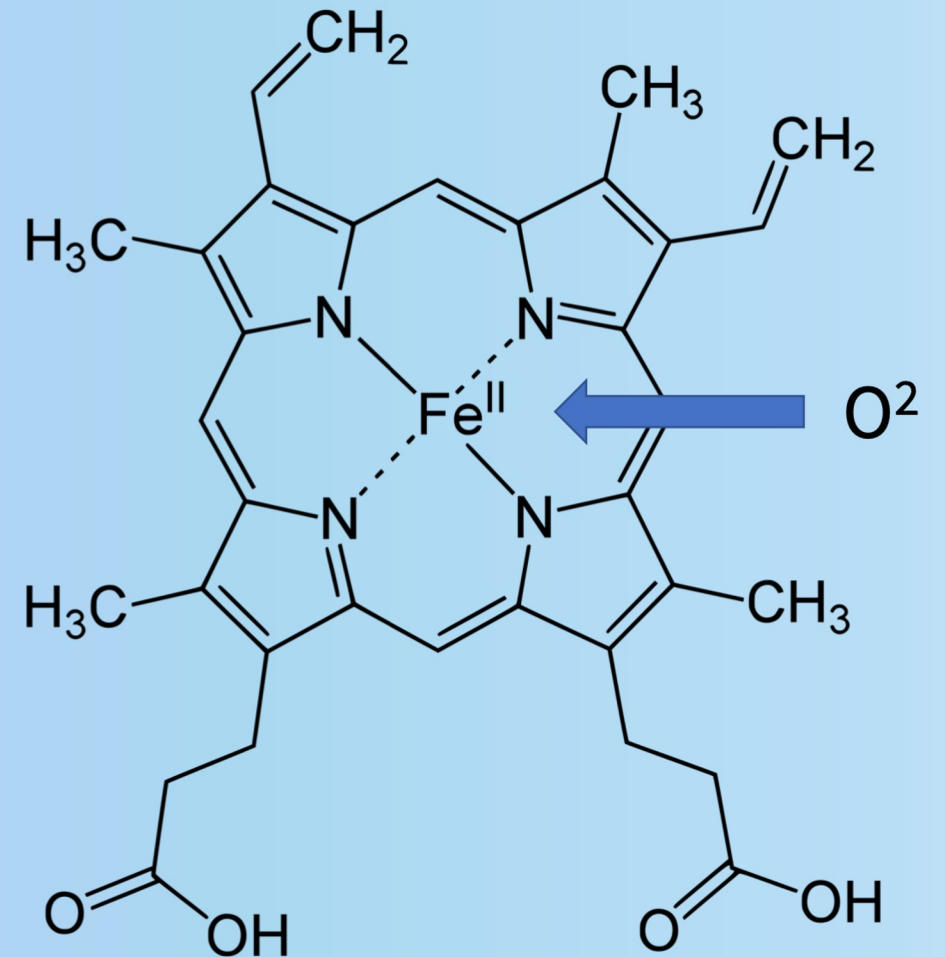


Heme Synthesis and Degradation

By Jacob Guzior

Plan for today:

- Synthesis pathway and enzymes
- Problems with synthesis
- Degradation pathway
- Problems with Degradation
- Other Nitrogen compounds

