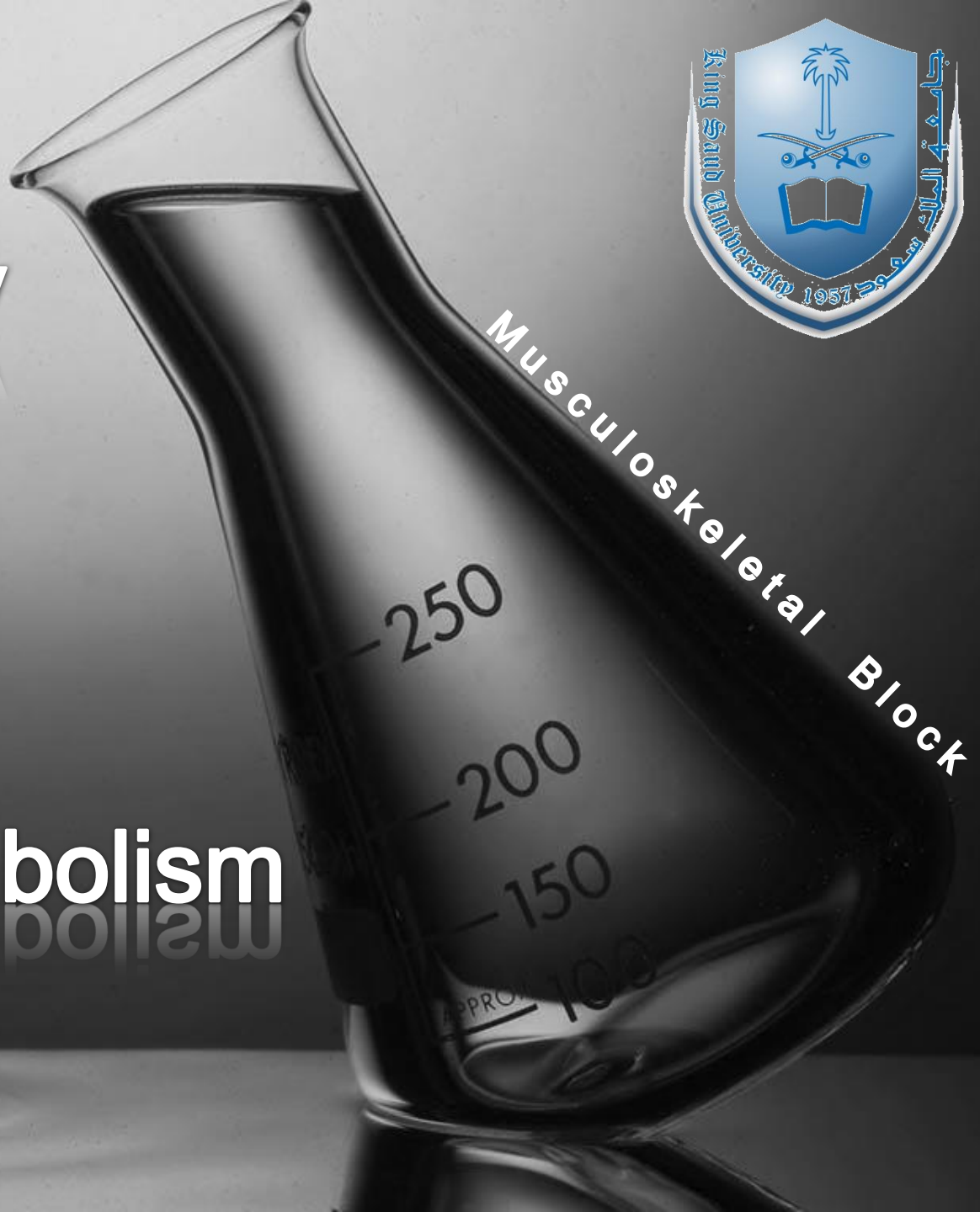


# Biochemistry Team

## Creatine Metabolism



Musculoskeletal Block



# **Objectives**

- 1. To study the importance of creatine in muscle as a storage form of energy**
- 2. To understand the biosynthesis of creatine**
- 3. To study the process of creatine degradation and formation of creatinine as an end product**
- 4. To understand the clinical importance of creatinine as a sensitive indicator of kidney function**
- 5. To study different types of creatine kinase (CK) and their clinical importance**

