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## Riboflavin Deficiency

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## Introduction

Riboflavin, vitamin B2, is a water-soluble and heat-stable vitamin that the body uses to metabolize fats, protein, and carbohydrates into glucose for energy. In addition to boosting energy, riboflavin is used as an antioxidant for proper function of the immune system, healthy skin and hair. This is done with the help of two main coenzymes, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD). Without an adequate amount of riboflavin, macromolecules like carbohydrates, fats, and proteins cannot be digested and maintain the body. With a healthy digestive system, the body can absorb most of the nutrients from the diet, so it is important to get most of the riboflavin from dietary sources. Riboflavin has a yellow-green fluorescent pigment, which causes urine to turn yellow and that means the body is absorbing riboflavin. Riboflavin also helps convert tryptophan to niacin, which activates vitamin B-6. Some diseases that can be prevented with adequate riboflavin are anemia, cataracts, migraines, and thyroid dysfunction. Riboflavin is necessary for normal development, lactation, physical performance, and reproduction.[1][2]

## Etiology

Riboflavin deficiency can be caused by an inadequate dietary intake or by endocrine abnormalities. Riboflavin deficiency is associated with other vitamin B complexes. Riboflavin is naturally found in some food such as eggs, dairy products, meats, green vegetables, and grains. The main antioxidant riboflavin works as is glutathione. Glutathione works to destroy free radicals and detox the liver, as free radicals can cause to develop several diseases. Riboflavin deficiency is also caused by chronic diarrhea, liver disorder, alcoholism, and hemodialysis.[3][4][5]

## Epidemiology

Riboflavin deficiency is extremely rare in the United States. Riboflavin deficiency is most common in developing countries in Asia and Africa. Older adults, alcoholics, and women who take birth control pills are most likely to suffer from riboflavin deficiency since the body cannot absorb much riboflavin when on birth control pills. Riboflavin deficiency can be related to many developmental abnormalities such as cleft lip and palate, growth retardation, and cardiac disease. Pregnant and lactating women, people with Brown-Vialetto-Van Laere syndrome (BVVL), and people who are vegan are also at risk of riboflavin deficiency.

## Pathophysiology

Research has shown that riboflavin deficiency can alter iron absorption and cause an anemia which leads to fatigue. Riboflavin is involved in red blood cell production and transportation of oxygen to the cells. Improving the amount of riboflavin in the body can increase circulating hemoglobin levels and increase red cell production. Collagen is a protein found in most skin and hair, so riboflavin is necessary to maintain a good collagen level. Taking supplements of riboflavin is also a cure for migraines. Research showed that 400 mg of riboflavin a day had demonstrated efficacy in prevention of a migraine in adults, but it must be taken for a minimum of 3 months for good results. This is most likely because mitochondrial dysfunction has been shown to play a role in migraines, and riboflavin is a precursor of

flavin cofactors of the electron transport chain. According to research, riboflavin supplements can help with mitochondrial complex I deficiency by improving muscle strength, cardiomyopathy, and encephalopathy. Cataract is an eye disorder causing blurry lens, and taking riboflavin supplements can help prevent cataract. Along with cataract, riboflavin can help other eye disorders such as glaucoma and keratoconus. Riboflavin drops are usually added to the patient's corneal surface to increase the strength of the cornea. Taking riboflavin supplements can also reduce homocysteine levels and blood pressure. According to research, lowering homocysteine by 25% can lower risk of coronary heart disease and stroke. Homocysteine is an amino acid that the body makes from methionine, which is obtained through nutritional factors.

## Toxicokinetics

Severe riboflavin deficiency can diminish levels of FAD and FMN and affect the metabolism of other nutrients especially all of vitamin B. Riboflavin is excreted out of the body while only 15% of it is absorbed. Carbohydrates received from food are converted to ATP, which is then used to produce energy in the body. It is important to consume riboflavin every day either by food or with supplement. Most of the riboflavin is absorbed in the small intestine and excess is passed out of the body as urine. Urinary excretion can also decrease with age and stress. Hydrolysis of FAD and FMN to riboflavin done by pyrophosphates and phosphatase must occur in the upper intestine for dietary riboflavin absorption. Individuals who eat nutritional diets may not need supplements; therefore, it is necessary that food being consumed is rich in B vitamins along with others. Also, nutritional foods provide better absorption of riboflavin compare to supplements.

## History and Physical

Riboflavin deficiency can cause fatigue, swollen throat, blurred vision, and depression. It can affect the skin by causing skin crack, itching, and dermatitis around the mouth. Hyperemia and edema around throat, liver degeneration, and hair loss can also occur along with reproductive issues. Usually, people with riboflavin deficiency also have deficiencies of other nutrients. In most cases, riboflavin deficiency can be reversed unless it is anatomical changes such as cataracts.

## Evaluation

In a therapeutic trial, riboflavin deficiency can be confirmed by measuring the rate of urinary excretion of riboflavin. Urinary excretion increases as riboflavin supplements are taken. If urinary riboflavin excretion is lower than 40 micrograms per day, then riboflavin deficiency is occurring. Measuring erythrocyte glutathione reductase can aid in detecting riboflavin deficiency. When enzyme activity coefficient with FAD is 1.4 or higher, riboflavin deficiency is indicated.[6][7][8]

## Treatment / Management

Riboflavin supplements come in 25 mg, 50 mg, and 100 mg tablets. According to the National Institutes of Health, the recommended daily nutrient intake of riboflavin is 1.3 mg for men, 1.1 mg for women, 1.3 mg for male adolescents (age 14 to 18), and 1.0 mg for female adolescents (age 14-18). It is recommended that pregnant women take 1.4 mg and breastfeeding women take 1.6 mg. For infants age of 0 to 6 months old is 0.3 mg, 7 to 12 months is 0.4 mg, 1 to 3 years old is 0.5 mg, 4 to 8 years old is 0.6 mg, and 9 to 13 years old is 0.9 mg. It is important to take riboflavin supplements between meals because absorption levels increase with food. If supplements cannot be taken orally, then injections can also be used.[9][10]

## Pearls and Other Issues

Taking certain medications such as anticholinergic, anticonvulsants, phenothiazines, and phenytoin can reduce the level of riboflavin by not being able to be absorbed effectively into the body. Riboflavin can also interfere with some medications such as tetracycline, which is an antibiotic and doxorubicin, a chemotherapy drug.

## Enhancing Healthcare Team Outcomes

Riboflavin deficiency is not common in the USA. The best way to prevent it is to educate the patient on a healthy diet. The primary care provider, nurse practitioner, pharmacist and the dietitian should regularly encourage patients about eating fruits and vegetables. In addition, most cereals are also fortified with multivitamins. Empirically recommending vitamins for everyone is not recommended.[11][12][13]

## Questions

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