LECTURE
BIOENERGETICS

WHAT IS METABOLISM?

Sum of all chemical reactions that occur in the body

Anabolic reactions

- Synthesis of molecules - proteins in training

Catabolic reactions - enzyme mediated reductions, when we eat - enzymes bind to substrates to break down

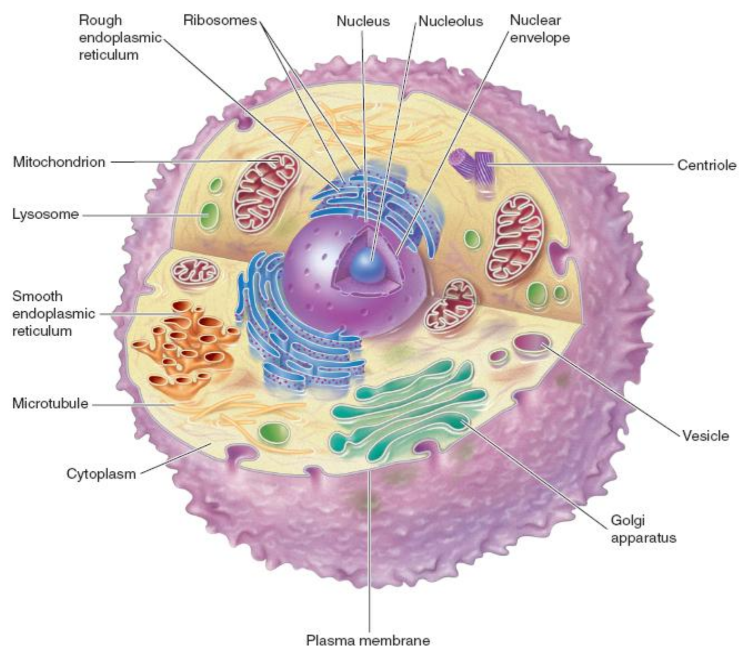
- Breakdown of molecules

Bioenergetics

- Converting foodstuffs (fats, proteins, carbohydrates) into energy

carbohydrates yield ATP in the cytoplasm

THE EUKARYOTIC CELL



The mitochondrion

'energy factory'

constantly making ATP
by burning lipids and proteins

action potential

Cellular membrane

major source of cellular electricity
and intrac-cellular signaling

Nucleus

home of the cell's genes

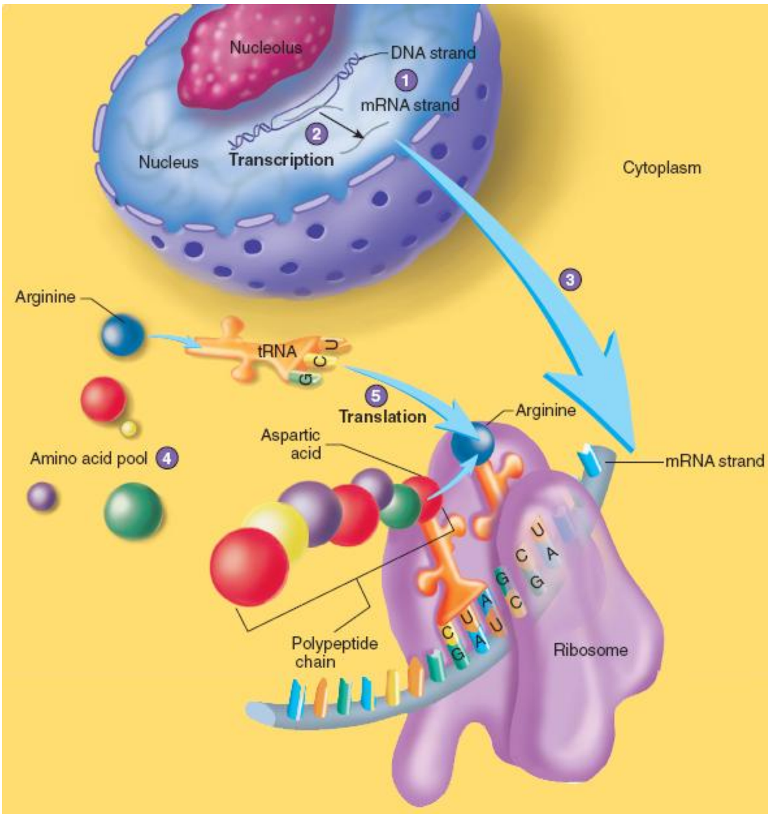
rate of glycolosys goes up significantly with exercise

1. signal --> exercise (post)
 --> nutrition (protein - whey)
2. supply of amino acids
strength --> myosin + actin (responsible for f.o.a. - muscle force
endurance --> enzymes

ATP = money

PROTEIN SYNTHESIS

1. DNA contains information to produce proteins.
2. Transcription produces mRNA.
3. mRNA leaves nucleus and binds to ribosome.
4. Amino acids are carried to the ribosome by tRNA.
5. In translation, mRNA is used to determine the arrangement of amino acids in the polypeptide chain.



Oxidation
- removing an electron
Reduction
- addition of an electron

oxidation and reduction are always COUPLED reactions
often involves transfer of hydrogen atoms rather than free electrons
- hydrogen atom contains 1 electron

Endergonic reactions

- Require energy to be added
- Endothermic

Exergonic reactions

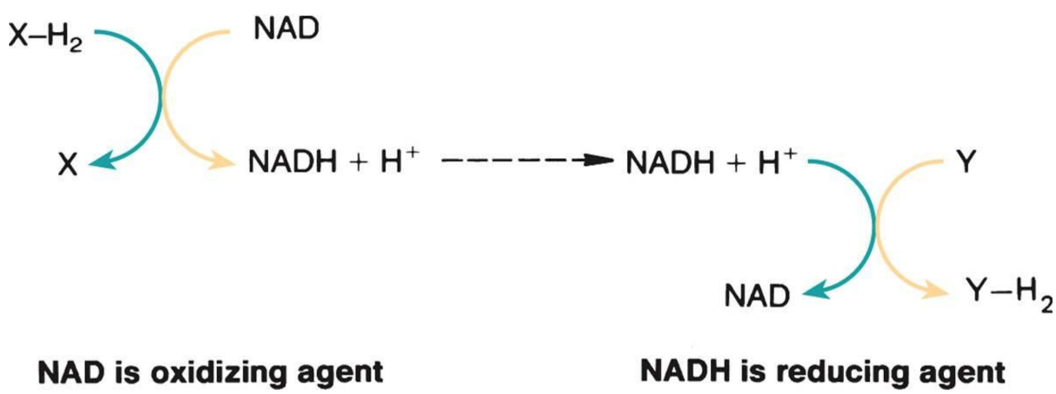
- Release energy (transfer to mechanical and/or chemical AND THERMAL)
- Exothermic

Oxidation

- Removing an electron

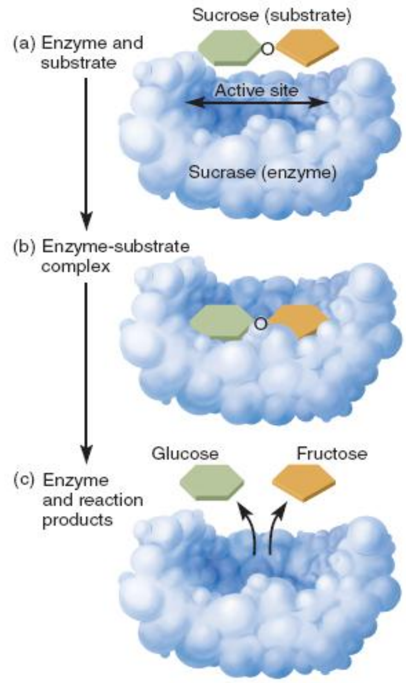
Reduction

- Addition of an electron
- Oxidation and reduction are always coupled reactions
- Often involves the transfer of hydrogen atoms rather than free electrons
  - Hydrogen atom contains one electron
  - A molecule that loses a hydrogen also loses an electron and therefore is oxidized



NAD -- molecule, niacin
--> electron accept/donor

all enzymes are proteins, but not all
proteins are enzymes



<u>WHAT ARE ENZYMES</u>?

