Nutrition and Metabolism

Clinical Physiology

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"Heart disease often begins in the kitchen

— and can be stopped in the clinic."

Saturday night · 10:00 PM

John Smith, 52 years old

Anterior STEMI · Cath Lab · PCI · We save him.

BMI	Blood Pressure	HbA1c	Triglyceride	Waist
34	175/105	8.1%	4.2 mmol/L	112 cm

This is not bad luck, this is the end of a metabolic story.

“How did it get here? And how could it have been stopped?”

The Body's Logic

The body does not optimize.

It survives.

ANABOLISM

Driven by insulin

Dominates after meals

Builds · Stores · Grows

ATP production ↑

CATABOLISM

Driven by glucagon

Dominates during fasting

Breaks down · Mobilizes · Energy

ATP production ↑
→ensures survival

Macronutrients — Through the Clinician's Eyes

CARBOHYDRATE

4 kcal/g

- Immediate insulin response
- Glycemic index = the rate and extent of blood sugar level increase
- Excess → fat→triglyceride → VLDL

PROTEIN

4 kcal/g

- Slow absorption
- During fasting: gluconeogenesis
- Immune function, enzymes

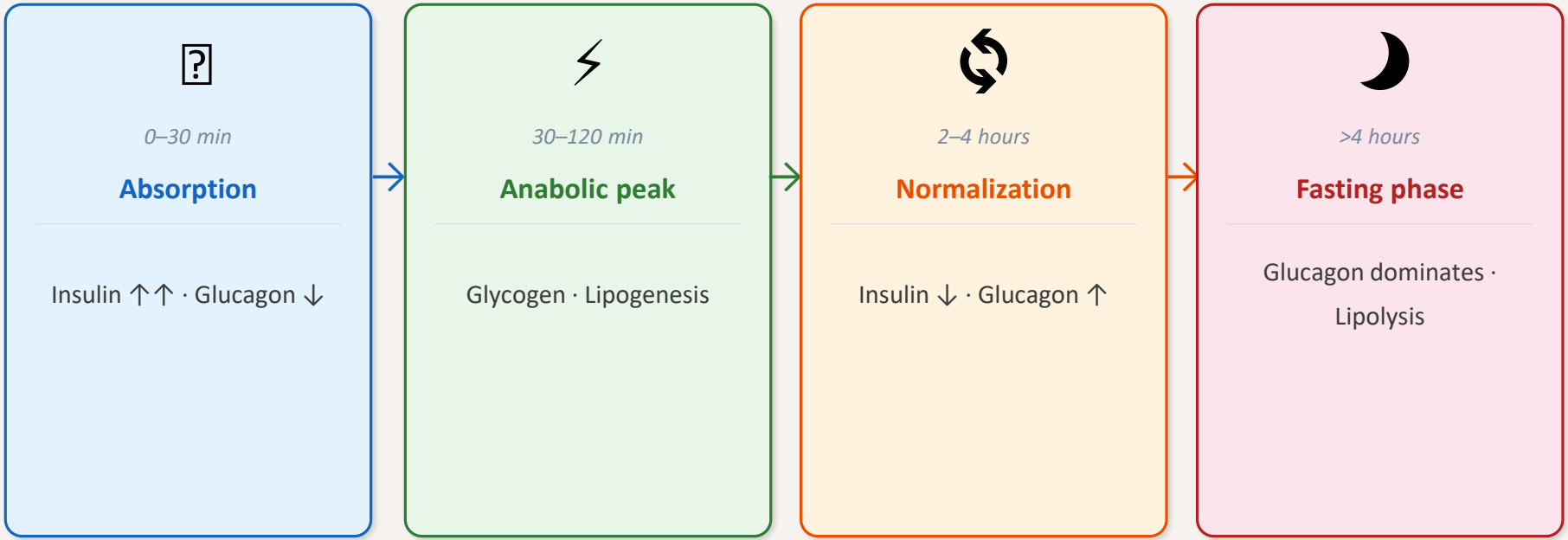
FAT

9 kcal/g !

- Most energy-dense
- Fatty acid → VLDL → LDL
- Balance is disrupted

What matters is not what we eat. But what the body does with it.

After a Meal — The Anabolic/Catabolic Rhythm



Clinical implication: standard labs only see the fasting phase.

For most of the day the patient is postprandial — and that is where the damage occurs.

