6. Carbohydrates, Proteins, and Fats – Digestion, absorption, and metabolism

Digestion, Absorption & Metabolism of Carbohydrates, Proteins and Fats

Use the interactive tables and chart above as you read—the data frames summarise enzymes, transporters, and key metabolic routes, while the bar chart contrasts ATP yield for representative fuels.

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1 · Carbohydrates

Stage	Process Highlights	Regulation / Clinical Note
Digestion	Oral α-amylase cleaves α-1,4 bonds → dextrins; pancreatic amylase in duodenum continues → maltose, α-limit dextrins; brush-border disaccharidases yield monosaccharides.	Lactase deficiency → lactose intolerance; amylase activity ↑ with high-starch diet.
Absorption	*SGLT-1* (Na^+ cotransport) uptakes glucose & galactose; fructose via *GLUT-5*. All exit enterocyte by *GLUT-2* to portal vein.	SGLT-1 mutations → glucose–galactose malabsorption.
Metabolism	Glycolysis (cytosol) → 2 ATP + pyruvate; aerobic PDH + TCA cycles; excess glucose stored as glycogen (liver/muscle) or converted to FA via acetyl-CoA.	Insulin ↑ glycogenesis & PFK-1 via dephosphorylation; glucagon/epinephrine trigger glycogenolysis. Pentose-phosphate pathway supplies NADPH for FA synthesis and ribose for nucleotides.

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2 · Proteins

Stage	Process Highlights	Regulation / Clinical Note
Digestion	Pepsin acts at pH 1-3; pancreatic endopeptidases (trypsin, chymotrypsin) and exopeptidases reduce chains; brush-border peptidases finish hydrolysis.	Pancreatic insufficiency → steatorrhoea + protein malabsorption.
Absorption	*PEPT-1* co-transports di-/tri-peptides with H^+; cytosolic peptidases liberate AA which exit via basolateral Na^+-independent carriers.	Competitive absorption explains why excess leucine may impair tryptophan uptake.
Metabolism	Transamination (ALT, AST) shuttles amino groups onto α-ketoglutarate → glutamate; oxidative deamination yields NH_3; urea cycle disposes N in liver. Carbon skeletons enter TCA (glucogenic) or generate ketone bodies (ketogenic).	Elevated ALT/AST signal hepatocellular injury; urea-cycle defects → hyper-ammonemia.

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3 · Fats (Lipids)

Stage	Process Highlights	Regulation / Clinical Note
Digestion	Emulsification by bile salts; pancreatic lipase–colipase hydrolyse TAG → 2-monoacyl-glycerol + FA; phospholipase A_2 yields lysophospholipids; cholesterol esterase releases free cholesterol.	Xenical (orlistat) inhibits pancreatic lipase to induce weight loss.
Absorption	Micelles ferry long-chain FA, 2-MAG, cholesterol, fat-soluble vitamins to enterocyte; re-esterification → TAG; assembly into chylomicrons (apo B-48) and secretion to lymph. SCFA/MCFA diffuse directly to portal blood bound to albumin.	Abetalipoproteinemia (no apo B) → fat/vit E malabsorption, acanthocytosis.

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Stage	Process Highlights	Regulation / Clinical Note
Metabolism	Hormone-sensitive lipase mobilises adipose TAG; liberated FA transported via albumin; inside mitochondria, carnitine shuttle (CPT-I) admits long FA for β-oxidation → lots of acetyl-CoA → TCA or **ketogenesis** in liver. Excess acetyl-CoA + insulin → cytosolic lipogenesis (ACC, FAS).	Low insulin/glucose (fasting) ↑ lipolysis; malonyl-CoA blocks CPT-I, coordinating fed/fasted switch. Carnitine deficiency → muscle weakness & hypoketotic hypoglycaemia.

Comparative Energy Efficiency

The bar chart confirms why fat is a dense energy store—palmitate oxidation (~ 106 ATP) dwarfs glucose (~ 32 ATP) and amino-acid catabolism (~ 15 ATP for alanine).

4 · Integration & Hormonal Control

A coordinated hormone network ensures that **fuel supply meets cellular demand** across fed, fasting, stress, growth and long-term energy-balance states.

