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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.
Folic acid

Dihydrofolate

Tetrahydrofolate

\[ \text{NADPH} + \text{H}^+ \leftrightarrow \text{NADP}^+ \]

\[ \text{NADPH} + \text{H}^+ \leftrightarrow \text{NADP}^+ \]
Inhibitors of DHFR are important therapeutics:
Methotrexate - chemotherapy
Trimethoprim - inhibits bacterial DHFR
Pyrimethamine - inhibits malarial DHFR
\[ \text{Gly} \rightarrow \text{N}^4, \text{N}^6 \text{methylene tetrahydrofolate} \rightarrow \text{N}^4 \text{formyl tetrahydrofolate} \]

- \( \text{N}^4 \) methyl tetrahydrofolate → Biosynthesis of methionine
- \( \text{N}^4, \text{N}^6 \) methylene tetrahydrofolate → Biosynthesis of thymidylate
- \( \text{N}^4 \) formyl tetrahydrofolate → Biosyntheses of purines

\[ \text{N}^4 - \text{methyl tetrahydrofolate} \]
\[ \text{N}^{14} - \text{formyl tetrahydrofolate} \]
Methionine Cycle
And Biological Methyl Groups
homocysteine → \( \text{N}^+\text{met} \text{yl THF} \) → vitamin \( B_12 \) → methionine
Tetrahydrofolate

Carbon donor (e.g. serine or glycine)

N⁰, N⁰ methylene tetrahydrofolate

methionine

homocysteine

NADH + H⁺

NAD⁺

N⁰ 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.