M1 - Renal, Fall 2007

Lyons, R.; Burney, R.

<http://hdl.handle.net/2027.42/64946>
http://hdl.handle.net/2027.42/64946
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
homocysteine $\rightarrow$ N°-methyl THF $\rightarrow$ vitamin B₁₂ $\rightarrow$ methionine
Tetrahydrofolate

Carbon donor (e.g., serine or glycine)

N^6, N^7 methylene tetrahydrofolate

N^6 methyl tetrahydrofolate

methionine

homocysteine

NADH + H^+

NAD^+
Other methyl acceptors:
DNA ("CpG Islands")
RNA

Methionine → S-Adenosyl methionine

Norepinephrine → SAH → Epinephrine

\[
\begin{align*}
\text{Methionine} & : \quad \text{ATP} \quad \text{PPi} + P_i \\
\text{Norepinephrine} & : \quad \text{SAM} \quad \text{SAH} \\
\text{Epinephrine} & : \quad \text{S-Adenosyl methionine}
\end{align*}
\]
**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.