M1 - Renal, Fall 2007

Lyons, R.; Burney, R.

<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)

Methyl-THF

Methionine Cycle

THF Cycle

THF

Diet:

DHF

Folate

Connects to Amino Acids

Donation of one carbon (from Ser, Gly)

Connects to Nucleic Acids lectures

Purine biosynthesis

Thymidylate synthetase

Formyl-THF

Methylene-THF
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
\[
\text{homocysteine} \xrightarrow{N^\circ\text{-methyl THF}} \text{methionine}
\]
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N^6, N^4 methylene tetrahydrofolate

N^6 methyl tetrahydrofolate

methionine

homocysteine

NADH + H^+

NAD^+
Other methyl acceptors:

DNA ("CpG Islands")
RNA

- Methionine
- S-Adenosyl methionine
- Norepinephrine
- 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.