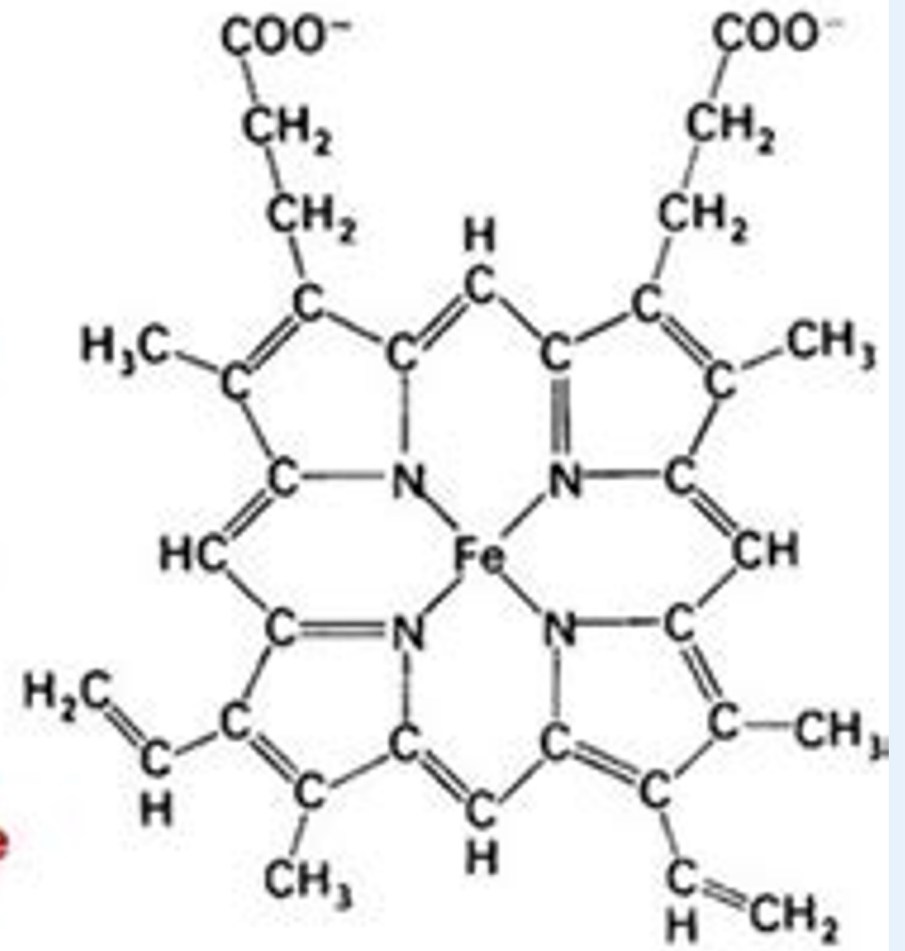


Polypeptide chain
 β chain

α chain

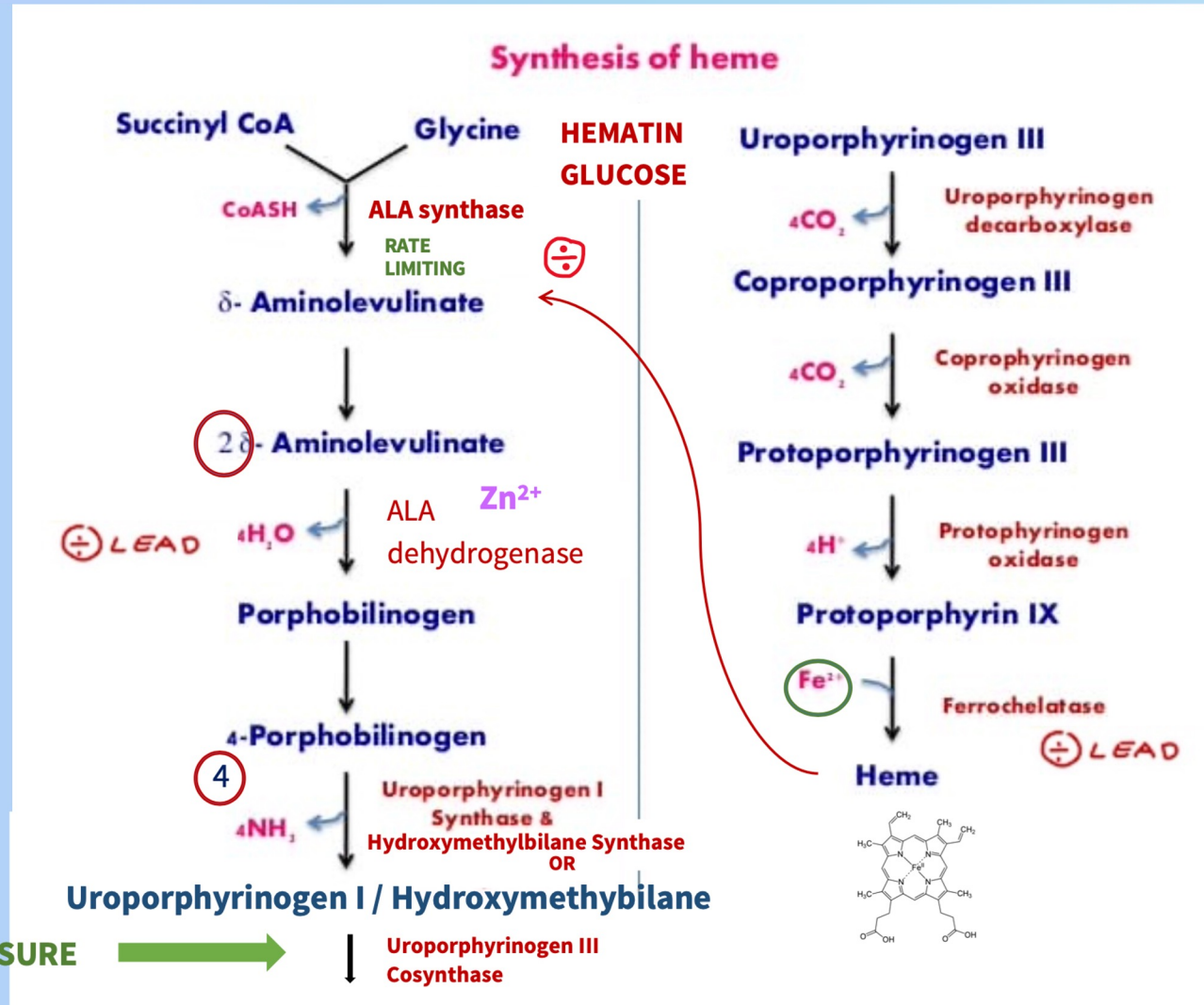
Iron **Fe**
Heme

Hemoglobin



Heme
(Fe-protoporphyrin IX)

Synthesis



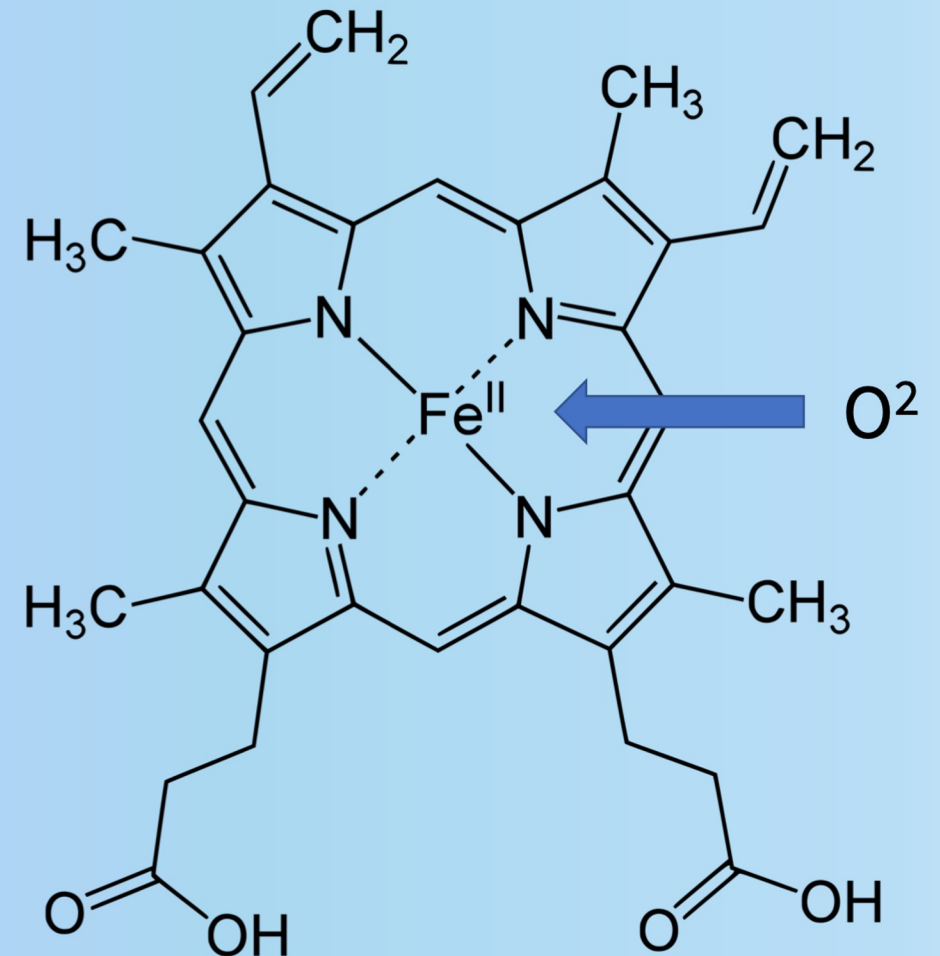
Where does synthesis occur?

