M1 - Renal, Fall 2007

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Viewer discretion advised: Material may contain medical images that may be disturbing to some viewers.
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 + $\text{N}^6, \text{N}^{10}$ methylene tetrahydrofolate

Tetrahydrofolate + glycine $\rightarrow$ $\text{N}^6, \text{N}^{10}$ methylene tetrahydrofolate
Methionine Cycle

And Biological Methyl Groups
\[
\begin{align*}
\text{homocysteine} & \quad \rightarrow \quad N^6\text{-methyl THF} \quad \rightarrow \quad \text{methionine} \\
\text{vitamin B}_12
\end{align*}
\]
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N^\text{\text{\textsuperscript{6}}} , N^\text{\text{\textsuperscript{5}}} methylene tetrahydrofolate

methionine

homocysteine

NADH + H^+
Other methyl acceptors:
DNA ("CpG Islands")
RNA

- Methionine
  - S-Adenosyl methionine

- Norepinephrine
  - Epinephrine

Reactions:
- Methionine + ATP → S-Adenosyl methionine
- Norepinephrine + SAM → Epinephrine
  - SAH formation
**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.