2007-09

M1 - Renal, Fall 2007

Lyons, R.; Burney, R.

http://hdl.handle.net/2027.42/64946
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 $\rightarrow$ glycine + $N^6, N^{10}$-methylene tetrahydrofolate

Tetrahydrofolate + glycine $\rightarrow$ $N^6, N^{10}$-methylene tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
Tetrahydrofolate

Carbon donor (e.g. serine or glycine)

$\text{N}^\text{r}, \text{N}^\text{o}$ methylene tetrahydrofolate

NADH + H$^+$

methionine

homocysteine

$\text{N}^\text{r}$ 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.