M1 - Renal, Fall 2007

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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 (PAABA)
sulfanilamide

Dietary folate: folic acid (meats, green veggies)
*requires* the intestinal enzyme ‘Conjugase’ for absorption.
Inhibitors of DHFR are important therapeutics:
Methotrexate - chemotherapy
Trimethoprim - inhibits bacterial DHFR
Pyrimethamine - inhibits malarial DHFR
Tetrahydrofolate + COO⁻ → H₂O + COO⁻ + N⁺, N⁻¹⁺ methylene tetrahydrofolate

NH₂-NH₂

Tetrahydrofolate + serine + NH₃⁻ → glycine + N⁺, N⁻¹⁺ methylene tetrahydrofolate

NH₂-NH₂

Tetrahydrofolate + NH₃⁻ + NH₄⁺ → N⁺, N⁻¹⁺ methylene tetrahydrofolate

NH₂-NH₂
Methionine Cycle
And Biological Methyl Groups
homocysteine $\rightarrow$ vitamin $B_{12}$ $\rightarrow$ methionine
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

\[ \text{N}^\circ, \text{N}^\circ \text{ methylene tetrahydrofolate} \]

\[ \text{N}^\circ \text{ methyl tetrahydrofolate} \]

methionine

homocysteine

\[ \text{NAD}^+ \]

\[ \text{NADH} + \text{H}^+ \]
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.