

# DIETARY SUPPLEMENTS IN THE TREATMENT OF INFERTILITY

## Introduction

Vitamins are organic molecules that are required for a wide-variety of cellular activities, but cannot be synthesized in the bodies of humans and must, therefore, be obtained through the diet. Minerals are inorganic molecules and are required for body structure (e.g. calcium and phosphorous for bone), as carriers of specific molecules (e.g. iron in hemoglobin) and as components or co-factors for many enzymatic reactions. In theory, a well-rounded complete diet will satisfy all the nutritional requirements of vitamins and minerals. However, modern lifestyles may interfere with proper nutrition. Moreover, the dietary content of vitamins and minerals may be insufficient to meet the additional requirements caused by stress and environmental factors.

Of particular note are antioxidants that act to detoxify oxygen radicals that have been linked to cellular degeneration and aging. It has been suggested that vitamin and micronutrient deficiencies may be responsible for some aspects of human infertility, and consequently that dietary supplementation may improve fertility in some cases. Specific herbs and other dietary supplements may mimic or aid in the action of vitamins and minerals.

## Oxygen Radicals and Antioxidants

Oxygen radicals are partially reduced, highly reactive oxygen intermediates including the superoxide anion, hydrogen peroxide and the hydroxyl radical. They are produced by a variety of oxidation reactions including NADPH oxidase and the electron transport chain, and can have severely detrimental effects on the structure and function of cell membranes, proteins, and DNA.

Oxygen radicals are produced in semen by nucleophils and/or by sperm but are normally detoxified by enzymatic reactions or by antioxidants such as vitamin E, vitamin C, reduced glutathione, carnitine and pyruvate. However, if the production of oxygen radicals exceeds the capacity of the antioxidants to detoxify them, then the sperm can be irreversibly damaged. Many studies have shown a direct relationship between the presence of oxygen radicals in semen and fertility, and most of the vitamin and mineral supplements used for the treatment of infertility in men are directly or indirectly linked to increasing the concentration of antioxidant activity in seminal plasma.

## Effects of Nutrient Supplementation on the Fertility of Women

**L-arginine**, an amino acid, is the substrate for the production of nitric oxide, a short-acting second messenger that stimulates ovarian blood flow and thereby improves follicular development. Treatment of women who had previously poorly responded to gonadotrophin stimulation resulted in increased numbers of oocytes retrieved and embryos transferred.

**Folic acid** is the precursor for 5-methyltetrahydrofolate, a co-enzyme that functions as a methyl donor in many synthetic reactions. Folate deficiency during pregnancy has been linked to spina bifida and other fetal neural tube defects and therefore it is recommended that all pregnant women, and women attempting to become pregnant, take a folic acid supplement of 0.4 mg/day.

**Vitamin C** (ascorbic acid) is required for collagen and steroid hormone synthesis, and acts as a general antioxidant and for the recycling of Vitamin E. Vitamin C supplementation of IVF patients during gonadotrophic stimulation resulted in significantly increased vitamin C concentrations in follicular fluid, and an increase in pregnancy rate, particularly in smokers.

**Vitamins with Herbal Supplements:** One study has shown a positive effect of a mixture of vitamins B6, B12 and E, and folic acid, iron, magnesium, selenium, zinc, L-arginine, chasteberry and green tea on infertility. Treatment of women who did not conceive after trying for 6-36 months resulted in 5 of 15 becoming pregnant, compared with 0 of 15 in the control group.

## **Effects of Nutrient Supplementation on the Fertility of Men**

**Vitamin B12** is a coenzyme in nucleic acid metabolism and is particularly important for the prevention of pernicious anemia. Vitamin B12 is found in meat and its deficiency is rare, except in strict vegetarians where it may affect fertility. Two Japanese papers have shown a positive effect of Vitamin B12 supplementation on sperm motility and sperm count, possibly reflecting the relatively lower amount of meat in the Japanese diet.

**Vitamin C** is the major antioxidant in seminal plasma and, in addition, serves to recycle the Vitamin E present in sperm membranes. Treatment with Vitamin C alone has been shown to increase sperm quality in smokers and to decrease the amount of oxidative damage to sperm DNA in healthy men.

**Vitamin E and Selenium:** Vitamin E associates with the sperm membrane where it is the principle antioxidant, and serves to inhibit lipid peroxidation. Selenium is required for the synthesis of glutathione peroxidase which, acts to reduce hydrogen peroxide and thereby inhibit the formation of lipid peroxides. Given alone, treatment with Vitamin E has been shown to produce increases in sperm motility, zona binding, and pregnancy rate. Combined treatment with Vitamin E and selenium resulted in increased sperm motility, percent live sperm, and percent normal sperm, and decreased the oxidation of membrane lipids.

**Carnitine** is required for the transport of long-chain fatty acids across the inner mitochondrial membrane for metabolism. Acetyl-carnitine is the major form of carnitine found in sperm. In three studies, treatment with carnitine or acetyl-carnitine resulted in increases in sperm concentration and motility.

**Folic Acid and Zinc:** Folic acid is the precursor for 5-methyltetrahydrofolate, a co-enzyme that functions as a methyl donor in many synthetic reactions. Zinc is a co-factor for many metalloenzymes and is involved in nucleotide and protein biosynthesis, cell division and membrane stability. It is found in high concentrations in seminal fluid, primarily from prostatic secretion. Treatment with folic acid alone resulted in increased sperm numbers and motility, and decreased number of round cells. Zinc alone produced increases in sperm count, morphology and motility. Given together, folic acid and zinc resulted in increased normal sperm count.

### **Conclusions**

The poor diets and stress associated with modern lifestyles may impair the fertility of both men and women. A daily dose of vitamins and minerals can correct for dietary deficiencies and thereby optimize a couple's potential for fertility.