

LE Magazine March 1999

## REPORT



## TREATING OSTEOPOROSIS

## The Youth Hormone

The answers to bone deterioration and breast and prostate cancer prevention may very well lie in progesterone

The skeleton is comprised of living tissue that continually renews itself throughout life. The living part of bone is an organic collagen matrix that is strengthened by minerals such as calcium and magnesium.

There are two types of bone regulating cells. The osteoclasts function to dissolve older bone and leave tiny unfilled spaces behind; the osteoblasts then move into these spaces to produce new bone. This process of dissolving older bone mass by osteoclasts and new bone formation by osteoblasts is the mechanism for the repair and continuing strength of bone.

Like all living cells, osteoblasts and osteoclasts require hormonal guidance to function properly. Osteoblasts depend primarily on progesterone and testosterone, while osteoclasts need estrogen-like hormones. In the absence of these hormones, osteoblasts and osteoclasts cease to function properly and rapid deterioration of the bone occurs. Osteoporosis can occur when osteoclasts dissolve more bone than what the osteoblasts are able to replace.

Estrogen regulates the activity of osteoclasts, which results in the slowing of the process of older bone dissolution. Progesterone, on the other hand, promotes the production of osteoblasts which are required to effect new bone formation. Natural progesterone has been shown to stimulate osteoblast-mediated new bone formation which is required to prevent and reverse osteoporosis.

The following is a simple description of the effect of estrogen and progesterone on bone:

- Estrogen can temporarily slow down but not reverse osteoporosis.
- Estrogen cannot protect against osteoporosis when progesterone is absent.
- The addition of natural progesterone may be the ideal hormone replacement for the prevention and treatment of postmenopausal osteoporosis. It appears that only natural progesterone is capable of reversing the osteoporosis process by providing increased numbers of osteoblasts to rebuild bone.
- The use of estrogen in the prevention of osteoporosis may be optional, or at least used in smaller doses or in natural phytoestrogen forms.

Osteoporosis can be caused by mineral and vitamin deficiencies, corticosteroid drugs, poor eating habits, lack of exercise, too much cortisol and too little testosterone. The major influence on age-associated bone deterioration, however, would appear to be a severe deficiency of ovarian-secreted progesterone.

## Progesterone may prevent breast cancer, alleviate PMS

There is a large base of evidence suggesting that progesterone is protective against, as well as a potential treatment for, breast cancer. A study by KJ Chang showed transdermal estradiol increased the cell proliferation rate by 230%, while transdermal progesterone decreased the cell proliferation rate by >400%. A combination estradiol/progesterone cream maintained the normal proliferation rate. This is direct evidence that estradiol (a potent estrogen) stimulates hyper-proliferation of breast tissue cells and progesterone prevents hyper-proliferation.

A second study by noted researcher Bent Formby, Ph.D. was just published with more insightful results. To determine the biologic mechanism of why progesterone inhibits the proliferation of breast cancer cells, a variety of cancer cell lines with different receptors and different expression of genes were exposed to progesterone. Exposure to progesterone induced a maximal 90% inhibition of cell proliferation in T47-D breast cancer cells and no measurable response to MDA-231 progesterone-receptor negative breast cancer cells. An impressive 43% of the T47-D cancer cells had undergone apoptosis (programmed cell death) within 24 hours after exposure to progesterone. Further analysis showed that the genetic expression by T47-D cancer cells of the bcl-2 gene was down regulated, and that of the p53 gene (tumor suppressor gene) was up regulated. Since the p53 gene expression induces cell apoptosis and the bcl-2 gene when expressed inhibits apoptosis, if one's cancer cells are progesterone-receptor positive, then progesterone as part of one's therapy appears to be very important. However, 50% of breast cancer cell lines have mutant or no p53 oncogene expression, so in this instance, genistein therapy might be helpful.

(This was pointed out in the January 1998 issue of *Life Extension magazine*, page 17.) In discussing the usefulness of genistein in treating breast cancer, it was stated that it worked better if the p53 gene was mutated or there was no functional p53 expression, and that coincides with this new information on progesterone. This all points to the fact that breast cancer patients should obtain an immuno-histochemistry test of tumor cells to help determine whether progesterone or genistein therapies might be helpful.

Previous retrospective studies show that women undergoing breast cancer operations during the luteal phase of the menstrual cycle, when progesterone is higher, have much longer survival times. Angiogenesis (new blood supply) is essential for tumor growth and vascular endothelial growth factor (VEGF) is one of the most potent angiogenic cytokines. K. Heer and colleagues suggest that since progesterone seems to lower VEGF expression, the lowering of this potent angiogenic cytokine in the luteal phase by progesterone could possibly decrease the potential for micrometastasis establishment. Dr. P.E. Mohr in the *British Journal of Cancer* reported that women with a progesterone level of 4 ng/ml or more at the time of their breast cancer surgery, had a significantly better survival rate at 18 years than those with a lower serum level of progesterone. This was particularly evident in node-positive women. In those women with good progesterone levels at the time of their surgery, it was revealed that approximately 65% were surviving 18 years later, whereas only 35% of the women with low progesterone levels at the time of surgery survived.

In a study conducted in 1981, published in the *American Journal of Epidemiology*, it was shown that the incidence of breast cancer was 5.4 times greater in women with low progesterone than in women who had good progesterone levels. Some final evidence confirming progesterone's protective effects on breast tissue comes from a study by J.M. Foidart in *Fertility and Sterility* where either a placebo gel, an estrogen gel, a progesterone gel or a combination estrogen/progesterone gel was applied to women's breasts for 14 days prior to breast surgery. The surgery was either aesthetic or to remove a benign lump. None of the participants were taking hormones and all were post-menopausal. After surgery, the breast tissue was analyzed and it was found that estradiol increased breast cell proliferation and that progesterone greatly decreased proliferation.

