











# Climate change and the impact on human metabolism

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- Acronym: INNO-SAFE-LIFE















### **Overview and Context**



The **Anthropocene** era marks unprecedented climate variability.



Global surface temperature ↑ by **1.1°C** since pre-industrial levels (IPCC 2023).



Climate change affects **metabolism** via:

Thermal homeostasis.

Nutrient supply and diet composition.

Pollutant exposure and oxidative stress.

Endocrine and microbiome alterations.



Metabolic physiology is environmentally sensitive. Temperature, food quality, and toxin exposure modulate enzymatic activity, hormonal control, and energy expenditure, influencing health outcomes in warming climates.













### Human Metabolism: Fundamental Overview



Energy balance: caloric intake vs expenditure.



Basal Metabolic Rate (BMR): influenced by temperature, thyroid activity, and body composition.



Mitochondrial metabolism: thermogenesis and oxidative phosphorylation.



Neuroendocrine regulation: hypothalamic integration of thermal and nutritional cues.



Metabolism is the sum of anabolic and catabolic processes driven by hormonal control. Environmental temperature modulates mitochondrial function and peripheral energy expenditure through thyroid and brown adipose tissue signaling.













### Thermal Physiology and Climate Stress

Heat stress increases cardiovascular strain and metabolic rate → dehydration and electrolyte imbalance.

Cold stress stimulates non-shivering thermogenesis (NST) via brown adipose tissue (BAT).

Chronic temperature elevation may suppress thyroid axis → metabolic adaptation.

Disruption of circadian thermoregulation alters glucose and lipid metabolism.

Temperature extremes push human physiology beyond adaptive thresholds. Heat-induced dehydration and electrolyte loss impact enzymatic efficiency, while chronic warmth downregulates energy-expensive thermogenesis.













### Climate Change and Energy Homeostasis



Environmental temperature modifies energy expenditure by ~5–15%.



Thermoneutral zones narrowing due to urban heat islands.



**Adaptive thermogenesis** reduced → potential for energy imbalance.



Rising temperatures may lower BMR, promoting adiposity.



Experimental and epidemiological data show that chronic exposure to warm climates may suppress metabolic energy expenditure, predisposing to weight gain and metabolic syndrome — a paradoxical outcome of global warming.













### Impacts on Macronutrient Metabolism

Carbohydrate metabolism: heat stress → impaired insulin sensitivity.

Lipid metabolism: oxidative stress enhances lipid peroxidation; altered HDL/LDL ratios.

**Protein metabolism:** dehydration and heat → muscle catabolism, nitrogen imbalance.

Climate-induced hypoxia (altitudinal, urban smog) → mitochondrial dysfunction.

Climate-linked stressors like hypoxia and dehydration perturb enzyme systems governing glucose and lipid metabolism. Heat-induced insulin resistance parallels the metabolic alterations seen in obesity and aging.













### Hormonal and Endocrine Modulation

**Thyroid hormones:** modulate thermogenesis; chronic heat reduces  $T_3/T_4$  secretion.

**Cortisol:** elevated under heat and psychosocial stress → gluconeogenesis, insulin resistance.

Leptin/ghrelin axis: disrupted by circadian and dietary changes.

**Sex hormones:** temperature-related fertility decline in both sexes.

The endocrine system mediates environmental adaptation. Chronic stress and circadian disruption under climate stress drive metabolic dysregulation, impacting appetite, insulin function, and reproductive health.













### Circadian and Chronometabolic Effects

Photoperiod disruption: extended heat and altered daylight affect melatonin secretion.

Clock gene expression (PER, CRY, BMAL1) modulates glucose and lipid metabolism.

Sleep deprivation from thermal discomfort exacerbates insulin resistance.

**Circadian misalignment** → metabolic inflexibility and obesity risk.

Circadian biology is temperature-sensitive. Global warming and light pollution synergistically distort circadian rhythms, impairing metabolic synchronization between liver, adipose, and muscle tissues.











## Oxidative Stress and Mitochondrial Dysfunction

Climate stress → **ROS overproduction** in mitochondria.

Antioxidant enzyme capacity (SOD, CAT, GPx) declines under chronic heat exposure.

Mitochondrial DNA mutations accumulate → decreased ATP efficiency.

Links to **metabolic disorders**: type 2 diabetes, sarcopenia, neurodegeneration.

Mitochondrial vulnerability to heat and pollution accelerates oxidative damage. Reactive oxygen species act as metabolic disruptors, bridging environmental exposure with chronic disease onset.













### Nutritional Transitions under Climate Change



**Crop yield reductions:** ↓ protein and micronutrient content.



**CO<sub>2</sub> enrichment:** ↓ zinc, iron, and B-vitamin concentration in grains.



Food insecurity → reliance on calorie-dense, nutrient-poor diets.



Metabolic consequence: micronutrient deficiency-induced mitochondrial inefficiency.



