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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.
Folic Acid is Synthesized By Bacteria

Dietary folate: folic acid (meats, green veggies)
*requires* the intestinal enzyme ‘Conjugase’ for absorption.
Folic acid

Dihydrofolate

Tetrahydrofolate
Inhibitors of DHFR are important therapeutics:
- Methotrexate - chemotherapy
- Trimethoprim - inhibits bacterial DHFR
- Pyrimethamine - inhibits malarial DHFR
Tetrahydrofolate + serine → glycine + N\textsuperscript{5}, N\textsuperscript{10} methylene tetrahydrofolate

Tetrahydrofolate + glycine → N\textsuperscript{5}, N\textsuperscript{10} methylene tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
N\textsuperscript{6} -methyl THF

[Diagram showing the conversion of homocysteine to methionine through the action of vitamin B\textsubscript{12} and THF.]
Other methyl acceptors:
DNA ("CpG Islands")
RNA

Methionine

S-Adenosyl methionine

Norepinephrine

Epinephrine

\[
\text{NH}_3^+ \quad \begin{array}{c}
\text{OOC} \quad \text{C} \quad \text{CH}_2 \text{CH}_2 \text{SC}_2 \text{H}_3 \\
\text{H} \\
\end{array}
\quad \text{ATP} \quad \text{PP}_i + \text{P}_i
\quad \begin{array}{c}
\text{OOC} \quad \text{C} \quad \text{CH}_2 \text{CH}_2 \text{SC}_2 \text{H}_3 \\
\text{H} \\
\end{array}
\]

\[
\begin{array}{c}
\text{NH}_3^+ \\
\text{HO} \\
\text{OH} \\
\text{C} \quad \text{CH}_2 \quad \text{NH}_3^+ \\
\text{H} \\
\end{array}
\quad \text{SAM} \quad \text{SAM} \quad \begin{array}{c}
\text{HO} \\
\text{OH} \\
\text{C} \quad \text{CH}_2 \quad \text{N} \quad \text{CH}_3 \\
\text{H} \\
\end{array}
\quad \text{SAH}
\]
**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.