# Creatine Metabolism

Arginine gives an amino group (called guanidino group < not important) to glycine to form Guanidinoacetate. And then Arginine comes out as Ornithine.

ornithine

Amidino-  
transferaase

GuanidinoAcetate

SAM gives a methyl group and comes out as SAH

Methyl-transferase

creatine

Note :To form creatine we need 2 enzymes , Amino-transferaase and Methyl-transferase

Note : SAM= S-adenosylmethionine  
SAH= S-adenosylhomocysteine

the reason we call creatine phosphate an energy source: the energy source gives the phosphate group to ADP and forms energy ATP

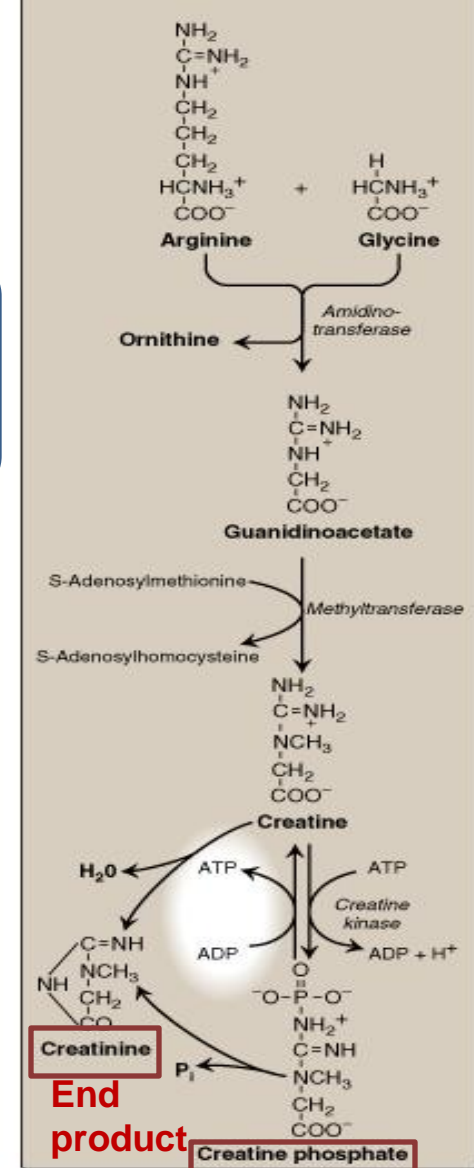


Figure 21.16 Energy Source  
Synthesis of creatine.

## Extra slide for your understanding 😊

\* Creatine Phosphate initiates the source of energy. It's not energy itself

-when we undergo physical activity we first use up the ATP that we previously have synthesized in the body. but it is not enough so our bodies start breaking down glycogen to give glucose and go into glycolysis. This takes too long so our body uses Creatine Phosphate as a rapid source of energy while glycogen is being broken down to glucose and get ATP from glycolysis.

\* In other words Creatine Phosphate fills in the gap between ATP instant usage and glycolysis to give a constant supply of energy.

# Creatine Metabolism

To make Creatine Phosphate from creatine → ATP is consumed to ADP. and to make creatine from creatine phosphate → ATP is formed from ADP.

Creatine



Creatine-kinase

Creatine phosphate

Note : although ATP here is consumed . creatine phosphate in the storage form will get high energy ,to be used in case of need

Creatine Kinase is a reversible enzyme that can change Creatine phosphate back to creatine (this is called dephosphorylation to give ATP) depending on the cells needs and the concentration gradient.

