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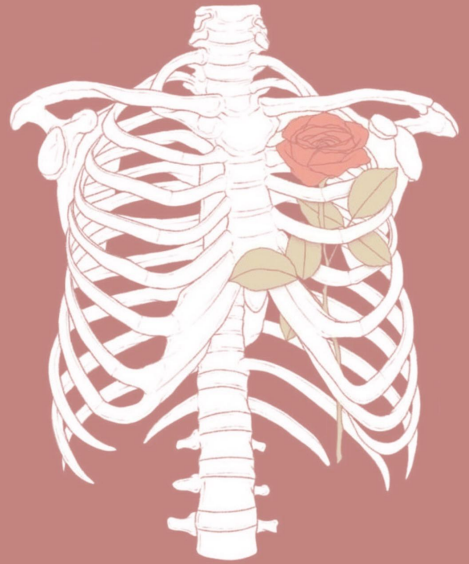
Aerobic and Anaerobic Metabolism



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Main text

IMPORTANT

Extra Info

Drs Notes

Muskuloskeletal Block - Biochemistry Team

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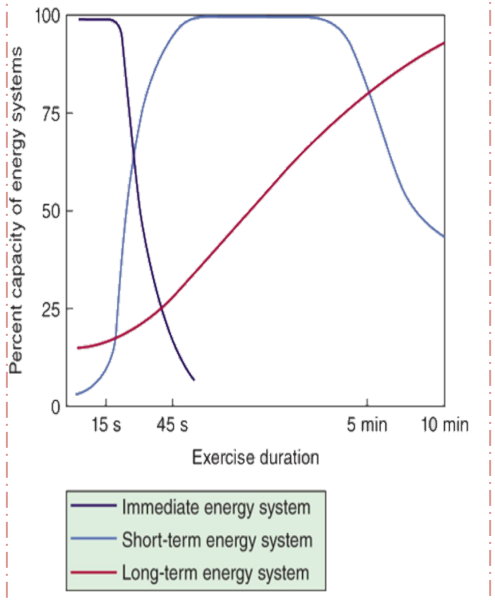
MED439

Objectives:

- Recognize the importance of ATP as energy source in skeletal muscle.
- Compare three systems of energy transfer in the body.
- Differentiate between energy metabolism in red and white muscle fibers.
- Understand how skeletal muscles derive ATP from aerobic and anaerobic metabolism.
- Discuss the importance of Cori and glucose-alanine cycles in energy metabolism.

Three systems of energy transfer

Type of System	Immediate System (ATP - PCr)	Short-term System (Glycolysis)	Long-term System (Aerobic)
Type of metabolism	Anaerobic	Anaerobic	Aerobic
Main Energy Source	Phosphocreatine (PCr)	Glucose	Fatty Acids
Type of Exercise	High intensity exercise	High intensity exercise	Continuous exercise
Duration	3 to 15 sec	15 sec to 2 min	Hours
Final product		Lactate	CO_2 and H_2O



- We can observe Phosphocreatine as fastest energy source, aerobic as latest and each is inversely proportional to its duration.
- Aerobic stays for hours thus it's recommended to do aerobic exercises after a fatty meal

