M1 - Renal, Fall 2007

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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.
Folic acid

\[
\text{NADPH} + \text{H}^+ 
\]

Dihydrofolate

\[
\text{NADP}^+ 
\]

Tetrahydrofolate

\[
\text{NADPH} + \text{H}^+ 
\]

\[
\text{NADP}^+ 
\]
Inhibitors of DHFR are important therapeutics:
Methotrexate - chemotherapy
Trimethoprim - inhibits bacterial DHFR
Pyrimethamine - inhibits malarial DHFR
\[
\text{NAD}^+ + \text{NH}_2\text{C} - \text{H} \rightleftharpoons \text{NADH} + \text{NH}_2\text{C}^+\text{H} + \text{CO}_2
\]
Methionine Cycle
And Biological Methyl Groups
\[
\text{homocysteine} \xrightarrow{\text{vitamin B}_12} \text{methionine} \xrightarrow{\text{N}^+\text{-methyl THF}} \text{THF}
\]
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N°, N° methylene tetrahydrofolate

N° methyl tetrahydrofolate

methionine

homocysteine

NADH + H⁺

NAD⁺
Other methyl acceptors:
DNA ("CpG Islands")
RNA

Methionine

S-Adenosyl methionine

Norepinephrine

Epinephrine
**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.