

UROLOGY FOR THE PRACTITIONER

ROLE OF DIETARY MODIFICATION AND VITAMINS IN PROSTATE CANCER

Horst W. H. SOMMERKAMP¹, Raja B. KHAULI²

Sommerkamp HWH, Khauli RB. Role of dietary modification and vitamins in prostate cancer. *Leb Med J* 2005 : 53 (2) : 103-106.

ABSTRACT : Prostate cancer incidence and nutrition are closely connected and show large food-related differences. Lowest cancer incidence in Asian countries is observed under low-calorie, soy-based food. Mediterranean nutrition has cancer protective components (fruit, vegetables, oil, seafood). The highest cancer incidence in the United States goes along with high-calorie food, red meat and fat ingestion. Changes in lifestyle and nutrition can influence the cancer risk. Dietary supplements and vitamins are in wide use and part of a complementary and alternative medicine.

Prevention of prostate cancer is a necessity for countries with a high prevalence of this disease and there are several ways to execute this. A change of dietary habits and the use of complementary medicine are two of the valuable and widespread tools. They encompass nutritional changes, food supplements and alterations in lifestyle. An increasing percentage of men make use of complementary and alternative medicine (CAM) for cancer prevention and as an adjunct to conventional therapy [1].

In prostate cancer there is ample evidence that nutrition plays a major role in tumorigenesis and progression. Furthermore some vitamins have shown to have a preventive or modifying effect in clinical and experimental settings [2-3].

DIETARY MODIFICATION

The wealth of information on the interrelation between nutrition and prostate cancer has led to the concerning question whether prostate cancer is a "nutritional disease" [4]. The vast differences in prostate cancer incidence between Eastern and Western countries [5] (Table I) with dissimilar dietary habits and food composition seem to offer an explanation for the observed facts.

A number of nutritional risk factors – components of

From the ¹Department of Urology, University Hospital of Freiburg, Germany, ²Division of Urology at the American University of Beirut - Medical Center, Beirut, Lebanon.

Correspondence : Dr. Horst W. H. Sommerkamp, Department of Urology, University Hospital of Freiburg, Wintererstr. 52 a, D-79104, Freiburg, Germany.

Phone : (49) 761 202 50 92 Fax : (49) 761 202 50 97
Email : hsommerk@aol.com

the **Western food** – have been identified :

- High total calorie uptake/body mass index over 30 [6]
- Total fat consumption/saturated fatty acids [7]
- Red meat (beef) [8]
- Milk and milk products [9]

Most of these risk factors are provided by the components of the Western nutrition, especially in the United States. Asian food in contrast lacks these factors in conjunction with a very low incidence of prostate cancer. Mediterranean diet has a position in between these extremes. Unfavorable changes in dietary habits can enhance the cancer incidence, as shown by Chinese and Japanese [10-11] immigrants to the United States : The adoption of the Western lifestyle lead to a significant rise in cancer prevalence after 2-3 decades. On the other hand the change from nutritional habits with increased risk to a superior lifestyle has shown to be effective [12].

There are components of the **Asian nutrition** [13] which may account for the worldwide lowest incidence in prostate cancer :

- Low calorie and animal protein uptake
- High uptake of vegetables and fibres
- Soy and soy products
- Green tea-consumption

A major preventive role is attributed to the *Phytoestrogens* provided by soy (Flavonoids) and linseed (Lignans). These have a weak estrogenic effect

TABLE I
COMPARISON OF PROSTATE CANCER INCIDENCE
BY REGION [Muir, 1987]

| REGION | Cases/100,000 men | |
|----------------------|-------------------|------|
| USA | | |
| California | WM* | 49.6 |
| | CM** | 82.5 |
| Michigan | WM | 51.2 |
| | CM | 91.1 |
| Connecticut | WM | 46.8 |
| | CM | 72.3 |
| MEDITERRANEAN | | |
| Greece | 8.1 | |
| Portugal | 11.3 | |
| Spain | 17.0 | |
| Italy | 17.6 | |
| France | 23.6 | |
| ASIA | | |
| China | 1.8 | |
| India | 4.8 | |
| Japan | 5.1 | |

