Muscle Metabolism

Page 1. Introduction

- Skeletal muscle must continuously make ATP to provide the energy for muscle contraction.

Page 2. Goals

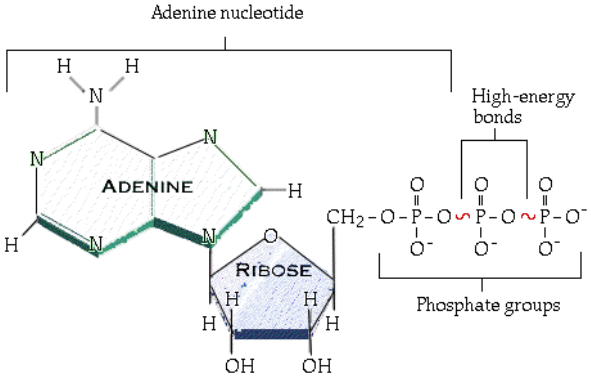
- To understand the cellular processes for synthesis of ATP.
- To compare and contrast aerobic and anaerobic processes in the muscle cell.

Page 3. Role of ATP

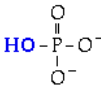
- Important roles of ATP in muscle contraction:
  1. ATP binds to myosin heads and upon hydrolysis into ADP and Pi, transfers its energy to the cross bridge, energizing it.
  2. ATP is responsible for disconnecting the myosin cross bridge at the conclusion of a power stroke.
  3. ATP provides the energy for the calcium ion pump which actively transports calcium ions back into the sarcoplasmic reticulum.

Page 4. Structure of Adenosine Triphosphate (ATP)

- Structure of ATP:



Note: ATP has three phosphate groups. The structure of a phosphate group (Pi) is:



- The bond between the last two phosphate groups is high energy and therefore blinking yellow.

Page 5. Hydrolysis of ATP

- This animation shows the hydrolysis of ATP.
- Summary of the hydrolysis of ATP:

$$ATP + H_2O \longrightarrow ADP + Pi + energy$$

- The hydrolytic enzyme binds the ATP and catalyzes the reaction. Two examples of hydrolytic enzymes within the muscle are:
  - The myosin head functions as a hydrolytic enzyme when it hydrolyzes ATP into ADP and Pi. The energy released is used to prop the myosin cross bridge up into its high energy position.

- The calcium ion pump which actively transports calcium ions back into the sarcoplasmic reticulum will act as a hydrolytic enzyme when it hydrolyzes ATP into ADP and Pi. The energy released is used to change the shape of the pump allowing the calcium ions to go back into the SR.

- During the reaction, the water (shown in blue) breaks the high energy bond between the last two phosphate groups. The water splits apart and the OH from the water ends up on the inorganic phosphate (sometimes abbreviated Pi) and the other H from the water goes onto the phosphate group which remains attached to the ADP.
- ADP is called adenosine diphosphate because only two phosphate groups remain on it.
- The energy contained in the bond between the last two phosphates on ATP has been released and is shown here as a glowing "E". There is still one additional high energy bond left in the ADP. (That high energy bond will not be important in this module.)
- The energy released from the ATP hydrolysis will be used to
  - Disconnect the myosin cross bridge from the binding site on actin at the conclusion of a power stroke.
  - Energize the power stroke of the myosin cross bridge.
  - Energize the calcium ion pump which actively transports calcium ions back into the sarcoplasmic reticulum.

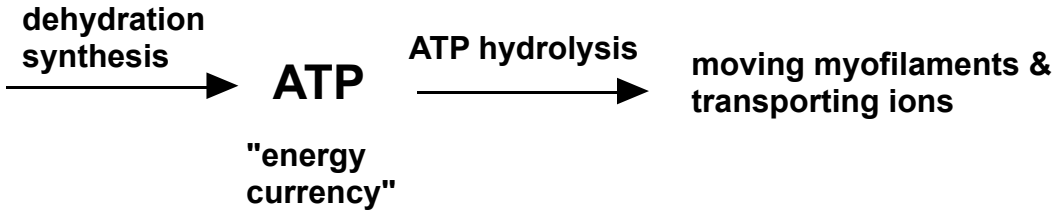
Page 6. Dehydration Synthesis of ATP

- This animation shows the dehydration synthesis of ATP. It is called "dehydration synthesis" because water is removed (dehydration) and a bigger molecule is synthesized from two smaller ones. Some textbooks call this process "condensation" because a water molecule is released.
- Summary of the dehydration synthesis of ATP:

