

Carbohydrate Metabolism

Glycolysis through galactosemia — the complete map of how the body builds, breaks, and rebalances sugar, with every regulatory switch and clinical correlate that examiners actually ask about.

Glycolysis

TCA Cycle

Gluconeogenesis

Cori & Ala Cycles

PPP

Glycogen

Inborn Errors

Glycolysis

R-L Cycle

TCA Cycle

Gluconeogenesis

Cori Cycle

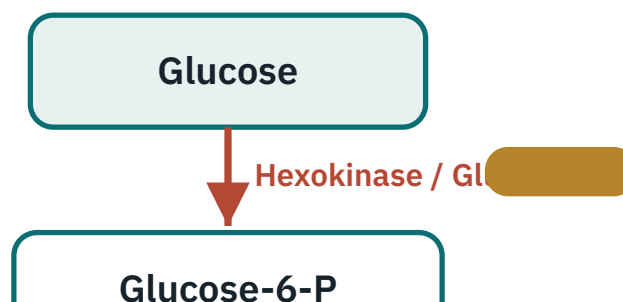
Ala Cycle

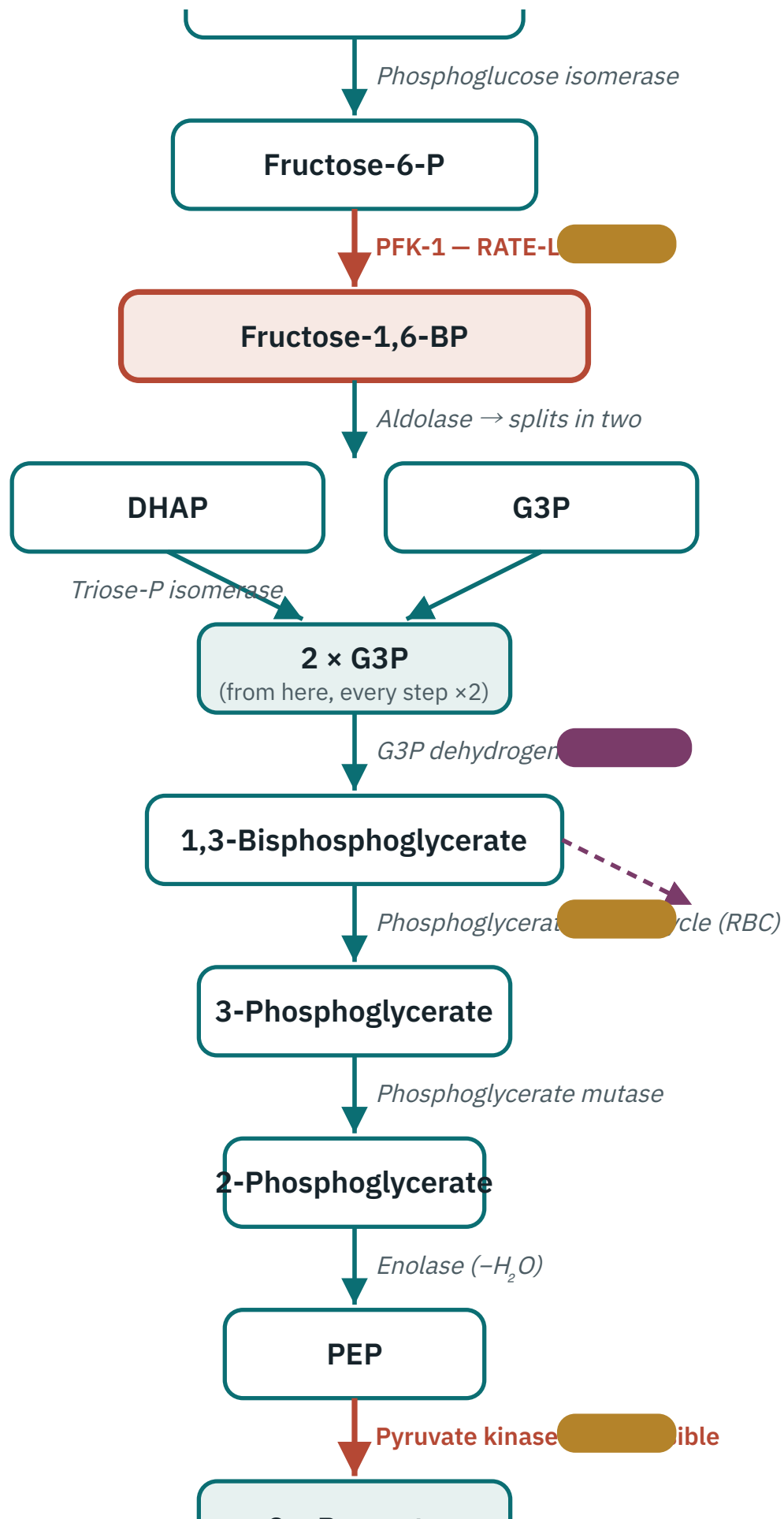
1 Glycolysis

Embden–Meyerhof–Parnas (EMP) pathway · cytoplasm · every cell

The universal, oxygen-independent route from glucose to pyruvate — 10 enzymatic steps split into an energy-investment phase and an energy-payoff phase.

