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M1 - Renal, Fall 2007

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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
Methionine Cycle
And Biological Methyl Groups
$\text{N}^6$-methyl THF \rightarrow \text{THF} \rightarrow \text{vitamin B}_12 \rightarrow \text{methionine}$

$\text{homocysteine}$

$\text{ORC} - \text{C} - \text{CH}_2 \text{CH}_2 \text{SH}$

$\text{NH}_3$

$\text{ORC} - \text{C} - \text{CH}_2 \text{CH}_2 \text{SC} \text{H}_3$

$\text{NH}_3$
Tetrahydrofolate

Carbon donor (e.g. serine or glycine)

\[ \text{N}^6, \text{N}^6 \text{ methylene tetrahydrofolate} \]

methionine

\[ \text{N}^6 \text{ methyl tetrahydrofolate} \]

homocysteine

\[ \text{NAD}^+ \]

\[ \text{NADH} + H^+ \]
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.