Understanding the integrated 3 energy system

★ extra explanation

100m Race

2000m Race

Marathon

PCR System

Glycolysis

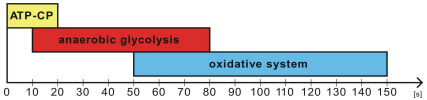
Krebs cycle

Oxidative phosphorylation

Electron transport chain

ATP

*All systems work together

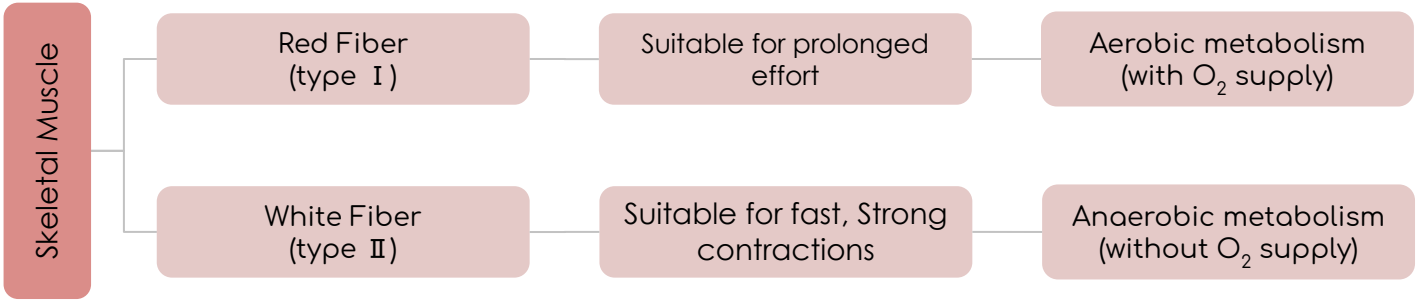


ATP as energy source

- The nucleotide coenzyme adenosine triphosphate (ATP) is the most important form of chemical energy stored in cells.
- Breakdown of ATP into ADP + PO_4 releases energy.
- This energy is used for all body functions (biosynthesis, membrane transport, muscle contraction, etc.).
- The main pathway for ATP synthesis is oxidative phosphorylation catalyzed by the respiratory chain.
- ATP synthase catalyzes the synthesis of ATP.
- ADP + P_i → ATP.

Energy metabolism in muscle

- Muscle contraction requires high level of ATP consumption.
- Without constant resynthesis, the amount of ATP is used up in less than 1 sec. of contraction.



The muscle can't store energy for more than 1-2 sec, so they need constant re synthesis. in humans the type of muscle is mixed "pink"

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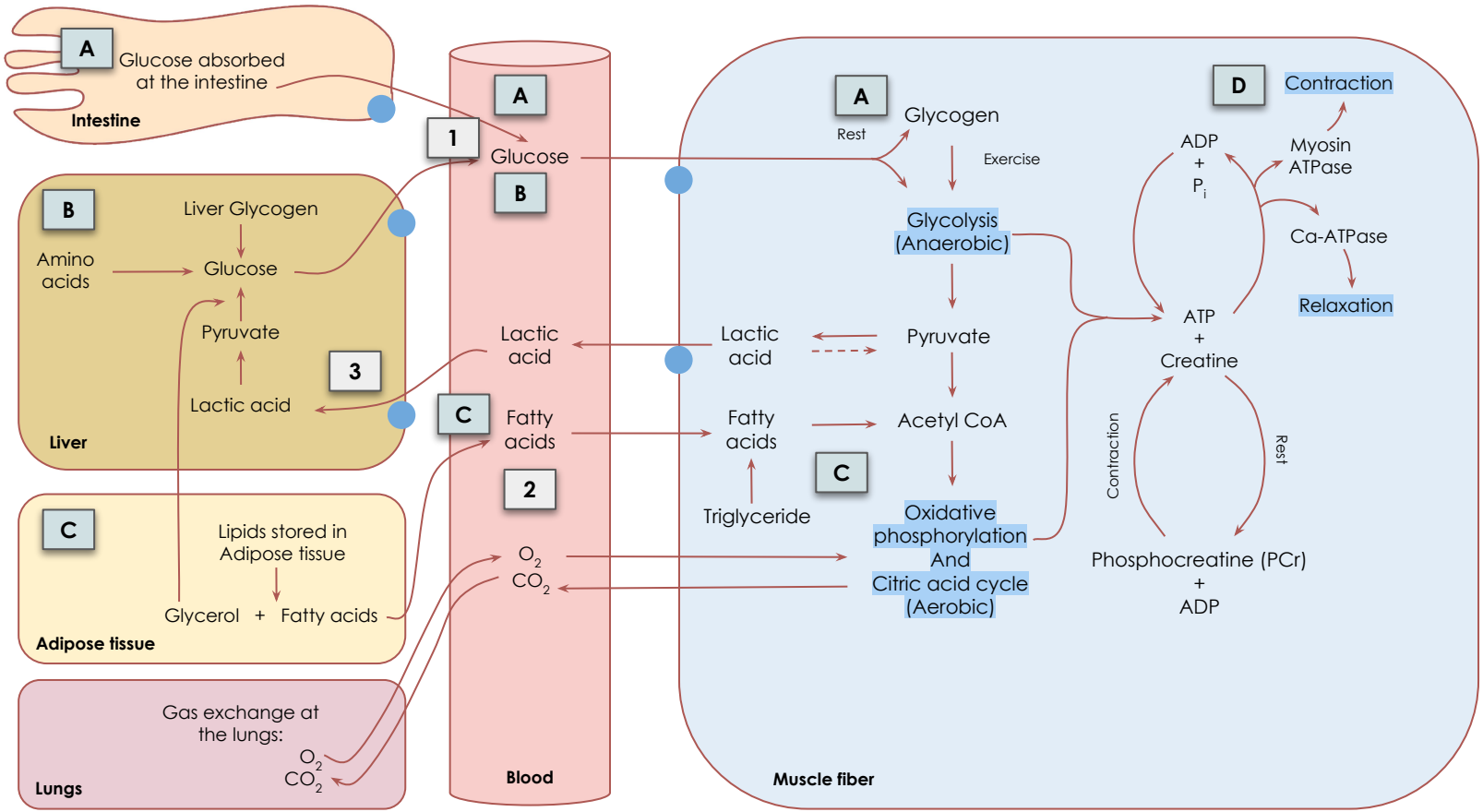
Overview of Energy metabolism