$$ADP + Pi + \text{energy} \longrightarrow ATP + H_2O$$

- The synthetic enzyme binds the ADP and catalyzes the reaction. During the reaction, water (shown attached to the ADP and phosphate groups in blue) splits off and the inorganic phosphate (Pi) attaches to the ADP to form ATP.
- This process requires energy since a high energy bond is formed. The energy is shown here as a glowing yellow ball which appears. One of the main functions of this section is to examine where that energy comes from.

Page 7. ATP as "Energy Currency"



Page 8. Overview of "ATP Synthesis"

- Muscle cells synthesize ATP these three ways:
  1. Hydrolysis of creatine phosphate
  2. Glycolysis
  3. The Krebs cycle & oxidative phosphorylation

Page 9. Creatine Phosphate

- The immediate source of energy for rebuilding ATP is the high energy molecule creatine phosphate. The phosphate in creatine phosphate, can be transferred to ADP to form ATP

in a process called substrate phosphorylation. However, there isn't much creatine phosphate stored in muscle cells.

Page 10. Sources of Glucose

- Two sources of glucose to muscles:
  1. Blood glucose.
  2. Breakdown of glycogen into glucose within the muscle cell.

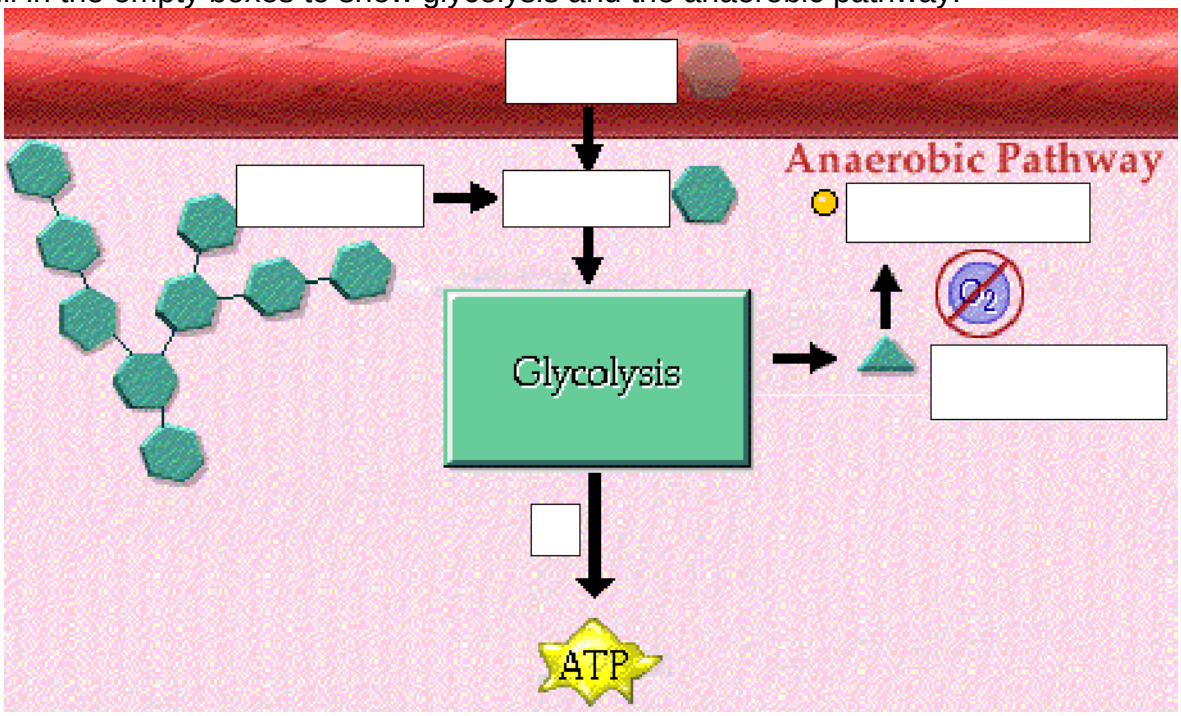
Page 11. Glycolysis

- Summary of the process of glycolysis:

