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M1 - Renal, Fall 2007

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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)

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

Diet:

Connects to Nucleic Acids lectures

Methyl-THF

Methylene-THF

Formyl-THF

THF Cycle

Methionine Cycle

Purine biosynthesis

Thymidylate synthetase
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 H_2O + glycine, N^\delta, N^\lambda methylene tetrahydrofolate

Tetrahydrofolate + glycine \rightarrow N^\delta, N^\lambda methylene tetrahydrofolate
Methionine Cycle
And Biological Methyl Groups
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.