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What Are Humans Designed to Eat?

Metabolic Flexibility, Energetic Resilience, and the Modern Food Environment

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INTRODUCTION

Modern nutrition debates have become increasingly polarized between low-fat, Mediterranean, plant-based, vegan, ketogenic, low-carbohydrate, and animal-based dietary models. Yet despite decades of nutritional guidelines and enormous scientific effort, chronic diseases—including obesity, type 2 diabetes, cardiovascular disease, autoimmune disorders, cancer, and neurodegenerative diseases—continue to rise globally.

This raises an important question:

What diets are actually most compatible with human physiology, metabolic biology, and long-term physiological resilience?

From an Integrative Orthomolecular Medicine (IOM) Systems Medicine perspective, nutrition should not be evaluated solely according to calories or isolated macronutrients, but according to broader systems-level effects on:

- metabolic flexibility,
- mitochondrial energetics,
- inflammatory regulation,
- nutrient density and bioavailability,
- toxicological burden,
- endocrine signaling,
- biological barrier integrity,
- and long-term energetic resilience.

Human physiology evolved under conditions of fluctuating food availability, intermittent fasting, prolonged physical exertion, and highly variable nutritional environments. As a result, humans developed remarkable metabolic flexibility—the ability to transition between glucose metabolism, fatty acid oxidation, and ketone utilization depending on energetic demands and nutrient availability.

Modern industrialized food systems differ profoundly from these ancestral conditions. Continuous feeding, ultra-processed foods, refined carbohydrates, industrial seed oils, circadian disruption, physical inactivity, and chronic hyperinsulinemia may progressively impair this adaptive fuel-switching capacity.

From a systems-level perspective, many chronic diseases may therefore reflect not simply isolated organ dysfunction, but progressive loss of metabolic flexibility and energetic resilience.

