

Nutrition Considerations for Patients With Prostate Cancer, Part 2

EVIDENCE-BASED ADJUNCTIVE NUTRITIONAL SUPPORT

James P. Meschino, DC, MS

Supplement Considerations (*continued from part 1*)

1. *Curcumin* (480 mg, three times per day) - Curcumin has been shown to inhibit the growth of breast, colon and prostate cancer cells via several important targeted effects (inhibits epidermal growth-factor receptors, the 12-lipoxygenase enzyme system and tyrosine kinase enzymes, which are commonly upregulated in cancer cells). If left unchecked, the upregulation of these pathways leads to uncontrolled cellular replication and indirectly inhibits apoptosis and increases angiogenesis (the ability of cancer cells to form blood vessels to fuel their growth). Animal and human studies indicate that curcumin can decrease proliferation rates of certain types of cancer. A human clinical trial demonstrated that curcumin supplementation (480 mg, three times per day) reduced the size and number of recurring polyps in patients with a previous history of genetically-induced colon cancer (Familial adenomatous polyposis).
2. *Essential Fatty Acids* (borage seed, flaxseed and fish oil) - This combination of oils provides the body with essential fatty acids that make local hormones (prostaglandin series 1 and 3), which are known to slow rates of cell division and reduce inflammatory reactions. Both of these activities are known to play a role in cancer prevention. The daily therapeutic dosage would be four to six capsules of a 1,200 mg essential oil capsule containing 400 mg each of borage seed, flaxseed and fish oil.
3. *Vitamin D* (2,000 IU per day) - Studies indicate that many human prostate cancer cells possess vitamin D receptors on their outer membrane. Stimulation of these receptors by vitamin D has been shown to increase the maturation of these cells (makes them look more normal), reduces their malignant behavior and slows down cell division. In experimental studies, vitamin D has been shown to suppress cancer cell proliferation, and induce apoptosis and differentiation.

A recent study showed that 2,000 IU of vitamin D administered daily to 15 patients with prostate cancer helped regulate blood prostate-specific antigen (PSA) levels. In nine patients, the PSA level decreased or remained unchanged (no further rise). These results were sustained during the 21-month course of vitamin D administration. The median PSA doubling time increased from 14.3 months prior to vitamin D administration to 25 months after starting vitamin D supplementation. In fact, 14 of the 15 patients showed a prolongation of the PSA doubling time after vitamin D supplementation was introduced. There were no reported side effects. The marked prolongation of PSA doubling time is extremely important to the administration of vitamin D, according to the recent work of Partin and fellow researchers (*Journal of Urology*, 2003). Partin, et al., showed that the risk of distal metastasis of prostate cancer (with respect to relapse after prostate cancer surgery) at five years was 65 percent to 75 percent when PSA doubling time was less than 10 months, compared with 10 percent to 20 percent when PSA doubling time was greater than 10 months.

Specific Prostate Support Supplements

1. *Prostate Support Nutrients* - It is known that prostate cancer cells divide and spread through the body under the influence of dihydrotestosterone hormone. Certain natural herbs have been shown to block the buildup of dihydrotestosterone, some of which have demonstrated an ability to slow or retard the progression of prostate cancer and/or slow the rate of rise in PSA blood levels.

For these reasons, prostate cancer patients (including those who have had their prostate gland removed) may wish to consider taking a combination product containing the following nutrients: saw palmetto, *Pygeum africanum*, beta-sitosterol, stinging nettle and lycopene. The daily dosage to be considered would include the following:

