specific U.S. population studies, mean PRAL values for those on a "High-PRAL Diet" (consistent with typical Western patterns) were approximately **23.35 mEq/day**.

•**Key Drivers:** The high PRAL is primarily due to a heavy intake of **animal proteins** (meat, cheese, eggs), **processed foods**, and **refined grains**, which are rich in acid-forming precursors like phosphorus and sulfur-containing amino acids.

•**Deficiencies:** The SAD is typically low in "base-forming" foods such as **fruits, vegetables, and legumes**, which would otherwise provide alkalizing minerals (potassium, magnesium, calcium) to neutralize the acid.

•**Health Implications:** A chronic high PRAL diet is associated with **low-grade metabolic acidosis**, which may increase the risk of:

- Chronic kidney disease and kidney stones.
- Insulin resistance and Type 2 diabetes.
- Hypertension and cardiovascular disease.
- Reduced bone mineral density and sarcopenia.

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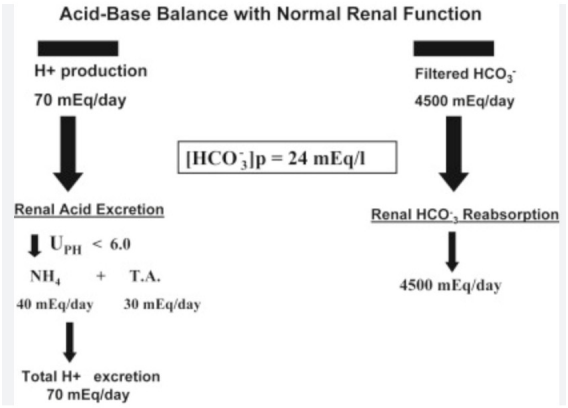

Graphic from ScienceDirect.com

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Exogenous sources of acid

- Animal foods (especially sharp/processed cheese, eggs and meat).
- Grains.
- Ketogenic/low-carb diets.
    - This generally only increases acid load until the body adapts to utilising ketones.
- Anaerobic exercise.
- Prolonged fasting.
    - ~48 hours or longer.

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Types of Acidic Foods

- **Animal Products:** Red meat, poultry, fish, eggs, and most dairy (cheese).
- **Grains & Starches:** Wheat, rice, corn, pasta, bread, and processed cereals.
- **Sugars & Processed Items:** Soda, sweets, sugary drinks, processed snacks, and artificial sweeteners.
- **Beverages:** Alcohol, coffee, and some fruit juices.
- **Condiments:** Ketchup, soy sauce, vinegar.

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What do you eat on an alkaline diet?

Food components that leave acidic ash include protein, phosphate, and sulfur, while alkaline components include calcium, magnesium, and potassium.

Certain food groups are considered acidic, alkaline, or neutral:

- **Acidic:** meat, poultry, fish, dairy, eggs, grains, alcohol
- **Neutral:** natural fats, milk, starches, sugars
- **Alkaline:** fruits, nuts, legumes, vegetables

SUMMARY

According to proponents of the alkaline diet, the metabolic waste — or ash — left from the burning of foods can directly affect the acidity or alkalinity of your body.

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Open access Editorial

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Low-grade metabolic acidosis as a driver of chronic disease: a 21st century public health crisis

James J DiNicolantonio , James O'Keefe

To cite: DiNicolantonio JJ, O'Keefe J. Low-grade metabolic acidosis as a driver of chronic disease: a 21st century public health crisis. *Open Heart* 2021;**8**:e001730. doi:10.1136/openhrt-2021-001730

Accepted 23 September 2021

INTRODUCTION

Metabolic acidosis is a chronic condition that many people in the Western world have but do not realise it.[1–3] It occurs when there is retention of acid in the body, which leads to a depletion in the bicarbonate stores of the body. The term metabolic acidosis is typically used when referring to low blood pH or acidemia due to a metabolic abnormality. However, this is inappropriate as most cases of metabolic acidosis do not have acidemia. In fact, a low blood pH is typically one of the last surrogate markers to become abnormal in those with low-grade metabolic acidosis.[2] This is because the body maintains a normal blood pH at the expense of bicarbonate reserves. Metabolic acidosis primarily occurs inside the cell and in the fluid that surrounds our tissues (interstitial fluid).[4] When checking for metabolic acidosis the clinician should look at blood). Thus, someone with a low blood pH has likely had low-grade metabolic acidosis for years or more likely decades.