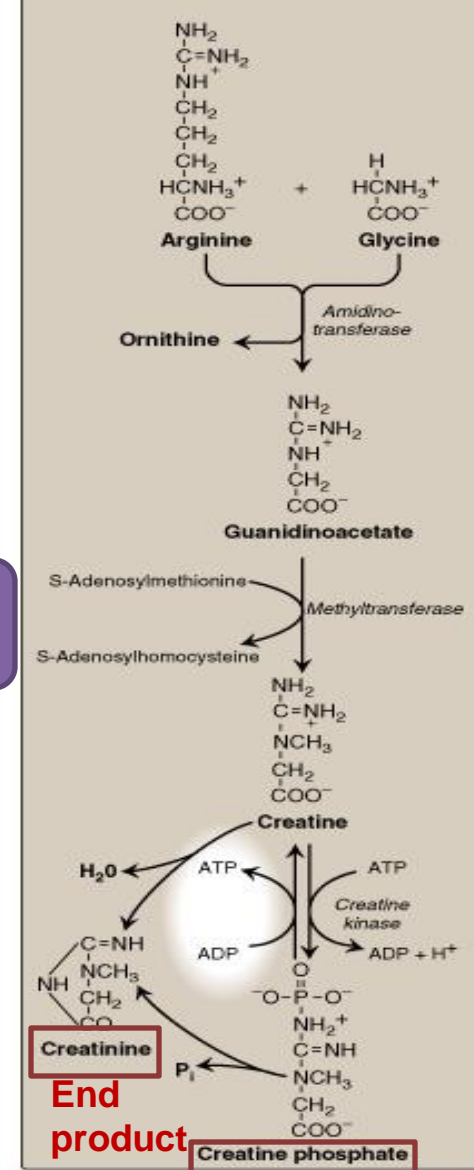
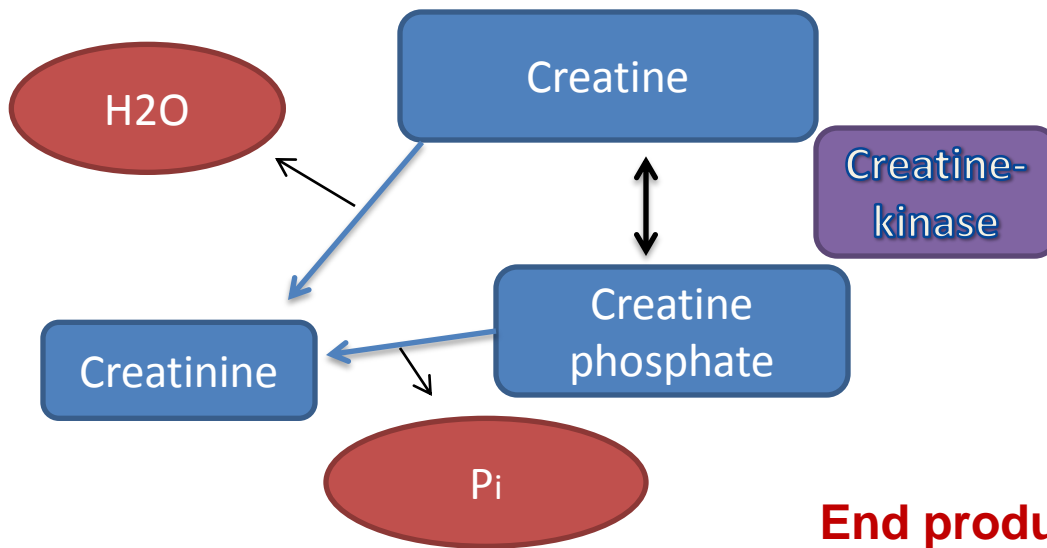


Figure 21.16 Energy Source  
Synthesis of creatine.

