

Metabolic Syndrome Is Not Just About Obesity

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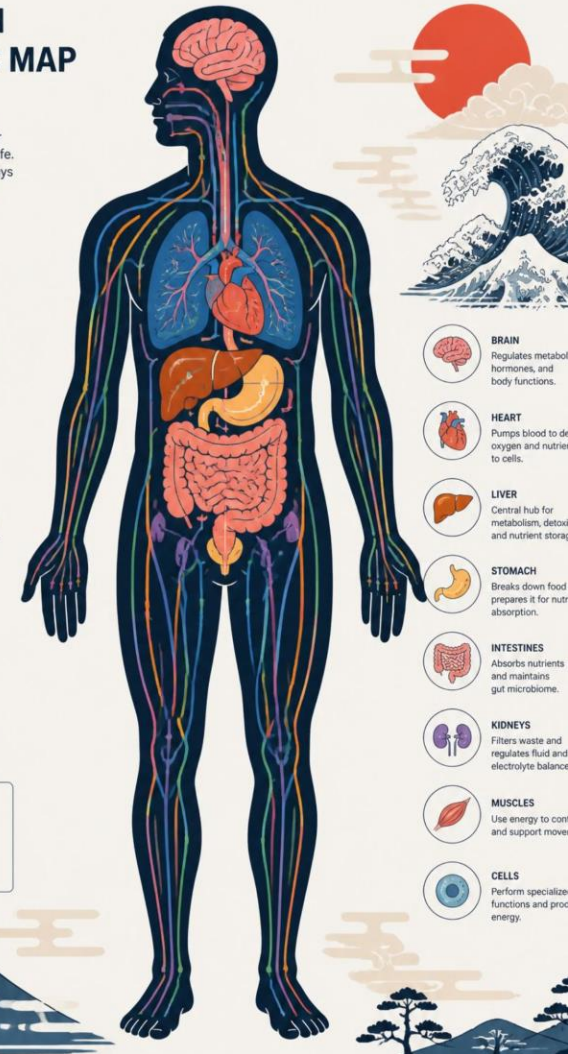
THE HUMAN METABOLIC MAP

Metabolism is the sum of all chemical reactions that occur in our bodies to sustain life. These interconnected pathways convert food to energy, build cellular components, and eliminate waste.

METABOLIC PATHWAYS

- CARBOHYDRATE METABOLISM**
Breaks down carbohydrates to produce energy.
- LIPID METABOLISM**
Processes fats for energy storage and cell structure.
- PROTEIN METABOLISM**
Breaks down proteins into amino acids and builds new proteins.
- NUCLEOTIDE METABOLISM**
Synthesizes and breaks down DNA and RNA components.
- ENERGY METABOLISM**
Generates ATP, the body's primary energy currency.
- DETOXIFICATION PATHWAYS**
Neutralizes and eliminates harmful substances.
- VITAMIN & COFACTOR METABOLISM**
Supports reactions through essential micronutrients.

EVERY REACTION SUSTAINS LIFE
All pathways are interconnected and work in harmony.



Why This Matters: The Silent Epidemic

>20%

Global Prevalence

Adults affected in America and Europe, surging in parallel with rising obesity rates

44%

Ages 60–69

Nearly half of older adults meet diagnostic criteria for metabolic syndrome

3X

Urban Risk

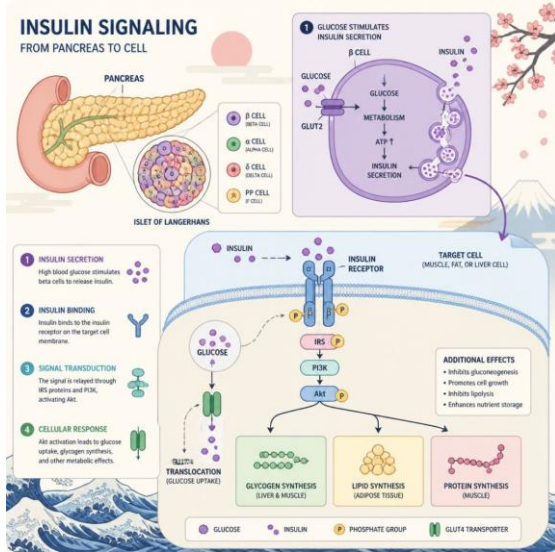
Urbanization, sedentary lifestyles, and dietary shifts drive exponential rise



Diagnostic Criteria: 3 of 5 Components

Metabolic syndrome is diagnosed when **any 3 of the following 5** criteria are met (NIH/NHLBI standards):

Component	Threshold	Clinical Significance
Abdominal Obesity	Waist >40" men / >35" women	Central adiposity marker
Elevated Triglycerides	≥150 mg/dL	Dyslipidemia indicator
Low HDL Cholesterol	<40 mg/dL men / <50 mg/dL women	Cardiovascular risk
Elevated Blood Pressure	≥130/80 mmHg	Endothelial dysfunction
Elevated Fasting Glucose	≥100 mg/dL	Insulin resistance proxy



The Core Problem: Insulin Resistance

Insulin resistance is the **central mechanism** underlying metabolic syndrome — not obesity alone.

