

# Are Hormones Safe

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Are you worried about developing breast cancer, or have been told not to take hormones as they will cause breast cancer. Your anxiety may be misplaced. Your risk of having breast cancer is far lower than your risk of having or dying from cardiovascular disease. Heart disease is responsible for more deaths in women than all forms of cancer combined and is the most significant health concern for women in the United States today, causing nearly 350,000 deaths each year compared to only 40,000 from breast cancer.

What is even more concerning is that the media and many practitioners fail to tell you that certain hormones will reduce the risk of cardiovascular disease as much sixty percent without increasing your risk of breast cancer! This is good news. Sadly, the media focuses on reports of breast cancer run rampant without educating and warning women about the more imminent danger of heart disease.

The media warns women about the risks of HRT *regardless of the types of hormones that were used in the studies*. No matter what type of hormones were used, bioidentical, synthetic, horse derived hormones, oral or transdermal, when presented to you the consumer, they all fall under the umbrella of HRT, which gives every type of hormone replacement a bad name.

In 2007, Fournier et al reported an association between various forms of HRT and the incidence of breast cancer in more than 80 000 postmenopausal women who were followed for more than eight postmenopausal years. Compared with women who had

never used any HRT, women who used estrogen only had a non-significant increase of breast cancer. If a synthetic progestin was used in combination with estrogen, the risk for breast cancer increased significantly. However, for women who used bioidentical progesterone in combination with estrogen, the increased risk for breast cancer was eliminated with a significant reduction in breast cancer risk compared with synthetic progestin use. In a previous analysis of more than 50 000 postmenopausal women, Fournier et al found that the risk for breast cancer was significantly increased if synthetic progestins were used, but was reduced if progesterone was used.

The WHI study clearly proved that Provera (medroxyprogesterone acetate) caused breast cancer and heart disease while Premarin (conjugated estrogens) taken alone showed a decreased incidence of breast cancer and a significant reduction of coronary calcium scores.

The WHI study came to an abrupt halt in July 2002 because the combination of Premarin and Provera also marketed as PremPro showed an increased risk of breast cancer, coronary heart disease, and stroke. Specifically, the study showed women who took the combination of Premarin and Provera had a twenty-four percent increased risk of breast cancer and an overall twenty-four percent increased risk of coronary heart disease then those who didn't.

**However, what is important to know is that the women, who took Premarin without Provera, had no increased risk of breast cancer. Also, after five years, the same group of women showed sixty-one percent less calcified plaque of their coronary arteries compared to the women who took a placebo.** However, Premarin did seem to increase the risk of clotting causing strokes and heart attacks. This risk was amplified when Provera was added. Recent research indicates that when bioidentical estrogen is taken through the skin by patch or cream, this problem is eliminated, and there seems to be no increased risk of clotting.

Several studies, including the Nurses' Health Study and the WHI showed that those women currently using estrogen replacement therapy or HRT have a significantly

lower risk of colorectal cancer. A new finding, published in the January 2009 issue of *Cancer Epidemiology, Biomarkers and Prevention*, found a seventeen percent reduced risk of colorectal cancer among women who had at one time used estrogen, a 25 percent reduced risk among women currently using estrogen, and a 26 percent reduced risk among those using estrogen for 10 or more years.

Now, hormone experts throughout the world have concluded that replacing your hormones is safe, and healthy women going through the first few years of menopause who need HRT to relieve symptoms should have no fears about its use.

The First Global Summit on Menopause-related Issues, held in Zurich on March 29 and 30, 2008, involved forty of the world's leading menopause experts who met to review public perceptions, risks, and benefits of hormone replacement therapy. They were looking at four main areas of controversy: cardiovascular health, breast issues, cognition, and bone issues. The Summit concluded HRT is safe and that healthy women going through the first few years of the menopause who need HRT to relieve symptoms should have no fears about its use.

The American Association of Clinical Endocrinologists and the North American Menopause Society have also come to similar conclusions. Further, Amos Pines, president of The International Menopause Society concluded in a 2007 press statement. "Weighing the overall benefits and risks of HT in the younger postmenopausal population clearly favors the use of HT for symptomatic women."

Heart disease is responsible for more deaths in women than all forms of cancer combined and is the most significant health concern for women in the United States today, causing nearly 350,000 deaths each year compared to only 40,000 from breast cancer. Unfortunately, many doctors misconstrued the results of the WHI believing women are better off not taking any hormone replacement therapy. Consequently, many women will needlessly suffer from and be at increased risk for depression, heart disease, stroke, osteoporosis, and colon cancer while it is clear that the right type of hormone

replacement therapy can significantly reduce the risk of heart disease while not increasing the risk of breast cancer.

