2007-09

M1 - Renal, Fall 2007

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<http://hdl.handle.net/2027.42/64946>
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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
\[ \text{N}^{\prime}\text{-methyl tetrahydrofolate} \rightarrow \text{Biosynthesis of methionine} \]

\[ \text{N}^{\prime}, \text{N}^{\prime}\text{-methylene tetrahydrofolate} \rightarrow \text{Biosynthesis of thymidylate} \]

\[ \text{N}^{\prime}, \text{N}^{\prime}\text{-methylene tetrahydrofolate} \rightarrow \text{N}^{\prime}\text{-formyl tetrahydrofolate} \rightarrow \text{Biosyntheses of purines} \]

\[ \text{N}^{\prime} \text{-methyl tetrahydrofolate} \]

\[ \text{N}^{\prime}\text{L formyl tetrahydrofolate} \]
Methionine Cycle
And Biological Methyl Groups
Tetrahydrofolate

Carbon donor (e.g. serine or glycine)

$N^\circ, N^\circ$ methylene tetrahydrofolate

methionine

homocysteine

$N^\circ$ methyl tetrahydrofolate

$NAD^+$

$NADH + H^+$
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.