* White men ** Colored men

TABLE II
VITAMIN RECOMMENDATIONS AND SUPPLEMENTATION IN PROSTATE CANCER

| | U.S. DAILY REQUIREMENT | RECOMMENDED DOSE IN CLINICAL TRIALS | FOOD | TOXICITY |
|------------------------------|---------------------------|--|--|---|
| Vitamin A Carotenes* | 3500 I.U. | | Carrots Tomato Broccoli Egg yolk Liver Meat | Liver function disturbance Nausea Headache Alopecia |
| Vitamin D[♦] | 400 I.U. | | Milk Egg yolk Fish oil Liver | Hypercalcemia |
| Vitamin E | 15-30 I.U. 6-30 mg/day | 400 mg/day (up to 800 IU/day) | Soybean oil Wheat germ oil Almonds & Nuts Milk non-fat Peas Olive oil Salmon | Very low toxicity (potential risk of bleeding when combined with blood thinners) |
| SELENIUM | 70 mg/day | 200 µg/day | Wheat germ Bran Brazil nuts Barley Brown Rice Garlic Orange Juice | GI upset Nail bed changes Fatigue Hair loss |

* β-carotene and vitamin A supplementation is only advised in men with initially low levels and in conditions of heightened oxidative stress : men receiving β-carotene supplements have been shown to have a higher risk for prostate cancer development and mortality, particularly smokers (see text).

♦ Vitamin D supplementation is not recommended for the prevention of prostate cancer, and is only advised by increasing intake of Vitamin D foods.

inducing an inhibitory effect on prostate cell growth and proliferation. Soy is one of the most protective agents and used for prevention and treatment [14]. Studies on dietary intervention [15-16] have shown that soy is PSA-effective in men at risk.

Green tea, which is regularly consumed in China, contains – like red wine – polyphenols, which have shown to be prostate cancer preventive [17].

Mediterranean food obviously has a preventive effect on prostate cancer incidence. The nutrition is based on plant-oils and seafood, combined with a high intake of fruit and vegetables. Components are :

- Plant oil (olive oil), fish oil
- Fish and seafood
- Vegetables and fruit (parsley, tomatoes)
- Spices (oregano, marjoram)
- Red wine

These components are preventive even in countries with a high uptake of saturated fat like in Saudi Arabia [18]. Mediterranean nutrition is rich in oils containing mono-unsaturated fatty acids (MUFA) with known cancer-preventive effects [19]. In Lebanon prostate cancer incidence is rather low and does not belong to the five

leading cancer causes [20-21]. This is in contrast to most European and overseas countries.

The preventive effect of seafood was investigated by Augustsson [22]. The consumption of fish more than three times per week lead to a drop in risk (0.56 RR, relative risk) in a follow-up-period of 12 years.

There is abundant proof of the beneficial effects of *Lycopenes* (tomato) in the literature. Prospective studies [23] have demonstrated that frequent tomato intake or the increased ingestion of tomato sauce led to a significant drop in prostate cancer risk. PSA-concentration in patients scheduled for surgery could be lowered within 3 weeks by tomato sauce ingestion [24]. These findings were sustained by animal experiments : tumor growth was substantially delayed under lycopene and vitamin E. Tomato powder but not lycopene inhibited carcinogenesis in chemically induced rat cancer [25].

Dietary supplements

In addition to the adoption of a risk-diminishing nutrition some dietary supplements have shown to be preventive and inhibitive with respect to prostate cancer. Supplements widely used for this purpose are :

- Soy products /Isoflavonoids
- Selenium
- PC-SPES

Genistein concentrated polysaccharide (GCP), obtained from a *soy extract*, is widely used as a part of complementary medical therapy in Japan, Korea and other parts of Asia [26]. In men with proven cancer results with 5 g/day were disappointing. However, interesting results were obtained by Ornish and coworkers [12] with GCP combined with a low-fat vegan diet and antioxidants in men with localized prostate cancer under watchful waiting. This regimen led to a drop in PSA-concentration by 5% in contrast to a rise of 1% in the control group.