## References

- Fernandez E; La Vecchia C; Braga C; Talamini R; Negri E; Parazzini F and Franceschi S, Hormone replacement therapy and risk of colon and rectal cancer. *Cancer Epidemiology Biomarkers & Prevention*, Vol 7, Issue 4 329-333
- Fournier et al, "Use of different postmenopausal hormone therapies and risk of histology- and hormone receptor-defined invasive breast cancer," *J Clin Oncol* 2008 Mar 10;26(8):1260-8.
- Fournier et al, "Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study," *Breast Cancer Res Treat* 2008 Jan;107(1):103-11.
- Fournier et al, "Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort," *Int J Cancer* 2005 Apr 10;114(3):448-54.
- L'Hermite et al, "Could transdermal estradiol+progesterone be a safer postmenopausal HRT? A review," *Maturitas* 2008 Vol 60, Issue 3, Pages 185-201. Adams MR et al. "Inhibition of coronary artery atherosclerosis by 17-beta estradiol in ovariectomized monkeys: Lack of an effect of added progesterone." *Arteriosclerosis* 1990;10:1051-7.
- Adams MR; Golden DL; Clarkson TB. Conjugated equine estrogens alone, but not in combination with medroxyprogesterone acetate, inhibit aortic connective tissue remodeling after plasma lipid lowering in female monkeys. *Atheroscler Thromb Vasc Biol* 1998 Jul;18(7):1164-71.
- Adams MR; Register TC; Golden DL; Wagner JD; Williams JK Medroxyprogesterone acetate antagonizes inhibitory effects of conjugated equine estrogens on coronary artery atherosclerosis *Arterioscler Thromb Vasc Biol* 1997 Jan;17(1):217-21 (ISSN: 1079-5642)
- Bolaji II; Grimes H; Mortimer G; Tallon DF; Fottrell PF; O'Dwyer EM. Low-dose progesterone therapy in oestrogenised postmenopausal women: effects on plasma lipids, lipoproteins and liver function parameters. *Eur J Obstet Gynecol Reprod Biol* 1993 Jan;48(1):61-8.
- Braunsberg HA; Coldham NG; Wong W. Hormonal therapies for breast cancer: can progestogens stimulate growth?. *Cancer Lett* 1986 Feb;30(2):213-8
- Bulbrook RD; Swain MC; Wang DY; Hayward JL; Kumaoka S; Takatani O; Abe O; Utsunomiya J. Breast cancer in Britain and Japan: plasma oestradiol-17beta, oestrone and progesterone, and their urinary metabolites in normal British and Japanese women. *Eur J Cancer* 1976 Sep;12(9):725-35.
- Bush TL; Barrett-Connor E; Cowan LD; Criqui MH; Wallace RB; Suchindran CM; Tyroler HA; Rifkind BM. Cardiovascular mortality and noncontraceptive use of estrogen in women: results from the Lipid Research Clinics Program Follow-up Study. *Circulation* 1987 Jun;75(6):1102-9.
- Chang HJ, Lee TTY et al. Influences of percutaneous administration of estradiol and progesterone on human breast epithelial cell cycle in vivo. *Fertil Steril*. 1995;63:785-791.

Clarkson TB. Progestogens and cardiovascular disease. A critical review. *J Reprod Med* 1999 Feb;44(2 Suppl):180-4

Colditz Ga. Hormones and breast cancer: evidence and implications for consideration of risks and benefits of hormone replacement therapy. *J Women's Health* 1999 Apr;8(3):354-7.

Colditz GA; Hankinson SE; Hunter DJ; Willett WC; Manson JE; Stampfer MJ; Hennekens C; Rosner B; Speizer FE. The use of estrogens and progestins and the risk of breast cancer in postmenopausal women. *N Engl J Med* 1995 Jun 15;332(24):1589-93.