Overview of Energy metabolism, Contd...

1 Glucose comes from liver glycogen or dietary intake.

2 Fatty acids can only be used in aerobic metabolism.

3 Lactic acid from anaerobic metabolism can be converted to glucose by the liver

A When we eat, Glucose is absorbed in the intestine → goes to bloodstream → goes to the muscle.
Inside to muscle fibers:
- **At rest:** its stored as glycogen.
- **During exercising:** It undergoes glycolysis (anaerobic pathway) to give ATP

B **In Liver**: it's also can give glucose from:
1. Its stored glycogen (glycogenolysis).
2. Using amino acids, fatty acid and pyruvate (gluconeogenesis).

glucose then will go to blood stream then to the muscle fibers.

C **In prolonged exercise:**
Adipose tissue will give fatty acid → goes to bloodstream → goes to muscle fibers → get converted into 6 Acetyl CoA (by β-oxidation) → undergoes oxidative phosphorylation + O_2 produced from the lung (Aerobic pathway) to give ATP.

D The produced ATP will be used for contraction and relaxation
- myosin ATPase (for **contraction**)
- Ca-ATPase (for **relaxation**)

Red muscle fibers (Aerobic metabolism)

- Red muscle fibers are suitable for prolonged muscle activity. Athletes have this kind of muscles because they exercise a lot.
- Their metabolism is mainly Aerobic and depends on adequate supply of O_2
- They obtain ATP mainly from fatty acids. That's why when a person needs to lose weight they focus on the aerobic exercise beacuse it uses fats
- Fatty acid are broken down by β-oxidation will produce acetyl CoA,, Krebs cycle, and respiratory chain.
- Why its called red?
- Red colour is due to the rich of myoglobin, mitochondria and capillaries.
- **Myoglobin:**
  - Has higher O_2 affinity than hemoglobin.
  - Each one myoglobin binds to one molecule of O_2 ,while hemoglobin bind with 4 O_2.
  - Myoglobin has higher O_2 affinity than hemoglobin.
  - It releases O_2 when its level drops.

How can muscles get ATP

★ extra explanation

- There are 4 ways for muscles fibers to get ATP:

1. Aerobic by red fibers
2. Anaerobic by white fibers
3. Creatine Phosphate
4. By the enzyme adenylate cyclase:
   (will take two ADP and produce 1 ATP and 1 AMP)

- What do we need the ATP for? It is used in both contraction and relaxation of the muscle.
- When the muscles at rest, it will store ATP as creatine phosphate "Phosphocreatine" and Glycogen and when we exercising it will start consuming ATPs that was

