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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.
Folic acid

Dihydrofolate

Tetrahydrofolate

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

\[ \text{NADP}^+ \rightarrow \text{NADPH} + \text{H}^+ \]
Inhibitors of DHFR are important therapeutics:
Methotrexate - chemotherapy
Trimethoprim - inhibits bacterial DHFR
Pyrimethamine - inhibits malarial DHFR
Methionine Cycle
And Biological Methyl Groups
Homocysteine $\rightarrow$ methyl THF $\rightarrow$ Vitamin B<sub>12</sub> $\rightarrow$ Methionine
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N^6, N^7 methylene tetrahydrofolate

methionine

NADH + H^+

homocysteine

NAD^+

N^6 methyl tetrahydrofolate
Other methyl acceptors:
DNA ("CpG Islands")
RNA

Methionine → S-Adenosyl methionine

Norepinephrine → Epinephrine
The image depicts a metabolic pathway involving the conversion of homocysteine to methionine. The pathway includes the following steps:

1. Homocysteine is converted to S-adenosyl homocysteine (SAH) using adenosine and ATP.
2. SAH donates a methyl group to methionine, forming methylated THF and S-adenosyl methionine.
3. The methylated THF is converted back to THF, completing the cycle.

Key molecules involved are:
- Homocysteine
- Methionine
- S-adenosyl homocysteine
- Methylated THF

The pathway also involves the use of NADH and NAD+ as electron carriers, and vitamin B12 as a coenzyme.
**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.