Pathway map — glucose → 2 pyruvate





2 × Pyruvate



O_2 present $\rightarrow$ Acetyl-CoA $\rightarrow$ TCA cycle

O_2 absent $\rightarrow$ Lactate (LDH, regenerates NAD^+)

NET PER GLUCOSE

Invested: 2 ATP (steps 1 & 3)

Produced: 4 ATP (steps 6 & 9, $\times 2$)

Net: **2 ATP + 2 NADH + 2 Pyruvate**

3 irreversible / regulated steps: 1, 3, 9

Irreversible / regulatory step

Reversible step

REGULATION OF PFK-1

Activated by AMP and fructose-2,6-bisphosphate (F2,6BP); inhibited by ATP and citrate. Insulin raises F2,6BP (via the bifunctional PFK-2/FBPase-2 enzyme) to favour glycolysis; glucagon lowers it to favour gluconeogenesis — the single biggest hormonal switch in carbohydrate flux.

CLINICAL CORRELATION

Pyruvate kinase deficiency is the second commonest cause of hereditary non-spherocytic haemolytic anaemia (after G6PD deficiency) — RBCs, being wholly dependent on glycolysis for ATP, are most vulnerable. Cancer cells favour aerobic glycolysis even with oxygen present — the Warburg effect.

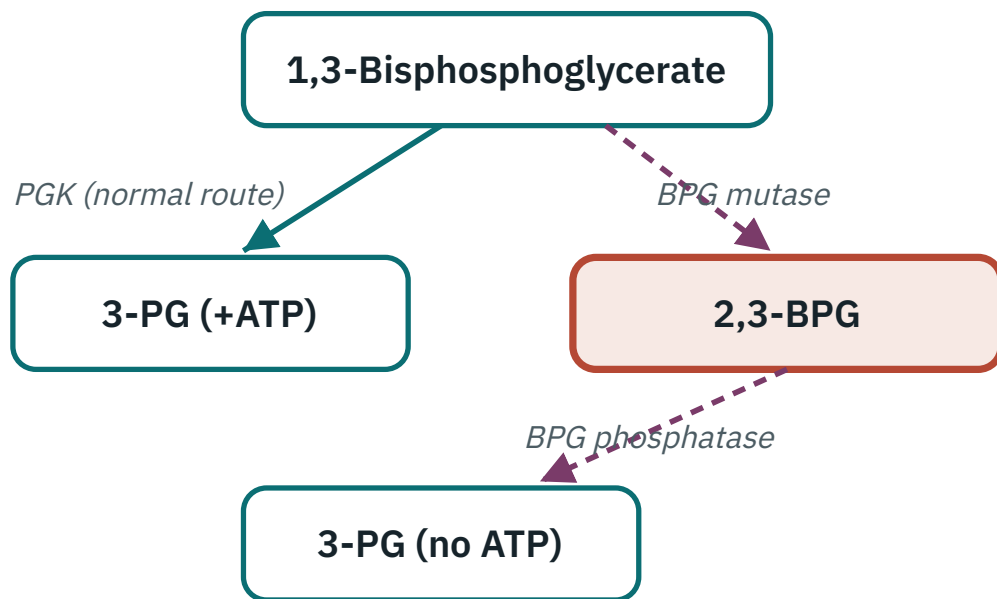
2 Rapoport–Luebering Cycle

2,3-Bisphosphoglycerate shunt · mature erythrocytes only

A short detour off glycolysis, unique to the RBC (which has no mitochondria and cannot run the TCA cycle), that trades one ATP for a powerful oxygen-delivery

signal.

Branch point at 1,3-BPG



2,3-BPG binds deoxyhaemoglobin →
↓ O₂ affinity → right-shifts the O₂ curve →
facilitates O₂ unloading at the tissues.

