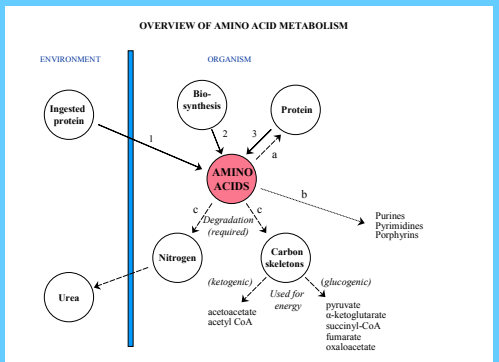
# Amino Acid Metabolism

Dr. Simmons




**Amino Acid Requirements of Humans**

| Nutritionally Essential | Nutritionally Nonessential |
|---|---|
| Arginine[a] | Alanine |
| Histidine | Asparagine |
| Isoleucine | Aspartate |
| Leucine | Cysteine |
| Lysine | Glutamate |
| Methionine | Glutamine |
| Phenylalanine | Glycine |
| Threonine | Proline |
| Tryptophan | Serine |
| Valine | Tyrosine |

[a] "Nutritionally semiessential." Synthesized at rates inadequate to support growth of children.

## NITROGEN BALANCE

Nitrogen balance = nitrogen ingested - nitrogen excreted
(primarily as protein) (primarily as urea)

Nitrogen balance = 0 (*nitrogen equilibrium)*
protein synthesis = protein degradation

Positive nitrogen balance
protein synthesis > protein degradation

Negative nitrogen balance
protein synthesis < protein degradation

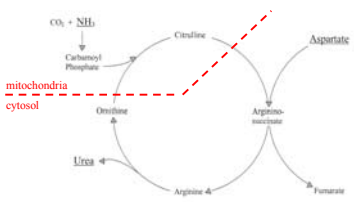
## TRANSAMINATION

**Family of Glutamate Transaminases**

| Transaminase | Reaction Catalyzed | | | | | |
|---|---|---|---|---|---|---|
| alanine | alanine | + | α-ketoglutarate | ⇌ | pyruvate | + **glutamate** |
| aspartate | aspartate | + | α-ketoglutarate | ⇌ | oxaloacetate | + **glutamate** |
| cysteine | cysteine | + | α-ketoglutarate | ⇌ | mercaptopyruvate | + **glutamate** |
| glycine | glycine | + | α-ketoglutarate | ⇌ | glyoxylate | + **glutamate** |
| leucine | leucine | + | α-ketoglutarate | ⇌ | α-ketoisocaproate | + **glutamate** |
| tyrosine | tyrosine | + | α-ketoglutarate | ⇌ | p-hydroxyphenylpyruvate | + **glutamate** |

pyridoxal phosphate
(active derivative of vitamin $B_6$)

## UREA CYCLE




Function: detoxification of ammonia
(prevents hyperammonemia)

## FATE OF THE CARBON SKELETONS

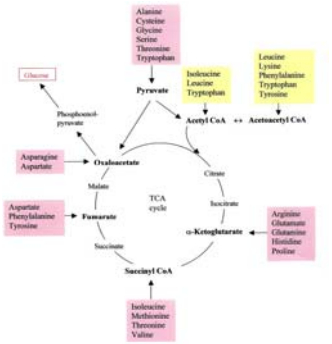
Carbon skeletons are used for energy.

**Glucogenic**: TCA cycle intermediates or pyruvate (gluconeogensis)

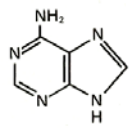
**Ketogenic**: acetyl CoA, acetoacetyl CoA, or acetoacetate

**Glucogenic and Ketogenic Amino Acids**

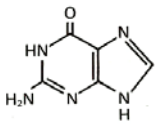
| *Glucogenic* | *Glucogenic and Ketogenic* | *Ketogenic* |
|---|---|---|
| Alanine<br>Arginine<br>Asparagine<br>Aspartate<br>Cysteine<br>Glutamine<br>Glutamate<br>Glycine<br>Histidine<br>Hydroxyproline<br>Methionine<br>Proline<br>Serine<br>Valine | Isoleucine<br>Phenylalanine<br>Threonine<br>Tryptophan<br>Tyrosine | Leucine<br>Lysine |




# *Purine and Pyrimidine Metabolism*



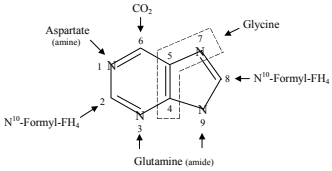
Adenine (A)



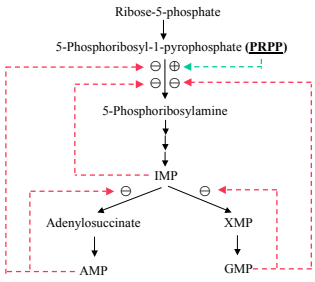
Guanine (G)

Major Bases

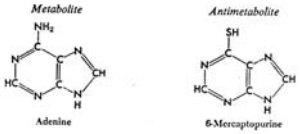
## Source of each atom in the purine ring



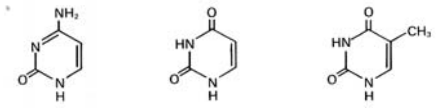

## Summary and Regulation



## Inhibition of Purine Biosynthesis by the Antitumor Agent, 6-Mercaptopurine



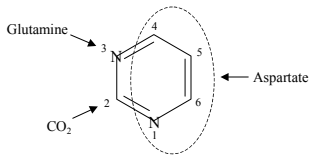

1) 6-Mercaptopurine is converted to a nucleotide.
2) The nucleotide inhibits purine biosynthesis at steps 2, 12a, 12b, and 13a.