-Liver and bone marrow

-Cytosol and mitochondria

Plan for today:

- ~~Synthesis pathway and enzymes~~
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Problems with heme synthesis

Anemias

- Lead poisoning
- ALA dehydrogenase • Ferrochelatase
- Iron deficiency
- Ferrochelatase
- Oxygen cannot bind heme

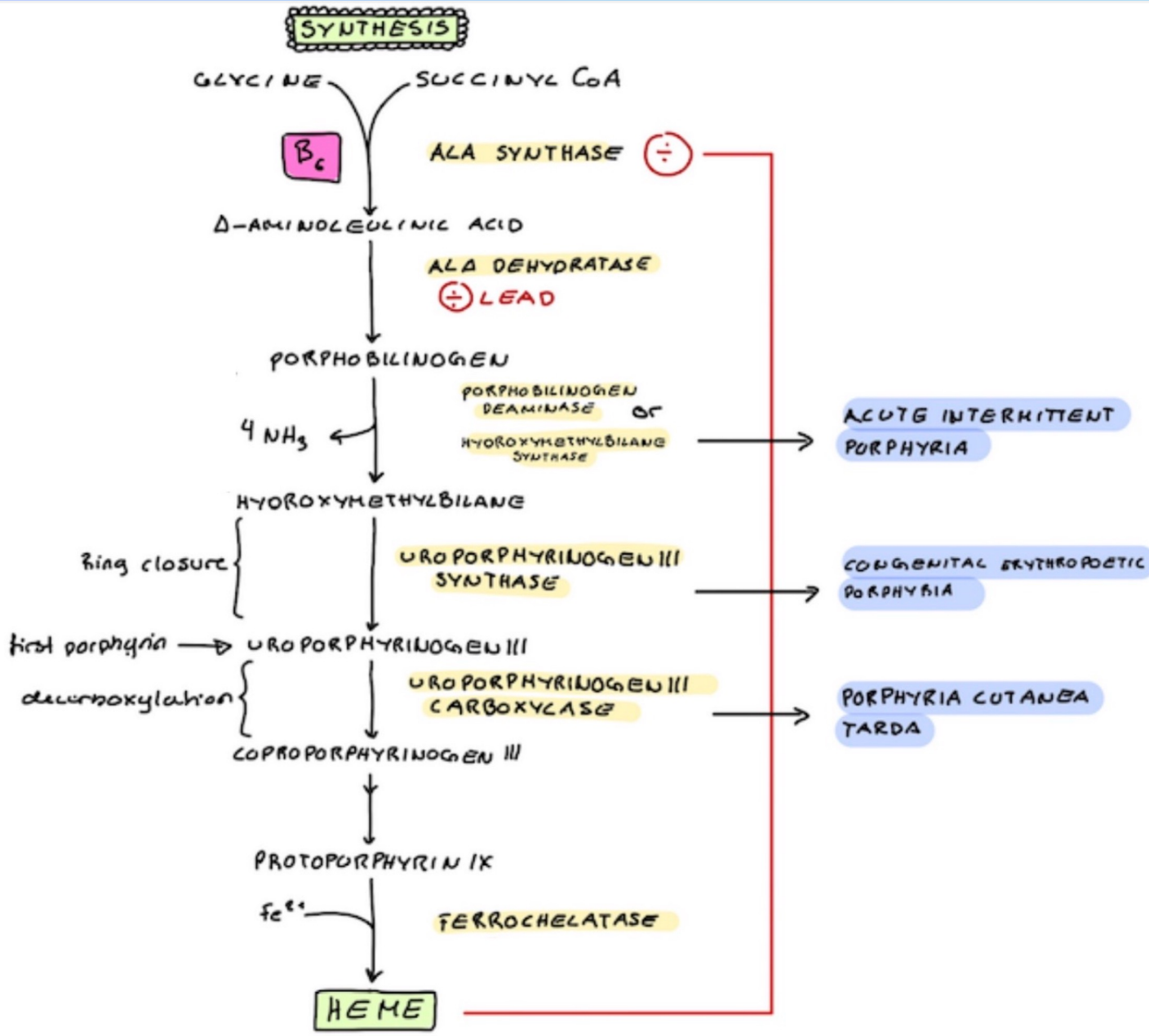
Porphyrias

Hepatic

- Drugs, alc, hormones, diet, infection
- Abd. pain + CNS

Erythropoietic

- Enzyme deficiency
- Cutaneous + photosensitivity



Acute intermittent porphyria

Congenital erythropoietic porphyria

Porphyria cutanea tarda

Acute intermittent porphyria (AIP)

