M1 - Renal, Fall 2007

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Viewer discretion advised: Material may contain medical images that may be disturbing to some viewers.
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

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

$N^\prime$-methyl tetrahydrofolate

$N^{14}$ formyl tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
$\text{N}^6\text{-methyl THF}$

homocysteine $\rightarrow$ vitamin $B_12$ $\rightarrow$ methionine
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

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

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

methionine

homocysteine

\[ \text{NAD}^+ + \text{H}^+ \]
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.