M1 - Renal, Fall 2007

Lyons, R.; Burney, R.

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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
Tetrahydrofolate + serine → H₂O + glycine + N⁶, N¹⁴ methylene tetrahydrofolate

Tetrahydrofolate + glycine → NAD⁺ + N⁶, N¹⁴ methylene tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
homocysteine \overset{N^6 -methyl THF}{\longrightarrow} \text{vitamin } B_{12} \overset{\text{THF}}{\longrightarrow} \text{methionine}
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N\textsuperscript{5}, N\textsuperscript{6} methylene tetrahydrofolate

methionine

homocysteine

NADH + H\textsuperscript{+}

NAD\textsuperscript{+}

N\textsuperscript{5} methyl tetrahydrofolate
Other methyl acceptors:

DNA ("CpG Islands")

RNA
**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.