Low-grade metabolic acidosis is something that many people in the Western world have.[2] Low-grade means there are no apparent or noticeable harms but the body is retaining acid, depleting bicarbonate stores and damage is occurring in numerous tissues in the body. Typically, with low-grade metabolic acidosis, the blood pH drops slightly, as does the bicarbonate levels, but they will still be in the 'normal' range. Thus, if blood pH and/or bicarbonate levels are at the lower end of normal this is highly suggestive that someone has metabolic acidosis.[2]

With low-grade metabolic acidosis, the total blood buffering capacity is reduced and thus a greater reliance on muscle, bone and connective tissue will be required for the

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Box 1 Ways to test for low-grade metabolic acidosis[2 12]

- Suboptimal fasting serum bicarbonate: <27 mEq/L.[28 29]
- Optimal bicarbonate level: 27–32 mEq/L.
- Optimal level prior to exercise: 31–38 mEq/L.
- Suboptimal blood pH: <7.42.
- Optimal blood pH 7.42–7.45.
- Optimal blood pH prior to exercise: 7.45–7.50.
- High urinary ammonium (NH4+):
  - Normal range is 15–45 ug/dL.
  - Optimal <40 mmol/day.
  - Urinary ammonium starts to fall when glomerular filtration rate (GFR) drops below 40 mL/min.
    - Thus, 24-hour urinary ammonium levels are not an appropriate way to look for low-grade metabolic acidosis once the GFR is <40 mL/min.
- High 24-hour urinary calcium (compared with calcium intake)
  - ~16.67% of dietary calcium gets excreted in the urine, so for a dietary calcium intake of 900 mg, 150 mg will typically come out in the urine.
    - If more than 16.67% of dietary calcium is coming out in the urine this suggests calcium loss, which may be due to metabolic acidosis.
- Low 24-hour urinary citrate
  - <320 mg/24 hours.[30]
  - Optimal urinary citrate level: 600–800 mg/24 hours.
- Low urinary pH
  - A urinary pH of <6.0 is formed from a diet that produces a net acid excretion of 70 mEq/day or higher, which for most people will lead to acid retention.[14]
  - Optimal urinary pH (net acid excretion of zero): ~6.8–7.5.[14]
    - Urine pH should not be taken first thing in the morning or less than 4 hours from eating. Spot urinary pH should be taken 4 hours or longer after eating but not first thing in the morning. The best time to take a urinary spot pH would be before dinner (at least 4 hours after eating lunch).
- Low partial pressure of carbon dioxide
  - < 35 mm Hg.
    - Suboptimal <38 mm Hg.

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Table 2 Strategies for suppressing the dietary acid load

Acid suppressor	Comments
Fruits and vegetables	See PRAL in table 1
Sodium citrate	5 g suppresses 60 mEq of acid. Should be taken with food.
Potassium citrate	3 g suppresses 30 mEq of acid. Typically, no more than 3 g is taken with each meal.
Sodium or potassium bicarbonate	This can suppress stomach acid and thus sodium or potassium citrate is the better option.
Bicarbonate mineral waters (low in sulfate)	1 mEq of bicarbonate inhibits 1 mEq of acid. Typically, the bicarbonate levels are fairly low and should not affect stomach pH. There is a slow accumulation of bicarbonate in the body when drinking bicarbonate mineral waters and this is a better option than sodium or potassium bicarbonate supplements.

PRAL, potential renal acid load.