Catalysts that regulate the speed of reactions

- Lower the energy of activation

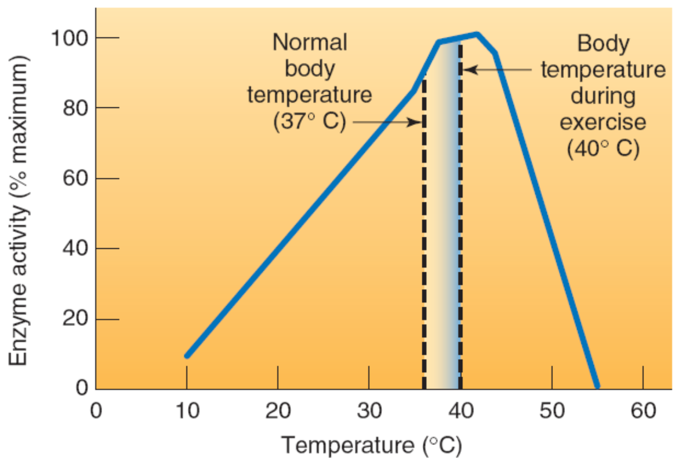
Factors that regulate enzyme activity

- Temperature
- pH

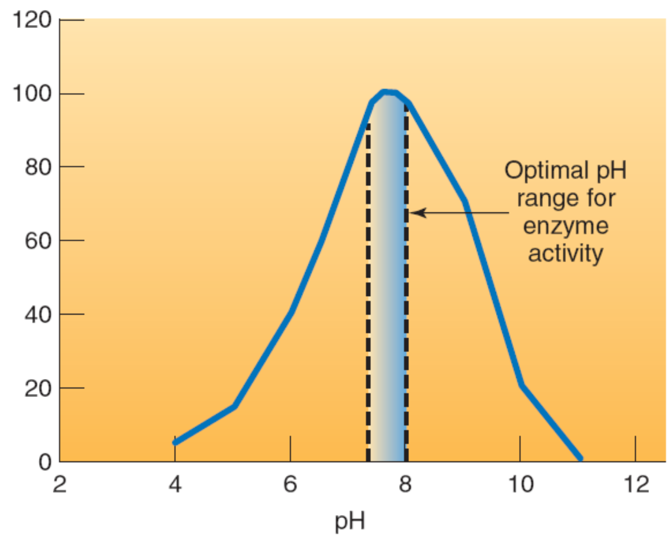
What role do enzymes play in metabolism?

a chemical reaction is sped up by enzymes

Effect of temperature



Effect of pH



<u>Where do we get our energy from?</u>

epinephrine increases the activity to break down stored muscle glycogen

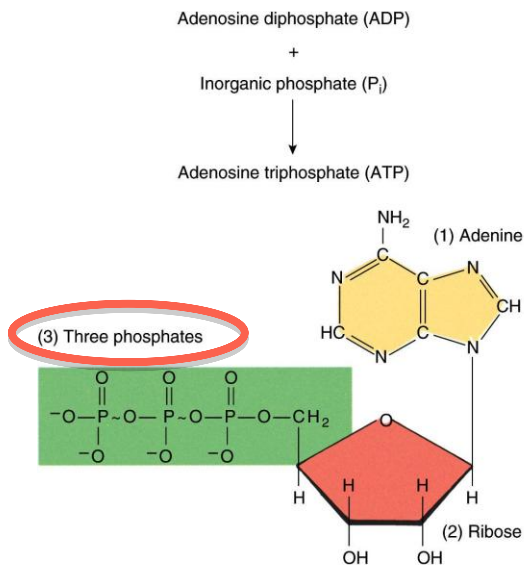
- Energy "substrates"
  - Carbohydrates, fats and proteins
- Where do these come from?
- Why do we need their energy?

to form ATP
exercise

3 consumers of ATP in exercise
1. Myosin (ATPase enzyme) --> works with actin (biomolecular motor)
2. Na+ / K+ ATPase found buried in cell membrane
3. SERCA (sarco endoplasmic reticulum Ca++ ATPase

- How do we get energy out of the substrates?
  - Depends on:
  - Substrate availability
  - Enzyme dynamics
  - Nervous system demand
  - Metabolic "backup"

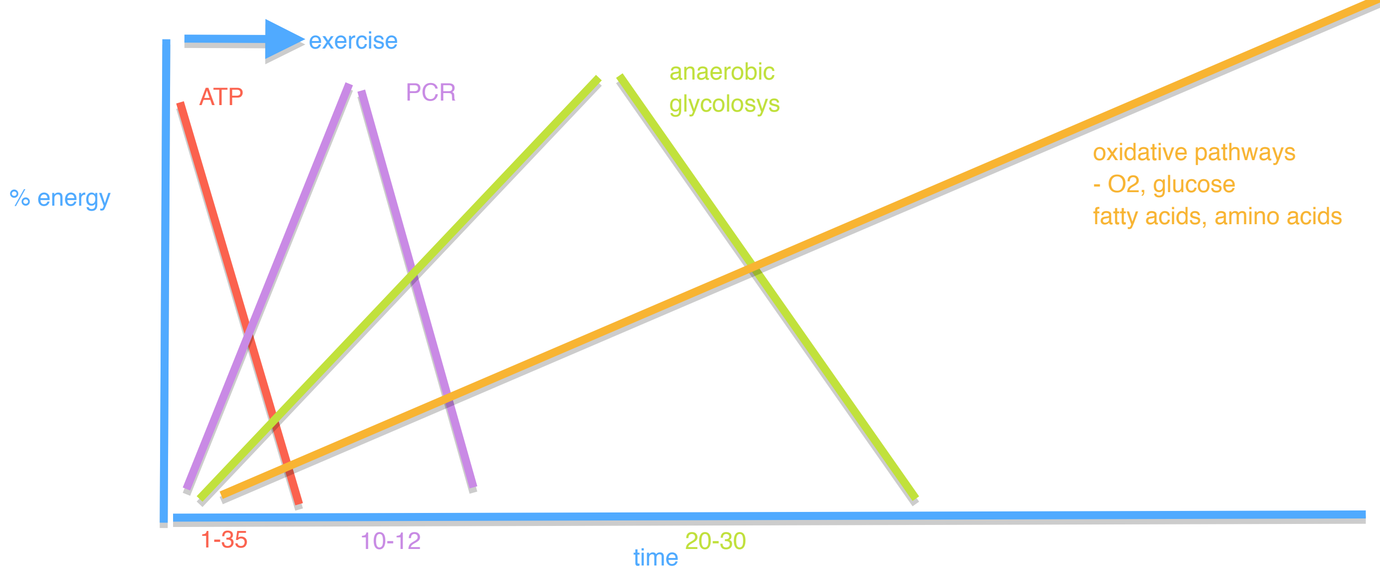
Cellular energy ($$)