- Deficiency of hydroxymethylbilane synthase (HMBS) -> Hepatic
- Triggers: **Diet, alcohol, drugs, infections, stress and hormonal changes**
- Women in puberty

- Symptoms:
 - Abdominal symptoms
 - CNS; seizures, hallucinations, confusion • Muscle pain and weakness
 - Heart palpitations
 - Tx: IV glucose - inhibits ALA synthase

Congenital erythropoietic porphyria (CEP)

- Deficiency of uroporphyrinogen III cosynthase (UROS)
- Photosensitivity of the skin
- Blisters, lesions and scarring of the skin
- Hands, feet and face
- Infancy
- Tx: Avoid sunlight



Porphyria Cutanea Tardea (PCT)

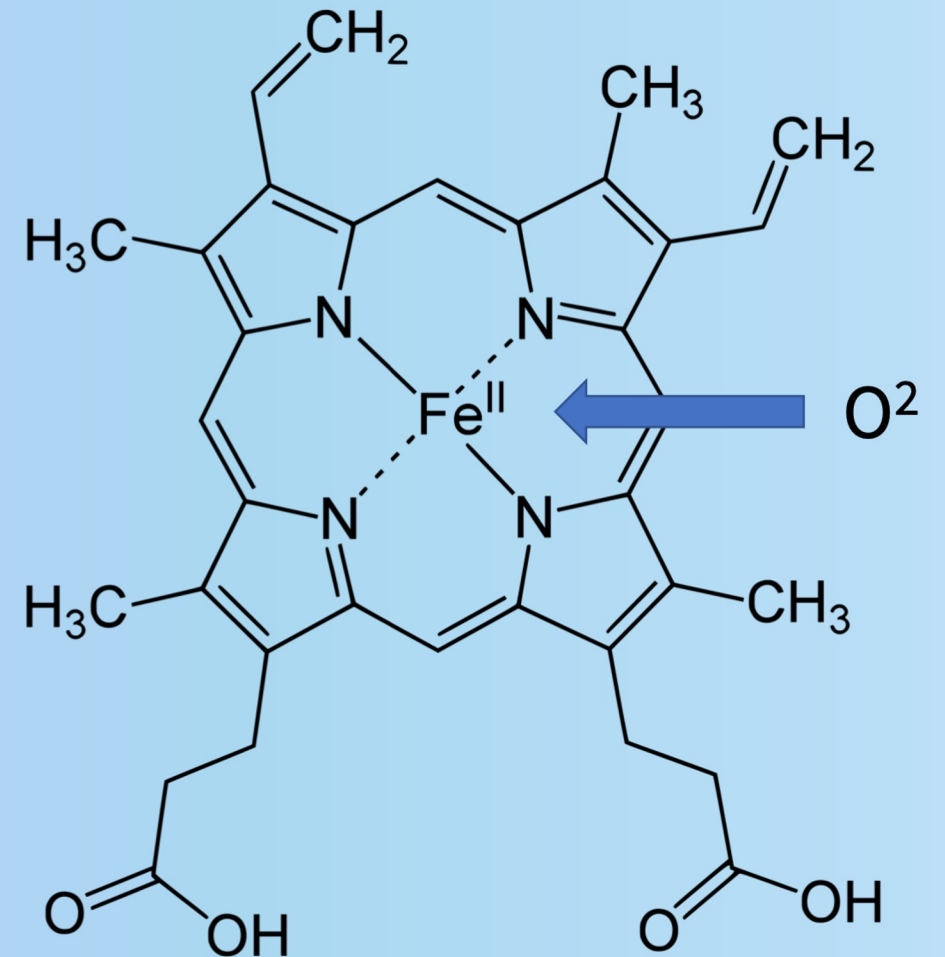
- Deficiency of uroporphyrinogen decarboxylase (UROD)
- Severe photosensitivity of the skin
- 1/3 – hereditary: early onset
- 2/3 – liver disease: late onset

