An Explanation of Cancer and the Increase in Cancer: High Testosterone, Low DHEA and Breast Cancer

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This is mentioned in *International Journal of Cancer* 2005; **115**: 497 and *Annals of Internal Medicine* 2005; **142**: 471-472, my publications.

New supporting material is below.

Sometime in the early 1990's, I developed my hypothesis that low dehydroepiandrosterone (DHEA; the major adrenal hormone) may trigger cancer. I sent this idea to a number of publications, including the *Journal of the National Cancer Institute*, April 11, 1994. However, prior to that, I had the following "letter to the editor" printed in *The Morning News of Northwest Arkansas*, March 14, 1994, page 4A. This briefly explains my explanation of cancer and low DHEA. I used the increase in breast cancer to explain this. (You should note that a connection of high testosterone and low DHEA had been noticed some time prior to my explanation. However, no one, other than I, has produced an explanation of how this combination of hormone levels could trigger cancer. I was not aware of the early findings of high testosterone and low DHEA when I developed my idea.) The Letter to the *News*:

> "During the past year, a lot has been published about increased cancer in this country. When this controversy began a few years back, it was refuted; the increase was attributed to better detection. Epidemiologists have now proven the increase is real. To account for this, some investigators at N.I.H. say the rise is caused by cancer-causing chemicals in the environment. One of the chief supporters of this idea, however, suggests these chemicals may account for only a minor part of the increase in cancer. I suggest the majority of the rise in cancer results from the same mechanism that produces the 'secular trend.'
> The secular trend is an increase in body size and earlier puberty in boys and girls with each generation. I suggest the trend results from increases in numbers of individuals of high testosterone, male and female. (Testosterone is not 'the' male hormone, males simply produce more. Testosterone increases size, aggression and sexuality in both sexes.) Males and females of higher testosterone arrive at puberty earlier and are more sexually active; they make more babies than low testosterone couples. The increase in cancer directly parallels the secular trend, that is, the increase in percentages of higher testosterone individuals. The best way to see this is in females. Breast cancer in females also parallels the secular trend, and early puberty is a key risk factor in female breast cancer. The simple answer is that testosterone advances old age, and breast cancer is mainly a phenomenon of old age.
> My work suggests all gene activity requires [is optimized by] the hormone, DHEA. That is, all genes compete for DHEA. DHEA is produced in a limited supply during the life-span and naturally begins to decline around 28 years old. Therefore, I suggest

loss of DHEA results in aging. Testosterone increases use of DHEA for 'testosterone-target' genes. Increased testosterone increases use of DHEA for these genes, that is, their tissues. This means that testosterone increases use of DHEA and advances the time when DHEA begins to decline. Testosterone advances aging. This is why men die, on average, earlier than women.

I suggest 'embryonic' or 'growth type' genes are activated when DHEA is readily available, and 'tissue type' or 'adult type' genes are activated by less DHEA. As we grow, overall DHEA availability is reduced because of our tremendous, early growth. As overall DHEA is reduced, tissues begin to form at the expense of growth. The ratio of growth genes changes as tissues begin to form. That is, the ratio changes from more growth to more tissue formation, and this continues until around age 28. At this time, tissues begin to experience reduced DHEA. Tissues begin to age. My work suggests this causes a few cells to reverse their ratio of DHEA availability. That is, some revert to embryonic type cells which grow rapidly.

Rapidly growing, normal embryonic cells and cancer cells have few 'cell adhesions.' Cell adhesions stick cells together; the more a cell has, the less free surface area it has to absorb DHEA, from blood. As cell adhesions form, the reduced DHEA pushes the cell toward the tissue ratio. (Most tissues are groups of cells literally stuck together for a unified purpose.) Loss of cell adhesion is characteristic of cancer cells. I suggest loss of cell adhesions increases the free surface area of cancer cells, and, therefore, increases their ratio of DHEA. This increased DHEA would then activate rapid cell growth, that is, it would activate 'embryonic type' genes in cells which absorb large amounts of DHEA. These cells would form tumors because of their rapid growth and increased absorption of DHEA.

Therefore, if I am correct, breast tumor tissue should absorb DHEA more rapidly than other tissues at the expense of DHEA in the rest of the person. It is known that breast tumors, but not normal breast tissue, concentrate DHEA (*Journal of Steroid Biochemistry* **26**: 151, 1987). Measurable levels of DHEA are reduced in women with breast cancer, and this reduction in DHEA occurs as early as nine years prior to diagnosis (*Geriatrics* **37**: 157, 1982). Once the breast tumor has begun to grow, it uses DHEA at the expense of the rest of the body. This severe loss of DHEA, caused by the cancer, will than advance aging in the rest of the body. I suggest this causes the wasting syndrome, called cachexia, seen in breast cancer, and other cancer, victims."

