2007-09

M1 - Renal, Fall 2007

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<http://hdl.handle.net/2027.42/64946>
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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^\text{6-methyl} \text{THF} \rightarrow \text{THF} \rightarrow \text{vitamin B}_12 \rightarrow \text{methionine}
Tetrahydrofolate

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

N^6, N^6 methylene tetrahydrofolate

methionine

homocysteine

NADH + H^+

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

Methionine → S-Adenosyl methionine

Norepinephrine → Epinephrine

SAM → 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.