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M1 - Renal, Fall 2007

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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
Homocysteine \[ \rightarrow \text{N}^6\text{-methyl THF} \rightarrow \text{THF} \rightarrow \text{vitamin } B_12 \rightarrow \text{methionine} \]
Other methyl acceptors:
  DNA ("CpG Islands")
  RNA

Methionine

\[
\text{OOC} - \text{CH}_2 - \text{CH}_2 \text{SH} + \text{ATP} \rightarrow \text{OOC} - \text{CH}_2 - \text{CH}_2 \text{NH}_3^+ + \text{PP}_i + \text{P}_i
\]

S-Adenosyl methionine

Norepinephrine

\[
\text{HO} - \text{C} - \text{CH}_2 - \text{NH}_3^+ + \text{SAM} \rightarrow \text{HO} - \text{C} - \text{CH}_2 - \text{N} - \text{CH}_3 + \text{SAH}
\]

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.