- Saw palmetto - This herb should be a standardized grade of 45 percent fatty acids and sterols, taken at a dosage of 720 mg, twice daily (or an 85 percent to 90 percent standardized grade of fatty acids and sterols, taken at a dosage of 160 mg twice daily).
 - *Pygeum africanum* - This herb should be a standardized grade of 12 to 14 percent triterpenes, taken at a dosage of 200 mg twice daily.
 - Beta-sitosterol - This plant-based substance should be taken at a dosage of 120 mg twice daily.
 - Soy isoflavones - This special class of flavonoids derived from soybeans should be taken at a minimum dosage of 50 mg per day (up to 200 mg per day).
 - Stinging nettle - This herb should be used with other prostate-support nutrients at a minimum dosage of 60 mg twice daily, using a 5:1 extract.
 - Lycopene - This is a carotenoid found in tomatoes and other red and pink fruits and vegetables. It accumulates in the prostate gland. There is some evidence that lycopene may be helpful in the treatment of prostate cancer. In one study, 26 men with prostate cancer were randomly assigned to receive lycopene (15 mg twice a day) or no lycopene for three weeks before undergoing prostate surgery. Prostate tissue was then obtained during surgery and examined. Compared to the unsupplemented men, those receiving lycopene were found to have significantly less aggressive growth of cancer cells. In addition, a case report has been published of a 62-year-old man with advanced prostate cancer who experienced a regression of his tumor after starting 10 mg of lycopene per day and 300 mg of saw palmetto three times per day.
2. *Ground Flaxseed* (50 g per day or 2 heaping tablespoons) - Enterolactone and enterodiol, formed from lignan precursors found in flaxseed, inhibit key enzymes that convert androgens into estrone hormone and estrone into estradiol. It has been shown that these forms of estrogen may encourage prostate cancer development and progression by decreasing the breakdown of dihydrotestosterone. Enterolactone and enterodiol also may compete with other estrogens for binding to estrogen receptors on prostate cells, toning down that estrogenic influence on prostate cancer cells.
 3. *Soy Isoflavones* (100-200 mg per day) - A study showed that men with prostate cancer who ingested 100 mg per day of soy isoflavones showed a slower rise in their blood PSA levels. Soy isoflavone supplementation was shown to decrease the rate of rise in serum PSA levels in patients with androgen-dependent and androgen-independent prostate cancer. The researchers concluded that soy isoflavones may help delay the development of symptoms,

improve quality of life and perhaps even prolong survival. A large body of experimental evidence suggests soy isoflavones and other derivatives of soy extract can inhibit the development and progression of prostate and other cancers via a number of mechanisms.

4. *Modified citrus pectin* (15 g three times per day) - Modified citrus pectin is a dietary supplement that has demonstrated an ability to prevent the spread of cancer (metastasis). It is a special form of pectin that has been altered in the laboratory by a proprietary process that shortens the length of pectin's polysaccharide chain. One of the dominant carbohydrates contained within modified citrus pectin is galactose. Galactose has a strong affinity for binding to the surface of metastatic cancer cells, which express a particular cell surface receptor known as galectin-3 (a galactoside-binding lectin). In turn, the binding of modified citrus pectin to the galectin-3 receptor on metastatic cancer cells creates a type of galectin-3 blockade. Cancer cells are then less able to adhere to other healthy tissues and cells, essentially inhibiting them from invading and spreading to new areas in the body. Additionally, the blockade of galectin-3 receptor prevents cancer cells from adhering to each other, discouraging their ability to form colonies (tumor mass). If cancer cells are deprived of their own adhesive ability, they fail to thrive and can be more easily destroyed by the body's immune system.

A pilot study involving prostate cancer patients who failed first-line androgen-deprivation therapy or were in relapse after radical prostatectomyexternal-beam radiation therapy or cryosurgery, and were not taking intermittent hormone blockade, demonstrated that supplementation with 15 g per day of modified citrus pectin (5 g three times per day) increased the length of the PSA doubling time by 30 percent in four of seven patients. One patient had a partial response, one was stable and one did not respond. The researchers concluded that modified citrus pectin appears to slow the PSA doubling time in patients with low levels of PSA. All patients were still alive three years after the end of the study.

Dilute modified citrus pectin powder in a favorite beverage. Up to 30 g per day may be taken safely. It is also available in capsules and tablets.

5. *Melatonin* (10-20 mg per day; requires physician monitoring) - Preliminary studies in Italy suggest melatonin can suppress growth of prostate cancer in human subjects. However, this is a high dosage and physician monitoring is required with this intervention.

Summary

The body of evidence suggests certain proactive dietary and supplementation interventions may help to arrest or slow the progression of prostate cancer in certain cases. It is unlikely that the patient will be provided with a comprehensive program of this nature by their attending oncologist or urologist. Thus, it is incumbent upon natural health care practitioners to provide prostate cancer patients with evidence-based recommendations pertaining to adjunctive nutrition support in situations in which the patient would appreciate becoming more enlightened on this subject.

This article has outlined the most current considerations pertaining to the adjunctive nutritional support for prostate cancer patients, based upon my interpretation of the scientific, peer-reviewed literature on this subject. These interventions are not to be used as a substitute for medical care, but rather to be considered as adjunctive nutritional support in these cases.

