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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

Dihydrofolate

Tetrahydrofolate

NADPH + H^+

NADP^+
Inhibitors of DHFR are important therapeutics:
Methotrexate - chemotherapy
Trimethoprim - inhibits bacterial DHFR
Pyrimethamine - inhibits malarial DHFR
Tetrahydrofolate + serine $\rightarrow$ H$_2$O + glycine

Tetrahydrofolate + glycine $\rightarrow$ N$^6$, N$^{10}$ methylene tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
homocysteine $\xrightarrow{\text{vitamin B}_12} \text{methionine}$
Tetrahydrofolate

Carbon donor (e.g. serine or glycine)

$N^\delta, N^\gamma$ methylene tetrahydrofolate

methionine

homocysteine

$N^\delta$ methyl tetrahydrofolate

$NADH + H^+$

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

- Methionine
- Norepinephrine
- Epinephrine

- S-Adenosyl methionine
**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.