M1 - Renal, Fall 2007

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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 + \text{serine} \rightarrow \text{glycine} + N^\delta, N^\epsilon' \text{methylene tetrahydrofolate}

Tetrahydrofolate + \text{glycine} \rightarrow \text{N}^\delta, N^\epsilon' \text{methylene tetrahydrofolate}
Methionine Cycle
And Biological Methyl Groups
\[
\begin{align*}
\text{homocysteine} & \rightarrow \text{N}^6\text{-methyl THF} \\
& \rightarrow \text{vitamin B}_12 \\
& \rightarrow \text{methionine}
\end{align*}
\]
Carbon donor  
(e.g. serine or glycine)

\[
\text{Tetrahydrofolate} \quad \xrightarrow{\text{carbon donor}} \quad \text{N}^\text{\textsuperscript{2}}, \text{N}^\text{\textsuperscript{4}} \text{ methylene tetrahydrofolate}
\]

\[
\text{methionine} \quad \xrightarrow{\text{NADH} + \text{H}^+} \quad \text{homocysteine}
\]

\[
\text{N}^\text{\textsuperscript{5}} \text{ methyl tetrahydrofolate}
\]
Other methyl acceptors:
DNA ("CpG Islands")
RNA
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.