

# Reversing Early Stage Prostate Cancer in a Hypertensive Patient: A Case Study on Nutritional Cum Phyto-Therapy

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**Abstract:** While prostate cancer is the most common male malignancy in the West, it is ranked as the number two cancer death for non-smokers in many developing countries. This case study demonstrates how an early stage prostate cancer might be treated by a comprehensive and evidence-based nutritional cum phytotherapy if patient is given the option of using it. According to the ANMP ([www.anmp.org.my](http://www.anmp.org.my)), a nutritional therapy is used to treat, control, or prevent chronic disorders by impacting on the hormonal, neurological, and immune functions of the patient. It may take a decade or longer to develop a malignancy. Three quarter of prostate cancer occurs in men over fifty five years when they go through andropause, which is evidenced partly by elevation in their oestrogen levels. However, being overweight or obese may trigger early progression of prostate cancer in men.

**Keywords:** Prostate cancer, dietary/lifestyle modifications, nutritional cum phyto-therapy, andropause, prostate specific antigen, metastasis.

## 1. CASE PRESENTATION

Jonathan M., age 46, a United States citizen who was working as a senior engineer with an oil corporation based in South East Asia. Two months' ago, he was diagnosed at a San Francisco men's clinic as having stage B prostate cancer. A digital rectal examination (DRE) was done after his serum Prostate Specific Antigen (PSA) shown a score of 9.3 µg/L. A subsequent needle biopsy confirmed his prostate malignancy although there was no evidence of metastasis. His employers in Jakarta, Indonesia recommended him to seek natural therapy(ies) at the DSY Wellness Center in Kuala Lumpur instead of the invasive treatment at a conventional medical center.

Besides on hypertensive drug for the past two years, the patient did not notice any major symptoms. However, he had nocturia, dribbling after urination, problems in the initiation and cessation of urination, occasional burning sensation during urination, and some chronic pain from his lower back and hips. Like most of his siblings, he was overweight for most part of his life. But he did notice that he was losing weight during the past three years. His father was diagnosed with prostate tumor at aged 51, whereas his mother was diagnosed with ovarian tumor during her late 30's.

The patient was not offered any advice on dietary and lifestyle changes to improve on his conditions after his adenocarcinoma was confirmed by an oncologist. Consequently, he continued his smoking and drinking habits.

The lifestyle modifications recommended to this patient included:

- (a) Moderate exposure to morning sunlight: Those living in sunny areas [1] and men with a history of exposure to high levels of sunlight [2] have lower risk of prostate cancer. Sunshine exposure causes cholesterol to be used to generate Vitamin D3, which improves the prognosis of prostate cancer patient [3] while it prevents progression of malignancy [4]. Men with vitamin D as measured by 25(OH)D levels below 16 ng/mL might suffer some 70% higher incidence rate of prostate cancer than those with levels above 16 ng/mL. Even younger men with 25 (OH)D levels below 16 ng/mL, their incidence of prostate cancer could be 3.5-fold higher than for those with levels of 16 ng/mL or above and incidence of invasive cancer could be 6.3-fold higher [5]. However, not all studies found such a strong association [6]. Those with darker skin do require longer sunlight exposure to generate the same levels of 25(OH)D compared to individuals with lighter skin tone.
- (b) Exercising: 30 minutes a day of moderate exercise such as walking could be healthful. Obesity elevates risk of developing prostate cancer. Body mass index (BMI) greater than 30 may carry 1.27-fold higher risk of developing and dying from the disease than non-obese men [7]. Furthermore, men with the highest waist-to-hip ratios might be 300% more likely to develop prostate cancer as those with the smallest waist-to-hip ratios [8]. Obesity is also associated with

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more aggressive and late-stage prostate tumours [9].

The patient was advised to temporarily avoid:

- (i) Calcium: Men on this supplement might *increase* their risk of prostate cancer [10].
- (ii) Cooking oils which oxidize easily such as those from corn and sunflower - both of which are rich in linoleic acid (omega-6) - stimulate growth of prostate cancer cells called DU145 [11]. Even high intake of alpha-linolenic acid (canola, soy, and flax seed oils) might increase risk of developing prostate cancer [12].
- (iii) Smoking: Men with prostate cancer who smoke tend to have poorer treatment outcomes than those who do not smoke [13].
- (iv) Alcohol: Up to 22 alcoholic drinks per week can raise risk of progressing prostate cancer [14].