Selected References

Curcumin

- Dorai Y, Cao Y, Dorai B, et al. Therapeutic potential of curcumin in human prostate cancer. III. Curcumin inhibits proliferation, induces apoptosis, and inhibits angiogenesis of LNCaP prostate cancer cells in vivo. *Prostate*, 2001;47(4):293-303.
- Dorai T, Dutcher JP, Dempster DW, Wiernik PH. Therapeutic potential of curcumin in prostate cancer - IV: Interference with the osteomimetic properties of hormone refractory C4-2B prostate cancer cells. *Prostate*, 2003;60(1):1-7.
- Sagar SM, Yance D, Wong RK. Natural health products that inhibit angiogenesis: a potential source for investigational new agents to treat cancer - Part 1. *Curr Oncol*, 2006;13(1):1-13.

Essential Fatty Acids

- Newcomer LM, King IB, Wicklund KG, Stanford JL. The association of fatty acids with prostate risk. *Prostate*, 2001;47:262-8.
- Simopoulos AP, Leaf A, Salem N Jr. Workshop statement on the essentiality of and recommended dietary intakes for omega-6 and omega-3 fatty acids. *Prostaglandins Leukot Essent Fatty Acids*, 2000;63(3):119-21.

Vitamin D

- Woo TCS, Choo R, Jamieson M, et al. Pilot study: Potential role of vitamin D (cholecalciferol) in patients with PSA relapse after definitive therapy. *Nutr Cancer*, 2005;5(1):32-6.
- Gahn PH, Ma J, Hennekens CH, et al. Circulating vitamin D metabolites in relation to subsequent development of prostate cancer. *Epidemiol Biomarkers Prev*, 1996;5(2):121-6.
- Veith R. Vitamin D supplementation, 25-hydroxy vitamin D concentrations and safety. *Am J Clin Nutr*, 1999;69(5):842-56.
- Rozen F, Yang XF, Huynh H, Pollak M. Antiproliferative action of vitamin D-related compounds and insulin-like growth factor - binding protein 5 accumulation. *J Natl Cancer Inst*, 1997;89(3):652-6.

Prostate Herbal Support Supplements:

- Kucuk O, Sarkar FH, Sakr W, et al. Phase II randomized clinical trial of lycopene supplementation before radical prostatectomy. *Cancer Epidemiol Biomarkers Prev*, 2001;10:861-8.
- Matlaga BR, Hall MC, Stindt D, Torti FM. Response of hormone refractory prostate cancer to lycopene. *J Urol*, 2001;166:613.
- Rao VA, Fleshner N, Agarwal S. Serum and tissue lycopene and biomarkers of oxidation in prostate cancer patients: a case-control study. *Nutr Cancer*, 1999;33(2):159-64.
- Hussain M, Banerjee M, Sarkar FH, et al. Soy isoflavones in the treatment of prostate cancer. *Nutr Cancer*, 2003;42(2):111-7.
- Boccafroschi, Annosica S. Comparison of *Serenoa repens* extract (saw palmetto) with placebo by controlled clinical trial in patients with prostatic adenomatosis. *Urologia*, 1983;50:1257-68.
- Brawley OW, Ford LG, Thompson I, et al. 5-Alpha-reductase inhibition and prostate cancer prevention. *Cancer Epidemiol Biomarkers Prev*, March 1994;3(2):177-82.
- Can men avoid prostate cancer? A brief review of diet and the prostate. *Nutrition Health Review*, 1995;72:3.
- Dufour B, Choquenot C. Trial controlling the effects of *Pygeum africanum* extract on the functional symptoms of prostatic adenoma. *Ann Urol*, 1984;18:193-5.
- Hartmann R, Mark M, Soldati F. Inhibition of 5 alpha reductase and aromatase by PHL-00801, a combination of *pygeum africanum* and *urtica dioica* extracts. *Phytomedicine*, 1996;3(2):121-8.
- McCaleb R. Synergistic action of *pygeum* and nettle root extracts in prostate disease. *Herbalgram*, 1996;40:18.
- Mitchell J, Duthie SJ, Collins AR. Effects of phytoestrogens on growth and DNA integrity in

human prostate tumor cell lines: PC-3 and LNCaP. *Nutr Cancer*, 2000;38(2):223-8.