Colditz GA; Rosner B Cumulative risk of breast cancer to age 70 years according to risk factor status: data from the Nurses' Health Study. *Am J Epidemiol* 2000 Nov 15;152(10):950-64

Collins JA, Blake JM, Crosignani PG. "Breast cancer risk with postmenopausal hormonal treatment." *Hum Reprod Update*. 2005 Nov-Dec;11(6):545-60. Epub 2005 Sep 8

Cowan LD; Gordis L; Tonascia JA; Jones GS. Breast cancer incidence in women with a history of progesterone deficiency. *Am J Epidemiol* 1981 Aug;114(2):209-17

Differential Effects of Oral Versus Transdermal Estrogen Replacement Therapy On C-Reactive Protein in Postmenopausal Women by Vanpen Vonpatanasin MD, et.al., *Journal of The American College of Cardiology*, Volume 41: 1358-1363, 2003

Effects of estrogen or estrogen/progestin regimens on heart disease risk factors in postmenopausal women. The Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. The Writing Group for the PEPI Trial. *JAMA* 1995 Jan 18;273(3):199-208

Estrogen Replacement therapy and Heart Disease: A Discussion of the PEPI Trial. Women's Health Information Center.

Ettinger, B., Reduced mortality associated with long-term postmenopausal estrogen therapy. *Obstetrics and Gynecology* 87(#1): January, 6-12 (1996).

Feeman WE. Thrombotic stroke in an otherwise healthy middle-aged female related to the use of continuous-combined conjugated equine estrogens and medroxyprogesterone acetate. *J Gend Specif Med* 2000 Nov-Dec;3(8):62-4;

Fitzpatrick La et al. Comparison of regimens containing oral micronized progesterone of medroxyprogesterone acetate on quality of life in postmenopausal women: a cross-sectional survey. *J Women's Health Gen Based Med* 2000 May;9(4):381-7

Fitzpatrick LA, Good A. Micronized progesterone: clinical indications and comparison with current treatment. *Fertil Steril* 1999 Sept;72(3):389-97.

Foidart JM; Colin C; Denoo X; Desreux J; Beliard A; Fournier S; de Lignieres B. Estradiol and progesterone regulate the proliferation of human breast epithelial cells. *Fertil Steril* 1998 May;69(5):963-9

Formby B, Wiley TS. "Bcl-2, surviving and variant CD44 v7-v10 are down regulated and p53 is up regulated in breast cancer cells by progesterone: inhibition of cell growth and induction of apoptosis." *Mol Cell Biochem*. 1999 Dec;202(1-2):53-61.

Formby B, Wiley TS. "Progesterone inhibits growth and induces apoptosis in breast cancer cells: inverse effects on Bcl-2 and p53." *Ann Clin Lab Sci*. 1998 Nov-Dec;28(6):360-9.

Fournier A, Berrino F, Clavel-Chapelon F. "Unequal risks for breast cancer associated with different hormone replacement therapies" results from the E3N cohort study *Breast Cancer Research and Treatment* 2007

Fournier A, Fabre A, Mesrine S, Boutron-Ruault MC, Berrino F, Clavel-Chapelon F. "Use of different postmenopausal hormone therapies and risk of histology- and hormone receptor-defined invasive breast cancer": *J Clin Oncol.* 2008 Mar 10;26(8):1260-8.

Glass AG, Lacey JV Jr, Carreon D, Hoover RN. Breast cancer incidence, 1980–2006: combined roles of menopausal hormone therapy, screening mammography, and estrogen receptor status. *J Natl Cancer Inst* 2007;99:1152–61

Godsland IF; Gangar K; Walton C; Cust MP; Whitehead MI; Wynn V; Stevenson JC. Insulin resistance, secretion, and elimination in postmenopausal women receiving oral or transdermal hormone replacement therapy. *Metabolism* 1993 Jul;42(7):846-53.

Gompel et al. Antiestrogen action of progesterone in breast tissue. *Breast cancer Res Treat* 1986; 8(3):179-88.

Hargrove, Osteen KG. An alternative method of hormone replacement therapy using the natural sex steroids. *Infertile Repro Med Clinics north Am.* 1995;6:563-674.DNH

Jensen J; Riis BJ; Strom V; Nilas L; Christiansen C. Long-term effects of percutaneous estrogens and oral progesterone on serum lipoproteins in postmenopausal women. *Am J Obstet Gynecol* 1987 Jan;156(1):66-71.

Lee WS; Harder JA; Yoshizumi M; Lee ME; Haber E. Progesterone inhibits arterial smooth muscle cell proliferation. *Nat Med* 1997 Sep;3(9):1005-8.

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Minshall RD; Stanczyk FZ; Miyagawa K; Uchida B; Axthelm M; Novy M; Hermsmeyer K. Ovarian steroid protection against coronary artery hyperreactivity in rhesus monkeys. *J Clin Endocrinol Metab* 1998 Feb;83(2):649-59.