CLINICAL CORRELATION

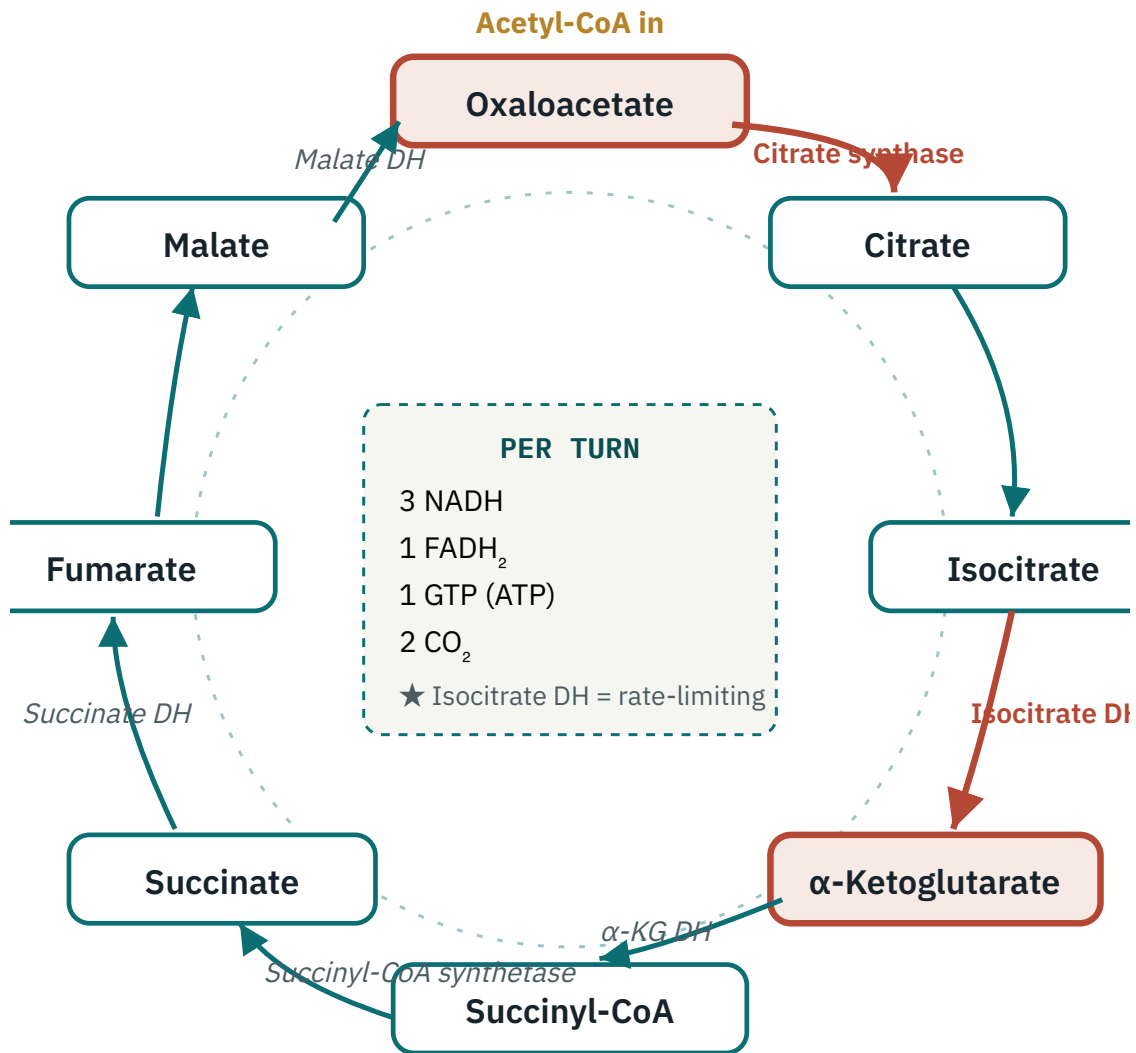
High altitude and chronic hypoxia raise 2,3-BPG to aid tissue oxygenation. Stored (banked) blood progressively loses 2,3-BPG, left-shifting the curve and impairing O₂ release after transfusion. Fetal haemoglobin binds 2,3-BPG poorly, giving it a higher O₂ affinity — essential for placental oxygen transfer.

3 TCA (Krebs) Cycle

Citric acid cycle · mitochondrial matrix

The final common oxidative pathway for carbohydrate, fat, and protein — and, critically, an **amphibolic** hub feeding biosynthesis as much as it drives ATP production.

