M1 - Renal, Fall 2007

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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 → vitamin B₁₂ → Methionine

Homocysteine: \(-\text{OOC-}C\text{-CH}_2\text{CH}_2\text{SH}\)

Methionine: \(-\text{OOC-}C\text{-CH}_2\text{CH}_2\text{SCH}_3\)
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N^\circ, N^\circ methylene tetrahydrofolate

methionine

homocysteine

NADH + H^+

NAD^+

N^\circ methyl tetrahydrofolate
Other methyl acceptors:
DNA ("CpG Islands")
RNA

Methionine

Norepinephrine

S-Adenosyl methionine

Epinephrine
**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.