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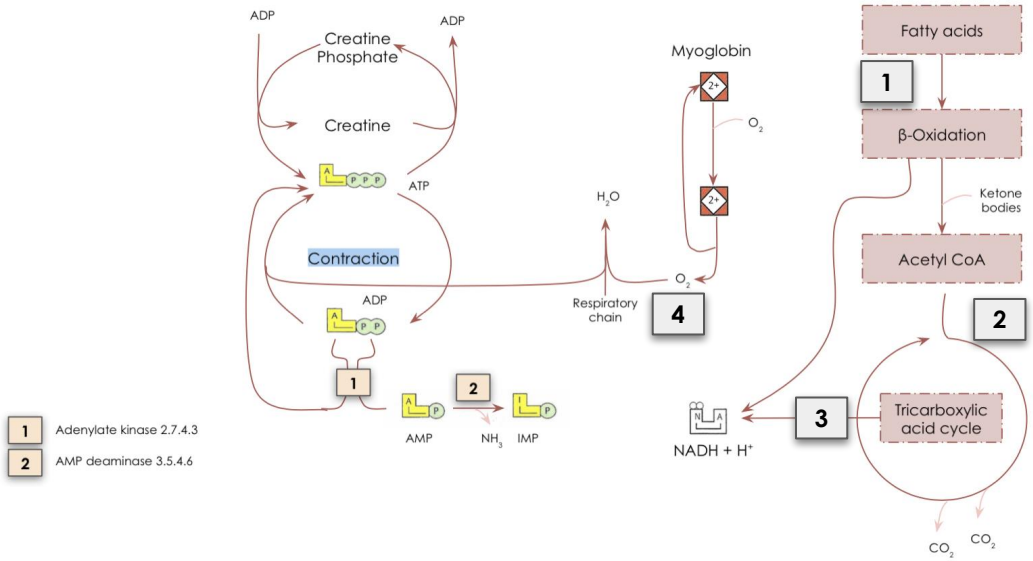
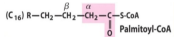
ATP metabolism in red muscle fibers



1 Fatty acids are oxidized to acetyl CoA, β-Oxidation helps in breakdown of fatty acids to acetyl coA.



Why it's called β-oxidation? Named after the carbon atom in the beta position of fatty acyl CoA which becomes the most oxidized during the cyclic redox reaction that remove C2 units in form of acetyl-CoA from the fatty acyl chain (a pathway that converts fatty acid to acetyl CoA)

2 Acetyl CoA enter the Krebs cycle. If you recall Krebs cycle breaks down larger molecules into acetyl coA then goes through several oxidation reactions to produce ATP.

3 Krebs cycle will give NADH, 1 Acetyl CoA gives: 3 NADH and 1 FADH.

4 NADH goes to respiratory chain in presence of O_2 given by myoglobin, O_2 grabs the carriers i.e. NADH and FADH and activates ATP Synthase.

White muscle fibers (Anaerobic)

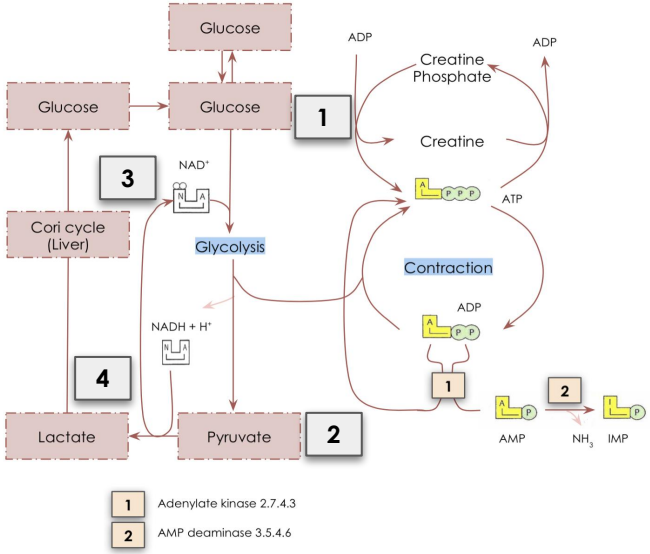
- White muscle fibers are suitable for fast, strong contractions.
- They mainly obtain ATP from anaerobic glycolysis.
- During intense muscle activity (weightlifting, etc.) O_2 supply from blood quickly drops, then the muscle will use anaerobic glycolysis.
- They have supplies of glycogen that is catabolized and undergoes glycolysis.

- They are white because they have less mitochondria, capillaries and myoglobin.
- They make energy from glycogen breakdown fast "Glycogen → Glucose-1-PO_4 → Glucose-6-PO_4 → Glycolysis → ATP".
- As we exercise, the body will start converting its energy source to anaerobic system.

