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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.
Inhibitors of DHFR are important therapeutics:
- Methotrexate - chemotherapy
- Trimethoprim - inhibits bacterial DHFR
- Pyrimethamine - inhibits malarial DHFR
Tetrahydrofolate + serine $\rightleftharpoons$ water + glycine

$\text{Tetrahydrofolate} + \text{glycine} \rightarrow \text{N}^\delta, \text{N}^{\delta'} \text{methylene tetrahydrofolate}$
\[ N^\prime \text{-methyl tetrahydrofolate} \rightarrow \text{Biosynthesis of methionine} \]

\[ \text{NAD}^+ \]

\[ N^\prime, N^\prime \text{-methylene tetrahydrofolate} \rightarrow \text{Biosynthesis of thymidylate} \]

\[ \text{NADH} + H^+ \]

\[ \text{Gly} \quad \text{Ser} \]

\[ \text{NADP}^+ \]

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

\[ \text{N}^\prime, \text{N}^\prime \text{-methenyl tetrahydrofolate} \]

\[ H_2O \]

\[ \text{N}^\prime \text{-formyl tetrahydrofolate} \rightarrow \text{Biosyntheses of purines} \]

\[ \text{N}^\prime \text{-methyl tetrahydrofolate} \]

\[ \text{N}^\prime \text{L formyl tetrahydrofolate} \]
Methionine Cycle
And Biological Methyl Groups
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

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.