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

1. THF
2. DHF
3. Methyl-THF
4. Methylene-THF
5. Formyl-THF

- Methionine Cycle
- THF Cycle

- Connects to Amino Acids
- Donation of one carbon (from Ser, Gly)
- Connects to Nucleic Acids
- Purine biosynthesis
- Thymidylate synthetase
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 + serine → H₂O + glycine + N⁶, N¹⁰ methylene tetrahydrofolate

Tetrahydrofolate + glycine → NAD⁺ + NADH + CO₂ + N⁶, N¹⁰ methylene tetrahydrofolate
\( \text{N}^\text{4}-\text{methyl tetrahydrofolate} \) → \( \text{Biosynthesis of methionine} \)

\( \text{N}^\text{4}, \text{N}^\text{5} \text{ methylene tetrahydrofolate} \) → \( \text{Biosynthesis of thymidylate} \)

\( \text{N}^\text{4} \text{ formyl tetrahydrofolate} \) → \( \text{Biosyntheses of purines} \)
Methionine Cycle
And Biological Methyl Groups
homocysteine $\rightarrow$ vitamin $\rightarrow$ methionine

$\text{N}^\text{6} - \text{methyl THF}$

$\text{THF}$
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N^6, N^6 methylentetrahydrofolate

NADH + H^+

NAD^+

methionine

homocysteine

N^6 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.