

2.8 Integration of metabolism: fed, fasting and diabetes

Name: _____ Class: _____ Date: _____ **Total: 24 marks**

KEY WORDS insulin

Objective

Predict fuel use across the fed–fasting timeline and read diabetes as a jammed switch.

1 Key knowledge and worked examples

■ The switch

Insulin: all organs store. Glucagon: liver releases. Timeline: glycogen (hours) → gluconeogenesis (days) → ketones (brain ~2/3 by day 3). HbA1c $\geq 6.5\%$ integrates ~120 days of glucose.

■ Worked example: the timeline of a fast

Hours 0–4 absorbed fuel; 4–12 glycogen drains; 12–24 gluconeogenesis; day 3+ ketosis with protein sparing ✓.

2 Practice

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]

3 Exam-style questions

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]

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]

Solutions

2.1

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

2.2

- Ketones supply $\sim 2/3$ of brain energy (glucose need falls to $\sim 30\text{--}40$ g/day).

2.3

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

3.1

- 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 ~ 2 g muscle protein (amino-acid carbon for glucose).

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.