

## **Cervical Dysplasia**

Cervical dysplasia describes abnormal cervical cells discovered upon pap smear analysis. Cervical dysplasia is usually graded according to its severity, which can range from mild inflammation to precancerous changes to localized cancer. Cervical cancer is a common, sometimes fatal disease. It is now known that human papilloma virus is the major cause of cervical dysplasia, which is transmitted via sexual intercourse. More than 90% of cervical cancers contain DNA of the higher risk HPV viruses and that DNA has been found to be present in the early stage lesions of cervical cancer.

There are no symptoms of cervical dysplasia until the disease has progressed into advanced cancer. Therefore, it is crucial that sexually active women, or women over age 20, have yearly Pap smears until the age of 65. Women who experience bleeding between menstrual periods, bleeding after intercourse, abnormal vaginal discharge, abdominal pain or swelling, urinary symptoms, or pelvic pain should be evaluated by a healthcare provider, even if it is not the regular time for a Pap test. The presence of cervical dysplasia requires medical attention in all cases.

From a lifestyle standpoint, cigarette smoking increases the risk of cervical dysplasia, and increases the likelihood that mild forms of dysplasia will progress to more severe forms. Women who become sexually active at an early age and have multiple sexual partners are at increased risk for developing cervical dysplasia. For those who are sexually active, using barrier methods of contraception, such as a condom or diaphragm, is associated with reduced risk of cervical dysplasia.

A superior level of nutritional status of vitamin A, carotenoids such as lycopene, vitamin C, vitamin E, and folic acid have been reported to be associated with a reduced risk of cervical dysplasia.

**Supplement Considerations:** In the early stages of cervical dysplasia doctors sometimes take a “wait and see what happens” approach, known also as “watchful waiting”. During this period it may be beneficial to consider an aggressive supplementation program involving nutrients that have shown promise in either preventing or reversing this condition. Supplementation considerations in this case include:

1. High Potency Multi Vitamin and Mineral – this will provide a foundation of nutrients that are important to the normal development of cervical cells and provides a boost in levels of antioxidants and B-vitamins that are associated with the prevention of cervical dysplasia and the promotion of healthy cervical cells.

2. Additional Beta-carotene-----50,000-90,000 IU per day - Beta-Carotene has been shown to influence cellular differentiation of surface lining cells (epithelial cells) and enhances immune-system function. Beta-Carotene was shown to halt the progression of cervical dysplasia and cause a reversal in some cases involving early and moderate stages of this condition, which is known to be a pre-cancerous condition.

Note that individuals who are smokers and individuals diagnosed with lung cancer should refrain from using high doses of beta-carotene (no higher than 10,000-15,000 IU), according to the implications of two clinical studies.

3. Folic acid-----5-10 mg per day (note that this is a very high intake of folic acid and requires physician consent and monitoring) - In clinical studies Folic Acid supplementation (10 mg per day) has been shown to reverse early and moderate stage cervical dysplasia as demonstrated by pap smear testing. Success rates vary from 20 to 100 percent. Folic Acid appears to improve the integrity (chromosomal linkages) of cervical DNA, making it less resistant to the effect of the human papilloma virus (HPV). The HPV is known to cause cervical dysplasia. The B-vitamin Folic Acid is critical to synthesis of normal DNA as cells divide from one generation to the next. Cells that line the cervix replace themselves every 7-14 days and, therefore, the cells must continuously form DNA as part of their genetic structure. Previous studies have demonstrated that poor Folic Acid status can lead to DNA abnormalities with subsequent development of cervical dysplasia or megaloblastic features of cervical cells (large abnormal cell appearance). Oral contraceptives are known to increase the rate of cell division of cervical cells, hence, escalating the need for adequate Folic Acid intake. Studies by Whitehead et al. and Butterworth et al. demonstrated that Folic Acid supplementation could reverse cervical megaloblastic changes and cervical dysplasia, respectively, in patients using oral contraceptives. In fact, oral contraceptive use is a known risk factor for cervical dysplasia, primarily due to its effect on speeding up cell division rates.

In the study by Butterworth et al., patients with mild and moderate degrees of cervical dysplasia showed reversal of their condition over a 3-month trial period with Folic Acid supplementation.

4. Additional Vitamin E Succinate - 400 IU per day - A number of large studies have shown that low levels of vitamin E are associated with a greater risk for cervical dysplasia and infection with the HPV virus, which causes cervical dysplasia. In addition to having antioxidant abilities, vitamin E also demonstrates anti-proliferative effects, slowing down cell replication. It has been shown that vitamin E forms a complex with a protein receptor that activates and/or increases the expression of the phosphatase gene A1 and A2 which encourages the de-activation of a protein called Kinase C. Decreased

activity of kinase C inhibits the activity of an important enzyme called ornithine decarboxylase, and, in turn, inhibits DNA synthesis of cells that are showing uncontrolled replication (such as precancerous cells). In summary, vitamin E may help put the brakes on precancerous cells, preventing them from replicating as quickly as they are inclined to do.

5. Additional Lycopene-25 mg per day – Low levels of lycopene is associated with an increased risk of cervical dysplasia.

#### **Beta-Carotene References :**

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2. Ho GY, Palan PR, Basu J, et al. Viral characteristics of human papillomavirus infection and antioxidant levels as risk factors for cervical dysplasia. *Int J Cancer* 1998;78:594–9
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4. Liu T, Soong SJ, Wilson NP, Craig CB, Cole P, Macaluso M, et al. A case control study of nutritional factors and cervical dysplasia. *Cancer Epidemiol Biomarkers Prev*. 1993;2(6):525-30.

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3. Butterworth CE Jr, Hatch KD, Macaluso M, et al. Folate deficiency and cervical dysplasia. *JAMA* 1992;267:528–33).

**Vitamin E References:**

1. Kwasniewska A, Tukendorf A, Semczuk M. Content of alpha-tocopherol in blood serum of human Papillomavirus-infected women with cervical dysplasias. *Nutrition and Cancer* 28(3):248-251, 1997.
2. Palan PR, et al. Plasma levels of antioxidant beta-carotene and alpha-tocopherol in uterine cervix dysplasias and cancer. *Nutr Cancer*. 1991;15(1):13-20.

**Lycopene References:**

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2. VanEenwyk J, Davis FG, Bowen PE. Dietary and serum carotenoids and cervical intraepithelial neoplasia. *Int J Cancer* 1991;48:34–8.