Amino Acid Metabolism

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OVERVIEW OF AMINO ACID METabolism

Environment

Ingested protein

Bio-synthesis

Protein

Amino Acids

Nitrogen

Carbon skeletons

Urea Degradation

(Required)

Purines

Pyrimidines

Porphyrins

Used for energy

pyruvate

α-ketoglutarate

succinyl-CoA

fumarate

oxaloacetate

acetoacetate

acetyl-CoA

(glucogenic)(ketogenic)

Amino Acid Requirements of Humans

<table>
<thead>
<tr>
<th>Nutritionally Essential</th>
<th>Nutritionally Nonessential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arginine</td>
<td>Alanine</td>
</tr>
<tr>
<td>Histidine</td>
<td>Asparagine</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>Aspartate</td>
</tr>
<tr>
<td>Leucine</td>
<td>Cysteine</td>
</tr>
<tr>
<td>Lysine</td>
<td>Glutamate</td>
</tr>
<tr>
<td>Methionine</td>
<td>Glutamine</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>Glycine</td>
</tr>
<tr>
<td>Threonine</td>
<td>Proline</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>Serine</td>
</tr>
<tr>
<td>Valine</td>
<td>Tyrosine</td>
</tr>
</tbody>
</table>

* "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

Function: detoxification of ammonia
(prevents hyperammonemia)

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 (gluconeogenesis)

**Ketogenic**: acetate CoA, acetoacetate CoA, or acetoacetate

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*Purine* and *Pyrimidine Metabolism*
**Major Bases**

Adenine (A)  
Guanine (G)

**Source of each atom in the purine ring**

- **Aspartate (amine)**
- **CO₂**
- **Glycine**
- **N⁵-Formyl-FH₄**
- **N⁵-Formyl-FH₄ Glutamine (amide)**

**Summary and Regulation**

- **Ribose-5-phosphate**
- **5-Phosphoribosyl-1-pyrophosphate (PRPP)**
- **5-Phosphoribosylamine**
- **Adenylosuccinate**
- **SMP**
- **AMP**
- **GMP**
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.

Major Bases

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

Sources of the atoms of the pyrimidine ring:

- Glutamine
- Aspartate
DNA and RNA Degradation

“Salvage Pathway” for Purines (~90%)

Enzyme: Hypoxanthine-guanine phosphoribosyltransferase (HGPRTase)

hypoxanthine + PRPP \(\rightarrow\) IMP + PP

guanine + PRPP \(\rightarrow\) GMP + PP

Lesch-Nyhan Syndrome
Degradation of Purines (~10%) 

Allopurinol 

Inhibits xanthine oxidase 

Heme
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