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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

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

\[ \text{NADPH} + \text{H}^+ \quad \text{NADP}^+ \]
Inhibitors of DHFR are important therapeutics:
Methotrexate - chemotherapy
Trimethoprim - inhibits bacterial DHFR
Pyrimethamine - inhibits malarial DHFR
Tetrahydrofolate + serine $\rightarrow$ glycine + N¹⁰, N¹⁰' methylene tetrahydrofolate

Tetrahydrofolate + glycine $\rightarrow$ N¹⁰, N¹⁰' methylene tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
Other methyl acceptors:
DNA ("CpG Islands")
RNA

Methionine

S-Adenosyl methionine

Norepinephrine

Epinephrine
The diagram illustrates the metabolic pathway involving homocysteine and methionine, with specific reactions catalyzed by enzymes and cofactors.

1. **Homocysteine** is converted to **S-adenosyl homocysteine** by Adenosine.
2. **NADH** and **NAD** are involved in redox reactions.
3. **Vitamin B<sub>12</sub>** is essential for the conversion of **N<sup>5</sup>-methyl THF** to **methionine**.
4. **Adenosyl homocysteine** is converted to **S-adenosyl methionine** by Adenosine.
5. **Methyl group donation to biological substrate** is facilitated by **S-adenosyl methionine**.
6. **ATP** and **PP<sub>1</sub>** are involved in energy transfer reactions.

The pathway highlights the importance of methyl group transfer and redox balance in metabolic processes.
**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.