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frontiers | Frontiers in Nutrition

TYPE Systematic Review
PUBLISHED 11 August 2023
DOI 10.3389/fnut.2023.1233746

OPEN ACCESS

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RECEIVED 02 June 2023
ACCEPTED 28 July 2023
PUBLISHED 11 August 2023

CITATION
Al-Hawary SIS, Mushabab F, Abullais SS, Althomali RH, Saleh EAM, Alnajjar SN, Oudaha KH, Romero-Parra RM, Hussien BM and Garousi N (2023) Metabolic syndrome in relation to dietary acid load: a dose–response meta-analysis of observational studies.
Front. Nutr. 10:1233746.
doi: 10.3389/fnut.2023.1233746

Metabolic syndrome in relation to dietary acid load: a dose–response meta-analysis of observational studies

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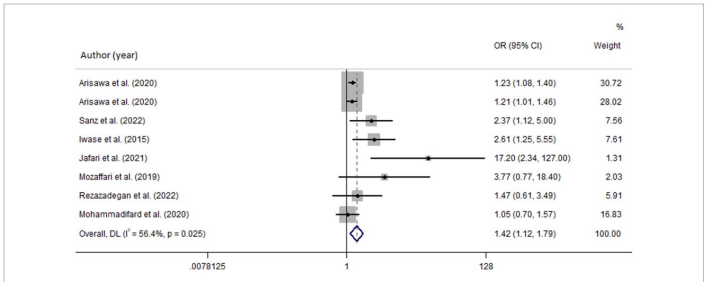

FIGURE 2
Forest plot of the pooled data for the association between high dietary acid load (based on NEAP) and odds of metabolic syndrome.

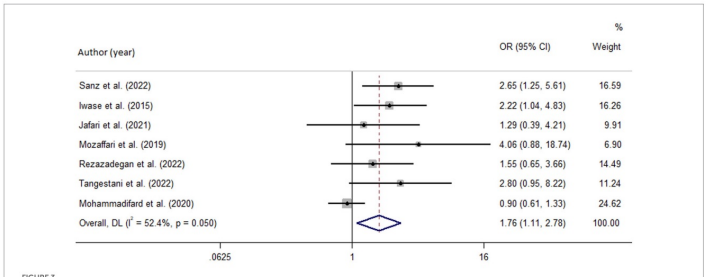

FIGURE 3
Forest plot of the pooled data for the association between high dietary acid load (based on PRAL) and odds of metabolic syndrome.

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ORIGINAL RESEARCH article

Front. Nutr., 28 May 2025

Sec. Clinical Nutrition

Volume 12 - 2025 | https://doi.org/10.3389/fnut.2025.1494617

Association between dietary acid load and risk of metabolic dysfunction-associated steatotic liver disease in patients with type 2 diabetes

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Objective: Considering the high prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) among patients with type 2 diabetes and its associated complications, this study aimed to investigate the relationship between dietary acid load (DAL) and the risk of MASLD in patients with diabetes.

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	Tertiles of dietary acid load			*P* trend
PRAL	T1 (< −21.2)	T2 (−21.2, −6.7)	T3 (−6.7 ≤)	
No. of cases	33	44	56	0.030
Model 1	ref	1.58 (0.76, 3.3)	2.63 (1.24, 5.56)	0.012
Model 2	ref	1.49 (0.66, 3.37)	2.17 (1.03, 5)	0.049
Model 3	ref	2 (0.8, 4.99)	3.1 (1.2, 7.7)	0.016

	Tertiles of dietary acid load			*P* trend
NEAP	T1 (< 28.3)	T2 (28.3–36.7)	T3 (36.7 ≤)	
No. of cases	30	45	58	0.001
Model 1	ref	1.7 (0.88, 3.66)	4.2 (1.8, 9.3)	<0.001
Model 2	ref	1.8 (0.79, 4)	4.3 (1.74, 10.8)	0.002
Model 3	ref	2.2 (0.9, 5.3)	7.3 (2.6, 20.3)	<0.001

Based on multiple logistic regression model. Model 1: adjusted for age and sex; Model 2: additionally adjusted for energy intake, BMI, smoking, physical activity; Model 3: additionally adjusted for duration of diabetes, FBS, TG, TC.

