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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
The image depicts a biochemistry diagram illustrating the biosynthesis of methionine and thymidine, and the biosyntheses of purines. The diagram shows the conversion of various substances:

- **N^1'-methyl tetrahydrofolate**
- **N^1, N^6 methylene tetrahydrofolate**
- **N^1', N^6 methylenyl tetrahydrofolate**
- **N^1' formyl tetrahydrofolate**

The reactions involve the transfer of hydrogen and the oxidation of reduced forms of pyridine nucleotides (NADH and NADPH) to produce oxidized forms (NAD^+ and NADP^+). The diagram also shows the role of glycine (Gly) and serine (Ser) in these processes. The final products are highlighted in red, indicating their significance in the biosynthetic pathways.

The chemical structures of **N^1'-methyl tetrahydrofolate** and **N^1' formyl tetrahydrofolate** are also included in the diagram, providing a visual representation of the molecules involved in these biochemical reactions.
Methionine Cycle
And Biological Methyl Groups
$\text{homocysteine}$

\[ \text{N}^6\text{-methyl THF} \rightarrow \text{THF} \]

\[ \text{vitamin B}_12 \rightarrow \text{methionine} \]
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N°, N° methylene tetrahydrofolate

methionine

homocysteine

NADH + H⁺

NAD⁺

N° 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.