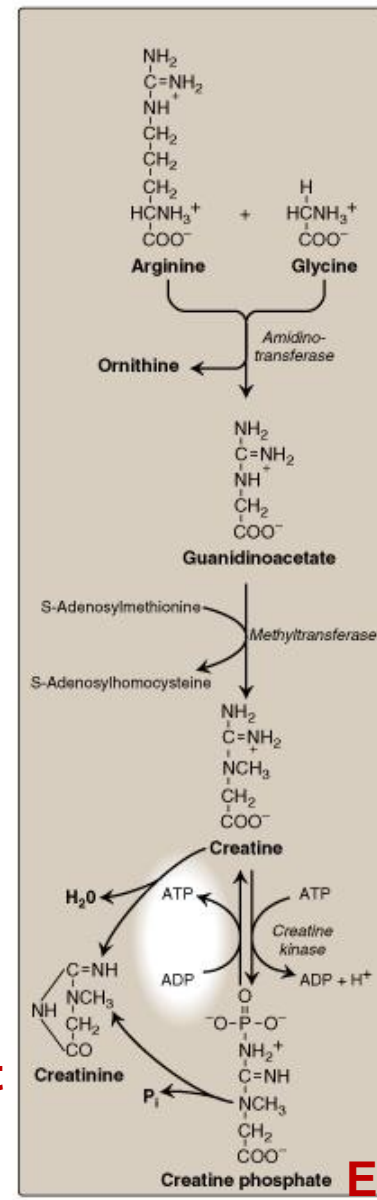
# Creatine Metabolism

You have to know that , creatinine is the end product whether from creatine or creatine-phosphate and the storage form is creatine-phosphate **which is the source of energy**



Note: No enzymes or energy are needed in phase of Creatinine synthesis ( End Product )

End product



Energy Source

Figure 21.16  
Synthesis of creatine.

# Creatine Biosynthesis

Three amino acids are required: **IMPORTANT**

**Glycine**

**Arginine**

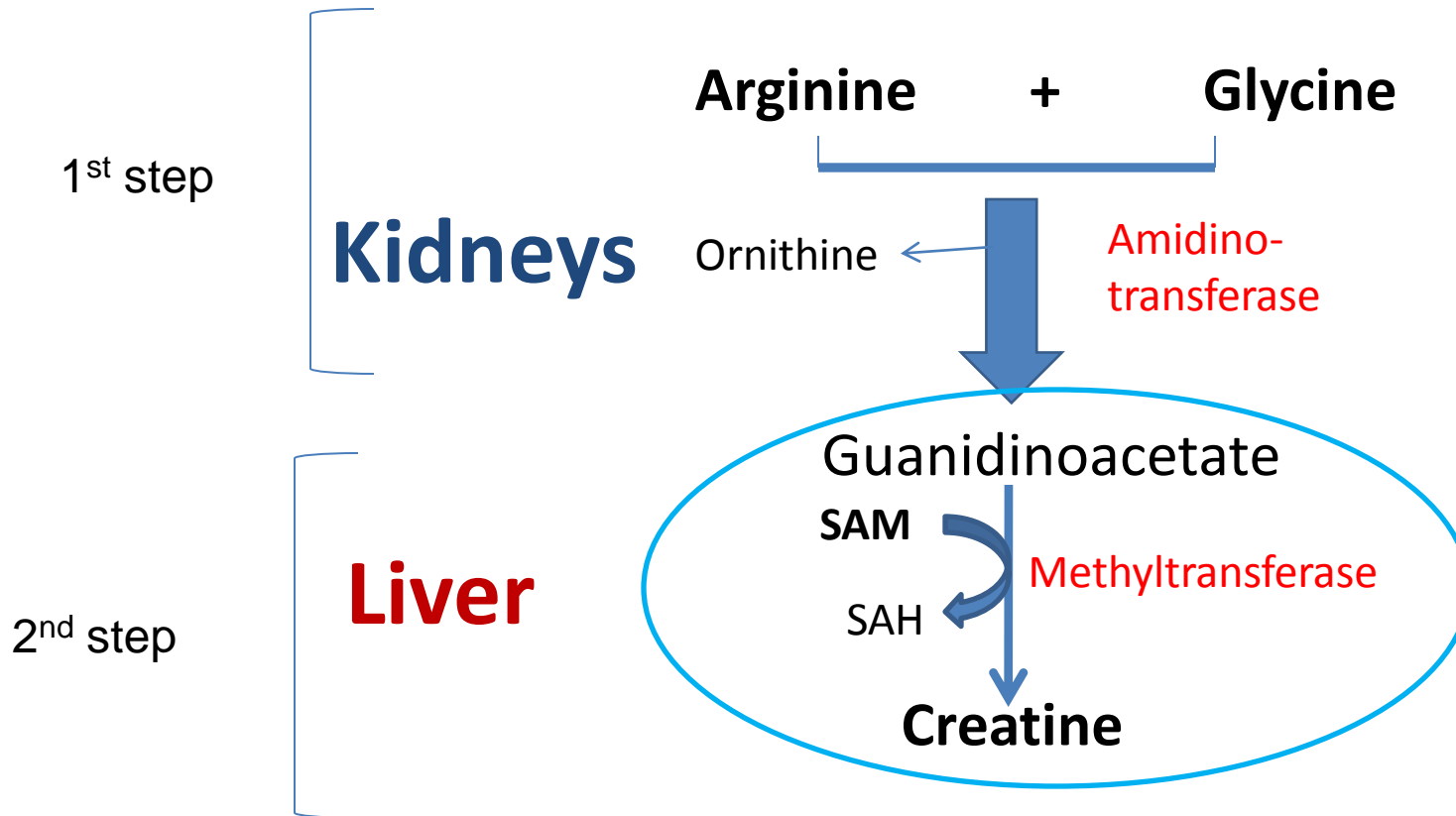
**Methionine (as S-adenosylmethionine)**