Glucose —glycolysis→ **2 Pyruvic Acid + 2 ATP**

Page 12. Anaerobic Pathway: Lactic Acid

- Fill in the empty boxes to show glycolysis and the anaerobic pathway:

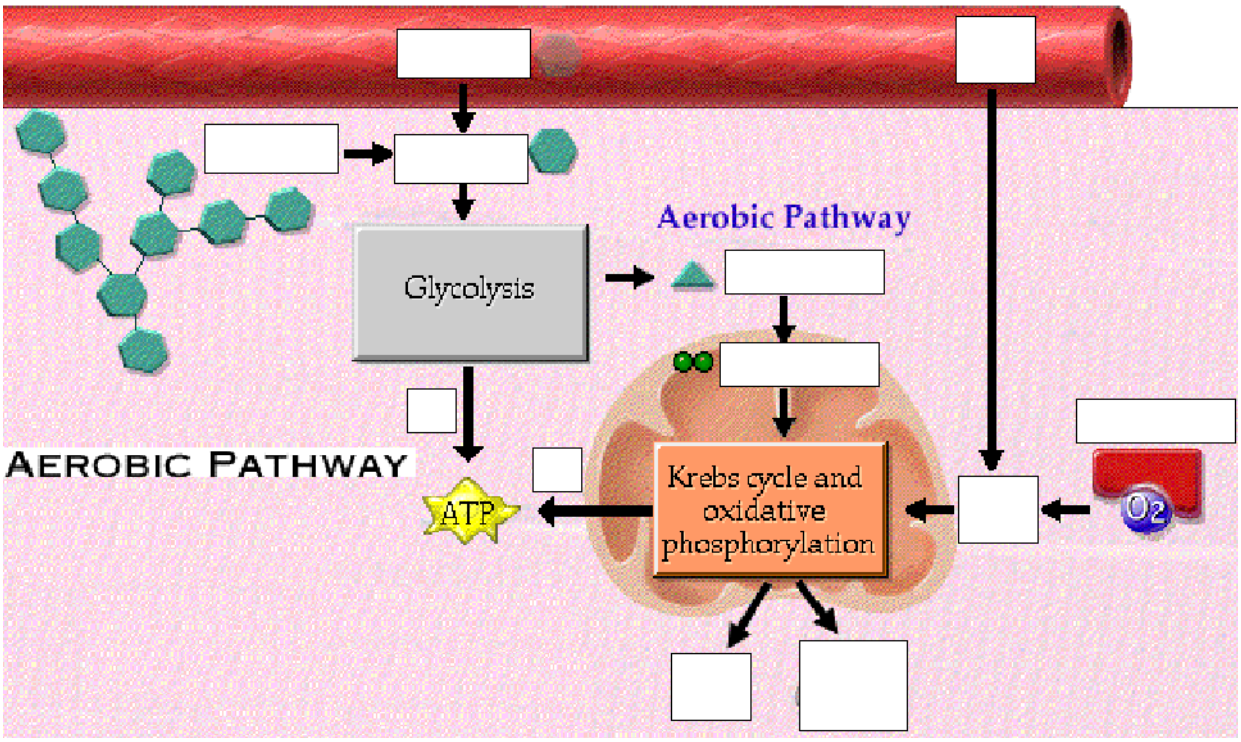


Page 13. Sources of Oxygen

- The oxygen needed for aerobic metabolism is available to muscle cells either directly from the blood or it can be stored in an oxygen binding protein called myoglobin.