An expert on progesterone therapy, Dr. John Lee states, "The goal of progesterone supplementation is to restore normal physiologic levels of bioavailable progesterone." That is why testing saliva or blood progesterone levels is important, especially for pre-menopausal women who are using progesterone cream to alleviate pre-menstrual syndrome (PMS) symptoms. In women whose doctors are prescribing excess amounts of supplemental estrogen, the administration of progesterone may enable the dose of estrogen to be reduced, since progesterone restores sensitivity to estrogen receptors on cell membranes. There are saliva tests available to ascertain progesterone and other hormone levels in the body. The Life Extension Foundation may be offering these tests in the future, subject to further validation studies.

Caution: Please refer to The Life Extension Foundation's "Osteoporosis Protocol" featured in this issue for a complete description in how to safely use progesterone and other natural hormone replacement therapies.

## Progesterone for men

New research by Bent Formby, Ph.D. at the Sansum Medical Research Institute in Santa Barbara, CA has uncovered evidence that progesterone may help men with prostate problems. Dr. Formby took prostate cancer cells and subjected them to different hormones to observe the effects and analyze what happened. The results showed that progesterone inhibits the growth of prostate cancer cells and that estradiol and dihydrotestosterone (DHT) accelerate prostate cancer cell growth. Dr. Formby also cited other research showing that testosterone can also inhibit prostate cancer cell proliferation because it opposes estrogen and energizes cells to use normal oxidative respiration, instead of being anaerobic like cancer cells. This research showing that testosterone inhibits prostate cancer was confirmed by Eugene Shippen, M.D., John Lee, M.D. and David Zava, Ph.D. at a recent scientific conference. (Further confirmation of this research is needed, because prostate cancer patients temporarily treat their disease by suppressing testosterone production.)

Progesterone opposes estrogen and its metabolites and it stops the conversion of testosterone to DHT by interfering with the enzyme 5-alpha-reductase. Essentially, it comes down to the following regarding male hormones and aging, and why prostate cancer is almost inevitable: In aging men, testosterone levels decline, estradiol increases (in fact serum estradiol concentrations in men average age 54 are higher than in women average age 59), DHT increases and men have practically nonexistent progesterone.

It is now becoming acceptable medical thought that at this stage in men, estradiol becomes dominant and it or one of its toxic metabolites starts the damage leading to cancer. So the question becomes, 'How to turn this dismal picture around and protect against benign prostatic hypertrophy (BPH) and eventually prostate cancer.' Previous studies indicate that selenium, vitamin E, and lycopene may cut the risk of prostate cancer in half, but on a hormonal basis, progesterone is the key, followed by testosterone. Progesterone opposes estradiol and keeps DHT levels down. Progesterone may induce mutated prostate cells to enter into the apoptosis (programmed death) cycle, and cell proliferation should be minimized. Clinicians have related case histories of men with benign prostate disease and cancer who have found relief with progesterone.

Testosterone is the primary hormone men require to maintain bone mass. For men undergoing testosterone ablation therapy to treat prostate cancer, progesterone can help protect against the acute loss of bone density that so often occurs.

## The potential dangers of FDA-approved progesterone-like drugs

The FDA has just approved a drug called Prometrium, an oral pill containing 200 mg of natural progesterone to be taken daily. This is overkill, as your liver will go into overdrive trying to excrete this acute, overabundant supply of progesterone. Most of this oral progesterone drug that is not detoxified by the liver will be bound to sex hormone-binding globulin (SHBG) and therefore become unavailable to cellular function. Progesterone cream is better utilized and much more economical. Dr. Foidart in his study on transdermal replacement hormone therapy states that avoidance of the "first passage effect"(through the liver) is ensured by the transdermal application of hormones and probably explains the superiority of this route of hormone administration. Natural progesterone should not be confused with the synthetic FDA-approved drug progestins that cause many side effects. Synthetic progestins do not provide the broad-spectrum of benefits that have been documented for natural progesterone.

The decline in progesterone production is correlated with increased bone loss and increased risk of cancer. Many of the effects associated with normal aging can be attributed to a progesterone deficiency, so progesterone replacement therapy may be another missing link to solving the human aging process. The beneficial effects of natural progesterone have now been shown in women and men. Progesterone protects against many of the detrimental changes of aging, and the only downside is that too much can make a person feel sleepy or even euphoric. Please note that it usually takes two to four weeks for topically applied progesterone to build up to sufficient levels in the body to the point where there are noticeable effects.

## Ahead Of The Times

While oncological researchers are now excited about the possibility of using progesterone for the prevention and treatment of certain breast cancers, here is what The Life Extension Foundation published way back in 1994:

"Breast cancer is far more likely to occur in women with normal-to-high estrogen levels and low progesterone levels. When surgical procedures are performed during the first half of the menstrual cycle when estrogen levels are high, the risk of metastasis is far greater than during the second half of the cycle (when progesterone is dominant)."

"The published data shows that premenopausal women with low progesterone levels are 5.4 times more likely to develop breast cancer and are 10 times more likely to die from all other forms of cancer than women with normal progesterone levels."

"Estrogen consistently shows itself to be a carcinogenic hormone while the proper amount of progesterone almost always blocks estrogen's cancer causing effect."

"The number of published studies showing that progesterone provides a protective effect against cancer is overwhelming, yet the edictal-industrial complex that dominates American medicine has consistently ignored these facts. The government's solution to the breast cancer epidemic is to offer free mammograms (which can cause breast cancer), yet the scientific literature shows that natural hormones like progesterone and melatonin could significantly reduce the epidemic of breast cancer that exists in the United States today."-

## Further Reading

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