Energy for muscle activity

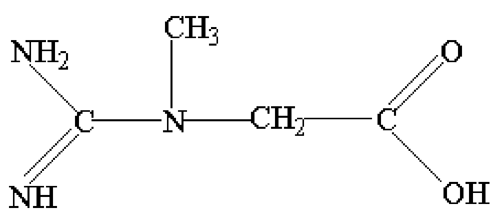
Bioenergetics

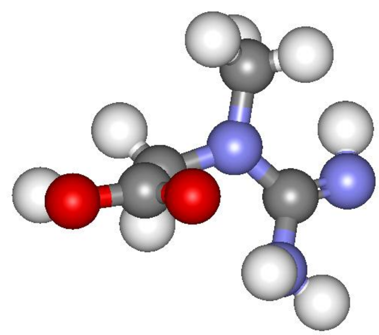
- Formation of ATP
  - Phosphocreatine (PCr) breakdown
  - Degradation of glucose
  - Oxidative formation of ATP
- Anaerobic pathways
  - Do not involve O_2
  - PC breakdown and glycolysis
- Aerobic pathways
  - Require O_2
  - Oxidative phosphorylation



What is creatine?

- Non-essential dietary element….found in meat and fish.
- Greek derivative, *kreas*, meaning flesh.
- Humans: made in 2 step process (liver and kidney).
- Where is it found? (mostly)……skeletal muscle, heart, spermatozoa, retinal cells.

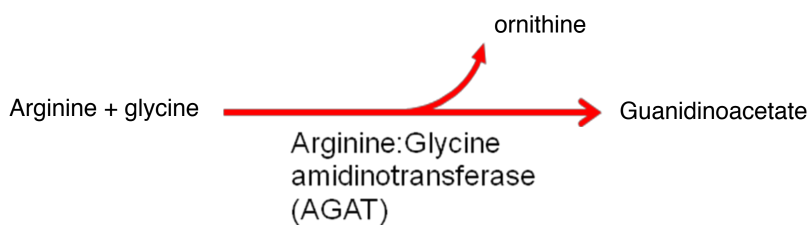




<u>Creatine biosynthesis?</u>

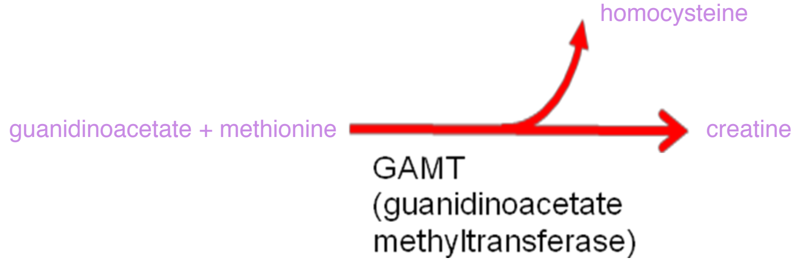
- 2 step process
- Step 1: Kidney: Arginine + glycine

methanine is an essential amino acid



Creatine biosynthesis?

- 2 step process
- Step 2: Liver: Guanidinoacetate + methionine

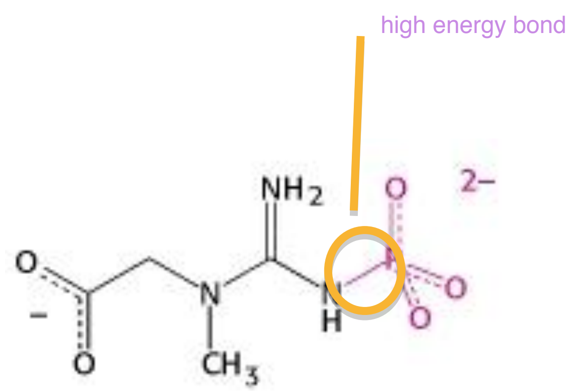


Why is creatine important?

- ATP re-synthesis for high intensity/velocity muscle contractions….how?

Creatine phosphate (phosphocreatine, PCr, CrP)

- Contains energy in phosphate bond



Creatine phosphate for energy……how does it make ATP?

PCr + ADP ATP + Cr

during exercise

Creatine Kinase - speeds up a chemical reaction, bringing two close PCr and ADP molecules together

What happens when we run out of creatine phosphate?

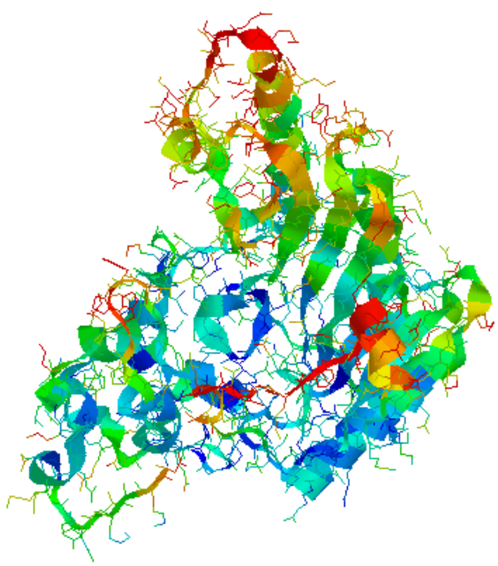
During Recovery (high intensity exercise)

Cr + ATP PCr + ADP

CK

oxidative pathways will make ATP when we are resting in between high intensity exercise

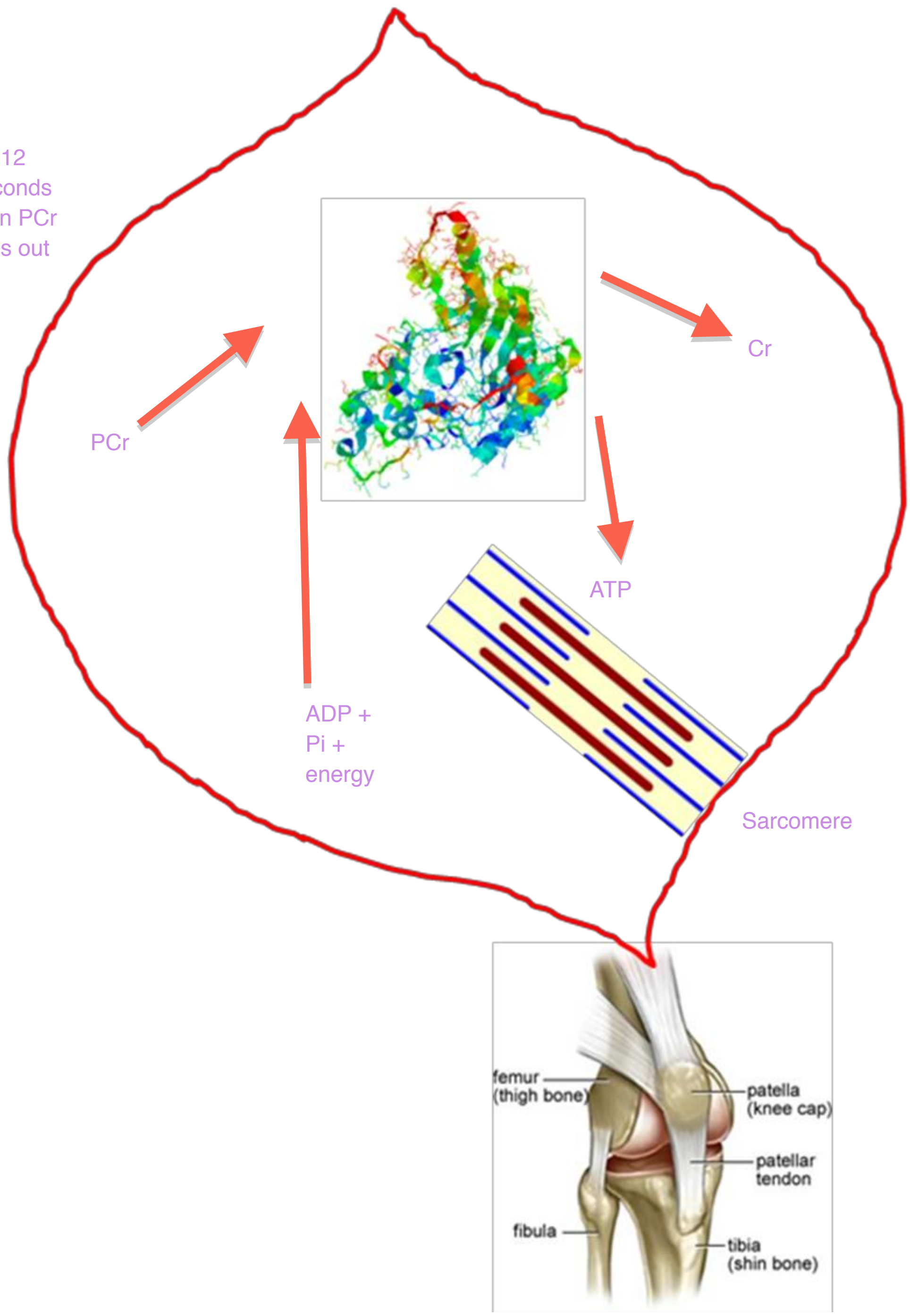
Creatine kinase: 381 amino acid sequence