One turn of the cycle



AMPHIBOLIC – NOT JUST CATABOLIC

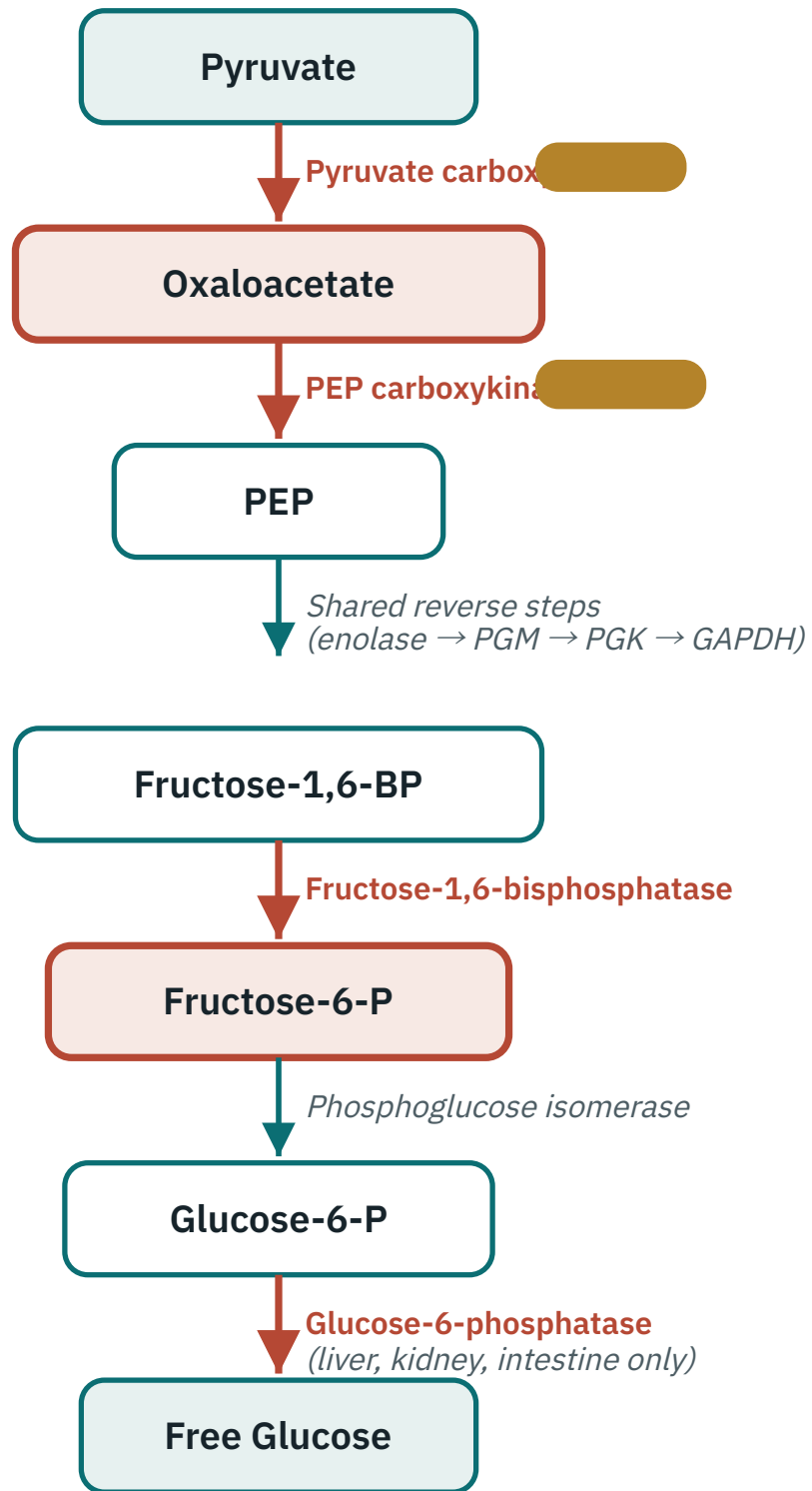
OAA feeds gluconeogenesis · Succinyl-CoA feeds haem synthesis ·
 α -Ketoglutarate and OAA transaminate to glutamate and aspartate · Citrate
exported to cytosol feeds fatty-acid synthesis. **Anaplerosis** (pyruvate
carboxylase replenishing OAA) keeps the cycle from stalling when intermediates
are siphoned off.

4 Gluconeogenesis

Liver & renal cortex (also intestine) · maintains fasting blood glucose

Glucose synthesis from lactate, glycerol, glucogenic amino acids and propionate — essentially glycolysis run backwards, except at the three irreversible steps, which are bypassed by four dedicated enzymes.

The four bypass reactions



4 BYPASS ENZYMES

- 1 & 2 — Pyruvate carboxylase + PEPCK
- 3 — Fructose-1,6-bisphosphatase
- 4 — Glucose-6-phosphatase