End of the Letter to the *News*

I suggest that low DHEA triggers oncogenes in people who have them, and this is why cancer is more common in old age. According to my work, all tissues, including cancers, must utilize DHEA for growth. Since DHEA is reduced in old age, this also explains why cancers, though more common in old age, grow less rapidly in old age. If proper DHEA levels prevent cancer, then DHEA should prevent cancers induced by known carcinogens. This has been determined in number of studies, such as "Exceptional Chemopreventive Activity of Low-dose Dehydroepiandrosterone in the Rat Mammary Gland," *Cancer Research*, 1996; **56**: 1724. So, the commonality of depression and cancer is low DHEA.

In 2002 and 2003, my connection of testosterone with breast cancer was supported: "testosterone might be more strongly associated with [breast cancer] risk than estradiol" (Journal of the National Cancer Institute 2002; 94: 606-616). "The estimated relative [breast cancer] risks between upper and lower tertiles were 2.07 (95% confidence interval [CI] 0.97-

4.41) for estrone in postmenopausal women, 2.01 (95% CI 0.96-4.21) for testosterone in premenopausal women, and 2.40 (95% CI 1.11-5.21) for testosterone in postmenopausal women, after adjusting for age at first live birth, waist-to-hip ratio, total calorie intake, a history of fibroadenoma, a family history of breast cancer and SHBG." (International Journal of Cancer 2003; 105: 92-7).

Here is the new material:

Two articles add support to my hypothesis regarding testosterone in women and breast cancer. That is I suggest increased testosterone is involved in triggering cancer. In the first article from the January, 2004, *Journal of the National Cancer Institute*, U.S.A., you will read the finding that "active smoking may play a role in breast cancer etiology." The second article demonstrates that smoking in women is connected with increased testosterone. "Current smokers had the highest testosterone concentrations with decreasing values in former and nonsmokers ($p = 0.0001$)." (The abstracts of these two articles are available at my explanation of breast cancer; click on the link.) Again, I suggest this adds support to my explanation of the mechanism of cancer.

Smoking is connected to breast cancer:

"Background: There is great interest in whether exposure to tobacco smoke, a substance containing human carcinogens, may contribute to a woman's risk of developing breast cancer. To date, literature addressing this question has been mixed, and the question has seldom been examined in large prospective study designs. *Methods:* In a 1995 baseline survey, 116 544 members of the California Teachers Study (CTS) cohort, with no previous breast cancer diagnosis and living in the state at initial contact, reported their smoking status. From entry into the cohort through 2000, 2005 study participants were newly diagnosed with invasive breast cancer. We estimated hazard ratios (HRs) for breast cancer associated with several active smoking and household passive smoking variables using Cox proportional hazards models. *Results:* Irrespective of whether we included passive smokers in the reference category, the incidence of breast cancer among current smokers was

higher than that among never smokers (HR = 1.32, 95% confidence interval [CI] = 1.10 to 1.57 relative to all never smokers; HR = 1.25, 95% CI = 1.02 to 1.53 relative to only those never smokers who were unexposed to household passive smoking). Among active smokers, breast cancer risks were statistically significantly increased, compared with all never smokers, among women who started smoking at a younger age, who began smoking at least 5 years before their first full-term pregnancy, or who had longer duration or greater intensity of smoking. Current smoking was associated with increased breast cancer risk relative to all nonsmokers in women without a family history of breast cancer but not among women with such a family history. Breast cancer risks among never smokers reporting household passive smoking exposure were not greater than those among never smokers reporting no such exposure. *Conclusion:* Our study provides evidence that active smoking may play a role in breast cancer etiology and suggests that further research into the connection is warranted, especially with respect to genetic susceptibilities." *Journal of the National Cancer Institute*, Vol. **96**, No. 1, 29-37, January 7, 2004

Smoking is connected to increased testosterone in women:

"While there is substantial evidence of the importance of endogenous and exogenous estrogen in reproductive health and chronic disease, there is little consideration of androgens in women's health. In the Michigan Bone Health Study (1992-1995), the authors examined the correlates of testosterone concentrations in pre- and perimenopausal women (i.e., age, menopausal status, body composition, and lifestyle behaviors) in a population-based longitudinal study including three annual examinations among 611 women aged 25-50 years identified through a census in a midwestern community. Current smokers had the highest testosterone concentrations with decreasing values in former and nonsmokers ($p = 0.0001$). Body composition measures (body mass index, body fat (%), weight (kg), lean body mass (kg), and fat mass (kg)) were significantly and positively associated with total testosterone concentrations in a dose-response manner. Hysterectomy with oophorectomy was associated with significantly lower testosterone concentrations. Alcohol consumption, physical activity, and dietary macronutrient intake were not associated with testosterone concentrations. This is one of the first studies to examine correlates of serum testosterone concentrations in anticipation of the growing interest in the role of androgens in women's health. The greater circulating levels of testosterone in obese women and smokers suggest that testosterone concentrations should be considered in the natural history of disease conditions

where obesity and smoking are risk factors, including cardiovascular disease."
American Journal of Epidemiology 2001 Feb 1; **153**(3): 256-64