CREATINE PHOSPHATE USE DURING EXERCISE

Knee extensor muscle cell

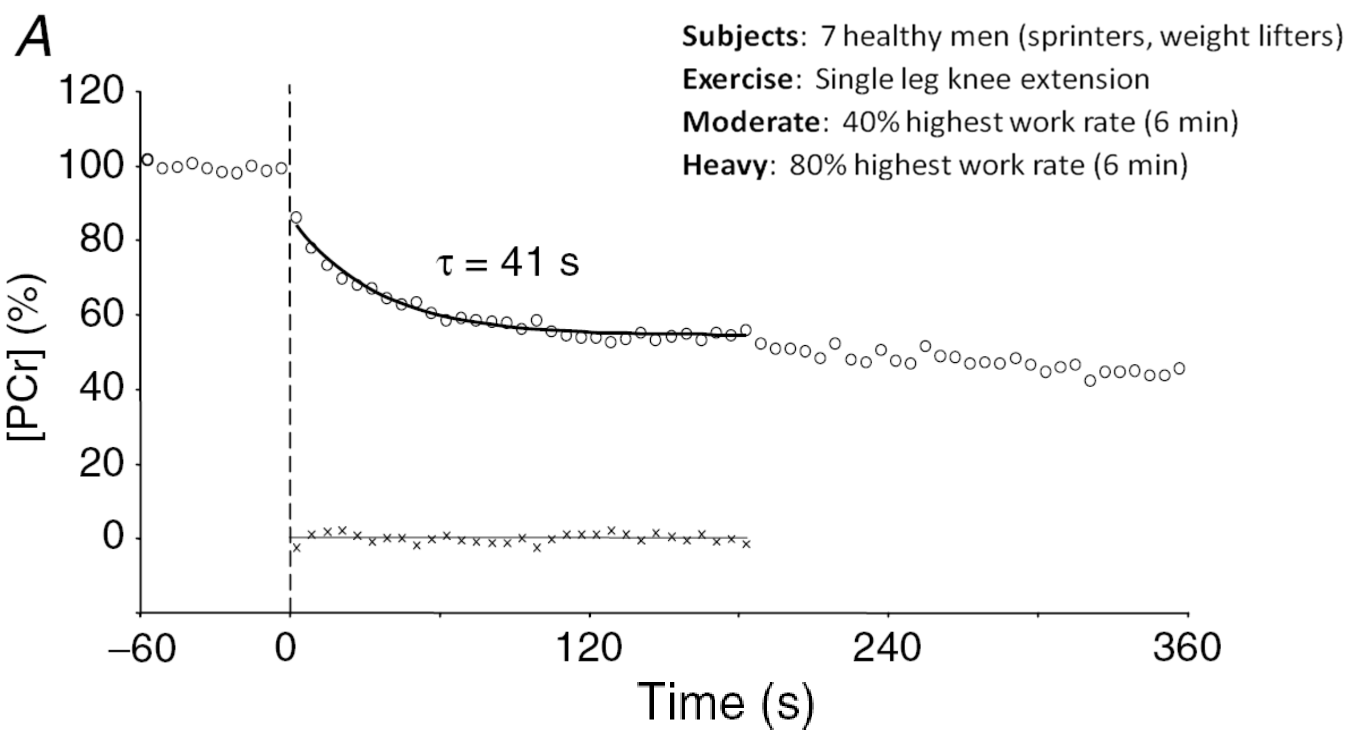
10-12 seconds then PCr runs out



CREATINE PHOSPHATE USAGE DURING EXERCISE

Andrew M. Jones, Daryl P. Wilkerson and Jonathan Fulford
J Physiol 586.3 (2008) pp 889–898

Muscle [phosphocreatine] dynamics following the onset of exercise in humans: the influence of baseline work-rate



CREATINE PHOSPHATE USAGE DURING EXERCISE (cont'd)

Creatine phosphate supplementation

- Idea……increase the muscle's stores of creatine phosphate….extends high intensity exercise and speeds muscle recovery.

Types:

- Creatine monohydrate (most popular)
- Creatine anhydrous (CON-CRET)
- Creatine phosphate
- Creatinol-O-phosphate

Creatine supplement forms

- Holds one molecule of water…….*creatine monohydrate*
- Drying of creatine monohydrate (at 100 deg C) yields *creatine anhydrous* (more concentrated form of creatine)
- Creatine salts created by combining creatine and a strong acid (pyruvic acid, malic acid, citric acid)

Creatine content

- Creatine anhydrous - 100%
- Creatine monohydrate - 88%
- Creatine malate - 75%
- Creatine citrate - 66%

Creatine solubility in water

- Greater solubility with creatine salts than creatine monohydrate

Creatine stability

- Creatine monohydrate most stable (i.e., takes a long time to degrade….therefore, long shelf life)
- Creatine degrades in warm, acidic water…..should be consumed immediately after dissolving in water