ENERGETICS & REGULATION

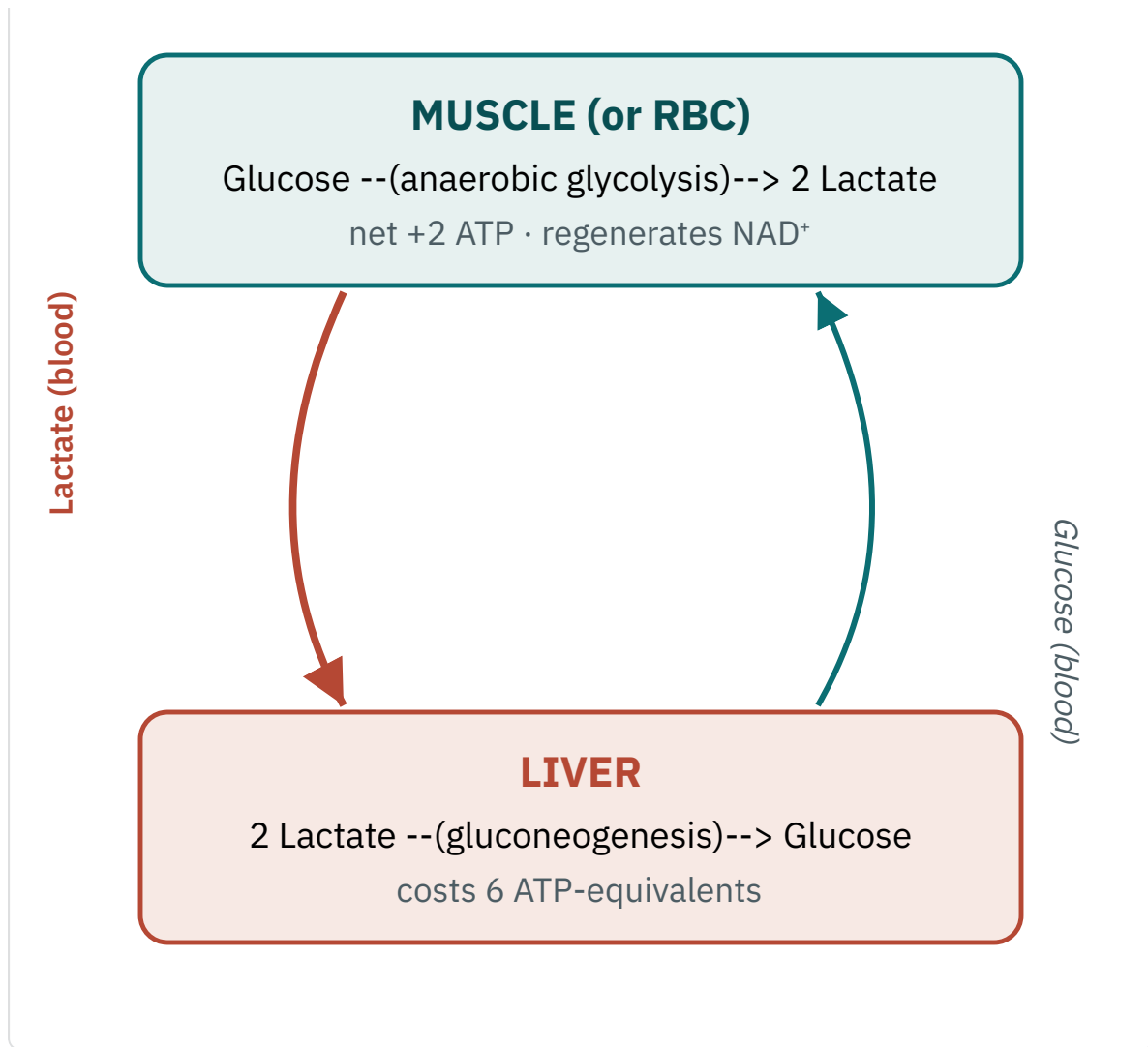
Costs 6 high-energy phosphates (4 ATP + 2 GTP) per glucose synthesized — energetically expensive, but essential. Low F2,6BP (glucagon-driven) activates FBPase-1 and shuts down PFK-1 simultaneously — the two pathways are never fully active at once, preventing a futile cycle.

5 Cori Cycle

Inter-organ lactate shuttle · muscle $\rightleftharpoons$ liver

Under anaerobic or high-demand conditions, muscle exports the lactate it cannot oxidise; the liver spends its own energy budget to turn that lactate back into glucose.

Muscle $\rightleftharpoons$ liver loop



WHY IT MATTERS

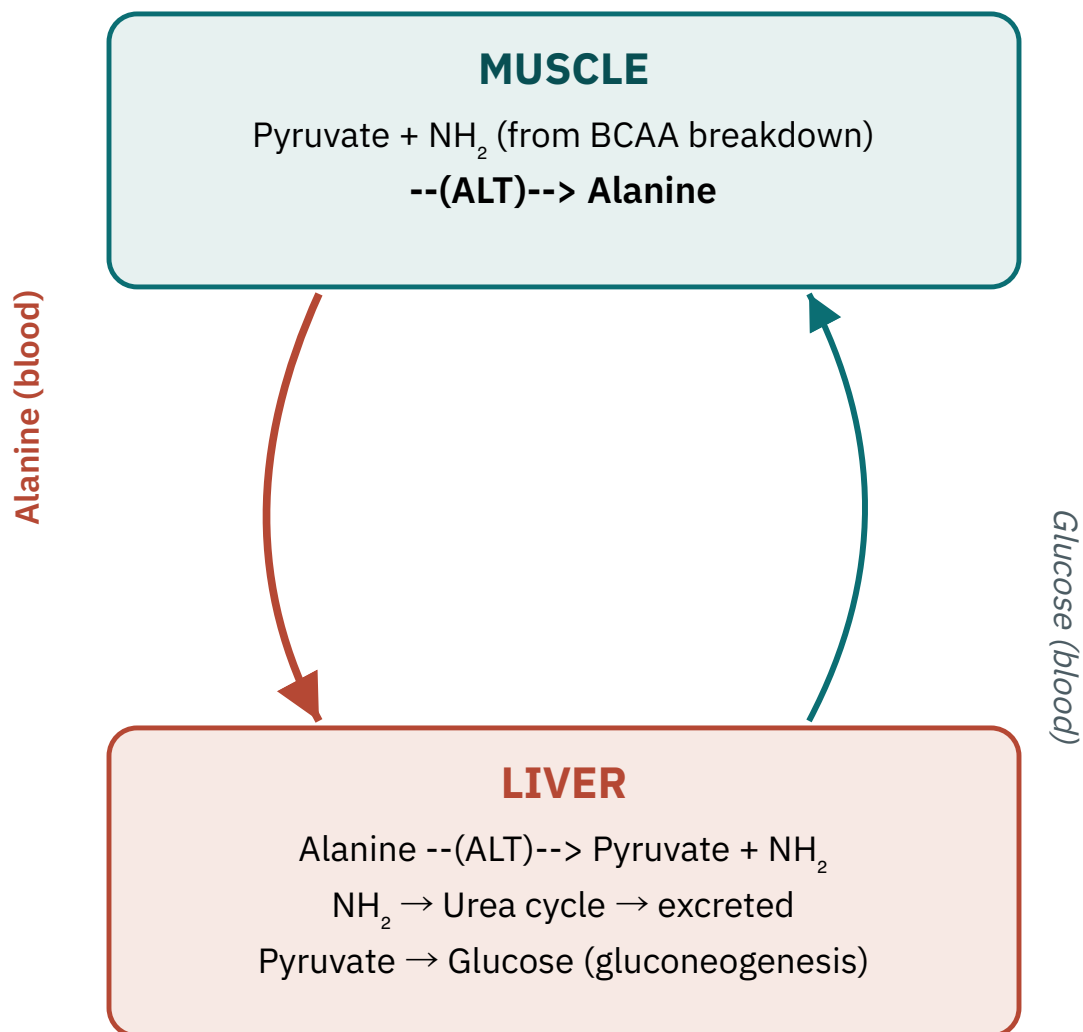
Prevents lactic acidosis by continuously clearing muscle/RBC lactate, and lets the liver — not the working muscle — bear the ATP cost of regenerating glucose. Central to metabolism during sprinting, hypoxia, shock, and sepsis.