Page 14. Aerobic Pathway

- Fill in the empty boxes to show the aerobic pathway:



Page 15. Summary of ATP Production

- This animation summarizes the three processes for producing ATP:
  - Creatine phosphate pathway
  - Glycolysis/anaerobic pathway
  - Aerobic pathway
- It also reminds us that ATP is needed by the muscle cell for the power stroke of the myosin cross bridge, for disconnecting the cross bridge from the binding site on actin, and for transporting calcium ions back into the SR.

Page 16. Summary

- ATP must be synthesized in muscle cells to replace ATP used for muscle contraction.
- ATP is synthesized by hydrolysis of creatine phosphate, glycolysis, and the Krebs cycle and oxidative phosphorylation.

Notes on Quiz Questions:

Quiz Question #1: Sequence of Metabolic Pathway

- This question allows you to predict the sequence of steps in the aerobic synthesis of ATP, starting with glycogen.
- Lactic acid is not used since this is an aerobic pathway.

Quiz Question #2: Anaerobic Process

- This questions asks you to predict what part of the sequence in question 1 is anaerobic.

Quiz Question #3: Aerobic Process

- This questions asks you to predict what part of the sequence in question 1 is aerobic.

Quiz Question #4: Storehouse of Glucose

- This question asks you to predict what part of the sequence in question 1 stores glucose in muscle cells.

Study Questions on Muscle Metabolism:

1. (Page 1.) Why is it necessary for muscle to have mechanisms to make ATP quickly?

2. (Page 3.) Which of these is not an important role of ATP in skeletal muscle contraction?
   a. Disconnecting the myosin cross bridge from the binding site on actin at the conclusion of a power stroke.
   b. Exposure of the myosin binding sites on actin.
   c. Energizing the power stroke of the myosin cross bridge.
   d. Energizing the calcium ion pump which actively transports calcium ions back into the sarcoplasmic reticulum.

3. (Page 4.) Which of these is not a part of the ATP molecule?
   a. adenine nucleotide
   b. phosphate groups
   c. ammonia
   d. high energy phosphate bonds

4. (Page 5.) Fill in the blanks in the following equation for the hydrolysis of ATP.

ATP + _____ → _____ + _____ + _____

5. (Page 5.) Why is the reaction that releases energy from ATP termed a "hydrolysis" reaction?

6. (Page 5.) Give a specific example of a hydrolytic enzyme that hydrolyzes ATP into ADP and Pi in muscle cells.

7. (Page 6.) Fill in the blanks in the following equation for the dehydration synthesis of ATP.

_____ + _____ + _____ → _____ + ATP

8. (Page 6.) Why is the production of ATP from ADP termed a "dehydration synthesis" reaction?

9. (Page 7.) Why is ATP often called "energy currency"?

10. (Page 7.) Muscle cells have only enough ATP to last for _____ during an active contraction period.

11. (Page 8.) List three processes that muscle cells use to make ATP when it is needed for muscle contraction.

12. (Page 9.) What is the most immediate source of energy for rebuilding ATP within muscle cells?

13. (Page 9.) Fill in the following blanks to show the production of ATP from Creatine phosphate:

_____ + _____ → _____ + _____

14. (Page 10.) What are the two sources of glucose to muscle cells?

15. (Page 11.) What are the end products of glycolysis?

16. (Page 12.) What happens to pyruvic acid in the absence of oxygen?

17. (Page 12.) What happens if a muscle is deprived of oxygen for too long when it is physically active?

18. (Page 13.) What is the name of the oxygen binding protein within muscle?

19. (Page 14.) Where, within a muscle cell, will the Krebs cycle and oxidative phosphorylation occur?

20. (Page 14.) What are the end products of the aerobic pathway?

21. (Page 14.) The total energy harvest from glycolysis, the Krebs cycle and oxidative phosphorylation is 38 ATP molecules for each glucose molecule metabolized.
    a. How much of that ATP is generated during glycolysis?
    b. How much of that ATP is generated during the Krebs cycle and oxidative phosphorylation?