Miyagawa K; Rosch J; Stanczyk F; Hermsmeyer K. Medroxyprogesterone interferes with ovarian steroid protection against coronary vasospasm. *Nat Med* 1997 Mar;3(3):324-7.

Moorjani S; Dupont A; Labrie F; De Lignieres B; Cusan L; Dupont P; Mailloux J; Lupien PJ. Changes in plasma lipoprotein and apolipoprotein composition in relation to oral versus percutaneous administration of estrogen alone or in cyclic association with utrogestan in menopausal women. *J Clin Endocrinol Metab* 1991 Aug;73(2):373-9.

Newham HH. Oestrogens and atherosclerotic vascular disease: lipid factors. *Baillieres Clin Endo Metab* 1993;7:61-93.

O'Meara, Rossing MA, Daling JR, Elmore JG, Barlow WE, Weiss N., et al. "Hormone replacement therapy after diagnosis of breast cancer in relation to recurrence and mortality." *J Natl Cancer Inst.* 2001 May 16;93(10): 733-4

Osborne MP, Bradlow HL, Wong GYC, Telang NT. (1993), Upregulation of estradiol C16 alpha-hydroxylation in human breast tissue: a potential biomarker of breast cancer risk. *J Natl Cancer Inst* 85:1917-1920.

Otsuki M; Saito H; Xu X; Sumitani S; Kouhara H; Kishimoto T; Kasayama S. Progesterone, but not medroxyprogesterone, inhibits vascular cell adhesion molecule-1 expression in human vascular endothelial cells. *Arterioscler Thromb Vasc Biol* 2001 Feb;21(2):243-8.

Ottosson UB; Johansson BG; von Schoultz B. Subfractions of high-density lipoprotein cholesterol during estrogen replacement therapy: a comparison between progestogens and natural progesterone. *Am J Obstet Gynecol* 1985 Mar 15;151(6):746-50.

Paganini-Hill A. Estrogen replacement therapy and colorectal cancer risk in elderly women. *Dis Colon Rectum*. 1999 Oct;42(10):1300-5

Register TC; Adams MR; Golden DL; Clarkson TB. Conjugated equine estrogens alone, but not in combination with medroxyprogesterone acetate, inhibit aortic connective tissue remodeling after plasma lipid lowering in female monkeys. *Arterioscler Thromb Vasc Biol* 1998 Jul;18(7):1164-71.

Rosano GM; Webb CM; Chierchia S; Morgani GL; Gabraele M; Sarrel PM; de Ziegler D; Collins P. Natural progesterone, but not medroxyprogesterone acetate, enhances the beneficial effect of estrogen on exercise-induced myocardial ischemia in postmenopausal women. *J Am Coll Cardiol* 2000 Dec;36(7):2154-9.

Ross RK; Paganini-Hill A; Wan PC; Pike MC. Effect of hormone replacement therapy on breast cancer risk: estrogen versus estrogen plus progestin. *J Natl Cancer Inst* 2000 Feb 16;92(4):328-32.

Rossouw JE, Anderson GL, Prentice RL, *et al*. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33

Scarabin PY; Alhenc-Gelas M; Plu-Bureau G; Taisne P; Agher R; Aiach M. Effects of oral and transdermal estrogen/progesterone regimens on blood coagulation and fibrinolysis in postmenopausal women. A randomized controlled trial *Arterioscler Thromb Vasc Biol* 1997 Nov;17(11):3071-8

Schairer C, Gail M, Byrne C, Rosenberg PS, Sturgeon SR, Brinton LA, Hoover RN. "Estrogen replacement therapy and breast cancer survival in a large screening study." *J Natl Cancer Inst*. 1999 Feb 3;91(3):264-70.

Schmidt JB, Binder M, Macheiner W, Kainz C, Gitsch G, Bieglmayer C. "Treatment of skin ageing symptoms in perimenopausal females with estrogen compounds." A pilot study. Department of Special and Environmental Dermatology, University of Vienna Medical School, Wien, Austria.

Wagner JD; Martino MA; Jayo MJ; Anthony MS; Clarkson TB; Cefalu WT. The effects of hormone replacement therapy on carbohydrate metabolism and cardiovascular risk factors in surgically postmenopausal cynomolgus monkeys. *Metabolism* 1996 Oct;45(10):1254-62