Harvard-MIT Division of Health Sciences and Technology
HST.151: Principles of Pharmacology
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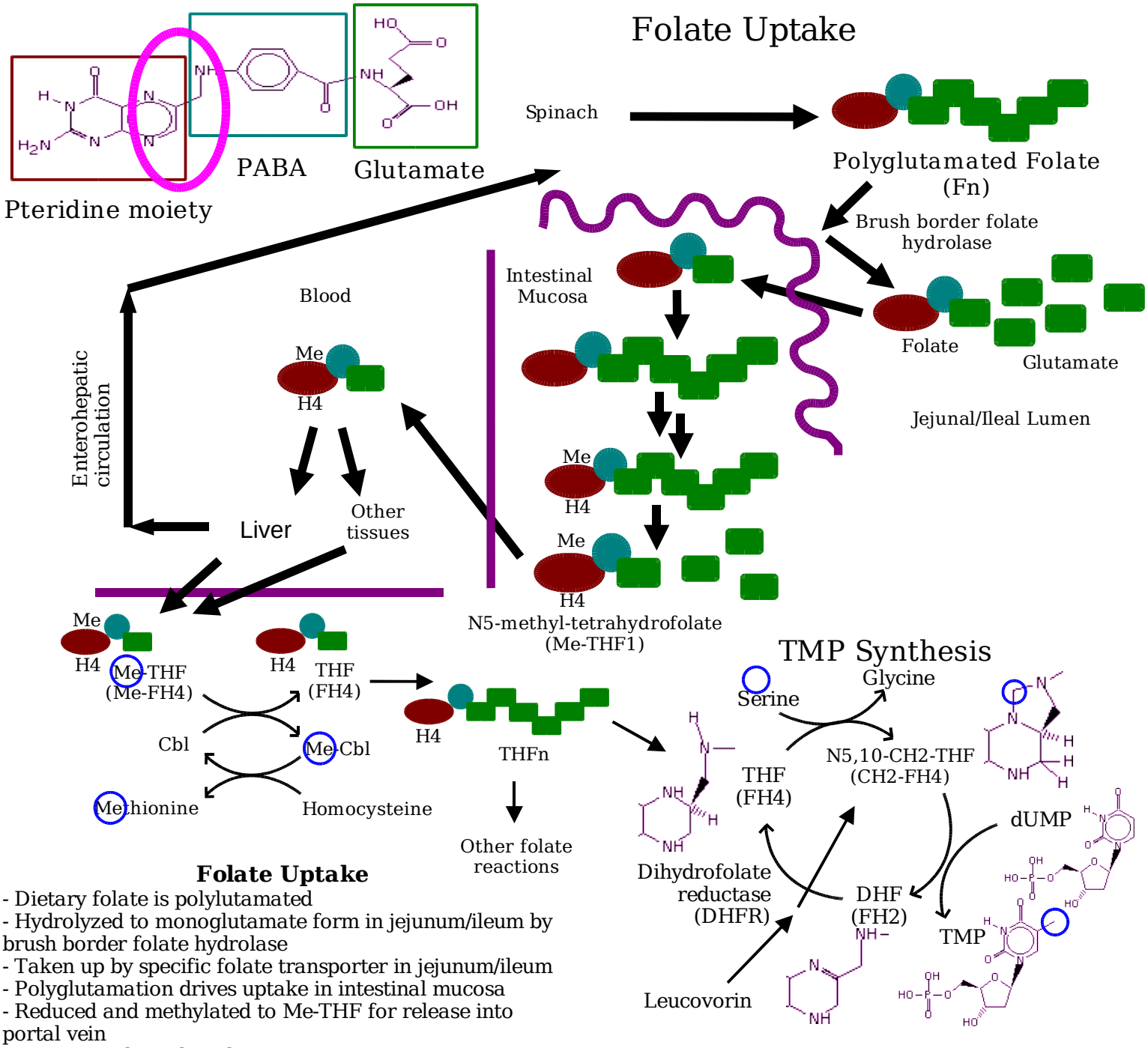
Folate Absorption and Biochemistry



Folate Uptake

- Dietary folate is polylutamated
- Hydrolyzed to monoglutamate form in jejunum/ileum by brush border folate hydrolase
- Taken up by specific folate transporter in jejunum/ileum
- Polyglutamation drives uptake in intestinal mucosa
- Reduced and methylated to Me-THF for release into portal vein
- 2/3 protein-bound in plasma
- Taken up by liver and other tissues; demethylated to THF and polyglutamated again
- Strong enterohepatic circulation
- Malabsorption or dietary deficiency can cause symptoms within weeks or months
- Vit. B12 (cobalamin) deficiency takes years to develop

Biochemical Activities of Folate

- One-carbon donor/acceptor
- Nucleotide synthesis: purines (AMP, GMP) can also be synthesized by “salvage pathway”, but thymidine (methylation of dUTP to TMP) strictly requires folate
- Amino acid metabolism: methionine synthesis from homocysteine; serine and glycine metabolism
- Histidine, betaine, choline catabolism

Causes of Folate Deficiency

- Decreased intake: poverty, famine, unusual diets
- Increased requirements: pregnancy/lactation, hyperemesis gravidarum, prematurity/infancy
- Malabsorption: congenital, drug-related?, tropical and non-tropical sprue
- Defective cellular uptake (congenital)
- Drugs: ethanol, sulfasalazine, oral contraceptives, anticonvulsants, antifolates (methotrexate, even trimethoprim and pyrimethamine in deficient patients)
- Acute idiopathic