**Site of biosynthesis:** (Of Creatine –not creatine phosphate)

**Step 1: Kidneys**

**Step 2: Liver**

# Creatine Biosynthesis

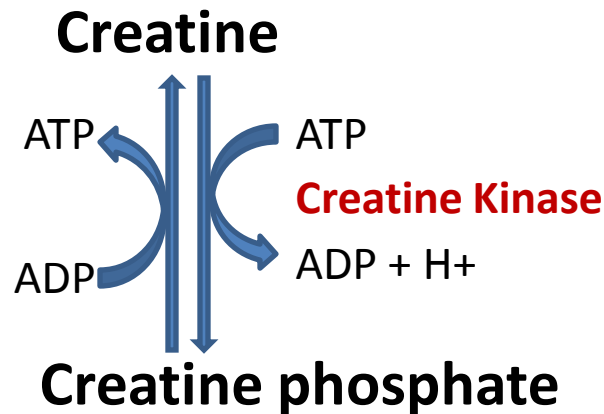


Note :Creatine is made in the liver then it is transferred to the muscle to transform into Creatine Phosphate



# Distribution of body creatine

- From liver, transported to other tissues
- **98% are present in skeletal and heart muscles**
- In Muscle, gets converted to the high energy source **creatine phosphate (phosphocreatine)**



# Creatine Phosphate

- Is a high-energy phosphate compound
- Acts as a storage form of energy in the muscle
- Provides a small but, ready source of energy during first few minutes of intense muscular contraction

**The amount of creatine phosphate in the body is proportional to the muscle mass**

# Creatine Degradation

1. Creatine and creatine phosphate spontaneously form **creatinine** as an **end product**
2. Creatinine is excreted in the urine
3. Serum creatinine is a sensitive indicator of kidney disease (Kidney function test)
4. Serum creatinine **increases** with the impairment of kidney function

because creatinine normally should be excreted in the urine and not get reabsorbed back

1

When should **creatine form creatinine** ?