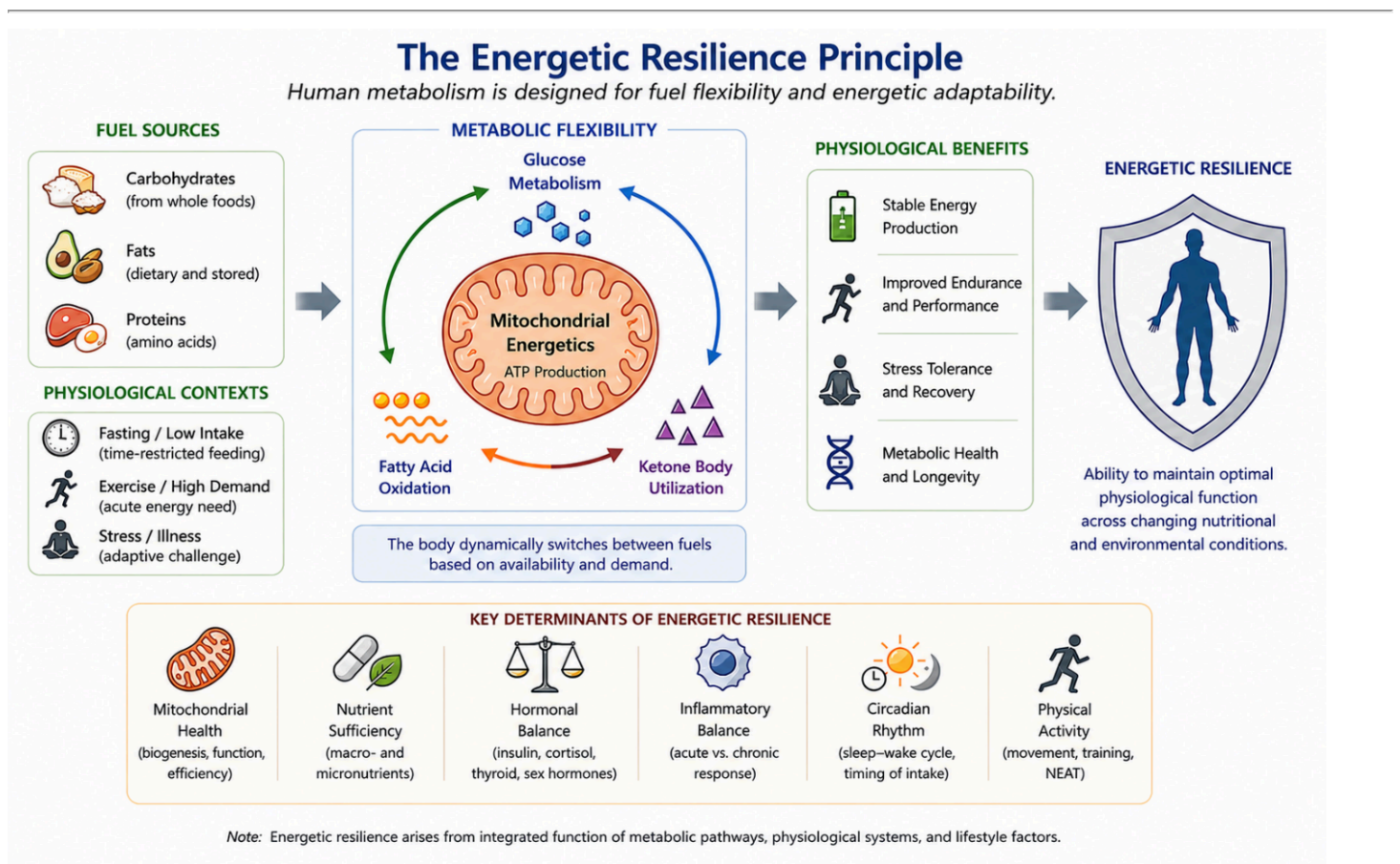


Figure 1. The Energetic Resilience Principle.

Human metabolism is inherently designed for flexible fuel utilization. Depending on nutrient availability and energetic demand, humans can transition between glucose metabolism, fatty acid oxidation, and ketone utilization to maintain stable energy production and physiological resilience. Adapted from Cheng RZ. *What Are Humans Designed to Eat? An IOM Systems Medicine Framework for Dietary Compatibility, Nutrient Density, and Toxicological Burden*. Preprints 2026, 2026050616. <https://doi.org/10.20944/preprints202605.0616.v1>

Fatty Acid Oxidation Is Normal Human Physiology

For many readers, the term "fatty acid oxidation" may initially sound harmful because the word "oxidation" is often associated with oxidative damage and free radicals.

However, fatty acid oxidation is actually the normal mitochondrial process by which humans convert stored fat into usable energy.

Fatty acid oxidation should not be confused with pathological oxidative stress. Rather, it is one of the body's most important energy-producing mechanisms and is essential for human survival during fasting, prolonged physical activity, and periods of reduced carbohydrate availability.

When food intake decreases-or when carbohydrate intake is reduced-the body begins breaking down stored fat (triglycerides) into fatty acids through a process called lipolysis. These fatty acids are then transported into mitochondria, where they undergo beta-oxidation to generate ATP, the body's primary energy currency.

At the same time, the liver can convert fatty acids into ketone bodies, including beta-hydroxybutyrate and acetoacetate. These ketones can then serve as highly efficient alternative fuels for the brain, skeletal muscle, and heart.

In other words, fatty acid oxidation and ketone utilization are not abnormal or dangerous metabolic states. They are normal components of human metabolic flexibility and evolutionary survival physiology.

Throughout most of human history, humans did not have constant access to food. Survival depended on the ability to maintain stable energy production during intermittent fasting, migration, hunting, environmental stress, illness, and fluctuating nutrient availability.

As a result, humans evolved remarkable fuel-switching capability-the ability to transition between glucose metabolism and fat-based metabolism depending on physiological conditions.

From an IOM Systems Medicine perspective, one major problem in the modern industrialized dietary environment is that many individuals gradually lose this metabolic flexibility due to:

- chronic hyperinsulinemia,
- continuous feeding patterns,
- ultra-processed foods,
- excessive refined carbohydrate intake,
- physical inactivity,
- circadian disruption,

- and persistent dependence on frequent glucose intake.

Over time, this may impair the body's ability to efficiently access stored fat for energy. Many individuals therefore become increasingly dependent on frequent carbohydrate intake simply to maintain perceived energy stability.

This loss of metabolic flexibility may contribute to:

- fatigue,
- unstable energy regulation,
- impaired endurance,
- insulin resistance,
- mitochondrial stress,
- chronic inflammation,
- and broader systems-level dysfunction.

Accordingly, the goal is not simply "low carbohydrate intake" alone. The deeper physiological objective is restoration of metabolic adaptability and energetic resilience—the ability to efficiently and safely transition between fuel systems without metabolic instability or "energy collapse."

