2007-09

M1 - Renal, Fall 2007

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http://hdl.handle.net/2027.42/64946
Amino Acid metabolism

- Amino acids
  - Glu, Gln, Asp, NH₃
  - Urea

Folate metabolism

- Methylene THF
- Met Cycle

Nucleic Acid metabolism

- Purines
  - DNA
  - RNA
  - Pyrimidines
  - Uric Acid
  - (energy)
Folate ("One-Carbon") Pathways

Click on any blue box to see details
(Start with the section with "Diet" and follow the paths with red arrows)
Folic Acid is Synthesized By Bacteria

Dietary folate: folic acid (meats, green veggies) *requires* the intestinal enzyme ‘Conjugase’ for absorption.

Para-aminobenzoic acid (PA.BA)  sulfanilamide
Inhibitors of DHFR are important therapeutics:

- Methotrexate - chemotherapy
- Trimethoprim - inhibits bacterial DHFR
- Pyrimethamine - inhibits malarial DHFR
\[
\text{N}^6, \text{N}^{10} \text{ methylene tetrahydrofolate} + \text{glycine} \rightarrow \text{serine} + \text{Tetrahydrofolate} + \text{H}_2\text{O} \]

\[
\text{N}^6, \text{N}^{10} \text{ methylene tetrahydrofolate} + \text{glycine} \rightarrow \text{Tetrahydrofolate} + \text{NAD}^+ + \text{NADH} + \text{CO}_2
\]
Methionine Cycle
And Biological Methyl Groups
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N^6, N^6 methylene tetrahydrofolate

NADH + H^+

methionine

homocysteine

N^6 methyl tetrahydrofolate

NAD^+
Other methyl acceptors:
DNA ("CpG Islands")
RNA
Folate Deficiencies: Symptom: megaloblastic anemia

Dietary deficiency:
Common especially in developing countries, lower socioeconomic classes
Folate deficiency secondary to bowel irritation:

- Conjugase is essential for adequate absorption of dietary folates

- Conjugase production may be compromised by bowel irritation:

  ‘Tropical Sprue’ - bowel irritation probably arising from bacterial origin, causes intestinal inflammation and malabsorption.

  ‘Celiac Sprue’ - similar outcome, but the original irritation is due to an allergic response, for example to gliaden (a component in gluten)
Folate Deficiency Secondary to B12 deficiency:
the ‘methyl trap’ hypothesis

B12 is also critical in other reactions, ones for which the deficiency has serious neurological consequences.