Screenshot

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TYPE Systematic Review
PUBLISHED 27 July 2022
DOI 10.3389/fnut.2022.891936

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Nutritional Epidemiology, a section of the journal Frontiers in Nutrition

RECEIVED 09 March 2022

Association between dietary acid load and cancer risk and prognosis: An updated systematic review and meta-analysis of observational studies

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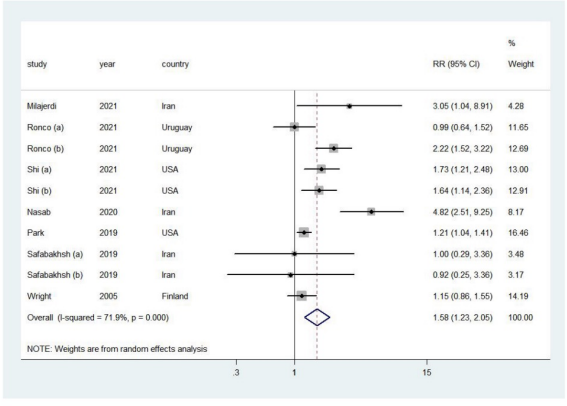

FIGURE 2
Forest plot (a random-effects model) of the association between DAL and cancer risk (highest vs. lowest). Squares indicate study-specific relative risk (RR), where the size of the square reflects the study-specific statistical weight; horizontal lines indicate the 95% CI; and diamonds denote the summary RR with 95% CI.

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Editorial · 26 October 2021 · Open access

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Low-grade metabolic acidosis as a driver of chronic disease: a 21st century public health crisis

Author affiliations · James J DiNicolantonio [1], James O'Keefe [1]

Introduction

Metabolic acidosis is a chronic condition that many people in the Western world have but do not realise it.[1–3] It occurs when there is retention of acid in the body, which leads to a depletion in the bicarbonate stores of the body. The term metabolic acidosis is typically used when referring to low blood pH or acidemia due to a metabolic abnormality. However, this is inappropriate as most cases of metabolic acidosis do not have acidemia. In fact, a low blood pH is typically one of the last surrogate markers to become abnormal in those with low-grade metabolic acidosis.[2] This is because the body maintains a normal blood pH at the expense of bicarbonate reserves. Metabolic acidosis primarily occurs inside the cell and in the fluid that surrounds our tissues (interstitial fluid).[4] When checking for metabolic acidosis the clinician should look at fasting serum bicarbonate, urinary pH (with a measurement at least 4 hours separated from the last ingested meal) and 24-hour urinary citrate levels. While there is not a universally accepted way to diagnose low-grade metabolic acidosis, this paper will help to give the clinician insights into checking for this condition in their patients.

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Defining metabolic acidosis

Acidemia, or too much acid in the blood, only occurs when the body's buffering capacity can no longer maintain a normal pH level. A normal blood pH is considered to be 7.35–7.45. However, even at a normal blood pH metabolic acidosis can occur. In fact, once the blood pH falls below 7.4, there is usually acid retention in the body and low-grade metabolic acidosis.[2] However, the blood pH does not drop below the normal range until metabolic acidosis has become severe. Once this occurs it is usually referred to as 'metabolic acidosis' by the clinician. However, this is actually acidemia (or too much acid in the blood). Thus, someone with a low blood pH has likely had low-grade metabolic acidosis for years or more likely decades.

Low-grade metabolic acidosis is something that many people in the Western world have.[2] Low-grade means there are no apparent or noticeable harms but the body is retaining acid, depleting bicarbonate stores and damage is occurring in numerous tissues in the body. Typically, with low-grade metabolic acidosis, the blood pH drops slightly, as does the bicarbonate levels, but they will still be in the 'normal' range. Thus, if blood pH and/or bicarbonate levels are at the lower end of normal this is highly suggestive that someone has metabolic acidosis.[2]

