
The Doctor's RESEARCH UPDATE

Natural Medicine for Women's Health

Michael A. Zelig, M.D.



Dr. Zelig earned a Masters degree in stress-physiology from the University of California, Santa Barbara, completed a fellowship in Molecular Immunology, and received his M.D. from the University of California, Irvine, College of Medicine. Dr. Zelig is a leading authority on diindolylmethane (DIM). He was awarded a patent for his microencapsulated formulation of absorbable DIM and has numerous issued and pending patents for novel uses of DIM in preventive medicine. As a physician-investigator, he has sponsored clinical trials for HPV, cervical dysplasia, uterine, and prostate health. These clinical trials are underway in collaboration with Cornell University, the NYU School of Medicine, Cancer Research UK, Wayne State University, and New York Medical College. The National Cancer Institute, under a clinical trials agreement with Dr. Zelig, has sponsored additional clinical trials investigating microencapsulated DIM as a natural preventive and therapeutic candidate for cancer.

The Doctor's Research Update Publications are available on the internet at: www.dimfaq.com

Nutritional Support for Uterine Health

The uterus, or womb, is the organ whose maturity defines feminine adulthood and provides for reproduction. The uterus consists of two primary tissues which are highly sensitive to estrogen and progesterone and whose monthly growth and decline produce the menstrual cycle. First is the glandular endometrium, or inner lining of the uterus, where monthly tissue loss with the fall in ovarian estrogen and progesterone results in menstrual bleeding. Second is the muscular myometrium, consisting of hormone sensitive smooth muscle which responds with significant growth and specialized contraction during pregnancy and the birth process. In middle age, both the endometrium and myometrium are prone to unwanted proliferation and growth due to increasing stimulation from estrogen. The absence of adequate progesterone in peri-menopause worsens this hormonal imbalance producing one form of "Estrogen Dominance". Obesity and smoking further contribute to disordered estrogen metabolism and excess proliferation of the endometrium.

Uterine Health Issues

Painful menstruation is severe and incapacitating for 1-3 days a month in some young women and more often in middle-aged women before menopause. Due to increasing estrogen production in the 3rd to 4th decade of life, most women develop irregular uterine bleeding and many proceed to excessive menses and occasional bleeding between

menses. Dysfunctional uterine bleeding is characteristic of excessive estrogen stimulation of the endometrium and, if not normalized, can progress to endometrial proliferation, hyperplasia, and cancer. Pelvic pain before and during menstruation can be caused by Endometriosis. Endometriosis is defined as endometrium persisting outside the uterus, typically in the pelvic abdominal space. Also causing abnormal menstruation are proliferation of myometrial smooth muscle with persisting benign overgrowths known as "fibroids" or leiomyomas. Both proliferative endometrium and fibroids can cause painful and excessive menstruation in women and these symptoms become worse in the years before menopause. Surgical intervention is the currently accepted treatment of both proliferative endometrium and uterine fibroids, but this approach does not consider the available benefits from nutritional intervention.

The Nutritional Connection to Uterine Health

Unfavorable estrogen metabolism, known by minimal production of 2-hydroxy estrogen and increased production of 16-hydroxy estrogen, has been linked to endometrial cancer¹. The use of natural and synthetic estrogen in perimenopausal and menopausal women also clearly increases the rate of dysfunctional uterine bleeding and increases the risk of subsequent endometrial cancer. Long term Tamoxifen use also results in uterine hyperplasia and dysfunctional bleeding.

Using nutritional intervention to promote more healthy estrogen metabolism is now considered an alternative means to prevent endometrial proliferation. Desirable estrogen metabolism for uterine health increases the 2-hydroxylation of estrogen². Nutritional factors, particularly the intake of cruciferous vegetables, are associated with greater 2-hydroxylation of estrogen³. Crucifers provide the indole phytonutrient, Diindolylmethane (DIM). Absorbable DIM supplements have been shown to reduce estrogen-driven uterine growth and help normalize proliferating endometrium and excessive bleeding in certain cases⁴. Studies also show that DIM causes the programmed death of endometrial cancer cells⁵.

Nutritional Supplement Approaches to Uterine Health

A healthy diet for uterine health includes regular intake of raw or lightly cooked cruciferous vegetables³. Supplemental Omega-3 oils have also been shown to benefit women with painful menstruation⁶.

Use of absorbable DIM supplements supports menstrual health where concerns exist regarding painful menstruation or endometriosis⁸. Use of absorbable DIM supplements (150-300 mg) taken once or twice daily depending on symptoms is highly successful in pre-menopausal women with uterine health concerns⁴.

Genistein (75-150 mg/day) from soy isoflavones, taken in conjunction with absorbable DIM, further supports uterine health where concerns exist regarding uterine fibroids⁷.

Absorbable DIM can provide a nutritional advantage and promote healthy estrogen metabolism in women seeking alternatives to surgery for the promotion of uterine health.

References:

1. Fishman J, Schneider J, Herschcope RJ, Bradlow HL. **Increased estrogen-16 alpha-hydroxylase activity in women with breast and endometrial cancer.** *J Steroid Biochem.* 1984 Apr;20(4B):1077-81.
2. Bradlow HL, Telang NT, Sepkovic DW, Osborne MP. **2-hydroxyestrone: the 'good' estrogen.** *J Endocrinol.* 1996 Sep;150 Suppl:S259-65.
3. Fowke JH, Longcope C, Hebert JR. **Brassica vegetable consumption shifts estrogen metabolism in healthy post-menopausal women.** *Cancer Epidemiol Biomarkers Prev.* 2000 Aug;9(8):773-9.
4. Zeligs, MA, Fulfs, JC, Peterson, R, Wilson, SM, McIntyre, L, Sepkovic, DW, and Bradlow, HL. **In vivo, uterine-protective activity of absorption-enhanced diindolylmethane: Animal and preliminary human use in combination with Tamoxifen.** *Proc Am Assoc Cancer Res.* 2003; 44:1268 (#6347).
5. Leong H, Firestone GL, Bjeldanes LF. **Cytostatic effects of 3,3'-diindolylmethane in human endometrial cancer cells result from an estrogen receptor-mediated increase in transforming growth factor-alpha expression.** *Carcinogenesis.* 2001 Nov;22(11):1809-17.
6. Sampalis F, Bunea R, Pelland MF, Kowalski O, Duguet N, Dupuis S. **Evaluation of the effects of Neptune Krill Oil on the management of premenstrual syndrome and dysmenorrhea.** *Altern Med Rev.* 2003 May;8(2):171-9.
7. Shushan A, Ben-Bassat H, Mishani E, Laufer N, Klein BY, Rojansky N. **Inhibition of leiomyoma cell proliferation in vitro by genistein and the protein tyrosine kinase inhibitor TKS050.** *Fertil Steril.* 2006 Oct 27
8. Zeligs MA. **Phytochemicals for the treatment of mastalgia and endometriosis.** *US Patent #6,689,387.* 2004 Feb 10.