- Naik HR, Lehr JE, Pienta KJ. An in vitro and in vivo study of anti-tumor effects of genistein on hormone refractory prostate cancer. *Anticancer Res*, 1994;14:2617-20.

Flaxseed

- Li D, Yee JA, Thompson LU, Yan L. Dietary supplementation with secoisolariciresinol diglycoside (SDG) reduces experimental metastasis of melanoma cells in mice. *Cancer Lett*, 1999;142(1):91-6.
- Thompson LU, Seidl MM, Rickard SE, et al. Antitumorigenic effect of mammalian lignan precursor from flaxseed. *Nutr Cancer*, 1996;26:159-65.
- Denis L, Morton MS, Griffiths K. Diet and its preventive role in prostate disease. *Eur Urol*, 1999;35(5-6):377-87.

Soy Isoflavones

- Hussain M, Banerjee M, Sarkar FH, et al. Soy isoflavones in the treatment of prostate cancer. *Nutr Cancer*, 2003;42;2:111-7.
- Kyle E, Neckers L, Takimoto C, et al. Genistein-induced apoptosis of prostate cancer cells is preceded by a specific decrease in focal adhesion kinase activity. *Mol Pharmacol*, 1997;51:193-200.
- Naik HR, Lehr JE, Pienta KJ. An in vitro and in vivo study of anti-tumor effects of genistein on hormone refractory prostate cancer. *Anticancer Res*, 1994;14:2617-20.
- Peterson G, Barnes S. Genistein and biochanin A. Inhibit the growth of human prostate cancer cells but not epidermal growth factor receptor auto phosphorylation. *Prostate*, 1993;22:335-45.
- Pollard M, Luckert PH. Influence of isoflavones in soy protein isolates on development of induced prostate-related cancers in L-W rats. *Nutr Cancer*, 1997;28(1):41-5.

Modified Citrus Pectin

- Eliaz I. The role of modified citrus pectin in the prevention of cancer metastasis. *Townsend Letter for Doctors & Patients*, July 1999(192):64.
- Kidd PM. A new approach to metastatic cancer prevention: modified citrus pectin (MCP), a unique pectin that blocks cell surface lectins. *Altern Med Review*, Jan 1997;1(1):4-10.
- Strum S, Scholz M, McDermed J. Modified citrus pectin slows PSA doubling time: A pilot clinical trial. Presentation: International Conference On Diet and Prevention of Cancer. Tampere, Finland. May 1999.
- Pienta KJ, Naik H, Akhtar A, et al. Inhibition of spontaneous metastasis in a rat prostate cancer model by oral administration of modified citrus pectin. *J Natl Cancer Inst*, March 1995;87(5):348-53.

Lycopene

- Levy J, Bosin E, Feldman B, et al. Lycopene is a more potent inhibitor of human cancer cell proliferation than either α -carotene or β -carotene. *Nutr Cancer*, 1995;24:257-66.
- Gann PH, Ma J, Giovannucci E, et al. Lower prostate cancer risk in men with elevated lycopene levels: results of a prospective analysis. *Cancer Res*, 1999;59(6):1225-30.
- Ansari MS, Gupta NP. Lycopene: A novel drug therapy in hormone refractory metastatic prostate cancer. *Urolog Oncol*, 2004;22(5):415-20.

Melatonin

- Lissoni P, Cazzaniga M, Tancini G, et al. Reversal of clinical resistance to LHRH analogue in metastatic prostate cancer by the pineal hormone melatonin: efficacy of LHRH analogue plus melatonin in patients progressing on LHRH analogue alone. *Eur Urol*, 1997;31(2):178-81.

- Fraschini F, Demartini G, Esposti D, Scaglione F. Melatonin involvement in immunity and cancer. *Biol Signals Recept*, 1998;7(1):61-72.
- Lissoni P, Barni S, Cattaneo G, et al. Clinical results with the pineal hormone melatonin in advanced cancer resistant to standard antitumor therapies. *Oncology*, 1991;48:448-50.
- Lissoni P, Barni S, Crispino S, et al. Endocrine and immune effects of melatonin therapy in metastatic cancer patients. *Eur J Cancer Clin Oncol*, 1989;25:789-95.
- Neri B, De Leonardis V, Gemelli MT, et al. Melatonin as biological response modifier in cancer patients. *Anticancer Res*, 1998;18:1329-32.

MARCH 2008