4.1 Hormonal Command Centre (table)

Hormone	Primary Stimuli	Major Target Organs	Key Metabolic Actions	Net Effect on Plasma Fuels
Insulin	↑ Blood glucose, ↑ AA, incretins	Liver, muscle, adipose	↑ Glucose uptake (GLUT-4), ↑ glycogenesis, ↑ lipogenesis, ↑ protein synthesis, ↓ lipolysis	↓ Glucose, ↓ FA, ↑ AA uptake
Glucagon	↓ Blood glucose, ↑ AA (alanine), catecholamines	Liver, adipose	↑ Glycogenolysis, ↑ gluconeogenesis, ↑ lipolysis, ↓ glycogenesis	↑ Glucose, ↑ FA, ↑ Ketones (prolonged)
Epinephrine / Norepinephrine	Acute stress, exercise, hypoglycaemia	Liver, muscle, adipose, pancreas	Rapid ↑ glycogenolysis & lipolysis; inhibits insulin secretion	↑ Glucose, ↑ FA, ↑ Lactate
Cortisol	Chronic stress, circadian early morning	Liver, muscle, adipose	↑ Proteolysis, ↑ gluconeogenesis, ↑ lipolysis; protein sparing for brain glucose	↑ Glucose, ↑ FA, ↑ AA
Growth Hormone	Sleep, hypoglycaemia, stress, puberty	Liver, adipose, muscle	↓ Glucose uptake in muscle/adipose, ↑ lipolysis, ↑ hepatic IGF-I production	Maintains glucose during fasting, ↑ FA
Thyroid Hormones (T3/T4)	TSH, low T3/T4 feedback	Whole body (nuclear receptors)	↑ Basal metabolic rate, ↑ Na^+/K^+-ATPase, ↑ lipid oxidation, potentiates catecholamines	Balances carb & lipid utilisation
Leptin	Adipose mass (↑ fat stores)	Hypothalamus, peripheral tissues	Suppresses appetite, ↑ energy expenditure, ↑ fatty-acid oxidation	Long-term ↓ food intake, stable glucose
Ghrelin	Empty stomach, caloric restriction	Hypothalamus, pituitary, GI	Stimulates appetite, ↑ GH release, ↓ fat oxidation	Short-term hunger signal, prepares for meal

The table **“Hormonal Control of Fuel Metabolism”** summarises:

Key insights

Insulin–Glucagon Axis drives rapid toggling between anabolic (storage) and catabolic (mobilisation) modes.
Catecholamines (epinephrine/norepinephrine) provide instant fuel for “fight-or-flight,” overriding insulin.
Cortisol & Growth Hormone act over hours to days, preserving glucose for the CNS during prolonged stress or fasting.

Key insights

Thyroid hormones set the basal metabolic rate and amplify lipolytic/catecholamine signals.

Adipokines (leptin) and gut hormones (ghrelin) modulate long-term appetite and energy expenditure, linking nutrient status to hypothalamic control.

The table details each hormone's stimuli, target organs, metabolic actions, and net effect on plasma fuels—use it as a quick-reference atlas.

4.2 Temporal Dynamics

The line chart **"Post-prandial to Fasting Shift: Insulin vs Glucagon"** captures the classic reciprocal pattern:

- **0–2 h post-meal** → Insulin peaks, promoting glycogenesis, lipogenesis and amino-acid uptake.
- **6–12 h** → Insulin falls; glucagon rises to maintain euglycaemia via hepatic glycogenolysis and initiation of lipolysis.
- **>12 h** → High glucagon/low insulin accelerates gluconeogenesis and ketogenesis, sparing muscle protein and glucose for the brain.

4.3 Integrated Organ Responses

State	Liver	Muscle	Adipose	Brain
Fed (high insulin)	↑ Glycogen & FA synthesis	↑ GLUT-4 glucose uptake, ↑ protein synthesis	↑ TAG storage	Utilises blood glucose
Early Fasting (↑ glucagon)	Glycogen → glucose, begins gluconeogenesis	Switches to FA oxidation	Initiates lipolysis	Still uses glucose
Prolonged Fasting (↑ glucagon + cortisol, GH; low insulin)	Predominant gluconeogenesis, ketone synthesis	Proteolysis reduced (GH), FA oxidation	Robust lipolysis; FA → liver	Gradual ketone uptake
Acute Stress/Exercise (↑ catecholamines)	Instant glycogenolysis & lactate output	Glycogen → lactate/pyruvate for ATP	Rapid lipolysis supplies FA	Relies on glucose + some lactate

