

■ Biochemistry of Cardiac Muscle – High-Yield Summary

1. Phosphocreatine–Creatine Kinase (PC-CK) System

- Function: Rapid ATP buffering and transfer system in cardiomyocytes.
- Reaction: Creatine + ATP ■ Phosphocreatine (PC) + ADP (reversible).
- Role: Provides a quick ATP source and transports high-energy phosphate to myofibrils (myosin heads).
- CK Isoenzymes: CK-MM (skeletal muscle), CK-MB (cardiac), CK-BB (brain), mi-CK (mitochondrial, 20–40% of total).
- mi-CK located on outer surface of inner mitochondrial membrane near ATP/ADP translocase.
- PC/ATP ratio ↓ in heart failure → poor prognosis.
- Disruption → ↓ contractility, ↑ arrhythmia risk.

2. Ketone Bodies

- Main types: Acetoacetate, β-hydroxybutyrate, acetone.
- Produced in liver mitochondria from Acetyl-CoA (from β-oxidation).
- Fuel for brain, heart, muscle during low glucose states.
- HMG-CoA: key intermediate (also in cholesterol synthesis).
- Triggered by: low glucose, low oxaloacetate, excess acetyl-CoA.

3. Ketosis & Ketoacidosis

- Ketosis = physiologic ↑ ketones (fasting).
- Ketoacidosis = pathologic accumulation → metabolic acidosis.
- Main causes: Diabetes, starvation, alcoholism, low-carb diet, enzyme deficiencies.
- Starvation: ↓ insulin / ↑ glucagon → heart & muscle use ketones first, later brain adapts.

4. Diabetic Ketoacidosis (DKA)

- Severe insulin deficiency → ↑ glucose + ↑ ketones → metabolic acidosis.
- Occurs mainly in type 1 DM; can appear in type 2 with stress/infection.
- Mechanism: ↓ insulin / ↑ counter-hormones → lipolysis → ↑ FFA → ketogenesis.
- Leads to hyperventilation (Kussmaul), dehydration, electrolyte loss.
- Diagnosis: Hyperglycemia + ketonuria + metabolic acidosis.

5. Ketolysis (Ketone Utilization)

- Used by heart, skeletal muscle, kidney, brain (during fasting).
- Liver & RBCs cannot use ketones (no mitochondria or thiophorase).
- Key enzyme: β-ketoacyl-CoA transferase (thiophorase) → converts acetoacetate to acetoacetyl-CoA.
- Requires TCA cycle to be active for energy production.

6. Heart Failure Metabolism

- ↓ Fatty acid oxidation, ↑ glycolysis and glucose oxidation, ↓ mitochondrial activity.
- ↓ PC/ATP ratio → decreased energy efficiency.

7. Cardiac Ischemia

- Caused by coronary occlusion → ↓ O₂ → ↓ oxidative phosphorylation.
- Results: ↓ ATP, ↓ PC, ↑ Pi, ↑ AMP → contractile dysfunction.
- Mild ischemia → glycolysis activation; prolonged → lactate accumulation → glycolysis inhibition.
- Leads to contractile failure, arrhythmias, cell death.

Exam Pointers

- CK-MB = cardiac injury marker.
- Liver produces but cannot use ketones (no thiophorase).
- β -hydroxybutyrate \leftrightarrow acetoacetate (via dehydrogenase).
- DKA = insulin deficiency + acidosis + Kussmaul breathing.
- Ischemia \rightarrow anaerobic glycolysis \rightarrow lactate accumulation \rightarrow acidosis.