Selenium-supply is of major importance for prostate cancer prevention [27] and a constituent of many trials [28-29]. Earlier studies [30] had shown that a daily supplementation with 200 µg of selenium was associated with a 63% reduction in prostate cancer incidence. Men with low plasma levels have a 4 to 5-fold increased risk of prostate cancer [31]. In the ongoing SELECT-Trial [28], selenium (200 µg) and vitamin E (400 mg) daily are combined for prevention, the results of which are to be published in 2013.

PC-SPES, a supplement composed of herbs, has strong estrogenic properties and is widely used in the United States. Due to the side effects and cost it is not suited for prevention but for therapeutic supplementation in cancer cases [32].

VITAMINS

Vitamin supplementation for prostate cancer is summarized in Table II.

Vitamin D (Calcitriol, D3)

Vitamin D is a constituent of food (egg yolk, fish-oil, liver, milk) or converted from precursors in the skin (D2) under ultraviolet exposure. Low vitamin D levels are associated with an increased risk for prostate cancer [33]. On the other hand calcitriol is a potent inhibitor of cell growth in prostate tumor cell lines [34], and in clinical investigations [35]. Deficiencies in vitamin D supply can thus be a dietary problem or due to a reduced synthesis in the skin. Asian and Mediterranean food contains sufficient vitamin D3 and offers one explanation for the low prostate cancer rate. Men living in regions with low sun exposure (Scandinavia) or reduced skin synthesis through pigmented skin (Afro-Americans) have significantly higher prostate cancer rates. Sun exposure has shown to be preventive for the development of prostatic carcinoma in a recent study [36]. As calcitriol productions decreases with age, deficiencies may result in men of old age even in countries with adequate supply by food composition. Supplements of 400-800 IU per day are recommended in these cases.

Vitamin E

Vitamin E is an important antioxidant preventing genetic damage and tumor-cell proliferation [37]. Lycopene

plus vitamin E leads to tumor necrosis [38] and reduced tumor growth rate [39] in experimental settings.

Its importance in prostate cancer prevention came into attention with the Finnish Study [40] which revealed a reduced incidence of prostate cancer by 32% in smokers supplemented by Vitamin E and carotene. A subsequent trial confirmed these findings [41] for current smokers or recent quitters with 100 IU of supplemental vitamin E daily. International prevention trials (ATBC study: “α-tocopherol-β-carotene”) were initiated with combining vitamin E with other preventive agents (β-carotene, selenium and others). Again only in smokers a weak preventive effect was seen on follow-up after 5-8 years of α-tocopherol supplementation [42].