→ Excess Visceral Fat

Free fatty acids flood the portal vein, accumulating in liver and muscle

→ Impaired Cell Signaling

Cells fail to respond adequately to insulin, triggering hyperinsulinemia

→ Metabolic Cascade

Glucose metabolism impairment, dyslipidemia, and hypertension follow

Pathophysiology: Beyond Simple Obesity

Metabolic syndrome emerges from a complex interplay of genetic predisposition, dysfunctional adipose tissue, and systemic inflammation — not simply excess weight.

Dysfunctional Adipose Tissue

Visceral fat is metabolically active and pro-inflammatory, secreting harmful adipokines that disrupt systemic homeostasis

Ectopic Lipid Accumulation

Fat deposits infiltrate the liver, skeletal muscle, and pancreas — impairing organ function independently of BMI

Systemic Inflammation

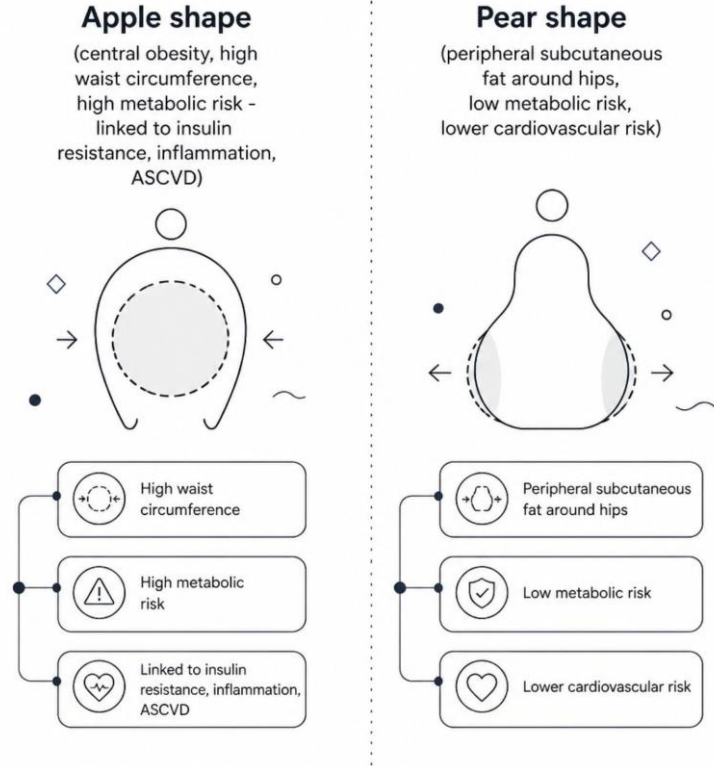
Elevated cytokines (TNF- α , IL-6) and oxidative stress perpetuate insulin resistance and vascular damage

Why Waist Circumference Matters More Than BMI

Body fat **distribution** — not total amount — determines metabolic risk. Two patients with identical BMI can have vastly different risk profiles.

- **Apple-shaped (central):** High visceral adiposity → drives insulin resistance, inflammation, and ASCVD risk
- **Pear-shaped (peripheral):** Subcutaneous hip fat → significantly lower metabolic risk
- A high waist-to-hip ratio reflects low muscle-to-fat mass and predicts metabolic complications independently of BMI

📌 Visceral adiposity is the key driver — measure the waist, not just the weight.



Cardiovascular Complications

Atherosclerotic CVD

Significantly elevated risk of ASCVD events — the leading cause of mortality in metabolic syndrome patients