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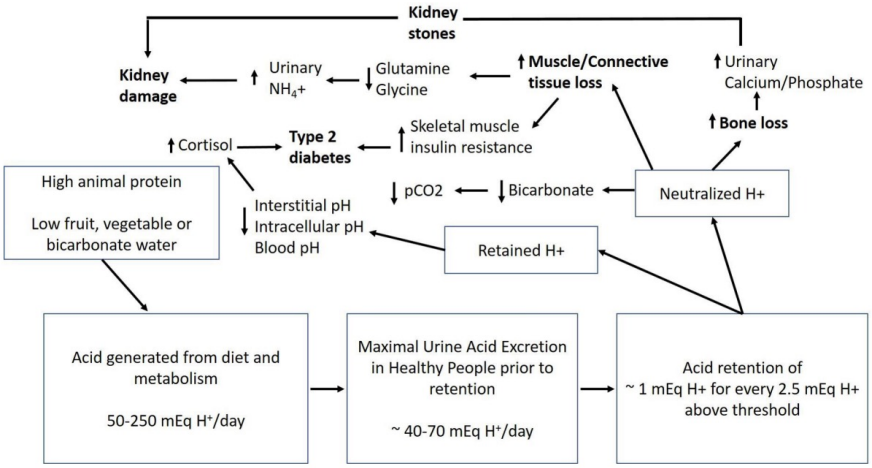

Figure 1 The harms of low-grade metabolic acidosis: adapted from Passey. Reducing the dietary acid load: how a more alkaline diet benefits patients with chronic kidney disease 2016.[21] pCO2, partial pressure of carbon dioxide.

DiNicolantonio JJ, O'Keefe J. *Open Heart* 2021;**8**:e001730. doi:10.1136/openhrt-2021-001730

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Pflügers Archiv - European Journal of Physiology (2024) 476:427–443
https://doi.org/10.1007/s00424-024-02910-7

REVIEW

Dietary acid load in health and disease

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Received: 27 October 2023 / Revised: 7 January 2024 / Accepted: 9 January 2024 / Published online: 29 January 2024

Abstract
Maintaining an appropriate acid–base equilibrium is crucial for human health. A primary influencer of this equilibrium is diet, as foods are metabolized into non-volatile acids or bases. Dietary acid load (DAL) is a measure of the acid load derived from diet, taking into account both the potential renal acid load (PRAL) from food components like protein, potassium, phosphorus, calcium, and magnesium, and the organic acids from foods, which are metabolized to bicarbonate and thus have an alkalinizing effect. Current Western diets are characterized by a high DAL, due to large amounts of animal protein and processed foods. A chronic low-grade metabolic acidosis can occur following a Western diet and is associated with increased morbidity and mortality. Nutritional advice focusing on DAL, rather than macronutrients, is gaining rapid attention as it provides a more holistic approach to managing health. However, current evidence for the role of DAL is mainly associative, and underlying mechanisms are poorly understood. This review focusses on the role of DAL in multiple conditions such as obesity, cardiovascular health, impaired kidney function, and cancer.

Keywords Nutrition · Chronic kidney disease · Acidosis

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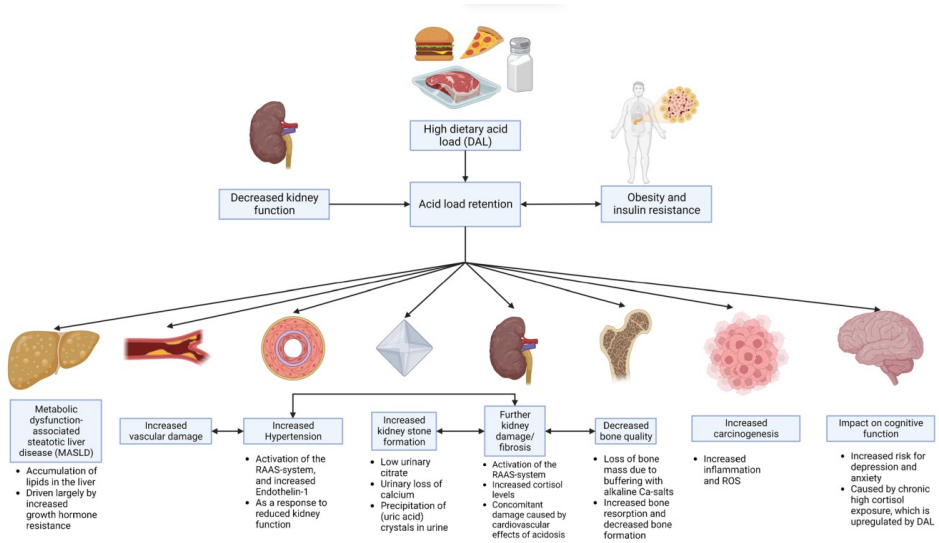