Bioavailability

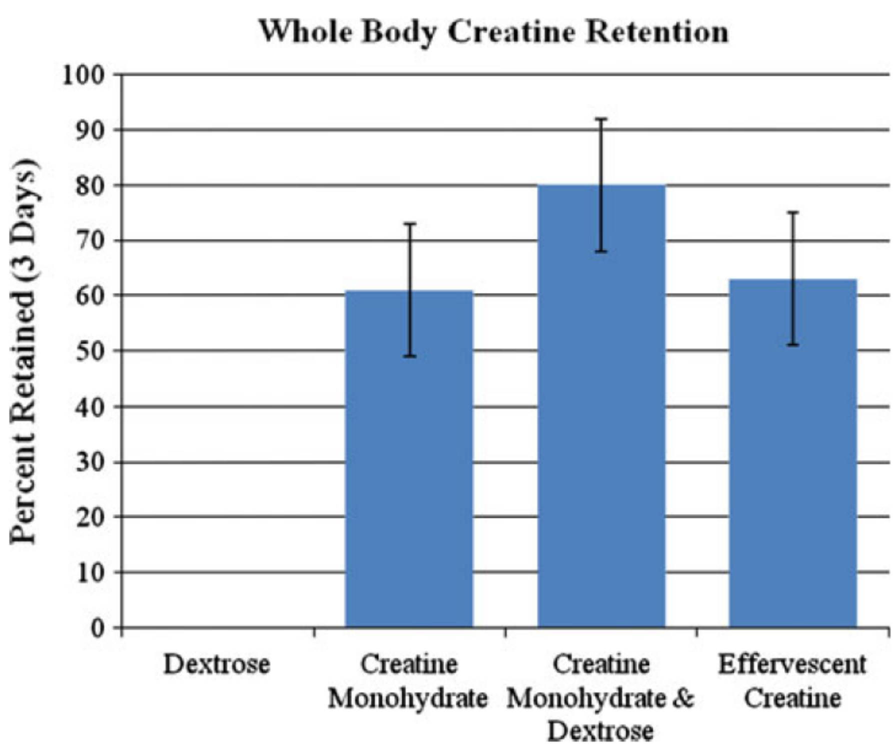
1) Absorb creatine from small intestine into blood
2) Uptake creatine into muscle tissue

Creatine solubility in water

- Greater solubility with creatine salts than creatine monohydrate
- Dietary creatine intestinal absorption close to 100%
- Muscle tissue uptake stimulated by insulin…….how do we get insulin secreted?

Analysis of the efficacy, safety, and regulatory status of novel forms of creatine

Ralf Jäger · Martin Purpura · Andrew Shao · Toshitada Inoue · Richard B. Kreider Amino Acids (2011) 40:1369–1383



Creatine dosage

- 1st 4-6 days: 20 grams/day (4, 5 gram servings)....*loading phase*
- 5 grams/day afterwards…..*maintenance phase*
- Takes 2-3 days for tissue creatine accumulation

Creatine and exercise performance

- 5-20% improvement in short-term exercise (cycling, sprinting, jumping, resistance exercise)

Side effects

- Increased weight gain (water retention in muscle)
- Nausea, vomiting, diarrhea……may occur with exercise
- Increased urinary creatine and creatinine…..may be related to kidney inflammation
- Altered fluid balance…..predispose to dehydration?
- Negative feedback from exogenous supply…..decreases natural production

Creatine phosphate RECOVERY FOLLOWING exercise

Influence of dietary creatine supplementation on muscle phosphocreatine kinetics during knee-extensor exercise in humans

Andrew M. Jones,[1] Daryl P. Wilkerson,[1] and Jonathan Fulford[2]

Am J Physiol Regul Integr Comp Physiol 296: R1078–R1087, 2009.

Subjects: 7 healthy men (sprinters, weight lifters)

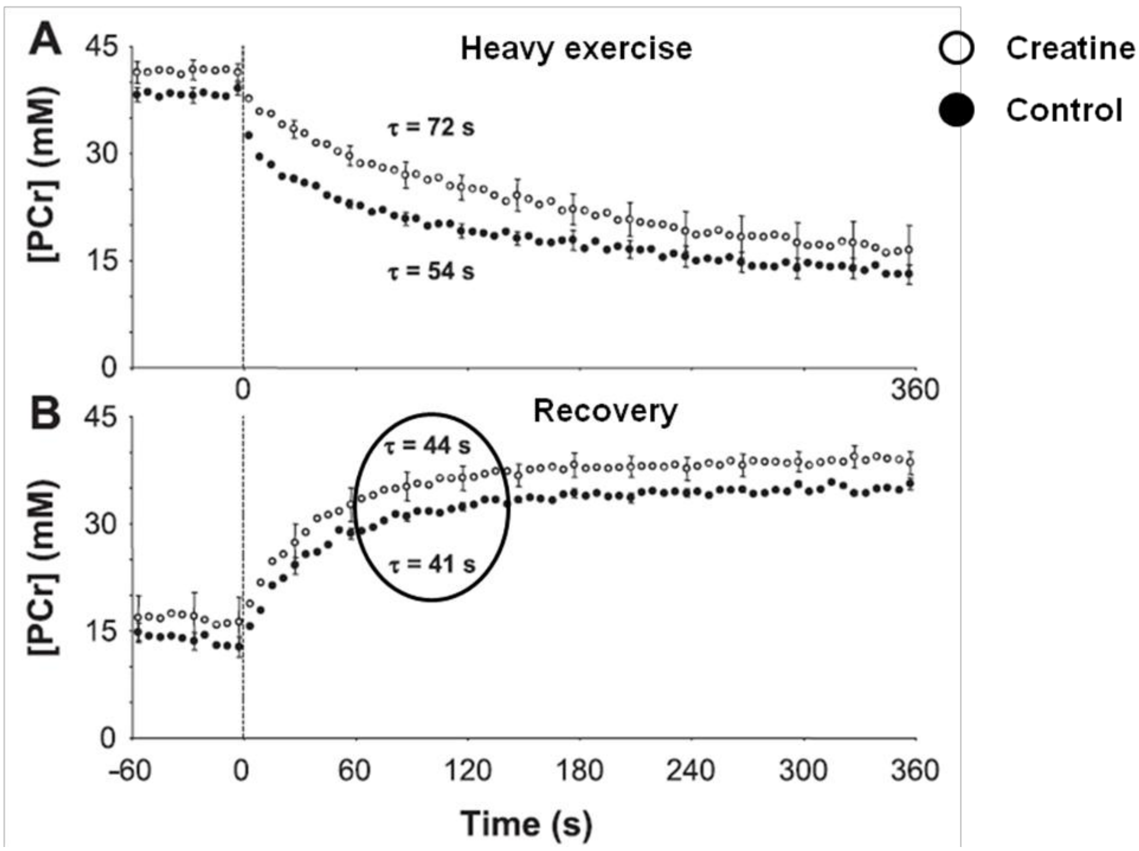
Exercise: Single leg knee extension

Moderate: 40% highest work rate (6 min)

Heavy: 80% highest work rate (6 min)

Creatine monohydrate supplementation:

- 20 g/day, 5-10 days
- Exercise performed prior to, and following, supplementation periods.



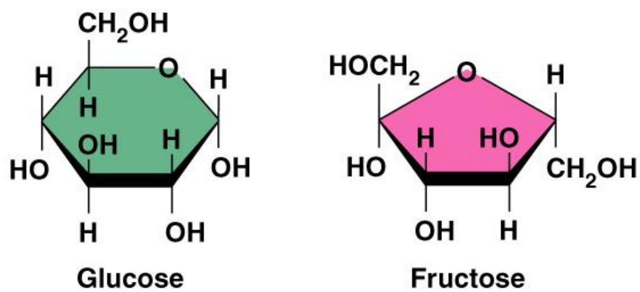
What was the effect of creatine supplementation?

1) Resting and exercise PCr levels.

2) Exercise and recovery time constants.