Since many cancer patients die from malnutrition created by their cancer progression, a comprehensive dietary plan consisting of these food items were recommended:

- (a) Fatty fish: Increased intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) decrease risk of developing prostate cancer, in general, and reduce risk of developing advanced stage disease in those already with prostate cancer [15]. It can inhibit the conversion of testosterone to dihydrotestosterone (DHT), which may be a factor in the development and progression of prostate cancer [16]. Fish rich in EPA/DHA include mackerel, cod, anchovy, and wild salmon.
- (b) Nuts and seeds: In raw form, they are a rich source of monounsaturated fats and vitamin E helpful to prostate cancer patient. Brazil nuts, for instance, may contain as much as 544 micrograms of selenium per ounce [17]. Just two Brazil nuts provide some 200mcg selenium sufficient to lower this cancer risk [18] while offering 50% reduced risk of cancer death [19].
- (c) Organic leafy vegetables, citrus and berries: The American National Cancer Institute recommends the ingestion of at least five servings daily of fruits and vegetables to fight the development and progression of prostate cancer [20]. These

foods contain anti-carcinogenic compounds such as chlorophyll, carotenoids, flavonoids, indole, polyphenols, sulforaphane, and protease inhibitors [21]. Although vitamin C intake from foods alone does not clearly appear to reduce rate of prostate cancer [22], several studies have linked higher dietary vitamin C intake with overall reduced risk of cancer including prostate [23-26]. Richest food sources of vitamin C include chilli, guava, bell pepper, green kiwi, and berries. Carotenoids and retinoids (pro-vitamin A) from say papaya and pumpkins could lower the incidence or preventing the occurrence of prostate cancers [27].

- (d) Lycopene-rich food: A diet high in tomatoes might offer 50% reduced incidence of cancer [28]. Lycopene lowers prostate cancer risk [29-32], enhances the level of apoptosis (programmed cell death) of prostate cancer cells [33] or inhibits its growth [34,35] while showing strong antioxidant activity [36] in prostate cancer patients. Lycopene is also found in carrots, green peppers, apricots, pink guava, watermelon, and pink grapefruit. Even frequent use of tomato sauce or paste is associated with a decreased risk of prostate cancer development [37,38]. As a fat soluble carotenoid, lycopene is a precursor of beta-carotene [39] but possesses at least twice the antioxidant capacity of beta-carotene [40]. When combined with food rich in vitamin E, it down regulates the levels of 5-*alpha-reductase*, an enzyme involved in the possible progression of prostate cancer [41].
- (e) Spices: These add flavour to food and also possess cancer-fighting properties. Those with strong anti-carcinogenic activity include garlic and ginger [42], as well as turmeric [43-45] which contains *curcumin* that inhibits cancer at its initiation, promotion and progression stages of development [46]. It is a *cyclooxygenase-2*(COX2)-inhibitor and it possesses both anti-inflammatory and antioxidant properties which inhibit prostate cancer growth by making natural cancer-fighting processes within the cell more effective [47]. It inhibits metastasis of prostate cancer to the bones [48]. It increases susceptibility of prostate cancer cells to any radiation therapy [49]. It is able to affect gene transcription and to induce tumour cell apoptosis [50]. Curry powder also contains a fair amount of genistein and other phytonutrients. Hot chilli

contains capsaicin, which has anti-tumour effects too [51].

- (f) Yellow or green Tea (Chinese or Japanese): This beverage reduces the risk of prostate cancer [52,53] and prevents development of tumors by blocking angiogenesis (growth of new blood vessels) [54]. It inhibits activity of *5-alpha-reductase*, the enzyme that converts testosterone to dihydrotestosterone (DHT), which has carcinogenic effects in the prostate [55] as well as other enzymes associated with the growth of prostate cancer cells [56]. Its most abundant and active polyphenol is epigallocatechin 3-gallate (EGCG) [57], which inhibits prostate cancer cells from multiplying [58,59] and promoting their destruction [60]. It also inhibits the activity of the enzyme *proteasome*, a key factor in the formation of prostate cancer [61] and the enzyme COX-2 involved in the progression of prostate cancer [62].

EGCG induces apoptosis and alters the expression of cell cycle regulating proteins that are critical for cell survival and apoptosis [63,64]. It has anticancer activity in patients with androgen-independent prostate carcinoma [65].

- (g) Soy: Intake of soy products is associated with a lower incidence of oestrogen-related cancers such as prostate [66,67]. Men with the highest consumption of tofu may have the lowest risk of developing prostate cancer [68,69]. Other valuable sources of soy include soy isolate, soy protein, fujuk, tempeh, soy flour, soy milk, and miso. The Protein Digestibility Corrected Amino Acid Score (PDCAAS) adopted by the USA-FDA and World Health Organization show soy isolate as having the same quality protein as egg white and human milk protein [70]. Saponins in soy beans possess a variety of anti-cancer properties [71]. Phytates or phytic acid (IP6) in soy increases natural killer cell activity in the body [72] while its phytoestrogens have anti-estrogenic effects [73] and 5-alpha reductase reduction activity [74]. Dietary concentrations of genistein, which is a natural protein tyrosine kinase (PTK) inhibitor, could stop prostate cancer cell metastasis [75] *via* cell detachment and cell invasion [76]. PTK inhibition is major factor in the inhibition of cancer [77].

- (h) Berries and citrus fruits: Consuming myricetin-rich berries can lower rates of prostate cancer [78]. Myricetin has antioxidant properties and its richest food sources per 100 grams are blueberries (2.66 mg), blackberries (0.67 mg), and cranberries (6.78 mg). Red onions and walnut are also a rich source.