#### **Speaker Notes:**

Climate-driven food degradation alters dietary macronutrient ratios and micronutrient density, influencing mitochondrial cofactor availability and systemic metabolic homeostasis.







# Environmental Pollutants and Endocrine Disruption



Climate change enhances **chemical mobility** (pesticides, plasticizers, heavy metals).



Endocrine-disrupting chemicals (EDCs): mimic hormones (BPA, phthalates).



**Bioaccumulation** in warming ecosystems → human exposure via diet.



EDCs linked to obesogenic and diabetogenic metabolic pathways.



Warming accelerates the release and bioavailability of endocrine disruptors, amplifying hormonal perturbations and increasing the prevalence of obesity and insulin resistance the "metabolic footprint" of climate pollution.













### Microbiome and Metabolic Interface

Gut microbiota sensitive to temperature, diet, and hydration status.

**Dysbiosis** from food insecurity and antibiotic use under changing climate.

Altered short-chain fatty acid (SCFA) production affects insulin sensitivity.

Microbiome shifts → systemic inflammation and metabolic reprogramming.

The gut microbiome acts as a climate-sensitive metabolic modulator. Environmental disruption modifies microbial diversity, impairing energy harvest efficiency and promoting lowgrade inflammation.







# Metabolic Adaptation and Evolutionary **Physiology**

Historical adaptation to thermal stress (e.g., Bergmann's and Allen's rules).

Epigenetic regulation: methylation of metabolic genes under environmental stress.

**Developmental plasticity:** fetal programming by maternal stress or malnutrition.

Climate-epigenome-metabolism axis as an emerging research field.

Evolutionary physiology offers insights into long-term adaptation. Climate stress imprints epigenetic modifications that alter metabolic set-points, possibly persisting across generations.















### Climate-Linked Disease Burden

**Metabolic syndrome** prevalence correlated with rising temperatures.

Diabetes risk increases 4% per 1°C rise (Lancet Planetary Health, 2017).

Chronic kidney disease of unknown origin (CKDu): heat-induced nephropathy in agricultural workers.

Climate-induced vector-borne diseases indirectly affect energy metabolism.

Epidemiological evidence connects heat exposure with rising metabolic diseases. Climate stress acts as both a direct and indirect driver — influencing organ function, infection risk, and systemic energy dynamics.













### **Vulnerable Populations**

**Elderly:** reduced thermoregulatory capacity.

Children: immature endocrine and metabolic regulation.

Low-income populations: higher exposure, limited nutrition.

Outdoor workers: chronic dehydration and kidney stress.

**Urban poor:** combined heat, pollution, and food insecurity risks.

Metabolic resilience is socioeconomically stratified. Vulnerable groups experience compounded exposure from environmental, nutritional, and occupational stressors.











### Biomarkers and Systems Biology Approaches

Metabolomics: climate-sensitive metabolites (glucose, lactate, acylcarnitines).

Proteomics: heat-shock proteins (HSP70, HSP90) as stress indicators.

**Epigenomic biomarkers:** methylation of PGC1α, UCP1 genes.

Integrative "exposomics" links environmental and metabolic datasets.

Multi-omics approaches quantify metabolic responses to environmental shifts. Systems biology models integrate thermal exposure with molecular biomarkers to predict metabolic resilience or vulnerability.













### Adaptation and Mitigation Strategies



Urban design: green infrastructure, passive cooling.



Dietary adaptation: plant-based, micronutrient-rich diets.



Occupational health: hydration, heat-exposure monitoring.



Precision medicine: metabolic phenotyping for personalized risk reduction.



Mitigating metabolic consequences of climate change requires cross-sectoral strategies, integrating health systems, nutrition policy, and urban planning to buffer physiological stressors.















### **Research Frontiers**



Thermo-metabolomics: mapping temperature-dependent metabolic flux.



Al modeling: predicting metabolic outcomes from climate scenarios.



Climate epigenetics: intergenerational metabolic reprogramming.



One Health frameworks: integrating human, animal, and ecosystem metabolism.



Emerging research uses integrative and computational approaches to understand metabolic adaptation at a planetary scale, emphasizing interconnected biological and environmental systems.













### **Ethical and Policy Considerations**

Climate-induced metabolic disease = inequality amplifier.

Ethical duty to mitigate disproportionate burdens.

Policy integration: planetary health and climate adaptation in healthcare planning.

Global collaboration: WHO, IPCC, and planetary health networks.

Equitable health adaptation requires global coordination. Climate–metabolic health must be embedded into international health frameworks, emphasizing sustainability and justice.



Climate change disrupts metabolic homeostasis through thermal, nutritional, and endocrine pathways.









Human metabolism reflects environmental adaptation and vulnerability.

Integrative biology, precision medicine, and climate policy are essential for resilience.

Future challenge: maintaining metabolic equilibrium in a warming world.

Conclusion

Climate change is not only an environmental crisis — it's a metabolic one. The interplay between global temperature and human physiology represents a defining research frontier for 21st-century medicine and public health.