- Summary in table for a better understanding: "extra explanation"

	Red muscle fibers	White muscle fibers
Force of contraction	Slow	Fast
Red color	High (aka Red fibers)	Low (aka White fibers)
Mitochondria and Myoglobin	High	Low
Oxidative capacity	High	Low
Capillary density and fatigue resistance	High	Low
Main source of energy	Triglycerides	Glycogen and Creatine Phosphate
Duration of use	Long	Short
Glycogen and Glycolytic capacity	Low	High
Power	Stamina	Strength

White muscle fibers (Anaerobic)



Now both creatine phosphate and aerobic glycolysis are no longer available, this is where **anaerobic** glycolysis takes place:

1. Glycogen stored in muscles will transfer to glucose by glycogen phosphorylase eventually ends up as G6P "Glycolysis starter molecule" and goes through glycolysis
2. Pyruvate is produced and NAD^+ is reduced to NADH.
3. $NADH + H^+$ is re-oxidized to maintain glucose degradation and ATP formation
   At some point NAD^+ will exhaust and NADH will accumulate so it will be re-oxidized back to NAD+ to maintain mitochondrial adaptation
4. Lactate is bad for muscles but we want to eliminate it in a way the body can benefit from, So Lactate is resynthesized into glucose by the cori cycle in the liver (More details in next slide)
   Lactate will accumulate as well and we need to get rid of it in a beneficial way thus it is transferred to liver where it goes through cori cycle.

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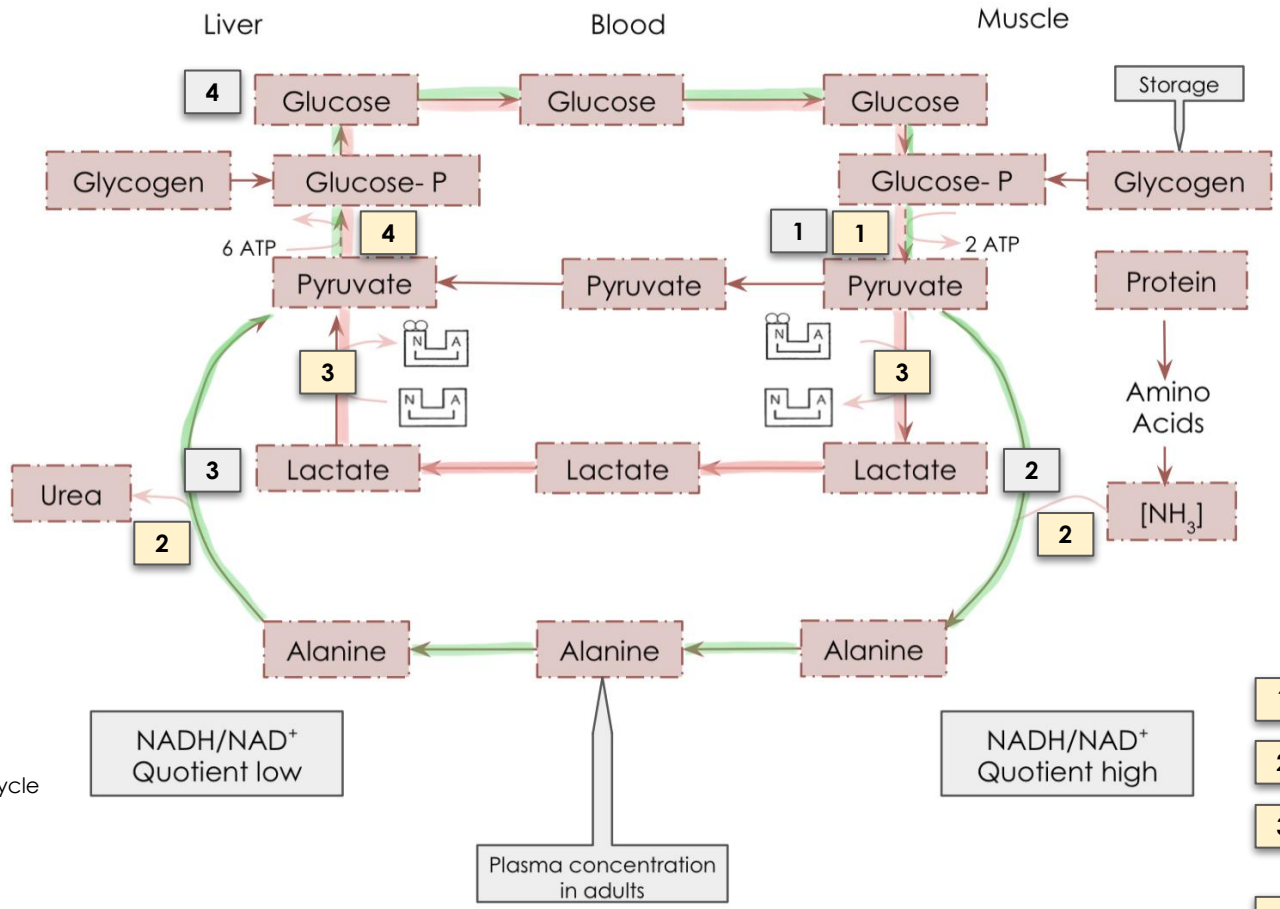
The Cori Cycle



The Cori Cycle, Contd...