6 Glucose–Alanine Cycle

Inter-organ nitrogen + carbon shuttle · muscle $\rightleftharpoons$ liver

A cousin of the Cori cycle that additionally ferries amino-nitrogen from muscle to the liver's urea cycle — important during fasting, starvation, and prolonged exercise.

Muscle $\rightleftharpoons$ liver loop, with nitrogen transfer



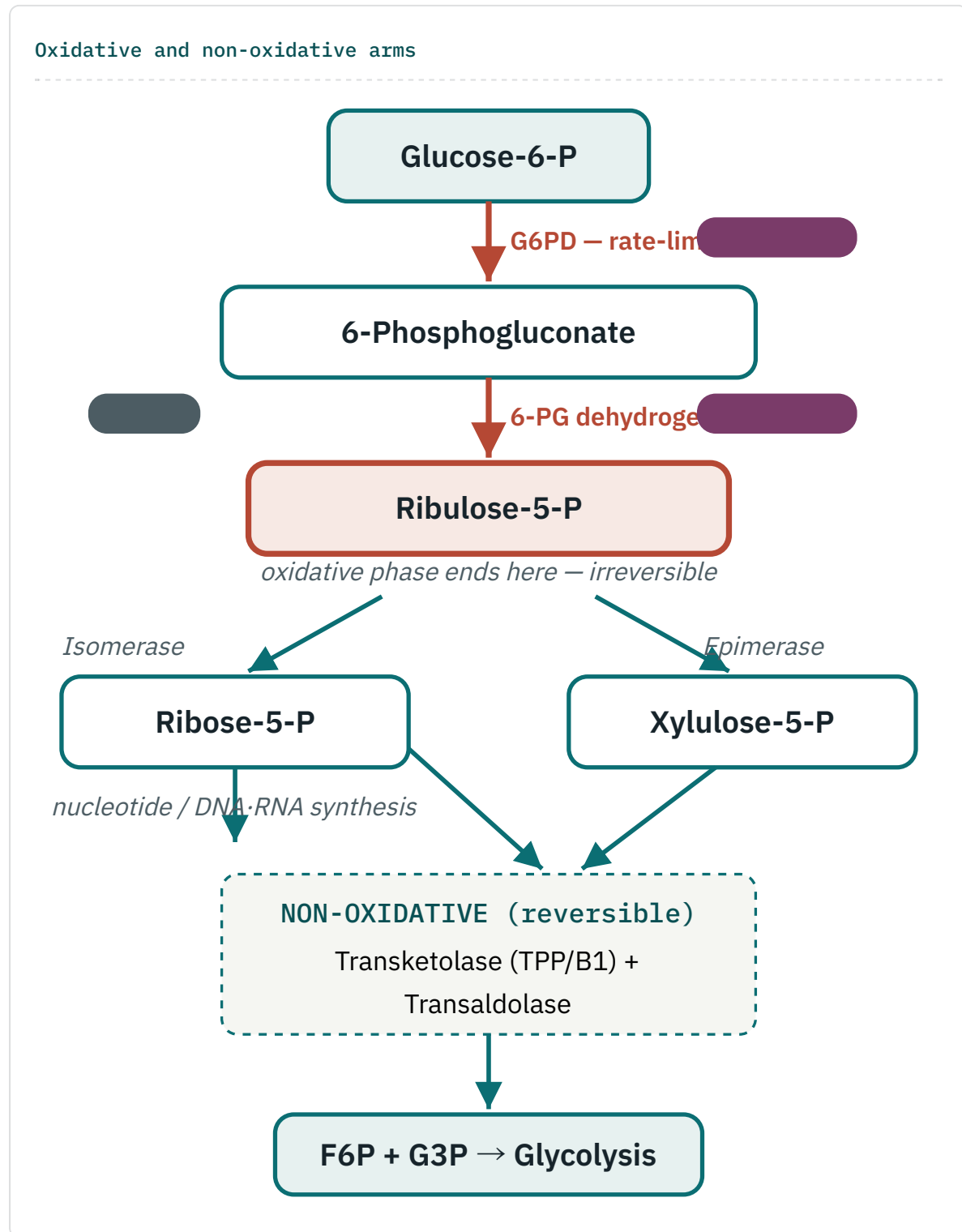
CORI VS. GLUCOSE-ALANINE – THE EXAM DISTINCTION

Both regenerate glucose in the liver from a 3-carbon unit made in muscle. Cori carries only carbon (as lactate); the alanine cycle carries carbon *and* nitrogen (as alanine), so it also detoxifies muscle-derived ammonia via the hepatic urea cycle.

7 Pentose Phosphate Pathway

HMP shunt · cytoplasm · liver, adrenal cortex, mammary gland, adipose, RBC