REFERENCES

1. Wu DS, Lubeck DP, Grossfeld GD, Carroll PR. Complementary and alternative medicine. In : Carroll, Grossfeld, editors. American Cancer Society. Atlas of Clinical Oncology. Prostate Cancer. Hamilton - London : BC Decker Inc, 2002 : 329-39.
2. Willis MS, Wians FH. The role of nutrition in preventing prostate cancer : a review of the proposed mechanism of action of various dietary substances. Clin Chim Acta 2003 ; 330 : 57-83.
3. Sommerkamp H. Nutrition and prostate cancer. Arab J Urol 2003 ; 1 : 24-5.
4. Fair WE, Fleshner NE, Heston W. Cancer of the prostate : a nutritional disease ? Urology 1997 ; 50 : 840-7.
5. Muir CS, Nectoux J, Staszewski J. The epidemiology of prostate cancer. Geographical distribution and time trends. Act Oncol 1991 ; 30 : 133-40.
6. Bergstrom A, Pisani P, Tenet V, Wolk A, Adami HO. Overweight as an avoidable cause of cancer in Europe. Int J Cancer 2001 ; 91 : 421-30.
7. Newcomer LM, King IB, Wicklund KG, Stanford JL. The association of fatty acids with prostate cancer risk. Prostate 2001 ; 47 : 262-8.
8. Michaud DS, Augustsson K, Rimm EB, Stampfer MJ, Willett WC, Giovannucci E. A prospective study on intake of animal products and risk of prostate cancer. Cancer Causes & Control 2001 ; 12 : 557-67.
9. Chan JM, Giovannucci E, Andersson SO, Yuen J, Adami HQ, Wolk A. Dairy products, calcium, phosphorus, vitamin D, and risk of prostate cancer. Cancer Causes & Control 1998 ; 9 : 559-66
10. Whittemore AS, Kolonel LN, Wu AH et al. Prostate cancer in relation to diet, physical activity, and body size in blacks, whites, and Asians in the United States and Canada. J Natl Cancer Inst 1995 ; 87 : 652-61.
11. Shimizu H, Ross RK, Bernstein L et al. Cancers of the prostate and breast among Japanese and white immigrants in Los Angeles County. Br J Cancer 1991 ; 63 : 963-6.
12. Ornish D, Fair W, Pettengil E et al. Can lifestyle changes reverse prostate cancer ? J Urol 2003 ; 169 : 74 (abstr 286).
13. Kamat AM, Lamm DL. Chemoprevention of urological cancer. J Urol 1999 ; 161 : 1748-60.
14. Moyad MA. Soy, disease prevention, and prostate cancer. Sem Urol Oncol 1999 ; 17 : 97-102.
15. Tsutsumi M, Suzuki K, Shiga Y, Ishikawa S, Ishikawa Y.