- Women > 30 yo
- Tx: avoid sunlight



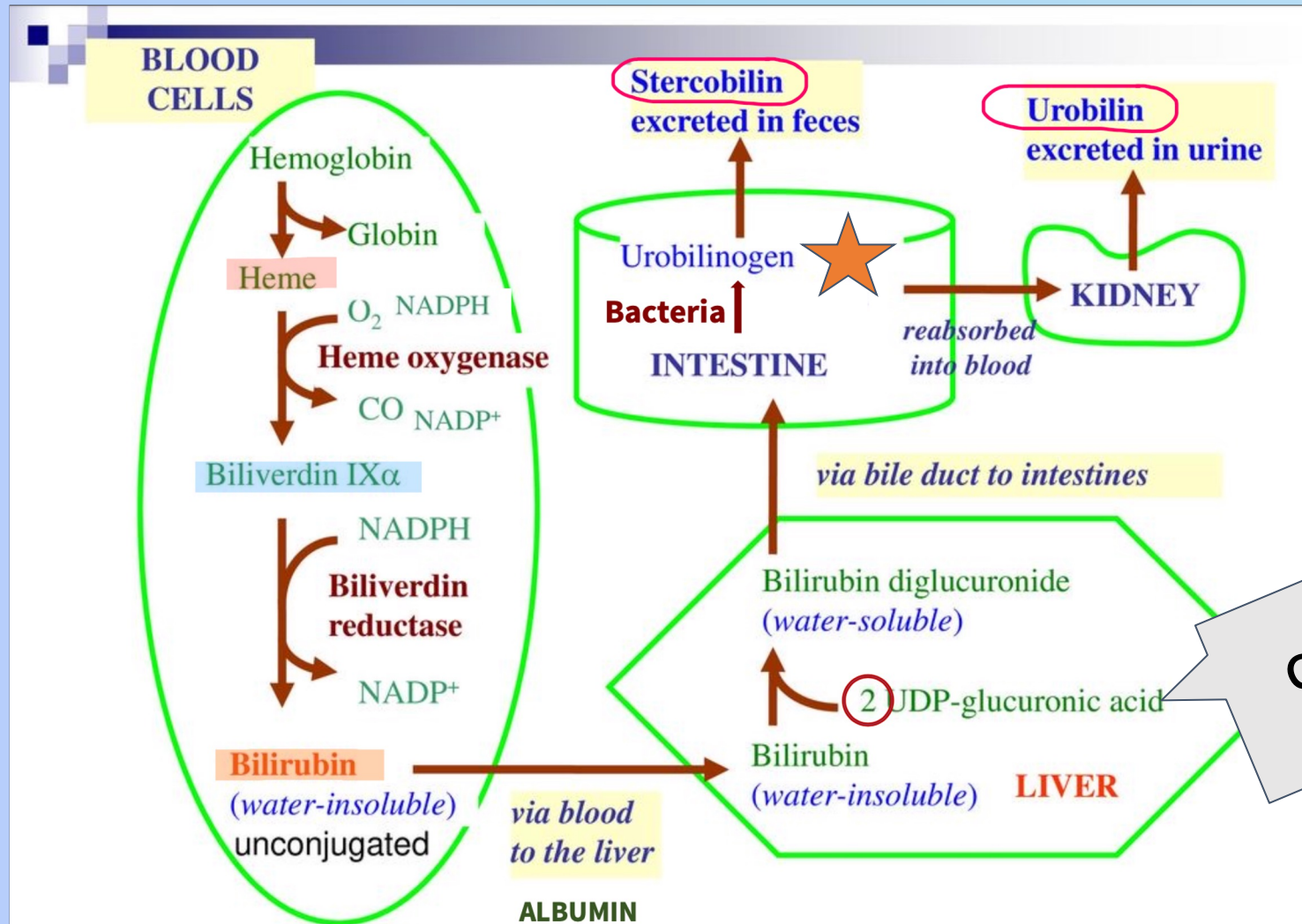
Plan for today:

- ~~Synthesis pathway and enzymes~~
- ~~Problems with synthesis~~
- Degradation pathway
- Problems with Degradation
- Other Nitrogen compounds



Degradation of Heme

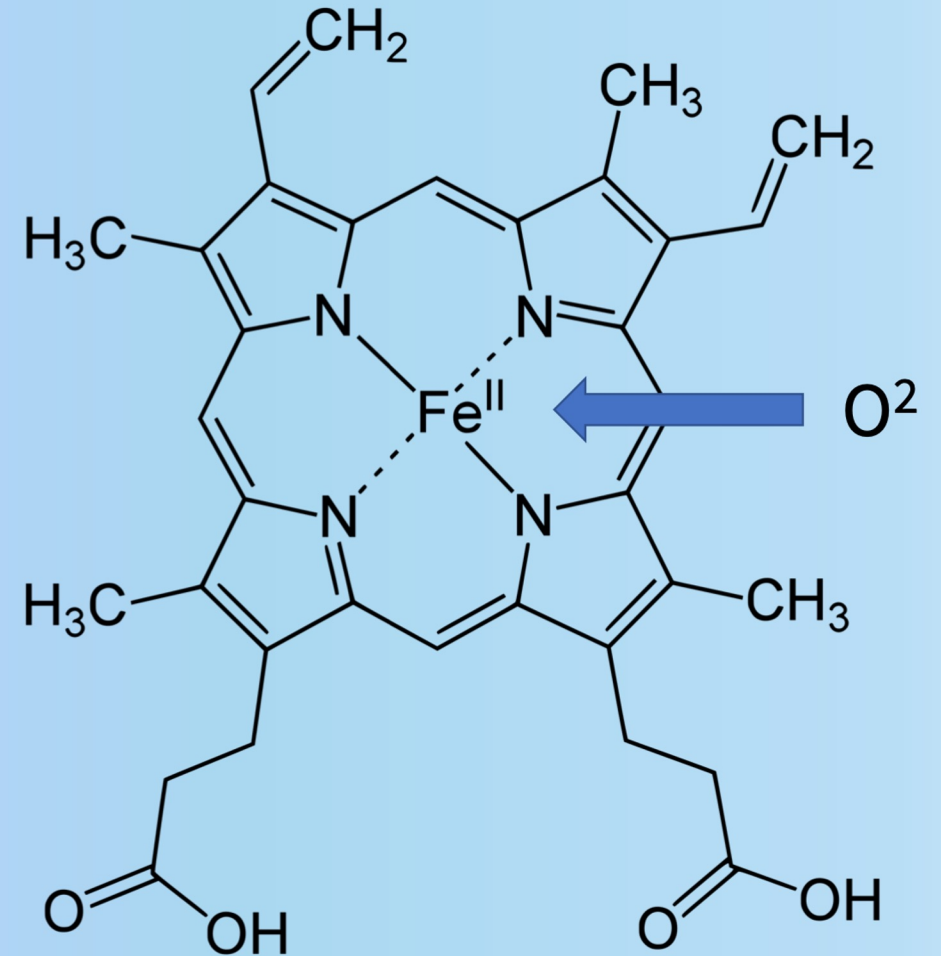
Stercobilin- Feces
Urobilin- Urine



Conjugation

Plan for today:

- ~~Synthesis pathway and enzymes~~
- ~~Problems with synthesis~~
- ~~Degradation pathway~~
- Problems with Degradation
- Other Nitrogen compounds