Several lifestyle and physiological factors may help support this adaptive transition, including:

- reducing ultra-processed foods,
- lowering excessive refined carbohydrate exposure,
- improving nutrient density,
- preserving skeletal muscle mass,
- regular physical activity,
- restoring circadian alignment,
- maintaining appropriate fasting intervals,
- improving insulin sensitivity,
- and ensuring adequate micronutrient and mitochondrial support.

Within this framework, nutritional ketosis should not necessarily be viewed as an abnormal metabolic condition, but rather as part of normal human physiological adaptability.

Modern Dietary Transition and Loss of Energetic Resilience

From adaptive fuel flexibility in our evolutionary environment to chronic glucose dependency in the modern environment.

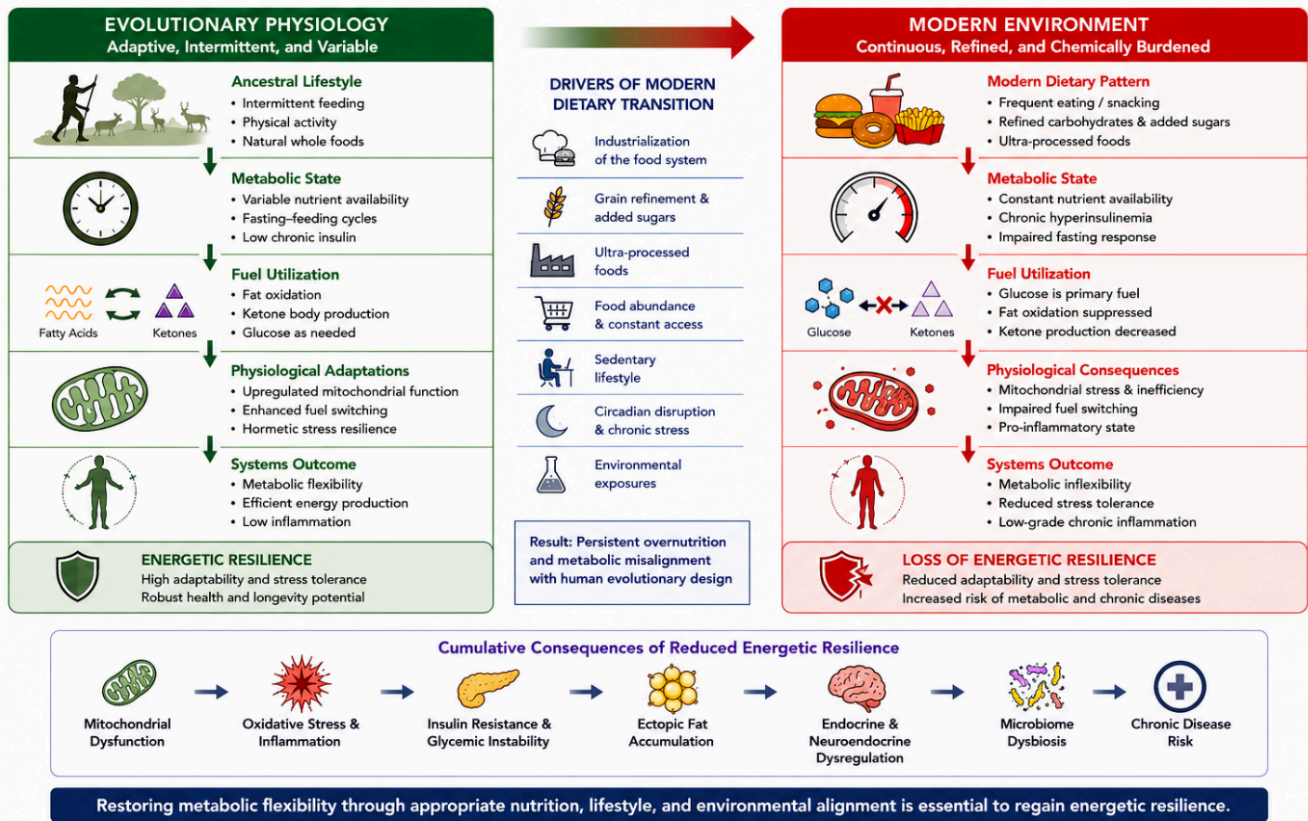


Figure 2. Modern Dietary Transition and Loss of Energetic Resilience.

Continuous refined carbohydrate exposure, ultra-processed foods, reduced fasting intervals, and sedentary lifestyles may progressively impair metabolic flexibility and mitochondrial resilience. Adapted from Cheng RZ. *What Are Humans Designed to Eat?* Preprints 2026.

