M1 - Renal, Fall 2007

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<http://hdl.handle.net/2027.42/64946>
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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

\[
\text{Folic acid} \quad \xrightarrow{\text{NADPH} + \text{H}^+} \quad \text{Dihydrofolate} \xrightarrow{\text{NADP}^+} \quad \text{Tetrahydrofolate} \xrightarrow{\text{NADPH} + \text{H}^+} \quad \text{Dihydrofolate} \xrightarrow{\text{NADP}^+} \quad \text{Folic acid}
\]
Inhibitors of DHFR are important therapeutics:
Methotrexate - chemotherapy
Trimethoprim - inhibits bacterial DHFR
Pyrimethamine - inhibits malarial DHFR
Methionine Cycle
And Biological Methyl Groups

Methionine

S-Adenosyl Methionine

Homocysteine

S-Adenosyl Homocysteine

Serine

Cysteine

(remainder of homocysteine degraded for energy)
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N°, N° methylene tetrahydrofolate

methionine

NADH + H⁺

homocysteine

NAD⁺

N° methyl tetrahydrofolate
Other methyl acceptors:
  DNA ("CpG Islands")
  RNA

\[
\begin{align*}
\text{Methionine} & \quad \xrightarrow{\text{ATP, PPi, P}_{i}} \quad \text{S-Adenosyl methionine} \\
\text{Norepinephrine} & \quad \xrightarrow{\text{SAM, SAH}} \quad \text{Epinephrine}
\end{align*}
\]
**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.