1. **In Muscle:**
   White muscle fibers (Fast and Strong contraction) obtain ATP from Anaerobic glycolysis.In anaerobic glycolysis, the glucose is converted to lactate.
2. **In The Bloodstream:**
   Lactate in muscle is released into bloodstream, then transported to the liver.
3. **In The Liver:**
   Liver converts lactate into glucose via gluconeogenesis. if lactate levels exceed (0.74-2.40) it will be taken up by the liver to start gluconeogenesis.
4. The newly formed glucose is transported to muscle to be used for energy again " complete cycle ".

- Summary: Liver converts lactate into glucose via gluconeogenesis, then the newly formed glucose is transported to be used for energy.

- Why skeletal muscles can't produce glucose from lactate?

Because:

- Muscles can't store energy as we preivoiusly noted.
- Gluconeogenesis requires much more ATP than the energy supplied by glycolysis in muscle.
- O_2 deficiencies do not arise in the liver even during intense exercise. Liver has two oxygen sources (arteries and hepatic portal vein) and is supplied with oxygen sufficiently far more than muscles.
- Therefore, liver always has sufficient ATP for gluconeogenesis.

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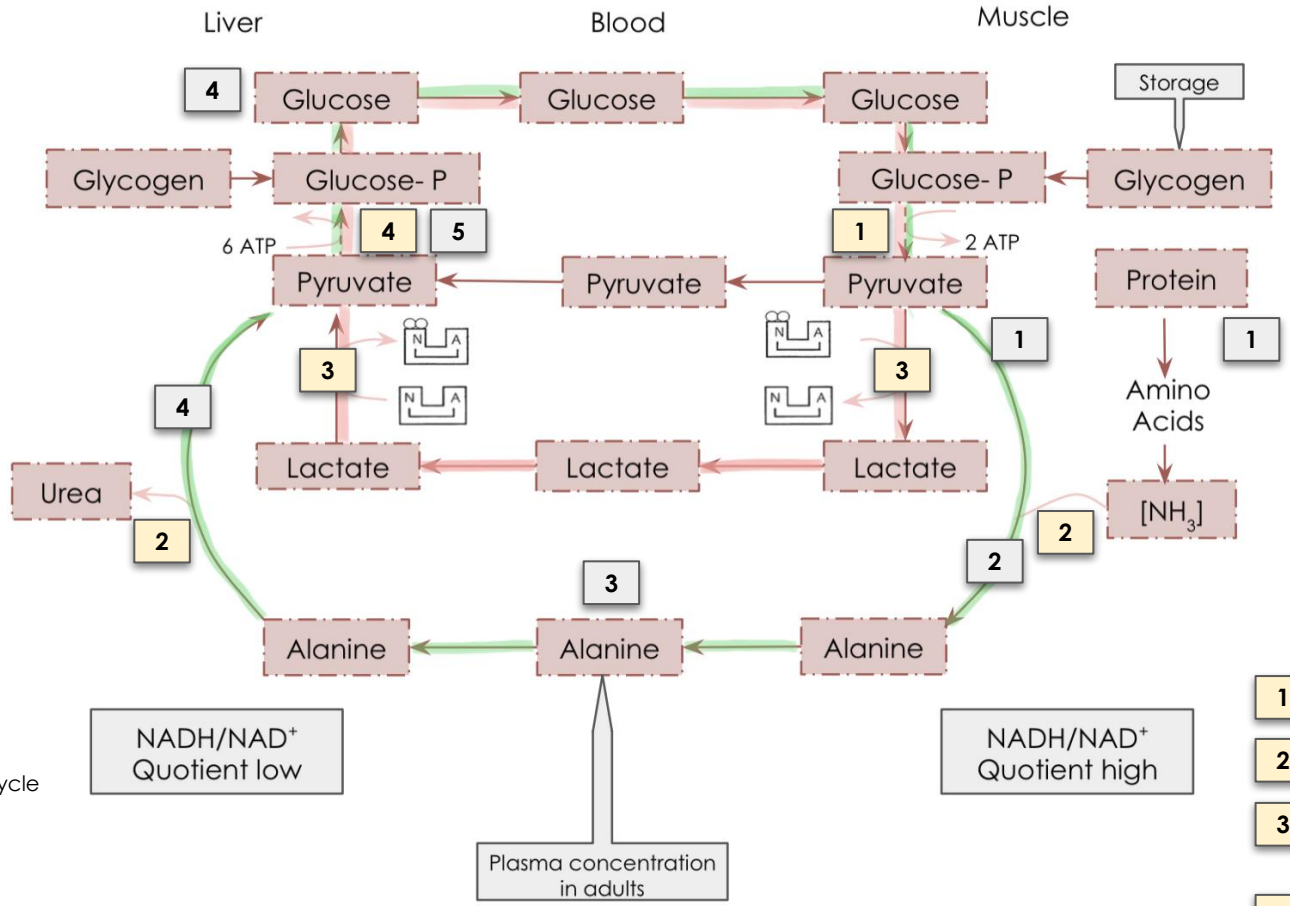
The glucose - alanine cycle



