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
 Rutamathvale  

**Biosynthesis of methionine**

1. N⁴, N⁵ methylene tetrahydrofolate
2. NAD⁺
3. NADH + H⁺

**Biosynthesis of thymidylate**

1. N⁴, N⁵ methenyl tetrahydrofolate
2. NADPH + H⁺

**Biosyntheses of purines**

1. N⁴-formyl tetrahydrofolate
2. H₂O

**Species**

- **N⁴-methyl tetrahydrofolate**
- **N⁴-formyl tetrahydrofolate**

**Structure diagrams**
Methionine Cycle
And Biological Methyl Groups
\[ \text{homocysteine} \rightarrow \text{vitamin B}_12 \rightarrow \text{methionine} \]
Carbon donor (e.g., serine or glycine)

Tetrahydrofolate

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

methionine

homocysteine

N\textsuperscript{5} methyl tetrahydrofolate

NADH + H\textsuperscript{+}

NAD\textsuperscript{+}
Other methyl acceptors:

- DNA ("CpG Islands")
- RNA

Chemical structures:

- 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.