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
Tetrahydrofolate + serine → glycine + N\textsuperscript{5}, N\textsuperscript{10} methylene tetrahydrofolate

Tetrahydrofolate + glycine → N\textsuperscript{5}, N\textsuperscript{10} methylene tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
\[
\text{homocysteine} \quad \rightarrow \quad \text{N}^6\text{-methyl THF} \quad \rightarrow \quad \text{THF} \quad \rightarrow \quad \text{methionine}
\]
Carbon donor (e.g., serine or glycine)

Tetrahydrofolate → N⁰, N⁰ methylene tetrahydrofolate

methionine → homocysteine

NAD⁺ → NADH + 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.