A glucose-6-phosphate offshoot that trades carbon skeletons for two indispensable currencies: NADPH for reductive biosynthesis and antioxidant defence, and ribose-5-phosphate for nucleotide synthesis.



WHAT NADPH IS SPENT ON

Reductive biosynthesis (fatty acid, cholesterol, steroid synthesis) · regeneration

of reduced glutathione (via glutathione reductase) to neutralise peroxide, protecting the RBC membrane and haemoglobin from oxidative damage · cytochrome P450 detoxification reactions.

CLINICAL CORRELATION

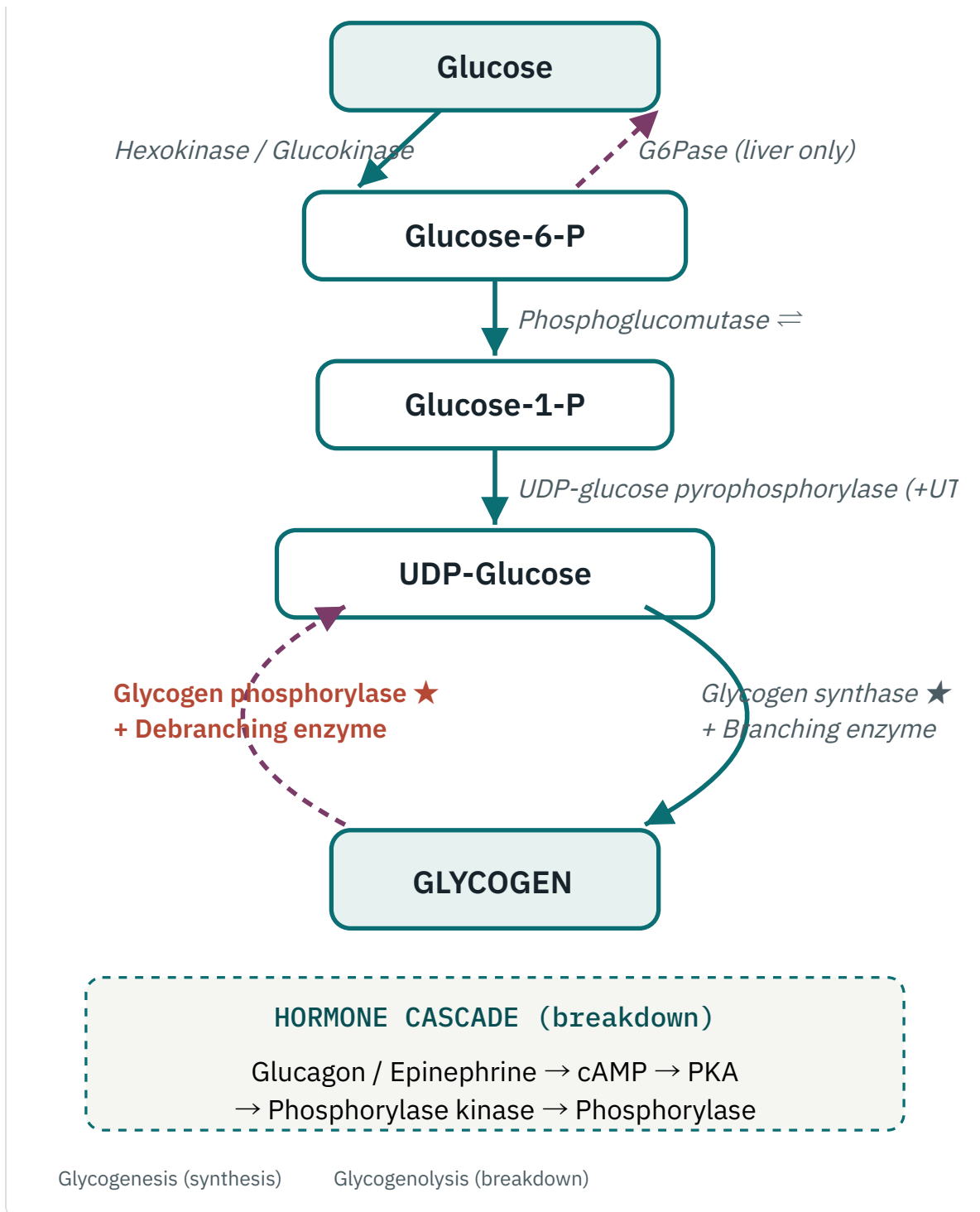
G6PD deficiency (X-linked) limits NADPH regeneration, leaving RBCs unable to keep glutathione reduced. Oxidative stress from infection, fava beans (favism), or drugs (primaquine, sulfonamides, dapsone) precipitates acute haemolysis with Heinz bodies and bite cells.