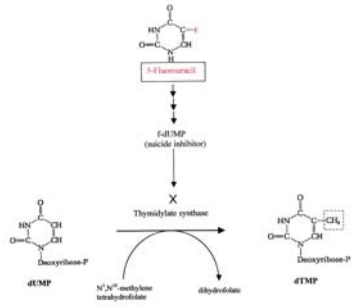


**Cytosine (C)** **Uracil (U)** **Thymine (T)**

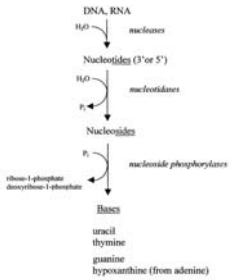
Major Bases

## Sources of the atoms of the pyrimidine ring:






DNA and RNA Degradation



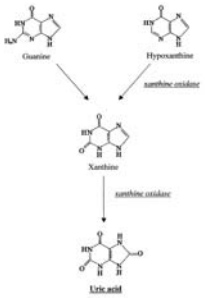

"Salvage Pathway" for Purines (~90%)

Enzyme: Hypoxanthine-guanine phosphoribosyltransferase (HGPRTase)

hypoxanthine + PRPP → IMP + $PP_i$
guanine + PRPP → GMP + $PP_i$

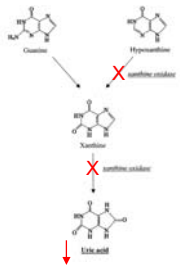
Lesch-Nyhan Syndrome

Degradation of Purines
(~10%)



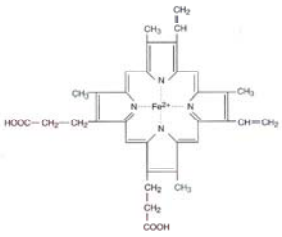

Allopurinol

*Inhibits xanthine oxidase*




# *Heme*

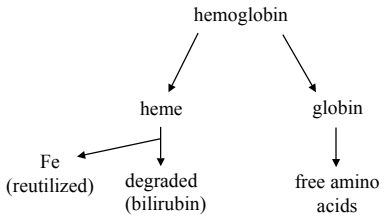
## Structure

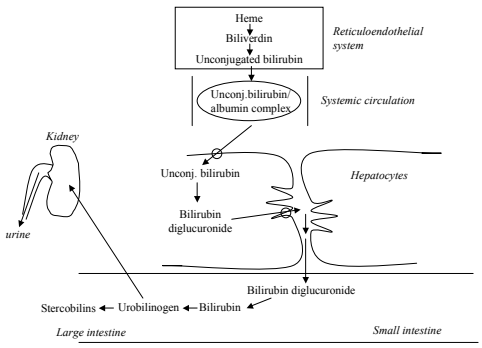


Pyrrole

## Porphyrias

| *Disease* | *Enzyme Deficiency (#)* | *Genetics* | *Pathology* |
|---|---|---|---|
| *More common:* | | | |
| Acute intermittent porphyria | Porphobilinogen deaminase (3) | Dominant | Nervous system |
| Porphyria cutanea tarda | Uroporphyrinogen decarboxylase (5) | Dominant | Skin |
| Erythropoietic protoporphyria | Ferrochetalase (8) | Dominant | Skin, gallstones, liver disease |
| *Less common:* | | | |
| Congenital erythropoietic porphyria | Uroporphyrinogen III cosynthase (4) | Recessive | Skin, appendages, reticuloendothelial system |
| Hereditary coproporphyria | Coproporphyrinogen oxidase (6) | Dominant | Nervous system, skin |
| Variegate porphyria | Protoporphyrinogen Oxidase (7) | Dominant | Nervous system, skin |




## HYPERBILIRUBINEMIA

-- elevated bilirubin in serum (above 1 mg/dL)

-- can be conjugated or unconjugated or both depending on the situation

-- elevated bilirubin can diffuse into tissues, making them appear yellow (jaundice)

## HYPERBILIRUBINEMIA

***Clinical Consequences:***

-- *Conjugated* hyperbilirubinemia: benign

-- *Unconjugated* hyperbilirubinemia: benign at concentrations < 25 mg/dL (albumin capacity)

-- At concentrations >25 mg/dL, *unconjugated* bilirubin is free (uncomplexed) and can enter the brain.

⇨ bilirubin encephalopathy (kernicterus)

## *Causes* of JAUNDICE

1) *Hemolytic anemia*
   -- ↑ destruction of erythrocytes
2) *Hepatitis or cirrhosis*
   -- ↓ conjugation and excretion of bilirubin
3) *Bile duct obstruction*
   -- conjugated bilirubin not delivered to intestine; it backs up, spills over into the blood
4) *Neonatal "physiological jaundice"*
   -- immature hepatic system of the newborn:
   ↓ uptake, conjugation, excretion of bilirubin