Problems with Heme Degradation

1. PRE-HEPATIC
2. HEPATIC
3. POST-HEPATIC

Jaundice

Jaundice = Icterus

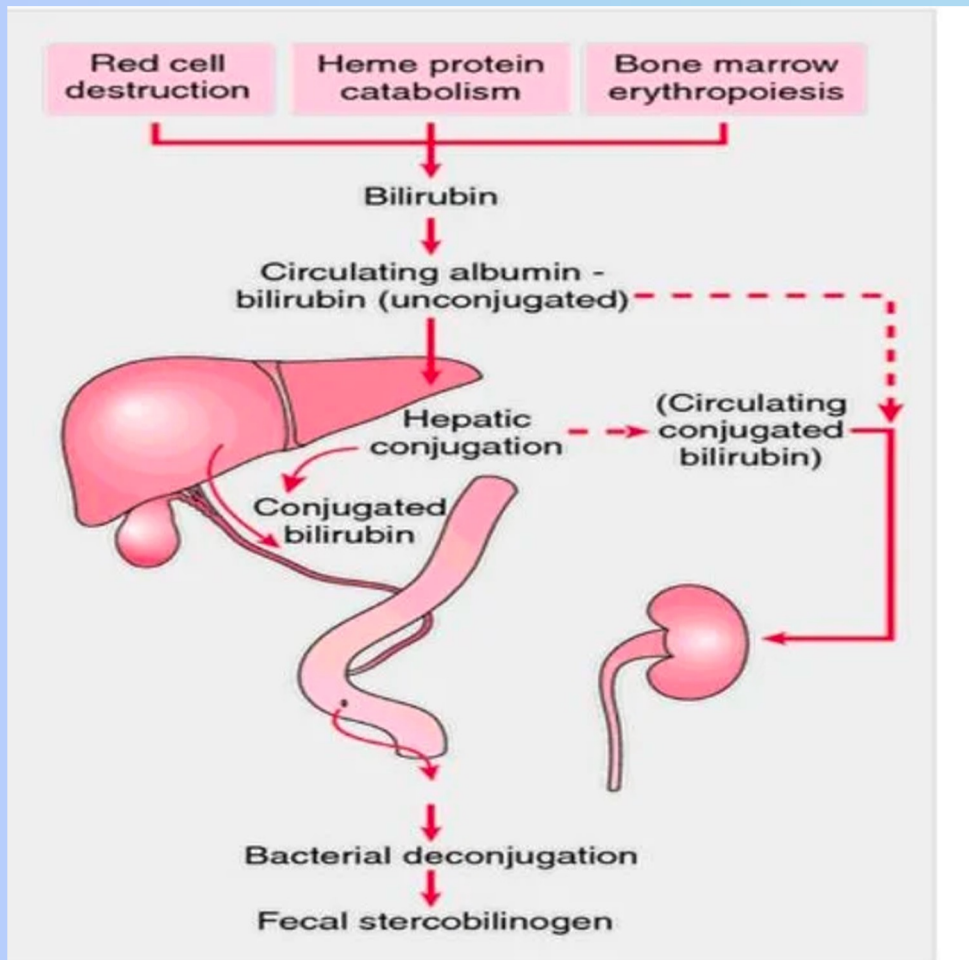
- Bilirubin > 3 mg/dL (normal < 1.3 mg/dL)
- Hyperbilirubinemia
- Neonatal jaundice

- Symptoms:
- Yellow discoloration
- Light colored stools
- Dark colored urine
- Itching of the skin





- 1. PRE-HEPATIC**
- 2. HEPATIC**
- 3. POST-HEPATIC**



PRE-HEPATIC

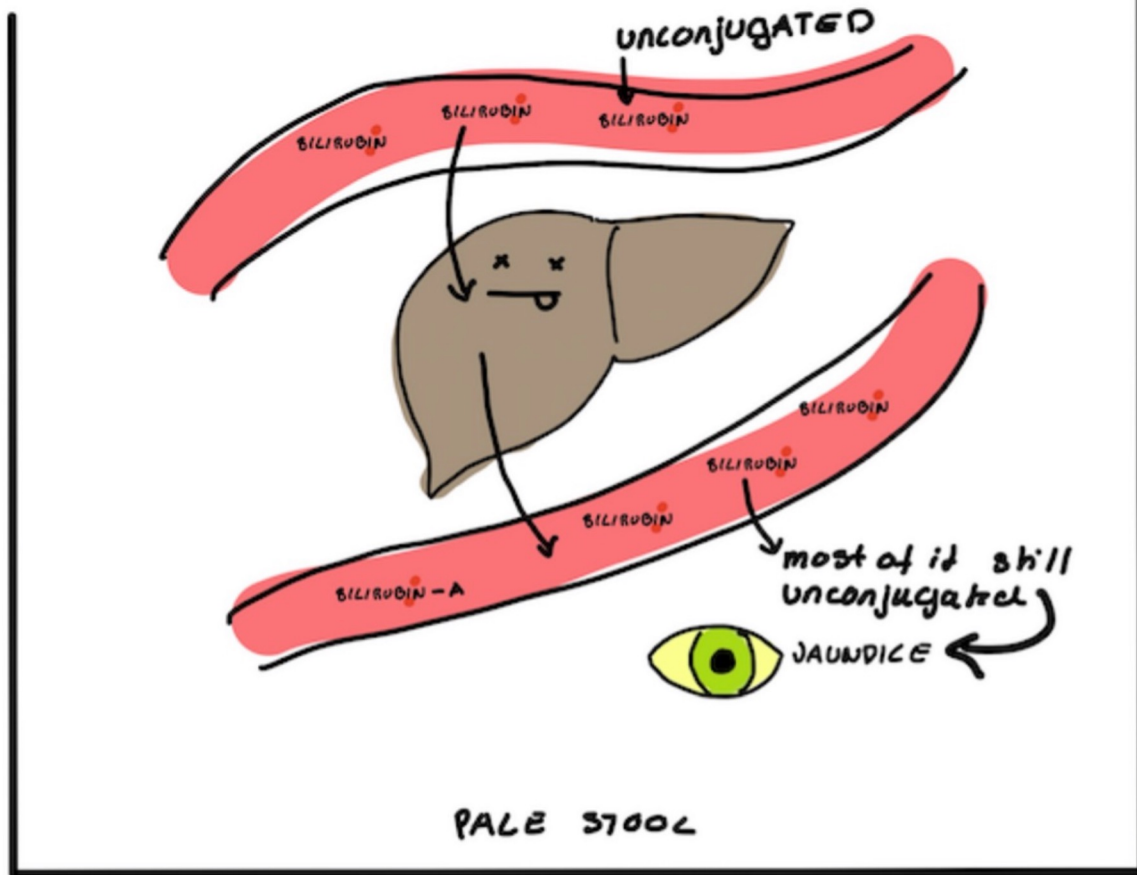
- ↑ Unconjugated bilirubin in serum
- ↑ Stercobilin in stool
- ↑ Urobilinogen in urine

