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Viewer discretion advised: Material may contain medical images that may be disturbing to some viewers.
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 + N^{\text{6, 7}} \text{ methylene tetrahydrofolate}

Tetrahydrofolate + glycine → N^{\text{6, 7}} \text{ methylene tetrahydrofolate}
The diagram illustrates the biosynthetic pathways of methionine, thymidylate, and purines involving N\textsuperscript{10}-methyl and N\textsuperscript{10}-formyl tetrahydrofolate. The reactions involve NAD\textsuperscript{+}, NADH, and NADPH.

- **Methionine Biosynthesis**: N\textsuperscript{10}-methyl tetrahydrofolate is converted to N\textsuperscript{10}-methylglycine (Gly) and N\textsuperscript{6}, N\textsuperscript{10}-methylene tetrahydrofolate.
- **Thymidylate Biosynthesis**: N\textsuperscript{5}, N\textsuperscript{10}-methylene tetrahydrofolate is converted to N\textsuperscript{5}, N\textsuperscript{10}-methylenetetrahydrofolate, which is further reduced to N\textsuperscript{5}, N\textsuperscript{10}-formyltetrahydrofolate and then to N\textsuperscript{5}-formyltetrahydrofolate.
- **Purine Biosynthesis**: N\textsuperscript{5}, N\textsuperscript{10}-formyltetrahydrofolate is converted to N\textsuperscript{5}, N\textsuperscript{10}-formyltetrahydrofolate and then to N\textsuperscript{5}-formyltetrahydrofolate.
Methionine Cycle
And Biological Methyl Groups
$N^\ominus$-methyl THF $\xrightarrow{\text{vitamin B}_12}$ THF $\xrightarrow{\text{homocysteine}}$ methionine
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

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

N\textsuperscript{5} methyl tetrahydrofolate

methionine

homocysteine

NADH + H\textsuperscript{+}

NAD\textsuperscript{+}
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.