Fig. 1 Summary of the consequences of a high dietary acid load (DAL)

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Anthropology, Human Biology and Nutrition Science

Received: 3 July 2016 | Revised: 3 November 2016 | Accepted: 15 November 2016
DOI 10.1002/ajpa.23148

AJPA YEARBOOK ARTICLE

WILEY American Journal of PHYSICAL ANTHROPOLOGY

Current views on hunter-gatherer nutrition and the evolution of the human diet

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Abstract

Diet composition and food choice are not only central to the daily lives of all living people, but are consistently linked with turning points in human evolutionary history. As such, scholars from a wide range of fields have taken great interest in the role that subsistence has played in both human cultural and biological evolution. Central to this discussion is the diet composition and nutrition of contemporary hunters and gatherers, who are frequently conscripted as model populations for ancestral human nutrition. Research among the world's few remaining foraging populations is experiencing a resurgence, as they are making the final transition away from diets composed of wild foods, to those dominated by domesticated cultigens and/or processed foods. In an effort to glean as much information as possible, before such populations are no longer hunting and gathering, researchers interested in the evolution of human nutrition are rapidly collecting and accessing new and more data. Methods of scientific inquiry are in the midst of rapid change and scholars are able to revisit long-standing questions using state of the art analyses. Here, using the most relevant findings from studies in ethnography, nutrition, human physiology, and microbiomes, we provide a brief summary of the study of the evolution of human nutrition as it has specifically pertained to data coming from living hunter-gatherers. In doing so, we hope to bridge the disciplines that are currently invested in research on nutrition and health among foraging populations.

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Summary: how acid-base status is maintained in the body and why low-grade acidosis is so common

- The average diet in the Western world leads to a net acid excretion of 50–100 mEq/day.
- The body loses 35 mEq of bicarbonate or bicarbonate forming substances per day.
- The kidneys must be relied on to prevent low-grade acidosis as the lungs cannot affect acid-base status over the long-run (one bicarbonate is neutralised to eliminate one hydrogen ion via the lungs).
- The kidneys of a healthy person can only excrete 40–70 mEq of acid per day before acid is retained in the body. Most Americans are consuming diets that produce this much acid or more per day.
- Animal-based or carnivore diets typically provide 150–250 mEq of acid per day, which means that these types of diets lead to significant acid retention unless exogenous bicarbonate forming substances are being consumed (bicarbonate mineral waters or supplements, fruits or vegetables).
- Once the kidneys reach their threshold (40–70 mEq of acid per day), approximately 1 mEq of acid is retained per 2.5 mEq of acid above the threshold.
- If the diet does not contain enough bicarbonate (bicarbonate-forming substances or citrate) and minerals (sodium, potassium, magnesium and calcium) to neutralise the excess acid then negative consequences to numerous bodily systems take place:
    - Bone will breakdown to increase bicarbonate buffering as well as alkaline minerals for sulfate excretion, which leads to mineral loss and weak bones.
    - Muscle and connective tissue will breakdown to eliminate hydrogen ions along with ammonium, which taxes glutamine and glycine status.
    - The kidneys will slowly become damaged from the high production of ammonia.
    - Kidney stones can form due to the increased reabsorption of citrate and the increased calcium out in the urine.
    - The increase in acid in the cell can reduce the function of numerous enzymes and processes and has harmful effects on all tissues.

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