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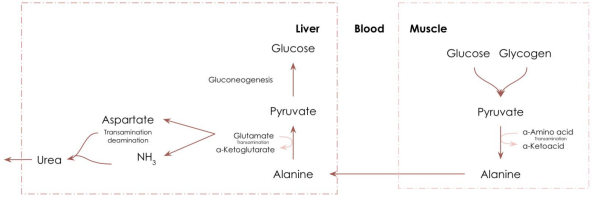
The glucose - alanine cycle, Contd...

1 **In Muscle:**
Muscles produce pyruvate from glycolysis during exercise and Amino nitrogen (NH_2) from normal protein degradation.

2 **In Muscle:**
Pyruvate (with NH_2) is converted to alanine in muscles
Pyruvate + NH_2 → Alanine "Amino group is transformed to pyruvate to give alanine (transamination)."

3 **In The Bloodstream:**
Transportation, Alanine is transported from the muscle by the blood into the liver. "Pyruvate is a charged molecule (it has a negative charge) so it can't be transported. That's why it's converted to Alanine"



4 **In The Liver:**
Liver converts alanine back to pyruvate (Alanine – NH_2 = Pyruvate). Once it's in the liver (the Alanine) it will give back the amino group to an acceptor. (The universal acceptor is a-ketoglutarate).

5 **In The Liver:**
Pyruvate is used in gluconeogenesis "to produce glucose". If Pyruvate comes from lactate then it's part of Cori cycle and if it comes from alanine then it's part of glucose-Alanine cycle.

6 **In The Liver:**
The newly formed glucose is transported to muscle to be used for energy again.

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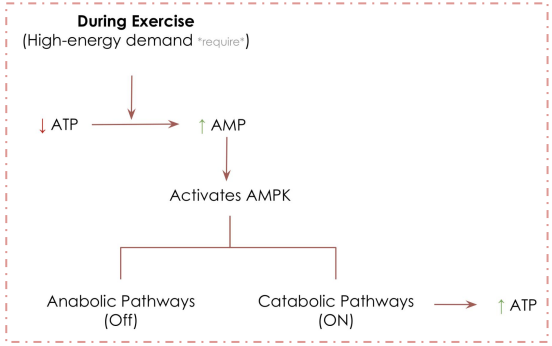
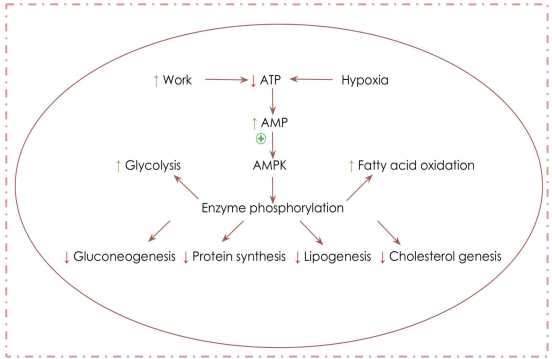
Exercise and AMPK

- In exercise, the metabolic enzymes are regulated through phosphorylation by AMP-activated protein kinase (AMPK).
- By this process the body tries to save energy.

