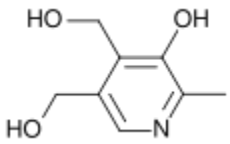
Vitamin B_6 and Pregnancy

Vitamin B_6 is the collective term for a group of three related compounds: pyridoxine, pyridoxal and pyridoxamine, and their phosphorylated derivatives. All six of these vitamers can be referred to as vitamin B_6, but pyridoxine is the vitamer that is typically used interchangeably with the term vitamin B_6. [1] The vitamers differ by the nature of the chemical group occupying the 4 position of the parent compound. Pyridoxine has a hydroxymethyl group in the 4 position. The molecular formula is $C_8H_{11}NO_3$ and the structural formula is shown below. [2]



Vitamin B_6 functions as a coenzyme in a variety of enzymatic reactions in the metabolism of amino acids, one-carbon units, lipids, and the pathways of gluconeogenesis, heme, and neurotransmitter biosynthesis. Pyridoxal 5-phosphate is the most common vitamin B_6 coenzyme. The structure makes it well suited to serve as a coenzyme for more than 100 different enzymes.

Action
Vitamin B_6, principally in the form of the coenzyme pyridoxal 5-phosphate, is involved in a wide range of biochemical reactions, including the metabolism of amino acids and glycogen, the synthesis of nucleic acids, hemoglobin, sphingomyelin and other sphingolipids, and the synthesis of the neurotransmitters serotonin, dopamine, norepinephrine and gamma-aminobutyric acid (GABA). Vitamin B_6 has antineurotoxic activity and may have activity in a number of inborn errors of metabolism, including pyridoxine-dependent seizures in infants, sideroblastic anemia, primary hyperoxaluria, homocystinuria and cystathioninuria. Vitamin B_6 has putative antiatherogenic, immunomodulatory, anticarcinogenic and mood-modulatory activities. [1] Pyridoxal 5-phosphate may affect steroid hormone function through modulation of steroid hormone receptor-mediated gene transcription, although the physiologic implications of this interaction are uncertain. [2]

Mechanism of Action
Until the specific actions of pyridoxine are determined, the mechanism of action is a matter of speculation. Vitamin B_6 deficiency was suspected in pregnant women based solely on its ability to relieve nausea [3], a therapeutic use which persists to date. Early evidence showed a biochemical disturbance in the vitamin B_6 metabolism beginning in the first trimester of pregnancy. Research now indicates the ability to synthesize pyridoxine 5-phosphate remains unchanged during pregnancy, as do the absorption of pyridoxine and the distribution of pyridoxine 5-phosphate. However, the metabolism of pyridoxine 5-phosphate appears to be markedly increased. The large increase in metabolic capacity may be primarily responsible for the decrease in plasma and tissue pyridoxine 5-phosphate concentrations in pregnancy. [4]

In recent years evidence has led to the consensus that during pregnancy most women have some level of deficiency of vitamin B_6 compared to age-matched nonpregnant women. [5-10] In addition, many experts consider the RDA for vitamin B_6 for pregnant women to be too low. [10-12]

Pharmacology
Phosphorylated forms of vitamin B_6 undergo hydrolysis in the small intestine. Nonphosphorylated forms are absorbed by passive diffusion in the intestine. The efficacy of absorption of vitamin B_6 is very high. [1] Bioavailability of vitamin B_6 in humans consuming a mixed diet is approximately 75%. [13] Vitamin B_6 enters into portal circulation and is bound to albumin in the plasma and hemoglobin in erythrocytes for transport. [14] Erythrocytes may serve as a component of vitamin B_6 transport between tissues. The liver is the primary site of vitamin B_6 metabolism through which pyridoxal 5-phosphate is generated for hepatic use and export to extrahepatic tissues. [2] Two hepatic enzymes oxidize excess pyridoxal in tissues to 4-pyridoxic acid, the primary form of the vitamin excreted in the urine. [1]

Indications and Usage
Vitamin B_6 has been used to reduce the severity of nausea and hyperemesis gravidarum associated with pregnancy since 1942. [3,15-18]

Research Summary
A double-blind trial indicated that vitamin B_6 alleviated the severe nausea and significantly reduced the vomiting associated with pregnancy in women who received vitamin B_6 in 25 mg doses every eight hours for three days. [16] Another double-blind, placebo-controlled trial showed a significant decrease in nausea scores among women taking 30 mg/day vitamin B_6 over a 5 day period. [17] A Cochrane Review of interventions for nausea and vomiting in early pregnancy indicated most of the drugs listed, including pyridoxine (vitamin B_6), have been shown to be more effective than placebo in reducing nausea and vomiting. Of the drugs listed in the review, pyridoxine was the least likely to cause side effects. [18] Additional observations suggest that maternal vitamin B_6 status may influence reproductive events throughout the entire course of pregnancy, from the time of conception through delivery. [19]

Contraindications
Vitamin B_6 is contraindicated in those hypersensitive to any component of a vitamin B_6-containing product. [1]

Precautions
Individuals who are being treated with levodopa without concurrently taking carbidopa should avoid taking B-natal. [1]

Drug Interactions
Certain medications interfere with the metabolism of vitamin B_6, and may result in deficiency if individuals taking such medications are not given supplemental vitamin B_6. The anti-tuberculosis medications, isoniazid and cycloserine, the metal chelator, penicillamine, and anti-Parkinsonian drugs, including L-dopa, form complexes with vitamin B_6, creating a functional deficiency. The efficacy of other medications may be altered by high doses of vitamin B_6. High doses of vitamin B_6 have been

found to decrease the efficacy of the anticonvulsants, phenobarbitol and phenytoin, and L-dopa. [20]

Food and Nutrient Interactions

Alcohol may increase the catabolism of pyridoxal 5-phosphate, a form of vitamin B_6. Chronic and excessive use of alcoholic beverages can result in vitamin B_6 deficiency. [1]

Adverse Reactions

Doses of vitamin B_6 of up to 200 mg/day are generally well tolerated. Adverse reactions reported with high doses (greater than 200 mg/day) of vitamin B_6 include nausea, vomiting, abdominal pain, loss of appetite and breast soreness. [1]

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