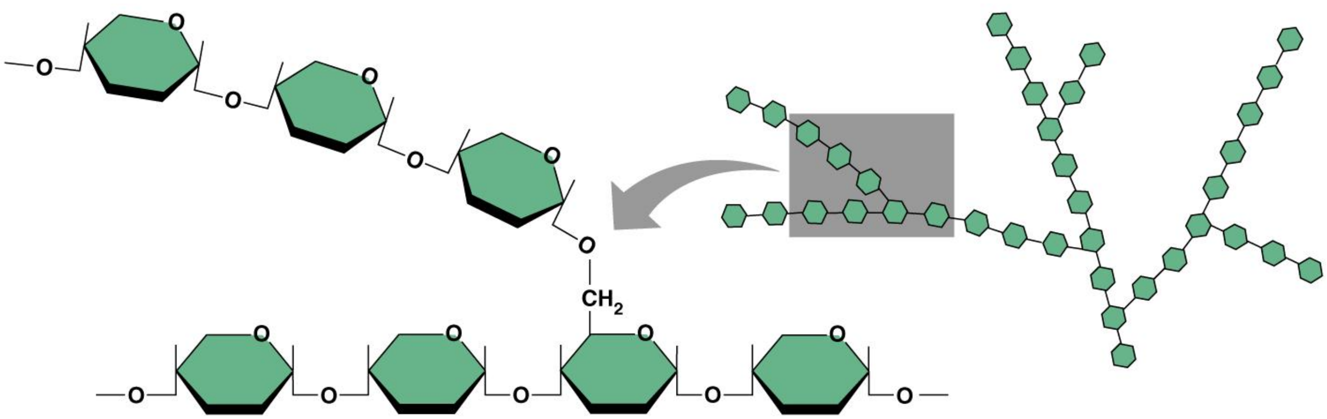
CARBOHYDRATES (GLUCOSE mainly)

- **Glucose**
  - Blood sugar "broken down" called GLYCOLYSIS
- **Glycogen**
  - Storage form of glucose in liver and muscle
    - Synthesized by enzyme *glycogen synthase*
  - **Glycogenolysis:** Breakdown of glycogen to glucose



GLYCOGEN

- Cleaved into individual glucose units:
    - In <u>muscle</u>, **myophosphorylase** (activated by epinephrine), followed by **phosphoglucomutase** (saves 1 ATP)
    - In <u>liver</u>, **phosphorylase** (activated by glucagon) followed by **glucose-6-phosphatase** (allows glucose to enter the blood)



GLYCOLYSIS/GLYCOGENOLYSIS

- Originally referred to as the **Embden-Meyerhof pathway**
- Exists both as anaerobic and aerobic pathways
- **Purpose**: re-synthesize ATP

Glycolysis: pathway start at glucose

Glycogenolysis: pathway start at glycogen

Metabolic pathway yield: 4 substrate level ATP (gross)
reducing equivalents (2 NADH + H+)
pyruvic acid (and lactic acid)

Metabolic pathway cost:
1 ATP (from muscle glycogen) 2 ATP (from muscle glucose)

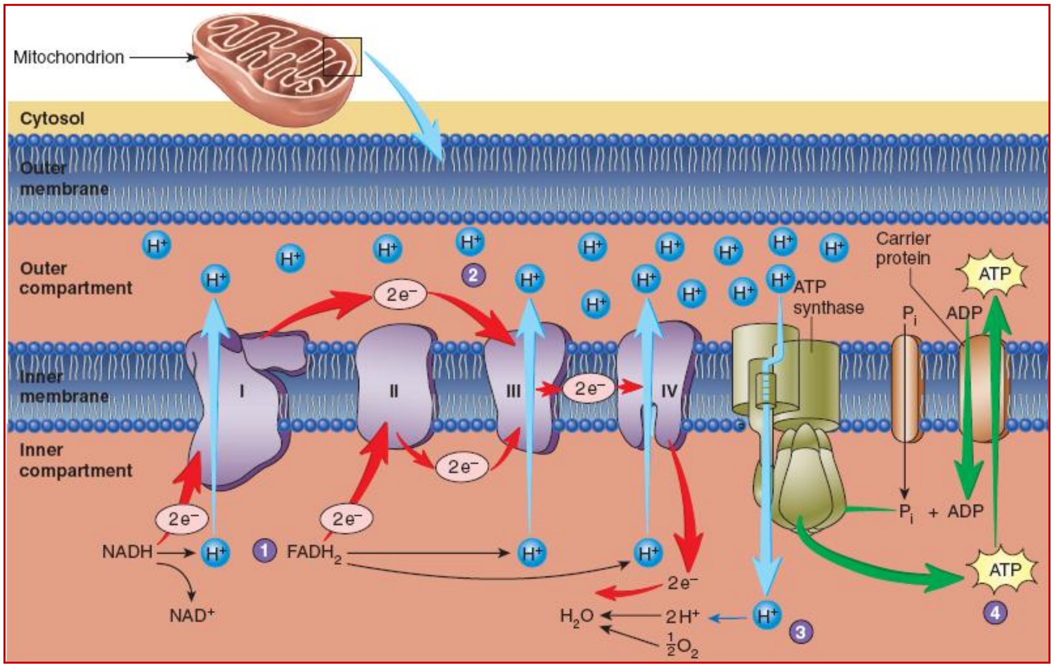
THE PATHWAY

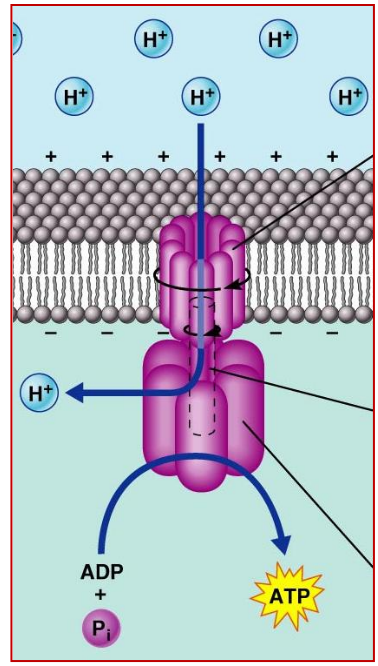
THE KREB'S CYCLE (TCA or citric acid cycle)

Pathway yield: 1 ATP, 2 CO_2, 3 NADH + H+, 1 $FADH_2$
- add in one more NADH + H+, for pyruvate conversion