- Explanation:
  - During exercise ATP level goes down and in the same time AMP level goes up.
  - When AMP level goes up is activated the AMPK enzyme.
    - ↳ The activation of AMPK enzyme will shot down the anabolic pathway (to save energy) and turn on catabolic pathway (to produce energy).

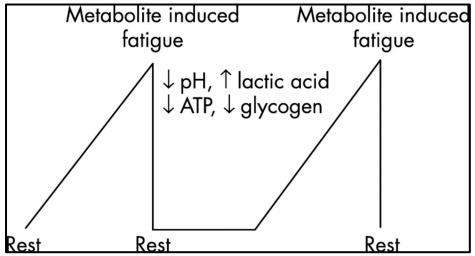




- AMPK activation shuts down ATP-requiring processes and stimulates ATP-producing processes

Muscle fatigue and endurance in athletes

- **Muscle fatigue:** is the Inability of muscles to maintain a particular strength of contraction over time.
  - Causes:
  1. Muscle damage.
  2. Accumulation of lactic acid.
  3. Decrease in pH in tissues.
- Athletes are able to change the proportions of red and white muscle fibers by targeted training
- The expression of muscle proteins can also change during the course of training.
- This provides them with:
  - High endurance during muscle activity.
  - Efficient energy production and consumption.
  - Delayed fatigue.



- Muscle fatigue can sometimes be pathological
- The red muscle fibers are better for them because it is suitable for prolonged effort + it is an aerobic which doesn't cause lactic acid formation which leads to muscle fatigue. A brief about muscle fatigue, click here

Summary of the enzymes

Enzymes	Function
ATP synthase	Catalyze the synthesis of ATP $ADP + P_i \rightarrow ATP$
Lactate dehydrogenase	Catalyze the conversion of lactate to pyruvate, as it converts NAD^+ to NADH
Myosin ATPase	Contraction of the muscles
AMP-activated protein kinase (AMP kinase)	When it is activated is shut down ATP- requiring processes and stimulate ATP producing processes
Adenylate cyclades	Take 2 ADP and produce 1 ATP and 1 cAMP
Ca- ATPase	Relaxation of muscles
AMP deaminase	Part of the auxiliary system of energy along with adenylate kinase
Adenylate kinase	Joint 2 ADP molecules to make 1 ATP and 1 AMP

Take home messages

- ATP is an important source of chemical energy needed by the cells to perform body functions.
- Muscular activity requires constant supply of ATP for energy either from aerobic or anaerobic metabolism.
- Cori and Glucose-alanine cycles play an important role in regenerating glucose for energy.
- Athletes are able to change proportions of their red and white muscle fibers with appropriate training.

Quiz

Q1 : Which enzyme is responsible contraction of muscles?			
A) Myosin ATPase	B) Ca- ATPase	C) Adenylate Cyclades	D) Adenylate Kinase
Q2 : Which of the following systems contain red muscle fibers?			
A) Immediate system	B) Short-term system	C) Intermediate-term system	D) Long-term system
Q3 : muscle fibers can get ATP via:			
A) Anaerobic by red fiber	B) Adenylate cyclase	C) Creatine phosphate	D) B & C
Q4 : Urea is produced when ..... is converted into			
A) Pyruvate, Alanine	B) Alanine, Pyruvate	C) Pyruvate, Lactate	D) Lactate, Pyruvate
Q5 : Biochemistry team 439 in musculoskeletal block is :			
A) The best team	B) The most impressive team	C) The most outstanding team	D) All of them

SAQs :

Q1: What are the causes of muscle fatigue?

Q2: what are white muscle fibers suitable for?

★ **MCQs Answer key:**

1) A 2) D 3) D 4) B 5) D

★ **SAQs Answer key:**

1) Muscle damage, accumulation of lactic acid.

2) Fast, strong contractions

Girls team:

Sara Alrashidi
Rania Almutiri
Alia Zawawi
Noura Alshathri
Reem Alamri
Renad Alhomaidi
Norah Alsheikh
Bdoor Almobarak

Boys team:

Abdullaziz Alomar
Nawaf Algarni
Abdullaziz Alrabiah
Abdullah Almazro
Mishal Alhamed
Omar Alsuliman
Abdullah Alanzan
Abdullaziz Alomar
Ahmed Alkhayyat
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