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
$N^\prime$-methyl tetrahydrofolate → Biosynthesis of methionine

Gly, Ser

$N^\prime$, $N^\prime$-methylene tetrahydrofolate → Biosynthesis of thymidylate

$N^\prime$-formyl tetrahydrofolate → Biosynthesis of purines

$N^\prime$-methyl tetrahydrofolate

$N^\prime$-formyl tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
N\textsuperscript{6} -methyl THF

\[ \text{homocysteine} \rightarrow \text{methionine} \]

\[ \text{vitamin B}_12 \]
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

\[ \text{N}^\circ, \text{N}^\circ \text{ methylene tetrahydrofolate} \]

methionine

homocysteine

\[ \text{N}^\circ \text{ methyl tetrahydrofolate} \]
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.