**If the level** of creatine is high and not needed

2

what does **spontaneous form** mean in biochemistry ? مهم

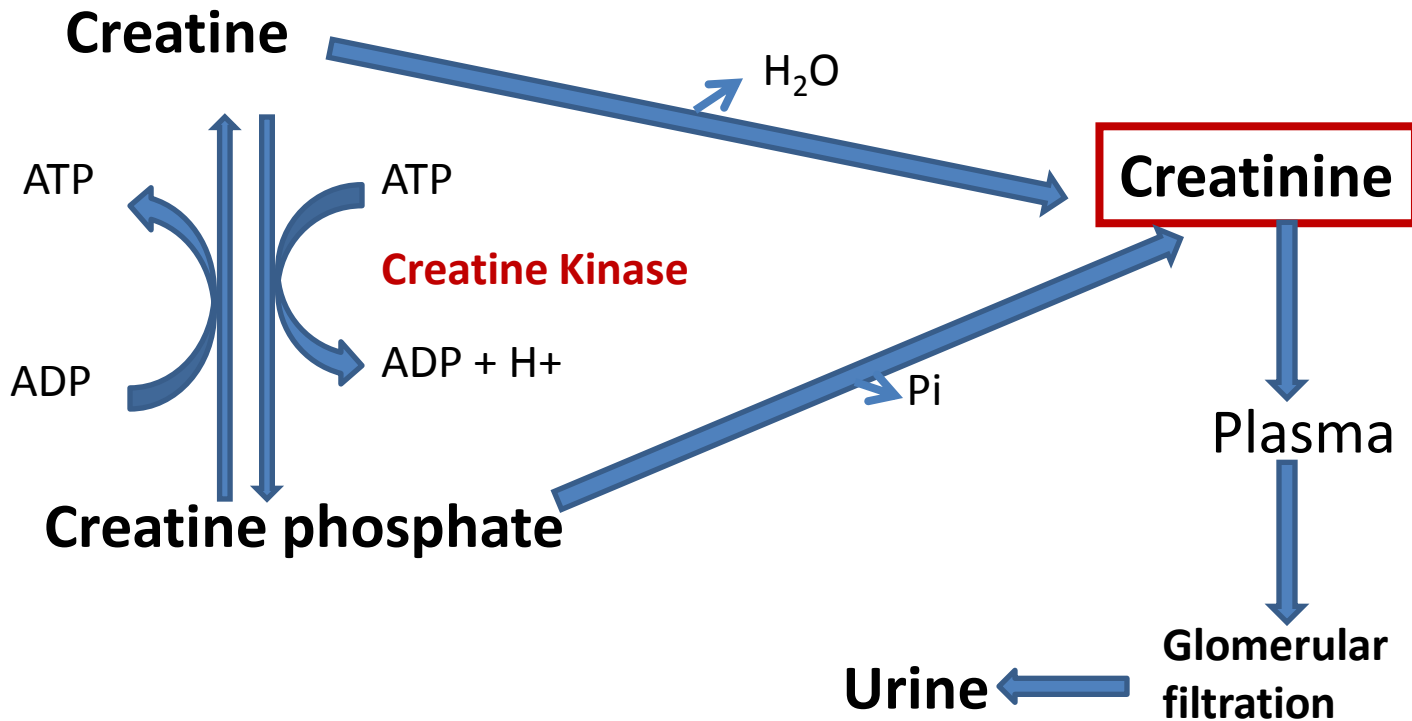
It means a **non-enzymitic reaction** , so Creatine and Creatine phosphate will form **Creatinine without use of enzymes or energy**

3

What is the difference between creatine phosphate and glucose ?

**Creatine phosphate** has a short pathway , so it produces fast energy

# Creatine Degradation



# Urinary Creatinine

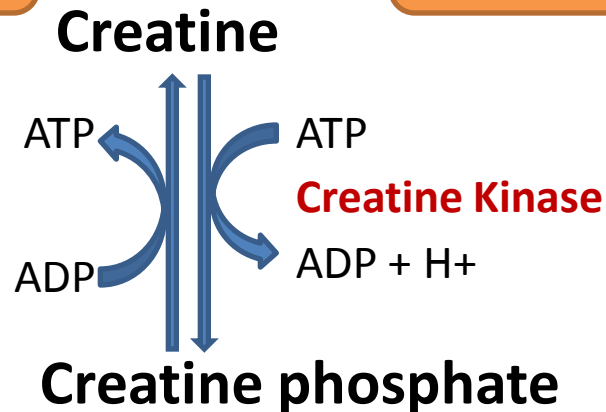
- A typical male excretes about 15 mmol of creatinine per day (women excrete a slightly smaller amount because of the decreased muscle content and size)
- A decrease in muscle mass due to muscular dystrophy or paralysis leads to decreased level of creatinine in urine
- The amount of creatinine in urine is used as an indicator for the proper collection of 24 hours urine sample

# Creatine Kinase (CK)

- CK is responsible for the generation of energy in contractile muscular tissues
- CK levels are changed in disorders of cardiac and skeletal muscle

It is used as a biochemical marker

Kinase: enzyme that phosphorylates (adds phosphate)



# Creatine Kinase (CK)

1. **CK** is required for conversion of creatine into creatine phosphate

2. **CK** has 3 **isoenzymes**:

Isoenzymes have the same function but different structures

**CK-MM**      mainly in skeletal muscle

**CK-MB**      mainly in heart muscle

**CK-BB**      mainly in brain

3. Serum total **CK** is increased in:

**Crush injuries (Damage of skeletal muscles)**

**Myocardial infarction (Damage of heart muscle)**

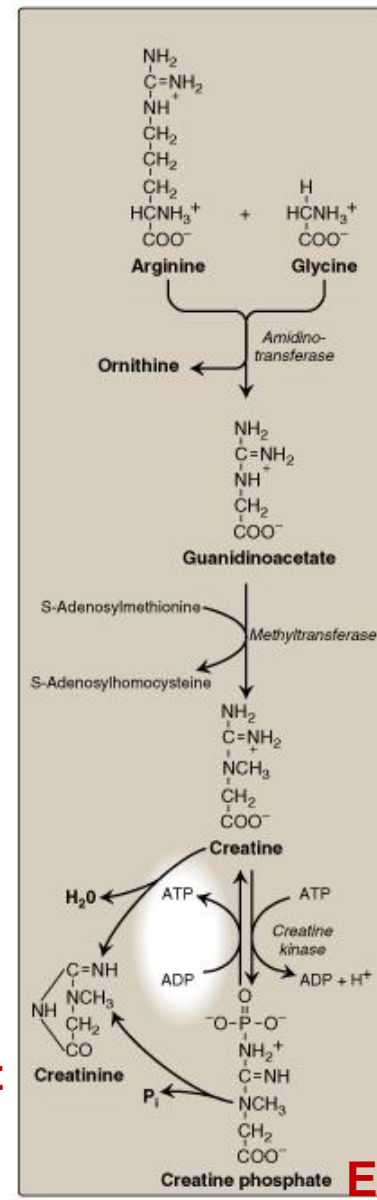


# Creatine Metabolism

## For your information

we get creatine from eating meat.  
Plants don't have any creatine. This  
means vegetarians have lower levels of  
creatinine in their system

A placebo-controlled double-blind experiment found that a group of subjects composed of vegetarians and vegans who took 5 grams of creatine per day for six weeks showed a significant improvement on two separate tests of **fluid intelligence**, **Raven's Progressive Matrices**, and the backward digit span test from the **WAIS**. The treatment group was able to repeat longer sequences of numbers from memory and had higher overall **IQ** scores than the control group. The researchers concluded that "supplementation with creatine significantly increased intelligence compared with placebo



End product

Energy Source

Figure 21.16  
Synthesis of creatine.

# References

- Lippincott, page 287-288
- Bishop 6<sup>th</sup> edition, page 223-227

Dr.Sumbul said we should know this :D

# Creatinine in urine and plasma

- Normal serum creatinine level is 0.7 to 1.4 mg/dl and serum creatine level is 0.2 to 0.4mg/dl
- The amount of creatinine excreted is proportional to the total creatine phosphate content of the body
  - **therefore can be used to estimate muscle mass**
- Serum creatinine is a sensitive indicator of kidney disease (Kidney function test)
  - **Because normally creatinine is rapidly removed from the blood and excreted**
- The amount of creatinine in urine is used as an indicator for the proper collection of 24 hours urine sample (normal urinary output is 15-25 mg/kg/d)

/Kg means that these levels won't change for adults and children

Not included in the boys slides ... :D

# Review question

- Which of the following is correct
  - A-1<sup>st</sup> step of Creatine Biosynthesis takes place in kidney
  - B- 1st step of Creatine Biosynthesis takes place in liver
  - C-2nd step of Creatine Biosynthesis takes place in kidney
  - d- none above



A

# Review question

- If the Serum total CK is increased ,which disease is the most likely cause ?
  - a-kidney disease
  - b-Myocardial infarction
  - c- liver disease
  - d- no effect

•  b

# Review question

- What the enzyme is used to form phosphate-Creatine from Creatine?
- A-Methyl-transferase
- B-Amino-transferase
- C- Creatine-kinase
- D- S-adenosylmethionine

C

# Review question

- Which of the following is not correct

A-CK is required for conversion of creatine into creatine phosphat

B- Methyltransferase is used to form creatine from GuanidineAcetate

C-creatinine Acts as a storage form of energy in the muscle

D-Creatine and creatine phosphate spontaneously form creatinine as an end product



C

# Review question

- To convert creatine to creatinine we need :

A- many enzymes

B-no enzymes needed

C- we only need Methyltransferase

D-none above



B