Insulin — The Commander-in-Chief

Anabolic effects

- Liver: glycogenesis ↑, gluconeogenesis ↓
- Muscle: GLUT-4 → glucose uptake ↑
- Fat: lipogenesis ↑, lipolysis ↓
- Vessel: NO ↑ → vasodilation

1st phase secretion — this fails first

IN EARLY T2DM:

- β-cell does not respond immediately to meals
- Glucose rises → normalizes slowly
- Postprandial hyperglycemia → endothelium

Insulin resistance is one of the main drivers of atherosclerosis.

Not a muscle problem. Not a glycemic question. A cardiovascular risk factor.

Glucagon — The Counterpart

Effects of glucagon

Glycogenolysis: hepatic glycogen mobilization

Gluconeogenesis: glucose from amino acids

Lipolysis: fatty acid release

Ketogenesis: acetyl-CoA → ketone bodies

Primary ketone body: acetoacetate → beta-hydroxybutyrate → acetone

DKA — insulin ≈ 0

Glucagon unchecked → ketones 8–25 mmol/L · pH 7.1

Treatment: fluids · insulin slowly! · K^+ replacement

Why insulin slowly?

Rapid insulin → K^+ into cells → hypokalemia → arrhythmia

There is only one difference between ketosis and ketoacidosis: the presence of insulin.

Physiology vs. emergency. Insulin: present = safety. Zero = life-threatening condition.

DKA: diabetic ketoacidosis

The Postprandial State — What Labs Don't Show Us

The damage does not occur on an empty stomach.

It occurs after meals.

✓ What the lab sees

Fasting glucose: 5.4 mmol/L

LDL: 3.1 mmol/L

Triglyceride: 1.8 mmol/L

→ "All fine"

⚠ What is happening meanwhile

Postprandial glucose: 9–10 mmol/L

Postprandial TG: 4–5 mmol/L

Endothelium: oxidative stress

3× daily · For years · John Smith

→ Fasting labs = snapshot. The patient's day = the peaks.

Obesity — What Matters

BMI	
< 18.5	Underweight
18.5–25	Normal
25–30	Overweight
30–35	Obese I.
35–40	Obese II.
> 40	Severe III.

Android — apple-shaped

Visceral fat

· Waist > hip, Waist: ♂ >94 cm, ♀ >80 cm

· More common in men

·CV risk, T2DM, NAFLD, hypertension

Gynoid — pear-shaped

Hips, thighs

· More common in women

· Metabolic impact lower — but mechanical and CV burden remains

Measuring waist circumference is a vital parameter — not aesthetics.

Adipocyte Biology — Why Is Obesity So Hard to Treat?

The number of adipocytes in adulthood does not decrease.

HYPERPLASTIC OBESITY

Childhood obesity

Adipocyte **NUMBER** increases

In adulthood: cell number remains

On weight loss: empty cells refill

→ Harder to treat

HYPERTROPHIC OBESITY

Adult-onset obesity

Adipocyte **SIZE** increases

Cell number relatively stable

Responds better to diet

→ Easier to treat

Childhood obesity is not a matter of willpower — it's a biological trap. Prevention is easier than treatment.

Leptin & Ghrelin — Not Appetite. Cardiovascular Regulation.

This is not appetite.

This is the autonomic nervous system and it affects the heart.

LEPTIN

Produced by adipose tissue

- Sympathetic nervous system ↑
- Noradrenaline ↑ → blood pressure ↑
- RAAS activation → aldosterone ↑

⚠ In obesity: leptin resistance

⚠ → no effect on appetite

⚠ → sympathetic activation PERSISTS

GHRELIN

Produced by stomach (before meals)

- Parasympathetic (vagus) ↑
- Heart rate ↓, antiarrhythmic
- AMPK activation → cardioprotective

⚠ GH secretion → anabolic

⚠ In obesity: basal level low

⚠ → cardioprotection lost

Adipose Tissue as an Endocrine Organ-

Not a storage depot. It is an inflammatory organ.

Adiponectin

- DECREASES in obesity — paradoxical!
- Antiatherogenic, antiinflammatory
- Insulin sensitivity ↑
- Cardioprotective effect

WILL BE MISSED

Leptin (CV effect)

- Elevated in obesity (resistance)
- Sympathetic ↑ → BP ↑
- RAAS activation
- Endothelial dysfunction

CV RISK

TNF-α / IL-6

- Chronic inflammation
- Damages endothelium
- Inhibits insulin signaling
- Triggers atherogenesis

INFLAMMATION

Measuring waist circumference: vital parameter. Not cosmetics — an active source of inflammation.