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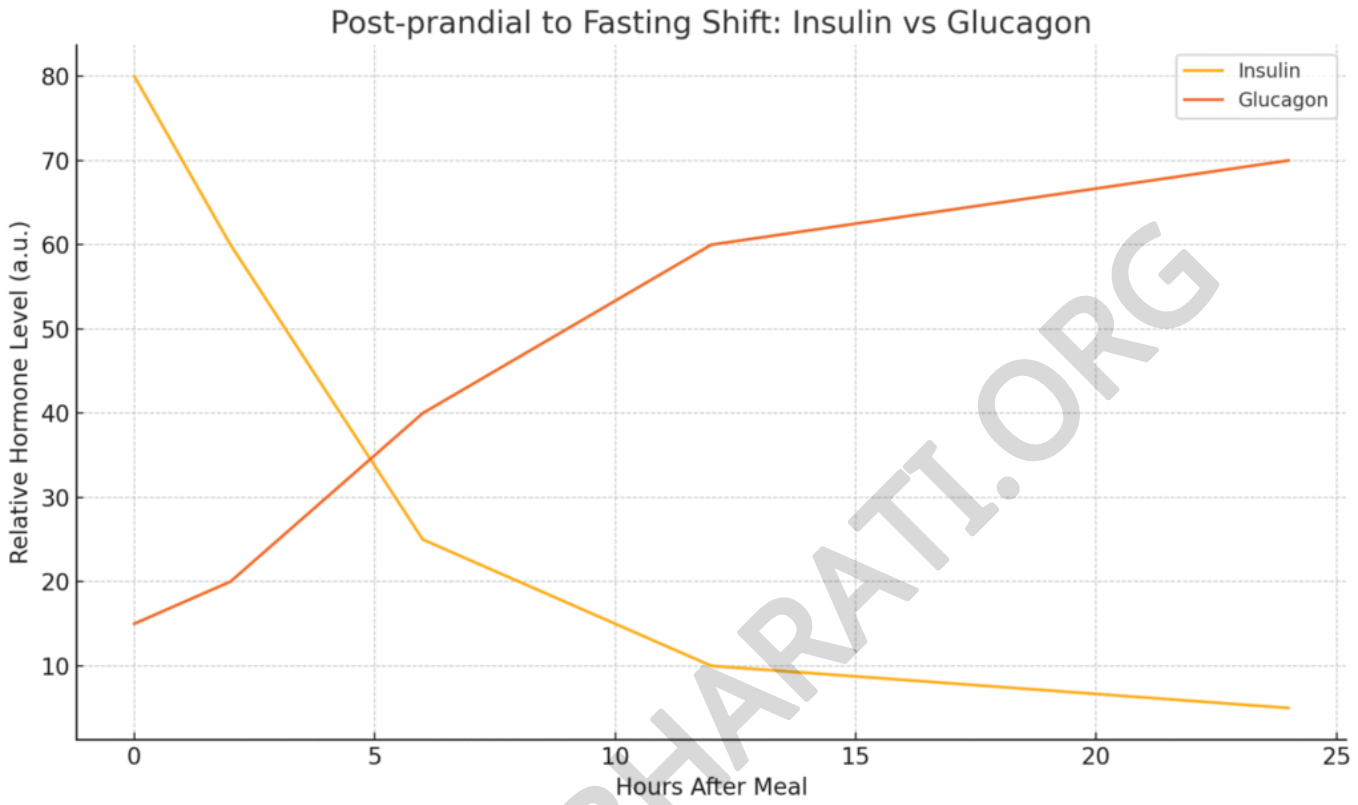
4.4 Regulatory Check-points & Clinical Pearls

- **Insulin/Glucagon ratio** is the master switch; T_2DM features impaired insulin signalling, so glucagon remains high → hyperglycaemia + hyperlipidaemia.
- **Malonyl-CoA** acts as a metabolic gate: high in the fed state (inhibits CPT-I, preventing FA entry into mitochondria) and low during fasting (allows β-oxidation).
- **AMP-activated Protein Kinase (AMPK)** senses cellular energy charge; activates FA oxidation and glucose uptake in muscle, suppresses lipogenesis in liver—exercise and metformin both stimulate AMPK.
- **Cortisol excess (Cushing's)** yields muscle wasting, hyperglycaemia and central obesity because of chronic proteolysis and lipogenesis.
- **Leptin deficiency or resistance** uncouples adipose mass from hypothalamic satiety, driving obesity despite adequate or excess energy stores.



Self-Assessment Tasks

1. Map the flow of dietary triacylglycerol from ingestion to oxidation in skeletal muscle, citing each transport form.
2. Explain why a defect in lactase affects calcium status in populations reliant on dairy.
3. Predict metabolic consequences of a genetic CPT-I deficiency during prolonged fasting.

Refer to the interactive tables for quick enzyme, transporter, and pathway look-ups while solving the tasks.