Atherogenic Dyslipidemia

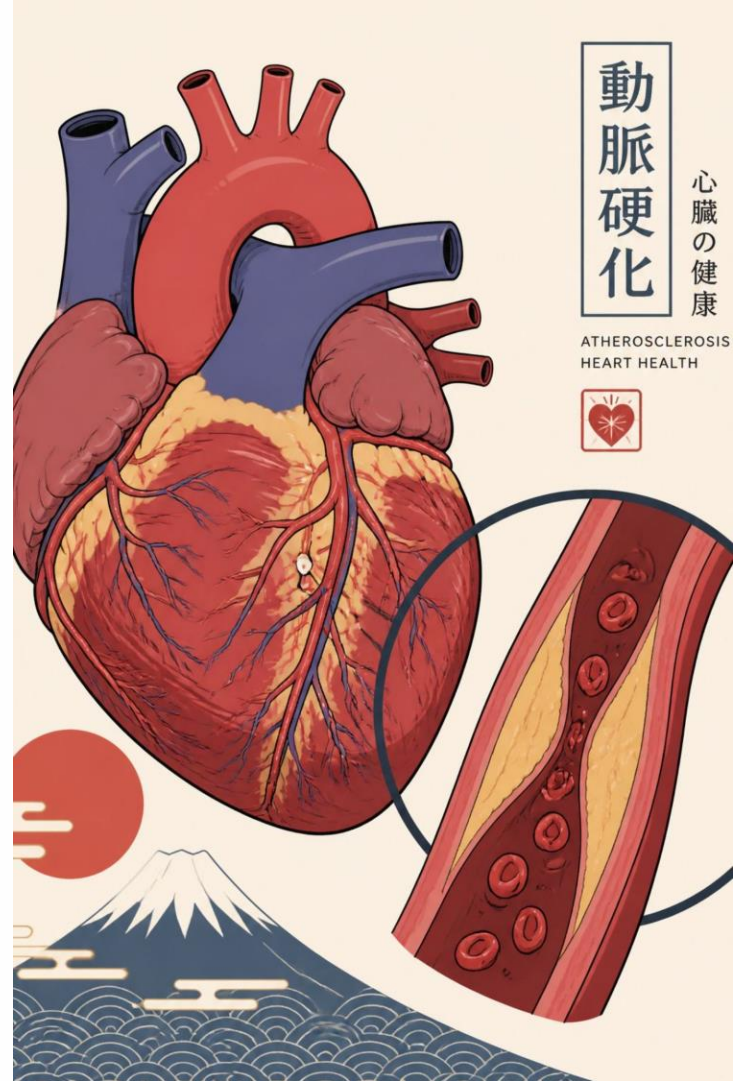
Classic triad: ↑ triglycerides, ↓ HDL, ↑ small dense LDL — highly pro-atherogenic even at normal total cholesterol

Hypertension

Driven by sodium retention, RAAS activation, and endothelial dysfunction from chronic hyperinsulinemia

Prothrombotic State

Elevated PAI-1 and fibrinogen increase thrombotic event risk, compounding cardiovascular vulnerability



動脈硬化

心臓の健康

ATHEROSCLEROSIS
HEART HEALTH



Metabolic Complications



Type 2 Diabetes

Progressive deterioration from impaired fasting glucose through overt T2DM as beta-cell reserve is exhausted



Hyperuricemia

Elevated serum uric acid — driven by insulin resistance-mediated impaired renal urate excretion — increases gout risk



NAFLD / MAFLD

Ectopic hepatic fat accumulation progressing from simple steatosis to NASH, fibrosis, and cirrhosis



PCOS

Polycystic ovary syndrome strongly linked to insulin resistance in women, creating a bidirectional metabolic relationship



Lifestyle Modification: First-Line Treatment

Lifestyle intervention remains the **cornerstone** of metabolic syndrome management — preceding and potentiating any pharmacological approach.

1 Weight Reduction

Even a modest **3–5% body weight loss** demonstrably improves triglycerides, fasting glucose, and blood pressure

2 Dietary Approach

DASH and Mediterranean diets preferred; emphasize whole grains, fiber, and restrict ultra-processed foods

3 Physical Activity

Minimum **150 min/week** moderate-intensity aerobic exercise; walking is the recommended starting point

Pharmacological Management

When lifestyle modification is insufficient, targeted pharmacotherapy addresses each metabolic component. **No single agent treats metabolic syndrome as a whole** – individualized, component-based therapy is required.



Antihypertensives

ACE inhibitors and ARBs preferred – provide metabolic benefits including improved insulin sensitivity and renal protection



Lipid-Lowering

Statins are first-line for ASCVD risk reduction; fibrates may be added for severe hypertriglyceridemia



Glucose Control

Metformin as foundational agent; GLP-1 receptor agonists and SGLT2 inhibitors offer cardiometabolic dual benefits



Insulin Sensitizers

Thiazolidinediones directly improve insulin sensitivity at the tissue level; monitor for fluid retention

Emerging Therapies & Novel Targets

The frontier of metabolic syndrome management is expanding beyond traditional risk factors to ward upstream mechanistic targets.



Gut Microbiota Modulation

Prebiotics, probiotics, and dietary fiber reshape the gut microbiome, reducing systemic inflammation and improving insulin sensitivity



Circadian Rhythm Optimization

Sleep quality, duration, and meal timing profoundly influence metabolic regulation — a modifiable but often overlooked target



Metabolic Surgery

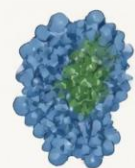
Bariatric procedures achieve metabolic syndrome remission in severe obesity — effects exceed what weight loss alone predicts



GLP-1 Receptor Agonists

Dual benefit on weight reduction and glycemic control positions GLP-1 agonists as transformative agents in metabolic syndrome management

DRUG DISCOVERY PROCESS



TARGET PROTEIN

PASSION
×
CURIOSITY
=
BREAKTHROUGH

