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M1 - Renal, Fall 2007

Lyons, R.; Burney, R.

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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
Tetrahydrofolate + glycine → N^6, N^10 methylene tetrahydrofolate

Tetrahydrofolate + serine → glycine

NAD^+ + NH_4^+ + CO_3^{2-} → NADH + NH_3 + H_2O
\[ \text{Gly} \quad \text{Ser} \quad \text{N}^1, \text{N}^6 \text{ methylene tetrahydrofolate} \quad \text{Biosynthesis of thymidylate} \]

\[ \text{N}^1, \text{N}^6 \text{ methenyl tetrahydrofolate} \quad \text{Biosynthesis of purines} \]

\[ \text{N}^1 \text{ formyl tetrahydrofolate} \]

\[ \text{N}^1 \text{ methyl tetrahydrofolate} \]

\[ \text{Biosynthesis of methionine} \]
Methionine Cycle and Biological Methyl Groups
\[
\begin{align*}
\text{homocysteine} & \xrightarrow{\text{vitamin B}} \text{methionine}
\end{align*}
\]
Tetrahydrofolate

Carbon donor (e.g. serine or glycine)

N\textsuperscript{5}, N\textsuperscript{10} methylene tetrahydrofolate

NADH + H\textsuperscript{+}

methionine

homocysteine

N\textsuperscript{5} methyl tetrahydrofolate
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.