M1 - Renal, Fall 2007

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<http://hdl.handle.net/2027.42/64946>
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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.
Inhibitors of DHFR are important therapeutics:
- Methotrexate - chemotherapy
- Trimethoprim - inhibits bacterial DHFR
- Pyrimethamine - inhibits malarial DHFR
Methionine Cycle
And Biological Methyl Groups
\[
\text{homocysteine} \xrightarrow{\text{N}^6\text{-methyl THF}} \text{methionine}
\]
Tetrahydrofolate

Carbon donor
(e.g. serine or glycine)

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

methionine

homocysteine

\[ \text{N}^\circ \text{ methyl tetrahydrofolate} \]
Other methyl acceptors:
- DNA ("CpG Islands")
- RNA

Methionine $\rightarrow$ S-Adenosyl methionine

Norepinephrine $\rightarrow$ Epinephrine

SAM $\rightarrow$ SAH
**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.