No Modern Food System Is Completely Toxin-Free

Modern dietary debates often portray particular food systems as either "healthy" or "toxic." In reality, no modern dietary system is entirely free of toxicological burden.

Plant-heavy dietary systems may involve greater exposure to:

- pesticide residues,
- herbicides,
- glyphosate,
- nitrates,
- mycotoxins,
- and naturally occurring plant defense compounds such as lectins, oxalates, and phytates.

Conversely, animal-heavy dietary systems may involve greater exposure to:

- persistent organic pollutants (POPs),
- dioxins,
- PCBs,
- heavy metals,
- and fat-soluble bioaccumulated pollutants concentrated within animal fat and marine food chains.

Thus, different dietary systems may shift toxicological exposure profiles rather than eliminate toxicological burden entirely.

From an IOM Systems Medicine perspective, the key question is not whether a diet is completely "toxin-free," but whether the overall dietary pattern:

- reduces cumulative physiological stress,
- supports mitochondrial function,
- maintains nutrient sufficiency,
- improves metabolic flexibility,
- supports detoxification systems,
- and enhances long-term physiological resilience.

Animal-Derived vs. Plant-Derived Foods: Key Comparison







Dimension	Animal-Derived Foods	Plant-Derived Foods	Comparative Conclusion
 Nutrient Density	<ul style="list-style-type: none"> • High nutrient density • Rich in bioavailable iron, B12, heme iron, DHA, EPA, and vitamin A 	<ul style="list-style-type: none"> • Lower nutrient density • Often lack B12, DHA/EPA, heme iron, vitamin D, and preformed vitamin A 	Animal foods provide more nutrients per unit energy.
 Amino Acid Bioavailability	<ul style="list-style-type: none"> • Complete amino acid profile • High digestibility and bioavailability 	<ul style="list-style-type: none"> • Often incomplete amino acid profile • Lower digestibility and bioavailability 	Animal proteins have superior overall quality and digestibility.
 Mitochondrial Support	<ul style="list-style-type: none"> • Rich in creatine, carnitine, CoQ10, heme iron, and B vitamins • Directly supports mitochondrial energy production 	<ul style="list-style-type: none"> • Lower or absent levels of key mitochondrial nutrients • Some precursors require conversion and are less efficient 	Animal foods better support mitochondrial function and energy production.
 Fiber / Phytochemicals	<ul style="list-style-type: none"> • Low to moderate fiber • Fewer phytochemicals 	<ul style="list-style-type: none"> • High fiber content • Rich in phytochemicals and polyphenols 	Plant foods excel in fiber and phytochemical content.
 Toxin Profiles	<ul style="list-style-type: none"> • Greater concern for bioaccumulated toxins (e.g., heavy metals, PCBs, dioxins) • Some marine sources higher in contaminants 	<ul style="list-style-type: none"> • Possible plant toxins: pesticides, lectins, oxalates, phytates • Generally lower bioaccumulation of persistent toxins 	Both food types can carry toxins; plant toxins are often reduced through preparation.
 Metabolic Effects	<ul style="list-style-type: none"> • Supports muscle maintenance, hormone production, and metabolic health • Often more satiating per calorie 	<ul style="list-style-type: none"> • Supports gut health and weight management • May require careful planning to meet protein needs 	Animal foods support metabolic resilience; plant foods support gut health and weight goals.

Table 1. Simplified comparison of animal-derived and plant-derived foods from an IOM Systems Medicine perspective.

Animal-derived foods generally provide higher nutrient density, superior amino acid bioavailability, and stronger mitochondrial support, whereas plant-derived foods contribute dietary fiber and diverse phytochemicals. Both food categories may carry distinct toxicological burdens depending on sourcing, processing, and environmental exposure. Optimal long-term dietary

strategies may integrate nutrient-dense minimally processed animal foods with selected low-toxin plant foods to support metabolic resilience and overall physiological function. Adapted from Cheng RZ. *What Are Humans Designed to Eat?* Preprints 2026.

Humans Evolved for Fuel Flexibility

Throughout most of human evolutionary history, survival depended not on continuous food availability, but on the ability to maintain stable energy production during intermittent fasting, migration, hunting, environmental stress, and fluctuating nutrient availability.

Humans therefore evolved highly adaptive fuel-switching physiology capable of utilizing:

- glucose,
- fatty acids,
- ketone bodies,
- and amino acids,











































depending on energetic demand and nutrient availability.