Metabolic Syndrome — One Root, Five Faces

BMI	Blood Pressure	HbA1c	Triglyceride	Waist
34	175/105	8.1%	4.2	112 cm

Abdominal obesity

♂ >94 cm, ♀ >80 cm

Hyperglycemia

Fasting ≥ 5.6 mmol/L

Hypertension

≥ 140/90 mmHg

Insulin resistance
+ abdominal obesity

Dyslipidemia

TG ↑, HDL ↓

John Smith: 5/5

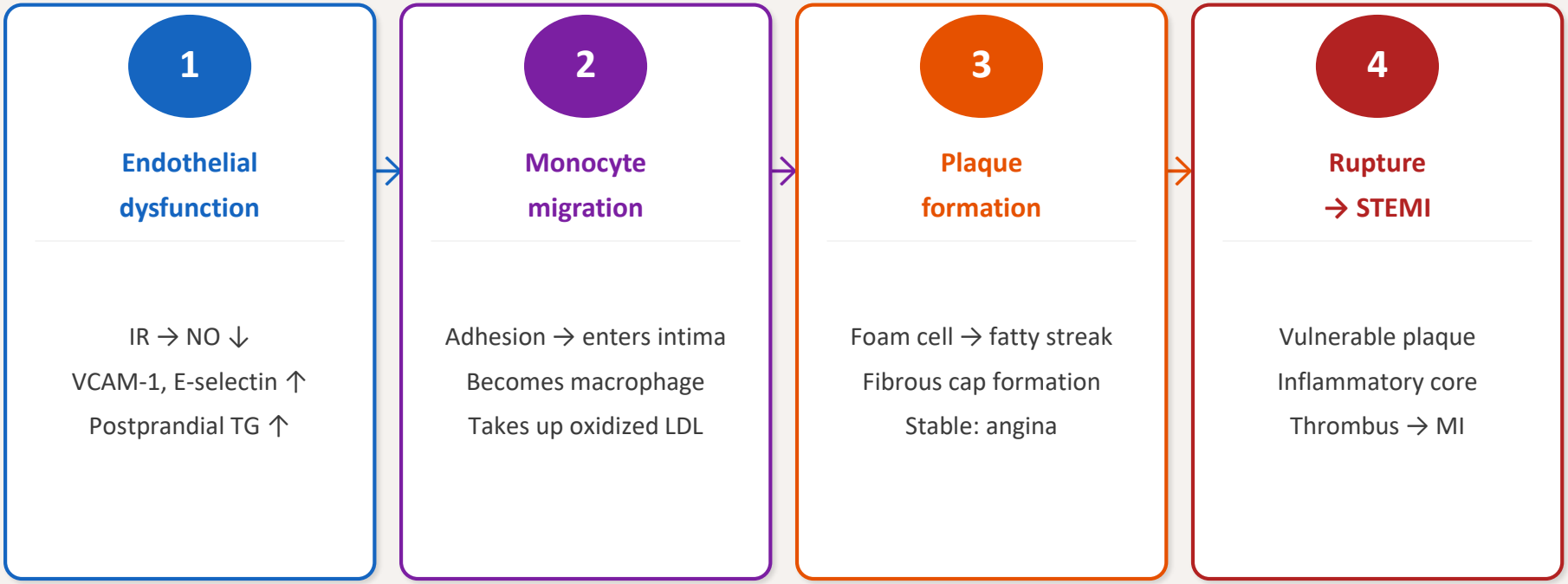
1 in 4 adults in the EU

Pro-inflammatory state

CRP ↑, inflammation

Not five diagnoses. Five manifestations of a single common root. · 4× mortality risk.

Atherosclerosis — How Did Mr. Smith Get Here?



Lipid panel: LDL-C matters, but apoB + non-HDL-C are more accurate. In metabolic syndrome: small dense LDL dominates.

LDL is not a number — it is a process.

NAFLD — The Liver as Metabolic Headquarters

NAFLD
(Non-Alcoholic Fatty Liver Disease)
Fatty liver

NASH
(Non-Alcoholic SteatoHepatitis)
Inflammation

Fibrosis
F1→F4

Cirrhosis /HCC
(HepatoCellular Carcinoma)
End stage

Why does this matter to us?