Pathway cost: pyruvate

OXIDATIVE PHOSPHORYLATION

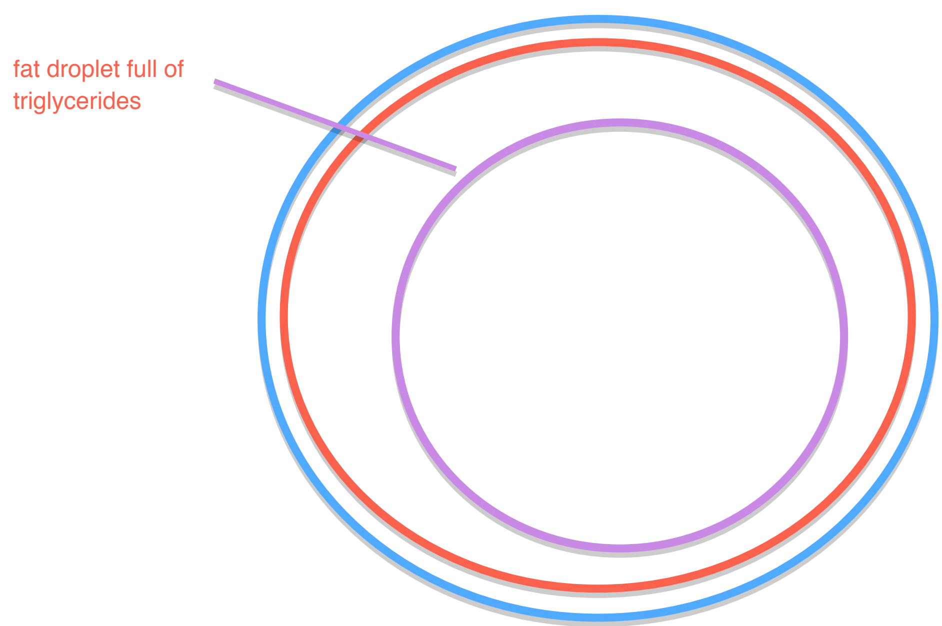




COST: reducing equivalents (NADH + H+ and FADH2), O2

YIELD: 2 ATP per FADH2 and 3 ATP per NADH+ H+

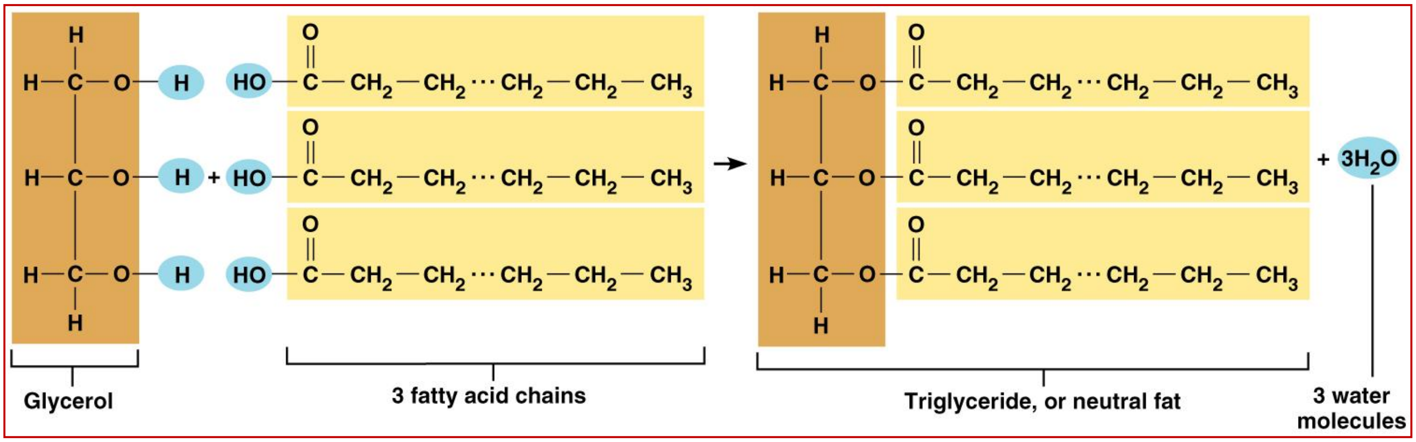
How much ATP do we get from one glucose molecule?



1. Mobilization
- enymes have to break it up
to allow it in the cardiovascular system
2. Activation - fatty acid must be activated takes place on the surface of the mitochondria
3. B-oxidation - surface and inside the mitochondria

FAT AS AN ENERGY SUBSTRATE

What is an adipocyte?



4 roles:

1) Building block of phospholipids and glycolipids
   two important components of all cell membranes