-Normal color of urine and stool

Causes:

- Hemolytic anemia
 - Malaria
- Blood transfusion
- Hemolytic drugs
- Ineffective hematopoiesis

HEPATOCELLULAR JAUNDICE



Causes:

- Liver damage
- Crigler-Najjar syndrome
- Dubin-Johnson syndrome
- Gilbert syndrome

HEPATIC JAUNDICE



Unconjugated and conjugated bilirubin in the serum



Urobilinogen in the urine

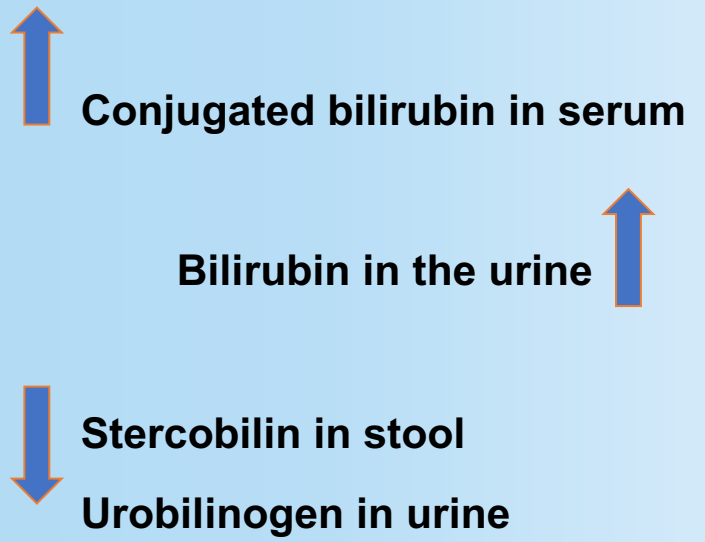
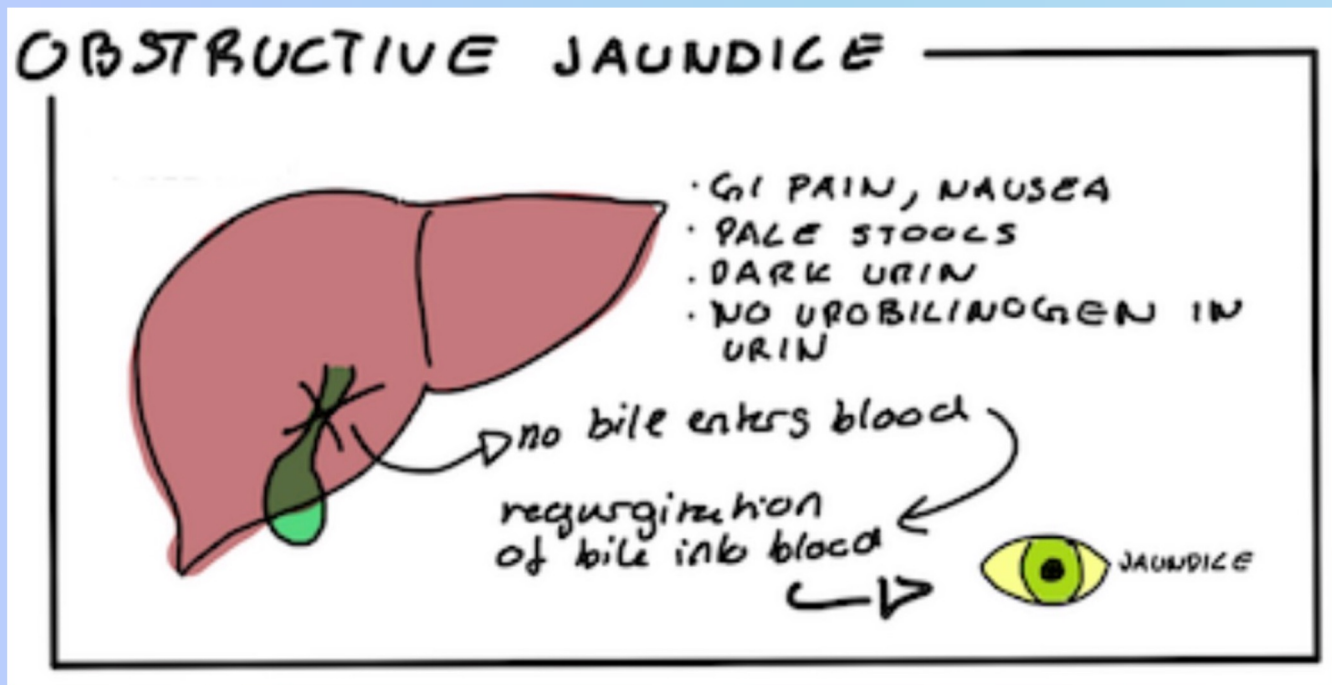
Stercobilin in stool

