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A Level Biology B (Advancing Biology)

H422/02 Scientific literacy in biology

Advance Notice Article

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Biochemistry of exercise-induced acidosis

The development of acidosis during intense exercise has a traditional explanation: an increase in lactic acid production. Each lactic acid molecule can release a proton and form the acid salt sodium lactate. Based on this explanation, if the rate of lactate production is high enough, the cellular proton buffering capacity will be exceeded, which results in a decrease in cellular pH. These biochemical events have been termed lactic acidosis. An increase in lactate production has long been considered one of several causes of muscle fatigue during intense exercise.

However, many scientists think there is no biochemical evidence that lactate production causes acidosis. In fact, lactate production reduces acidosis rather than causing it. There is a wealth of research evidence to show that acidosis is caused by reactions other than lactate production.

Protons do not accumulate in cells when the ATP demand of muscle contraction is met by mitochondrial respiration. Instead, protons are used by the mitochondria for oxidative phosphorylation, maintaining the proton gradient across the inner mitochondrial membrane. It is only when exercise intensity increases that there is a greater reliance on ATP regeneration from non-mitochondrial sources: glycolysis and the creatine phosphate system.

Creatine phosphate is used as a source of ATP during vigorous exercise. Production of ATP in this way consumes protons.

creatine phosphate + ADP + H^+ $\rightleftharpoons$ creatine + ATP

Glycolysis is usually considered to start with glucose. However, in muscle cells, glycogen is an important respiratory substrate. Glycogen is converted to glucose phosphate, not glucose, as shown in **Fig. 1**.

There are proton transport systems between the cytosol and the mitochondria. These transport systems reveal the power of mitochondrial respiration in helping to control the balance of protons within the cell. Mitochondrial metabolism releases electrons and protons from substrates and uses these electrons and protons to eventually produce ATP. Protons, ADP and P_i are transported into the mitochondria from the cytoplasm. The protons are required for the reduction of molecular oxygen; ADP and P_i are required to generate more ATP for muscle contraction.

A proton is released every time ATP is broken down to ADP and P_i. Metabolic acidosis occurs when the rate of ATP hydrolysis, and therefore the rate of ATP demand, exceeds the rate at which ATP is produced in the mitochondria.

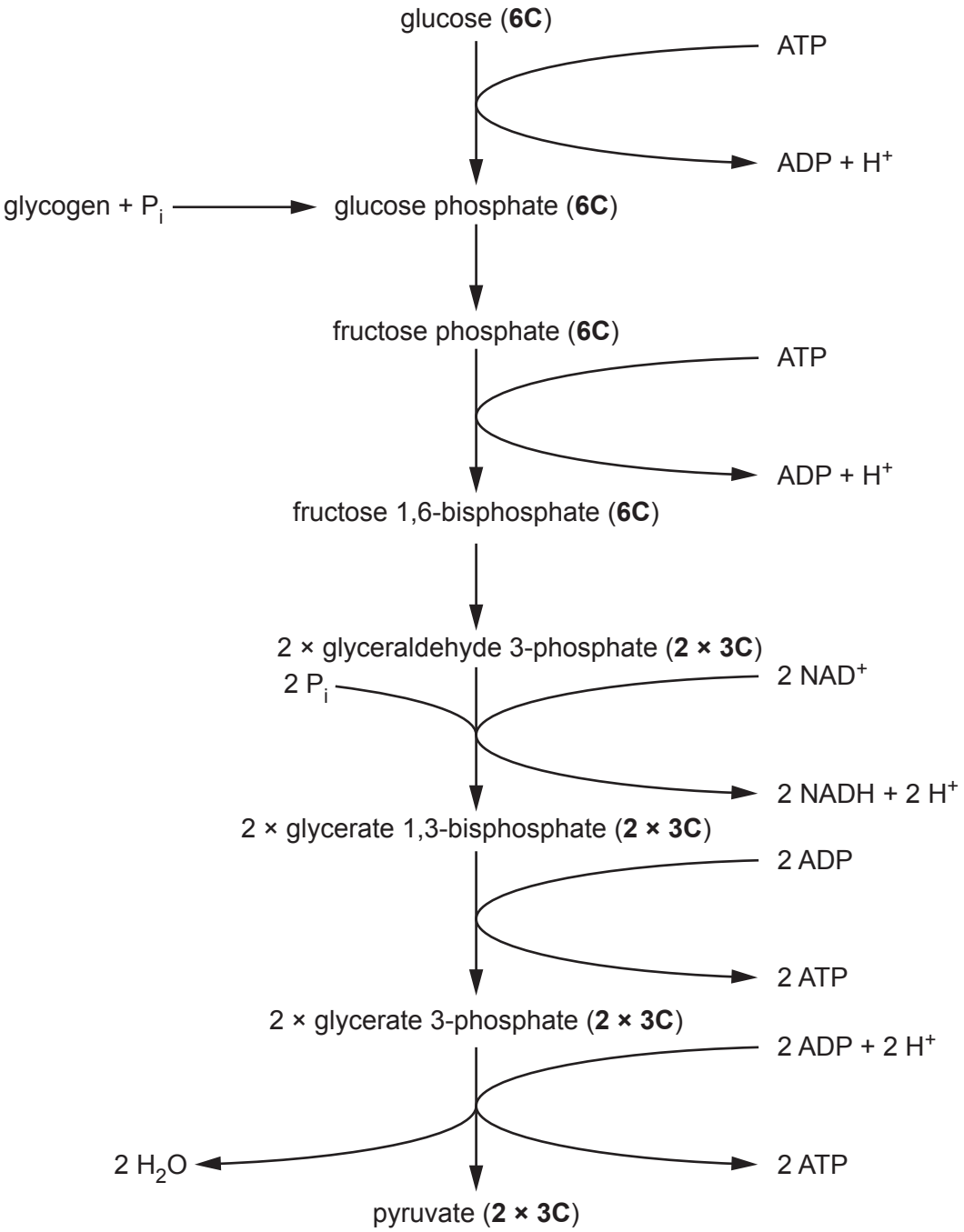

Fig. 1 The reactions of glycolysis using glucose or glycogen as the respiratory substrate

In muscle cells, the ATP that is supplied from non-mitochondrial sources is eventually used to fuel muscle contraction. This increases proton release and is responsible for the acidosis of intense exercise. Lactate production increases under these cellular conditions to prevent pyruvate accumulation and supply the NAD^+ needed for glycolysis. Increased lactate production therefore coincides with cellular acidosis, but it does not **cause** it. Nonetheless, lactate production remains a good indirect marker for the metabolic conditions that induce metabolic acidosis in cells. If muscles did not produce lactate, acidosis and muscle fatigue would occur more quickly and exercise performance would be severely impaired.

Any factor that reduces the ability of muscles to contract is likely to cause muscle fatigue. Another explanation for muscle fatigue does not involve acidosis. During intense exercise, ATP is hydrolysed to ADP and P_i. Scientists have suggested that the P_i combines with calcium ions in the sarcoplasmic reticulum to form insoluble calcium phosphate. This reaction is thought to represent another cause of muscle fatigue during exercise.