By contrast, many modern industrialized dietary environments promote almost continuous glucose exposure through:

- refined carbohydrates,
- ultra-processed foods,
- sugar-containing beverages,
- frequent snacking,
- and prolonged hyperinsulinemia.

Over time, this may impair access to endogenous fat stores, reduce mitochondrial flexibility, and increase dependence on continuous carbohydrate intake for perceived energy stability.

Systems-Level Comparison of Major Dietary Patterns

Dimension	SAD (Standard American Diet)	Mediterranean Diet	Plant-Based Diet	Keto Diet	Carnivore Diet
 Glycemic Burden	 High	 Moderate	 Variable	 Very Low	 Minimal
 Nutrient Density	 Low	 High	 Moderate	 High*	 High*
 Metabolic Flexibility	 Impaired	 Moderate	 Variable	 High	 High
 Mitochondrial Support	 Low	 Strong	 Moderate	 Strong	 Strong
 Ultra-Processing Burden	 High	 Low-Moderate	 Variable	 Low	 Very Low
 Energetic Resilience	 Low	 Moderate	 Variable	 High	 High
 Toxicological Burden	 High	 Moderate	 Variable	 Moderate-Low	 Low

Legend:  High / Poor  Moderate  Variable / Depends  Low / Good  Very Low / Optimal

* Quality depends on food choices and nutrient adequacy.

Adapted from Cheng RZ. *What Are Humans Designed to Eat? An IOM Systems Medicine Framework for Dietary Compatibility, Nutrient Density, and Toxicological Burden*. Preprints 2026, 2026050616. <https://doi.org/10.20944/preprints202605.0616.v1>

Table 2. Simplified systems-level comparison of major dietary patterns within the IOM Systems Nutrition Framework. Major dietary patterns differ substantially in glycemic burden, nutrient density, metabolic flexibility, mitochondrial support, energetic resilience, processing burden, and toxicological exposure profiles. Adapted from Cheng RZ. *What Are Humans Designed to Eat?* Preprints 2026.



Figure 3. Systems-level dietary framework based on metabolic flexibility and clinical context.

Different dietary approaches may be appropriate under different metabolic and clinical conditions. From an IOM Systems Medicine perspective, dietary strategies should be individualized according to metabolic flexibility, inflammatory burden, mitochondrial function, and overall physiological resilience.

CONCLUSION

Human nutrition cannot be adequately understood through simplistic calorie-based or ideology-driven frameworks alone.

Humans evolved as metabolically flexible omnivores capable of adapting to fluctuating nutritional environments through dynamic fuel switching between glucose metabolism, fatty acid oxidation, and ketone utilization.

From an IOM Systems Medicine perspective, optimal nutrition should therefore be evaluated according to its effects on:

- metabolic flexibility,
- mitochondrial energetics,
- nutrient density,
- inflammatory regulation,
- toxicological burden,
- endocrine signaling,
- biological resilience,

- and long-term energetic adaptability.

No single dietary model is universally ideal under all conditions. Rather, nutritional compatibility likely varies according to:

- metabolic health,
- mitochondrial function,
- physical activity,
- environmental exposures,
- microbiome status,
- inflammatory burden,
- and individual physiological context.

However, several common principles consistently emerge across systems-level nutritional analysis:

- reduction of ultra-processed foods,
- reduction of excessive glycemic burden,
- improved nutrient density,
- restoration of metabolic flexibility,
- preservation of mitochondrial function,
- reduction of cumulative toxicological burden,
- and support of long-term physiological resilience.

The modern chronic disease epidemic may therefore reflect not merely excess calories, but a broader mismatch between industrialized dietary environments and human evolutionary metabolic physiology.

For readers interested in the full scientific systems-level analysis, including detailed mechanistic discussion, comparative dietary frameworks, nutrient density analysis, and toxicological considerations, see the complete preprint paper:

Cheng RZ.

What Are Humans Designed to Eat? An IOM Systems Medicine Framework for Dietary Compatibility, Nutrient Density, and Toxicological Burden.

Preprints 2026, 2026050616. <https://doi.org/10.20944/preprints202605.0616.v1>

Additional systems-level discussions on nutrition, metabolic flexibility, orthomolecular medicine, and chronic disease are available through Dr. Cheng's ongoing educational publications on Substack: <https://rzchengmd.substack.com>.