- Globally: 25–30% prevalence
- In T2DM: >70% (!)
- CV risk: 2–3× the average

Clinical action:

- T2DM + obesity → check transaminases!
- UH
- The NAFLD patient is essentially a cardiac patient

This is not hepatology. It is the same metabolic process in the liver.

Starvation & Stress — The Other Side

Under stress, the body does not conserve — it breaks down.

This cannot be reversed with nutrition alone.

Starvation phases

0–24 h: glycogen depleted

1–3 days: muscle protein breakdown

3–7 days: ketogenesis

>1 week: brain adapts to ketones

Ketosis: 0.5–3 mmol/L — OK

DKA: 8–25 mmol/L — URGENT

Stress starvation (hospital)

IL-1, IL-6, TNF-α: protein catabolism

Cortisol, glucagon: catabolism

Oedema masks weight loss

Catabolism cannot be

reversed by nutrition alone!

Clinician's action

NRS-2002 screening on admission

If gut works: early EN!

30–60% malnourished on admission

10–25% severely

Worsens in hospital — don't let it!

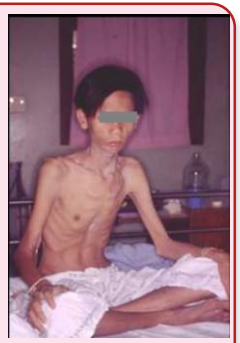
Hospital malnutrition is a silent epidemic. If the gut works — we feed the patient.

Because cachexia kills — slowly but surely.

Malnutrition — Two Different Conditions

Not all starvation is the same.

MARASMUS –
energy and protein deficiency



Chronic, severe caloric deficit

Albumin: normal or mildly ↓

NO oedema

Muscle and fat are consumed

Cortisol ↑, IGF-1 ↓ — adaptive catabolism

Hair loss not typical, prominent ribs, dry wrinkled skin

Ketogenesis initiates — the brain is protected

→ The body adapts

KWASHIORKOR–
severe protein deficiency

Protein deficiency — caloric intake may be n

Albumin markedly ↓ → oncotic pressure ↓

OEDEMA — characteristic sign!

Fatty liver — inflamed, non-adaptive

IL-6, TNF-α ↑ — inflammatory catabolism

Hair loss, pigment changes, skin disease

Distended abdomen — ascites + weak musculature

→ The body loses control

Malnutrition is not a uniform condition. In marasmus the body adapts — this saves. In kwashiorkor adaptive control is lost — this kills. ***Albumin and oedema decide.***

John Smith — There Was a Chance at Every Step

Age 30	Age 38	Age 44	Age 50	Age 52
BMI 27 TG mildly ↑	Prediabetes Fasting: 6.2	T2DM diagnosis Metformin started	Coronary artery disease Stent	STEMI ← THIS IS WHERE WE ARE TODAY
✗ Nobody told him: STEMI in 20 years	✗ DPP: –58% T2DM with lifestyle → never told	✗ 5-minute counseling not enough	✗ There was still a chance to stop progression	✗ Disabled. He will not return to work.

A failure of the system. This is our responsibility too.

One Patient — Two Paths

✕ No intervention

Age 30 Warning signs — nobody speaks up

Age 38 Pre-diabetes — lifestyle unchanged

Age 44 T2DM — 5 minutes of counselling

Age 50 Coronary artery disease, stent

Age 52 **STEMI** — Disabled

VS

✓ Early recognition

Age 30 Waist circumference measured, risk explained

Age 38 Lifestyle programme — −58% T2DM risk

Age 44 Intensive care, lifestyle change

Age 50 No coronary artery disease

Age 52 **Working. Living.**

Same patient. Same disease. A different system.

If You Take Away Three Things:

1

Metabolism is a clinical discipline.

Not biochemistry. Every patient who sits before you is somewhere on the metabolic spectrum.

2

Insulin resistance is the common root.

Cardiovascular disease, T2DM, NAFLD, hypertension — all start here. Understand this, and the rest follows.

3

Obesity = inflammatory cardiovascular disease.

At every consultation: what does this person eat? It is both a diagnostic and therapeutic tool.

"Heart disease often begins in the kitchen — and can be stopped in the clinic."