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Viewer discretion advised: Material may contain medical images that may be disturbing to some viewers.
Amino Acid metabolism

Amino acids

Glu, Gln, Asp, NH₃

Urea

Folate metabolism

Methylene THF

Met Cycle

Nucleic Acid metabolism

Purines

DNA

RNA

Pyrimidines

Uric Acid

(energy)
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)

- Connects to Amino Acids
- Donation of one carbon (from Ser, Gly)
- THF
- DHF
- Folate
- THF Cycle
- Methyl-THF
- Methylene-THF
- Formyl-THF
- THF

Diet:
- Folate
- DHF
- THF

Connects to Nucleic Acids lectures

- Purine biosynthesis
- Thymidylate synthetase

Methionine Cycle
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 $\rightarrow$ glycine + water

Tetrahydrofolate + glycine $\rightarrow$ $N^6, N^{10}$ methylene tetrahydrofolate

NAD$^+$ + glycine $\rightarrow$ NADH + $N^6, N^{10}$ methylene tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
N\textsuperscript{6} -methyl THF

\[\text{homocysteine} \rightarrow \text{vitamin B_12} \rightarrow \text{methionine}\]
Carbon donor (e.g. serine or glycine)

Tetrahydrofolate

N<sup>5</sup>, N<sup>10</sup> methylene tetrahydrofolate

methionine

NADH + H<sup>+</sup>

homocysteine

NAD<sup>+</sup>

N<sup>5</sup> methyl tetrahydrofolate
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.