-Dark urine due to conjugated bilirubin in the urine

-Pale stool due to decreased stercobilin in stool



POST-HEPATIC / OBSTRUCTIVE JAUNDICE



Causes:

- Calculus Cholecystitis
- Acalculus Cholecystitis
- Carcinoma of head of Pancreas
- Pancreatic edema
- Hepatic swelling/fibrosis

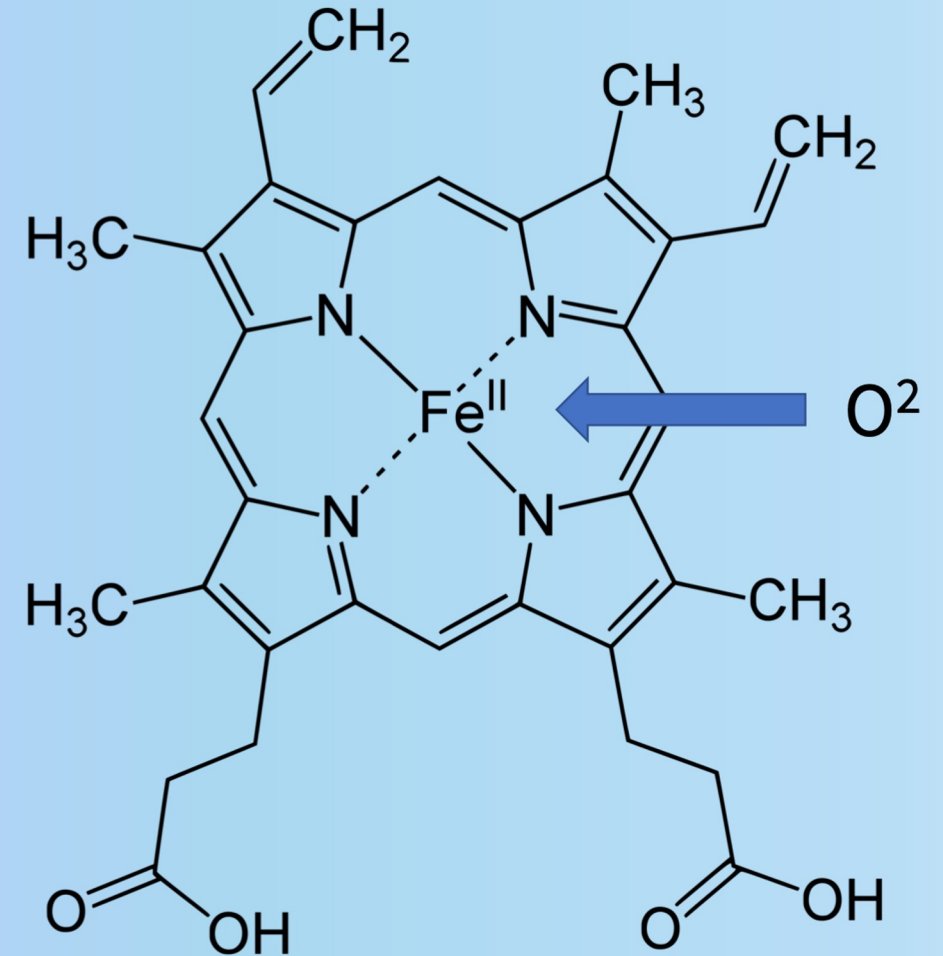
Dark urine due to increased conjugated bilirubin in the urine

Pale stool due to lack of stercobilin



Plan for today:

- ~~Synthesis pathway and enzymes~~
- ~~Problems with synthesis~~
- ~~Degradation pathway~~
- ~~Problems with Degradation~~
- Other Nitrogen compounds



Other Nitrogen Containing Compounds

Nitrates



Elemental nitrogen



Catecholamines

Function: CNS signalling

Synthesized from: Tyrosine

Degradation by: Monoamine oxidase (MAO)

Low Catecholamines: Parkinson's Disease

Dopamine



When ur happy the warm weather is finally here but the pollen count is 1 million



Relate-ability to the max.
(@tank.sinatra)

Histamines

Function: Inflammation and Allergic Response

Melanin

Function: Pigment to protect tissue from sun

Synthesis: Tyrosine

Serotonin

Function: CNS signalling, produced in gut
Synthesized from: Tyrosine



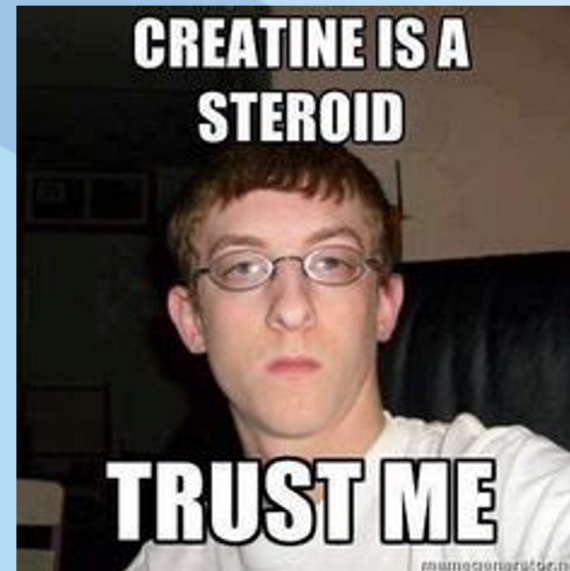
Creatine

Function: phosphorylated creatine provides high energy during muscle contraction

Synthesized from: glycine and the guanidino group of arginine, plus a methyl group from SAM

Degradation: spontaneously breaks down into creatinine and excreted through the urine

High blood creatinine means kidneys are not working



Wooclap!
-BSOPGO



