

Exercise walk-through

2.8

Integration of metabolism: fed, fasting and diabetes

University Medicine

Integration of metabolism: one lever, four organs

- 1 Timeline** Hours 0-4 absorbed fuel; 4-12 liver **glycogen**; 12-24 **gluconeogenesis** ramps; day 3+ brain on $\sim 2/3$ ketones.
- 2 Switch Insulin** sets every organ to store; glucagon (liver-only) opens the banks - one signal, coherent arrows.
- 3 Tape** $\text{HbA1c} \geq 6.5\%$: glycation integrates glucose over the ~ 120 -day red-cell life - recorder, not snapshot.

Fed and fasting: the fuel-flow ledger

FED

insulin high — store

liver	glycogen ↑, fat ↑
muscle	glucose in, glycogen ↑
fat	take up, store TAG
brain	glucose (120 g/day)

FASTING

glucagon high — release

liver	glycogen → glucose out, then gluconeogenesis
muscle	export amino acids
fat	lipolysis → fatty acids
brain	glucose, then ketones

Fed: store everywhere. Fasting: liver releases, muscle exports, fat liberates, brain adapts - the same map, two settings.

Check yourself

- **Glycolysis** net ATP per glucose? (2, plus 2 NADH.)
- NADH $\rightarrow$ ATP (modern count)? (2.5; FADH₂ 1.5.)
- Palmitate total? (106 ATP.)
- HbA1c diabetes threshold? ($\geq$ 6.5 %.)

Exercises 2.1-2.3

2.1 Name the hormone high in the fed state and one hepatic action it drives. [3]

2.2 What changes in the brain's fuel mix by day 3 of fasting? [3]

2.3 What does HbA1c measure, and over what window? [3]

Exercises 2.1-2.3

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2.1

- Insulin; drives hepatic glycogen synthesis (and lipogenesis).
-

2.2 What changes in the brain's fuel mix by day 3 of fasting? [3]

2.2

- Ketones supply $\sim 2/3$ of brain energy (glucose need falls to $\sim 30\text{--}40$ g/day).
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2.3 What does HbA1c measure, and over what window? [3]

2.3

- Non-enzymatic glycation of haemoglobin, integrated over the ~ 120 -day red-cell lifetime.

Exercise 3.1

3.1 Map the fasting timeline for liver, fat and muscle.

For each of hours 6, 18 and day 4, state the dominant fuel source of each organ. Justify the switch points with the glycogen budget (100 g vs 480 kcal/day brain). Explain protein sparing quantitatively (ketone substitution). [8]

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- Hour 6: liver on glycogenolysis, fat basal release, muscle glucose/ fatty acids. Hour 18: glycogen near-empty – gluconeogenesis from amino acids/glycerol/lactate; fat lipolysis high. Day 4: liver exports ketones; muscle largely fatty acids; brain $\sim 2/3$ ketones.
- Switch justified: $100 \text{ g bank} \div \sim 120 \text{ g/day brain demand} \approx \text{one day}$.
- Protein sparing: each gram of brain glucose replaced by ketones spares $\sim 2 \text{ g}$ muscle protein (amino-acid carbon for glucose).

Exercise 3.2

3.2 (Fictional) type 1 diabetic with ketoacidosis.

Explain how absent insulin makes cells read “fasting” despite hyperglycaemia. Trace four symptoms to the switch (ketoacidosis, Kussmaul breathing, osmotic diuresis, weight loss). Contrast the type 2 picture in one sentence. [7]

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3.2

- No insulin $\Rightarrow$ glucagon programme runs: lipolysis (free fatty acids $\rightarrow$ ketones $\rightarrow$ acidosis), proteolysis (weight loss), glycogenolysis + gluconeogenesis despite high glucose; glucose above renal threshold $\rightarrow$ osmotic diuresis (polyuria, thirst); acidosis drives Kussmaul (deep) breathing.
- Type 2: insulin present but resisted – same ledger, milder arrows, years not hours.