fat is used as an important fuel source

2) Protein modification by attaching to fatty acids

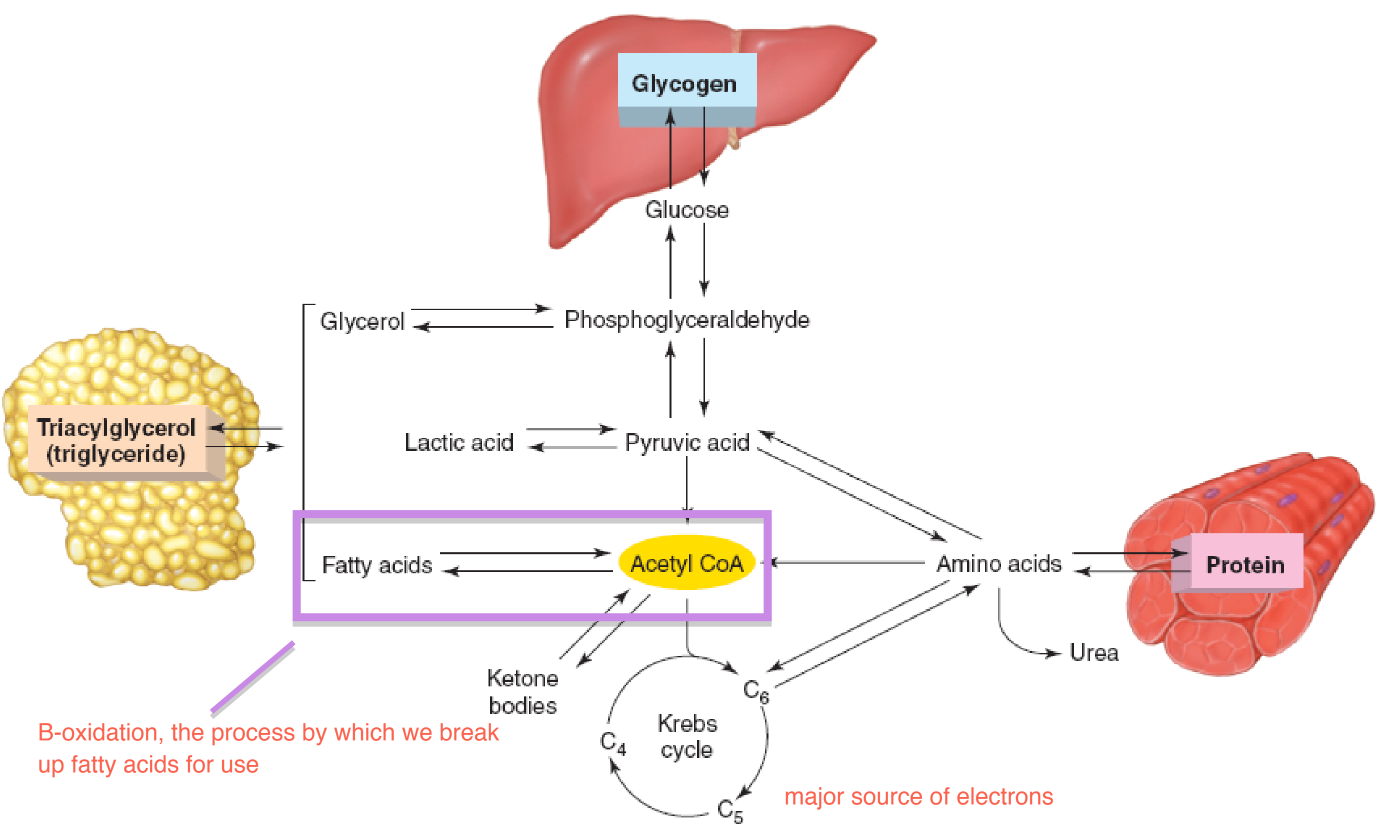
3) Fuel

4) Derivatives serve as hormones and intracellular messengers

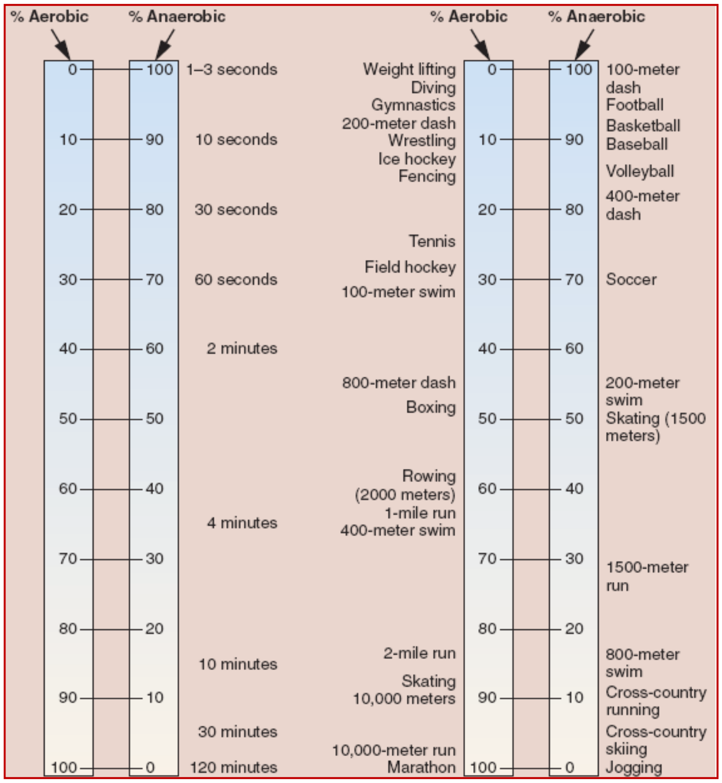
PROTEIN AS AN ENERGY SUBSTRATE

1. Amino acids (20 in total) are assembled in various combinations in 4 levels of structures (primary, secondary, tertiary, quartenary)
2. Gluconeogenesis
3. Conversion to metabolic intermediates

OVERALL SUBSTRATE UTILIZATION



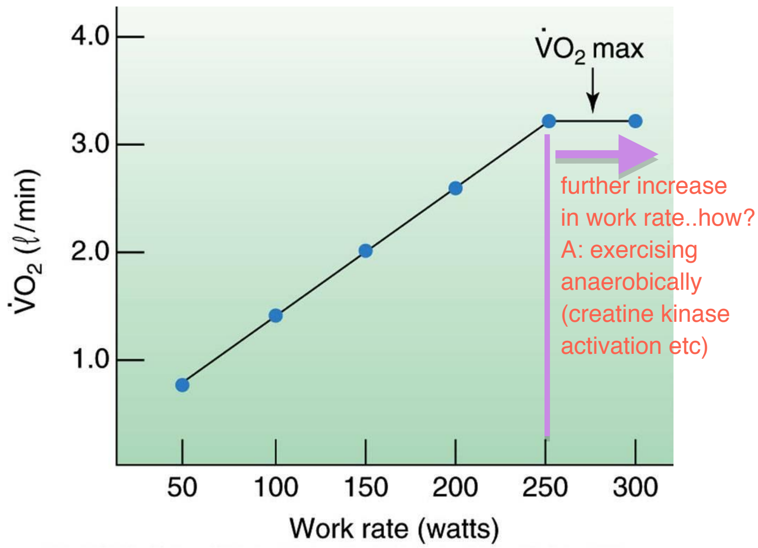
ENERGY EXPENDITURE



Incremental exercise

Oxygen uptake increases linearly until maximal oxygen uptake (VO_2 max) is reached

No further increase in VO_2 with increasing work rate



VO_2 max

- "Physiological ceiling" for delivery of O_2 to muscle
- Affected by genetics and training
- How is it quantified?

Physiological factors influencing VO_2 max

- Maximum ability of cardiorespiratory system to deliver oxygen to the muscle
- Ability of muscles to use oxygen and produce ATP aerobically

Glycolysis - how much ATP?

1. glucose ----> 2 pyruvate

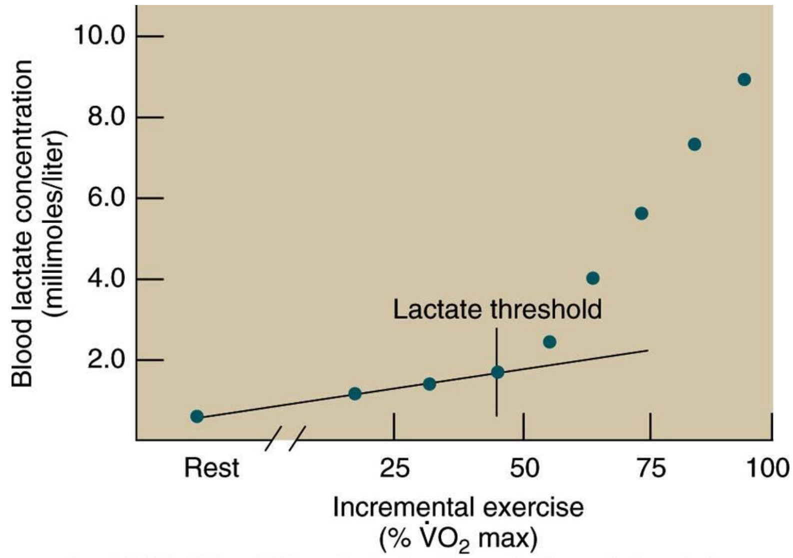
   2 lactic acids

   4 ATP

2. glucose --> 2 pyruvate ---> Acetyl CoA

   32 ATP

Lactate threshold



Abrupt (non-linear) increase in blood lactate

Reasons for the lactate threshold:

- Low muscle oxygen (hypoxia)
- Accelerated glycolysis
- NADH produced faster than it is shuttled into mitochondria
- Excess NADH in cytoplasm converts pyruvic acid to lactic acid
- LDH isozyme in fast fibers promotes lactic acid formation
- Reduced rate of lactate removal from the blood

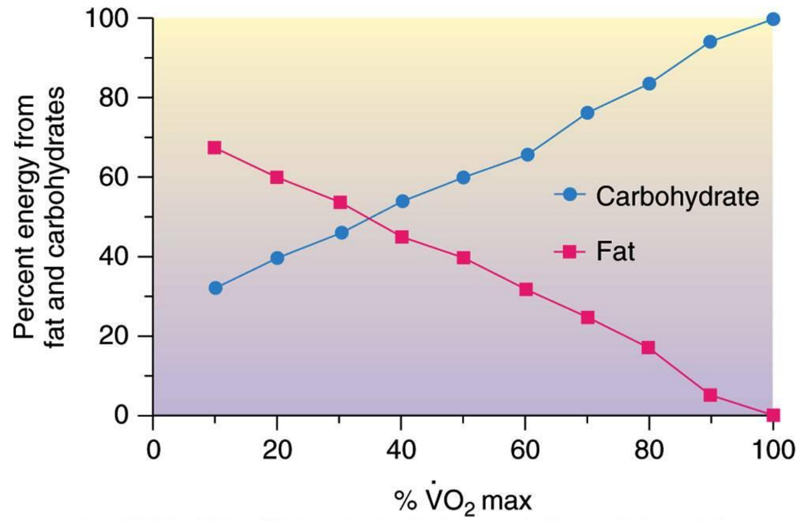
Exercise and fuel selection

Incremental exercise

Low-intensity exercise (<30% VO_2 max)

High-intensity exercise (>70% VO_2 max)

"Crossover" concept



Due to:

Prolonged, low-intensity exercise

- Shift from carbohydrate metabolism toward fat metabolism

Due to an increased rate of lipolysis