- A low-fat and high soybean protein diet for patients with elevated serum PSA : alterations of QOL and serum PSA level after the dietary intervention. *Hinyokika Kyo* 2002 ; 48 : 207-11.
16. Schroeder FH, Kransse R, Dijk MA et al. Dietary intervention in prostate cancer patients. Results of a randomized, double blind placebo controlled cross-over study. *J Urol* 2001; 165 : 65 (abstr 267).
 17. Gupta S, Ahmad N, Mukthar H. Prostate cancer prevention by green tea. *Sem Urol Oncol* 1999 ; 17 : 70-6.
 18. Hanash KA, Al-Othaimen A, Kattan S et al. Prostatic carcinoma. A nutritional disease ? Conflicting data from the Kingdom of Saudi Arabia. *J Urol* 2000 ; 164 : 1570-2.
 19. Norrish AE, Jackson RT, Sharpe SJ, Skeaff CM. Men who consume vegetable oils rich in monounsaturated fat, their dietary patterns and risk of prostate cancer (New Zealand). *Cancer Causes & Control* 2000 ; 11 : 609-15.
 20. ElSaghir NS, Adib S, Mufarrij A et al. Cancer in Lebanon : analysis of 10,220 cases from the American University of Beirut Medical Center. *J Med Liban* 1998 ; 46 : 4-11.
 21. Adib SM, Mufarrij AA, Shamseddine AI, Kahwaji SG, Issa P, ElSaghir NS. Cancer in Lebanon : an epidemiological review of the American University of Beirut Medical Center Registry 1983-1994. *Ann Epidemiol* 1998 ; 8 : 46-51.
 22. Augustsson K, Michaud DS, Rimm EB et al. A prospective study of intake of fish and marine fatty acids and prostate cancer. *Cancer Epidemiol Biomarkers Prev* 2003 ; 12 : 64-7.
 23. Miller EC, Giovannucci E, Erdman JW, Bahnson R, Schwartz SJ, Clinton SK. Tomato products, lycopene, and prostate cancer risk. *Urol Clin North Am* 2002 ; 29 : 83-93.
 24. Chen L, Stacewicz-Sapuntzakis M, Duncan C et al. Oxidative DNA damage in prostate cancer patients consuming tomato sauce-based entrees as a whole food intervention. *J Natl Cancer Inst* 2001 ; 93 : 1872-9.
 25. Boileau TW, Liao Z, Kim S, Lemeshow S, Erdman JW, Clinton SK. Prostate carcinogenesis in N-methyl-N-nitrosourea (NMU)-testosterone-treated rats fed tomato powder, lycopene, or energy-restricted diets. *J Natl Cancer Inst* 2003 ; 95 : 1578-86.
 26. Devere White RW, Hackman RM, Soares SE, Beckett LA. An evaluation of genistein ability to lower PSA in patients with prostate cancer. *J Urol* 2003 ; 169 : 446 (abstr 1668).
 27. Sommerkamp H, Khauli RB. Vitamins and selenium in the prevention of prostate cancer : an update. *Arab J Urol* 2003 ; 1 : 18-23.
 28. Klein EA, Thompson IM, Lippman SM et al. SELECT : The next prostate cancer prevention trial : Selenium and vitamin E Cancer prevention trial. *J Urol* 2001 ; 166 : 1311-15.
 29. Costello AJ. A randomized, controlled chemoprevention trial of selenium in familial prostate cancer : Rationale, recruitment, and design issues. *Urology* 2001 ; 57 : 182-4.
 30. Clark LC, Dalkin B, Krongrad A et al. Decreased incidence of prostate cancer with selenium supplementation : results of a double-blind cancer prevention trial. *Brit J Urol* 1998 ; 81 : 730-4.
 31. Brooks JD, Metter EJ, Chan DW et al. Plasma selenium level before diagnosis and the risk of prostate cancer development. *J Urol* 2001 ; 166 : 2034-8.
 32. Small E, Frohlich M, Bok R. Prospective trial of the herbal supplement PC-SPES in patients with progressive prostate cancer. *J Clin Oncol* 2000 ; 18 : 3595-603.
 33. Schwartz GG, Hulka BS. Is vitamin D deficiency a risk factor for prostate cancer ? *Anticancer Res* 1990 ; 10 : 1307-11.
 34. Schwartz GG, Wang MH, Zhang M. 1,25-Dihydroxyvitamin D (calcitriol) inhibits the invasiveness of human prostate cancer cells. *Cancer Epidemiol Biomarkers Prev* 1997 ; 6 : 727-32.
 35. Peehl DM. Vitamin D and prostate cancer risk. *Eur Urol* 1999 ; 35 : 392-4.
 36. Bodiwala D, Luscombe CJ, French ME et al. Prostate cancer risk and exposure to ultraviolet radiation : studies on interactions between ultraviolet exposure and polymorphisms in genes that mediate skin pigmentation and vitamin D-dependant pathways. *J Urol* 2003 ; 169 : 72 (abstr 276).
 37. Moyad MA, Brumfield SK, Pienta KJ. Vitamin E, alpha- and gamma-tocopherol, and prostate cancer. *Seminars in Urologic Oncology* 1999 ; 17 : 85-90.
 38. Lein MT, Jung K, Abramjuk C, Schnorr J, Wagner S, Loening SS. Lycopene and vitamin E increase the rate of necrosis in prostate cancer. *J Urol* 2003 ; 169 : 90 (abstr 349).
 39. Van Weerden WM, De Ridder CM, Bolder CA, Wildhagen M, Kraemer K, Schroder FH. Oral supplementation of vitamin E and lycopene reduces orthotopic growth of PC-346C prostate tumors. *J Urol* 2003 ; 169 : 218 (abstr 843).
 40. Heinonen OP, Albanes D, Virtamo J et al. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene : incidence and mortality in a controlled trial. *J Natl Cancer Inst* 1998 ; 90 : 440-6.
 41. Chan JM, Stampfer MJ, Ma J et al. Supplemental vitamin E intake and prostate cancer risk in a large cohort of men in the United States. *Cancer Epidemiol, Biomarkers & Prevention* 1999 ; 8 : 893-9.
 42. Virtamo J, Pietinen P, Huttunen JK et al. Incidence of cancer and mortality following alpha-tocopherol and beta-carotene supplementation : a postintervention follow-up. *JAMA* 2003 ; 290 : 476-85.