8 Glycogenesis & Glycogenolysis

Storage form of glucose · liver (blood-glucose buffer) & muscle (local fuel)

Two opposing, reciprocally-controlled pathways sharing common intermediates — synthesis builds branched glycogen from a glycogenin primer; breakdown strips it back down, one glucose unit at a time.

Shared intermediates, opposite enzyme sets



LIVER VS. MUSCLE

Liver expresses glucose-6-phosphatase, so liver glycogen releases **free glucose into the blood** — a systemic buffer. Muscle lacks G6Pase, so muscle glycogen is broken down only for **local** ATP production during contraction, never exported. Insulin favours synthesis; glucagon (liver) and epinephrine (liver + muscle) favour breakdown, with Ca^{2+} /calmodulin an added trigger in contracting muscle.

9 Inborn Errors of Metabolism

Glycogen storage diseases & disorders of galactose metabolism

Glycogen Storage Diseases (GSDs)

Type	Enzyme deficient	Organ(s)	Key features
0	Glycogen synthase	Liver	Fasting hypoglycemia; no hepatomegaly (too little glycogen made)
I — Von Gierke	Glucose-6-phosphatase	Liver, kidney	Severe fasting hypoglycemia, marked hepatomegaly, lactic acidosis, hyperuricemia, hyperlipidemia, "doll-like" face
II — Pompe	Lysosomal acid α -1,4-glucosidase	All organs (heart, muscle)	Cardiomegaly, hypotonia, early death — a lysosomal storage disease, not a classic glycogenolysis defect
III — Cori/Forbes	Debranching enzyme	Liver, muscle	Milder than type I; hepatomegaly; normal lactate/uric acid; limit-dextrin accumulates
IV — Andersen	Branching enzyme	Liver	Abnormal, poorly-branched glycogen (amylopectin-like); progresses to cirrhosis
V — McArdle	Muscle glycogen phosphorylase	Skeletal muscle	Exercise intolerance, cramps, myoglobinuria; classic "second-wind" phenomenon
VI — Hers	Liver glycogen phosphorylase	Liver	Mild hypoglycemia, hepatomegaly
VII — Tarui	Muscle phosphofructokinase	Muscle, RBC	Exercise intolerance plus hemolysis

Disorders of Galactose Metabolism

Condition	Enzyme deficient	Severity / features
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Classic galactosemia	GALT (galactose-1-P uridylyltransferase)	Most severe — cataracts, hepatomegaly with jaundice, intellectual disability, ↑ risk of <i>E. coli</i> sepsis; galactose-1-P accumulates
Galactokinase deficiency	Galactokinase	Milder — cataracts only, from galactitol accumulating in the lens; no liver/brain involvement
GALE deficiency	UDP-galactose-4-epimerase	Variable severity depending on tissue distribution of residual enzyme

WHY CATARACTS RECUR ACROSS THESE DISORDERS

Excess galactose is reduced by aldose reductase to galactitol, an osmotically active sugar-alcohol that cannot cross back out of the lens easily — it draws in water, and the resulting osmotic stress and oxidative damage produce cataracts. The same logic underlies diabetic cataracts, but with glucose → sorbitol instead.

10 Exam Corner

Practice question set — end-semester format

B.Sc. Biochemistry — End-Semester Examination

Paper: Carbohydrate Metabolism

Full Marks: 30

Time: 1.5 Hrs

GROUP A — LONG ANSWER (ANSWER ANY TWO)

- Describe the reactions of glycolysis with the help of a suitable diagram. Discuss its regulation, and add a note on the significance of the Rapoport-Luebering cycle in erythrocytes. **10**
- Outline the pathway of gluconeogenesis, clearly identifying the four key bypass reactions. How is the pathway regulated, and how does it interface with the Cori cycle and the glucose-alanine cycle? **10**
- Give an account of the pentose phosphate pathway. Discuss the

biomedical importance of NADPH and the metabolic consequences of glucose-6-phosphate dehydrogenase deficiency.

10

GROUP B – SHORT NOTES (ANSWER ANY TWO)

a. The TCA cycle as an amphibolic pathway

5

b. Glycogen storage diseases

5

c. Galactosemia

5