The nutritional supplements prescribed for this patient were:

- (i) Zinc citrate (32% elemental zinc): 40mg twice a day equivalent to 25mg. This mineral inhibits the enzyme 5-alpha-reductase activity, which reduces the conversion of testosterone to DHT [79,80]. It prevents the specific binding of androgens to nuclear and cytosol androgen receptors [79]. Zinc is absolutely vital to the apoptosis of prostate cancer cells through its effects on the compound known as *fetuin* [81]. It also regulates tumor cell invasion of other tissues in the prostate [82]. Zinc inhibits prolactin secretion by the pituitary gland [83,84]. Increased prolactin secretion leads to higher levels of DHT [85].
- (ii) Vitamin D: 2,000 IU of this vitamin three times a day may be helpful for treating prostate cancer [86] since these cancer cells lack a component of vitamin D that is typically present in healthy prostate cells [87]. It inhibits prostate cancer cell growth or proliferation [88,89] *via* a number of cellular pathways, including cell cycle arrest, induction of apoptosis, and altered activation of growth factor signalling [90]. However, vitamin D metabolites produce inhibitory effects on specific receptors in prostate cancer cells [91]. It also protects non-malignant prostate epithelial from oxidative stress-induced cell death [92].
- (iii) Soy isoflavones (standardized to 25% genistein): 500mg three times a day. Just 60 mg daily could moderately reduce PSA levels [93]. Lower intake of genistein is associated with higher rates of cancer [94]. It is a strong inhibitor of angiogenesis, which is a major factor in the growth of cancer cells [95]. Besides, it induces tumour cell apoptosis [96]. Isoflavones inhibits many different prostate cancer cell lines, but its daidzein component may not have the same effect [97]. Just three weeks' therapy could result in increased antioxidant activities resulting in inhibition of prostate cancer cell formation [98].

Even low doses of its genistein can induce apoptosis in prostate cancer cells [99]. Genistein and daidzein counteract the negative effects of DHT on the prostate gland and its cancer cells [100].

- (iv) Selenium yeast: 350mg once a day (equivalent to 150mcg elemental selenomethionine) since the patient included some mixed nuts in his diet. Selenium deficiency increases the risk of cancer [101] and is associated with an increased risk of fatal cancer [102]. This micro-nutrient could reduce prostate carcinoma cell growth by 50% [103]. It plays a key role in the induction of apoptosis of prostate cells [104]. Higher levels of selenium counteract the prostate cancer cell-stimulatory effects of cadmium *in vitro* [105]. Apparently, selenium destroys prostate cancer cells by interfering with the metabolism of a compound called *5-lipoxygenase* that is critical to its growth [106]. The combination of selenium and vitamin E can offer additive effects on the destruction of enzymes important in the progression of prostate cancer [107]. While supplementation can reduce cancer risk [108], serum selenium levels higher than 150ng/mL may negatively affect patient's mortality rate [109].
- (v) Mixed tocopherols: 400 IU twice a day. Natural vitamin E supplementation can significantly reduce risk of developing prostate cancer [110-113]. D-alpha-tocopherol, when combined with lycopene, inhibits prostate cell proliferation [114] although when consumed individually gamma-tocopherol might be more effective [115]. The inhibitory effects on prostate cancer cells are likely to be linked to its androgen suppression [116].

Additionally, these herbal extracts were prescribed:

- (a) *Serenoa repens* extract: 500mg three times a day. This oily palm extract inhibits the conversion of testosterone to DHT in the prostate [117]. It has anti-estrogenic and receptor site-binding effects too [118]. Recent research suggests that estrogen strongly contributes to prostate cancer partly because this hormone reduces the ability of the prostate gland to clear its DHT levels. *Serenoa repens* extract for 90 days can result in lower receptor values for estrogen [117]. It significantly improves symptoms such as

dysuria, nocturia, prostate volume, and residual urine [119,120]. It also reduces the expression of *cyclooxygenase-2*, a newly recognized factor in the development of prostate cancers [121]. Although *Silybum marianum* inhibits conversion of testosterone to DHT [122], the patient did not also suffer from sluggish liver to justify its use.

- (b) Panax Ginseng (standardized to 60% ginsenosides): 400mg thrice a day. Ginsenoside Rg3 inhibits growth of prostate carcinoma cell line [123].
- (c) *Annona muricata* leaf tea: 1g three times a day. Its leaf contains compounds which might be selectively cytotoxic to prostate cell line (PC-3). Prostate cancer cell toxicity is estimated to be between 10 and 100-fold the potency of the chemotherapy drug Adriamycin [124]. Other study suggests a potency of up to 10,000 times compared to this drug [125].
- (d) Pygeum (standardized to 14% triterpenes including betasitosterol and 0.5% n-docosanol): 1g three times a day. This seed inhibits the progression of both prostate cancer and benign prostate hyperplasia [126]. It can induce prostate cancer cell apoptosis [127]. Like *Serenoa repens*, it improves a variety of urinary symptoms such as urinary frequency, nocturia, flow interruption, after-dribbling, weak stream, and hesitation [128]. Additionally, pygeum increases prostatic secretions and improve the composition of the seminal fluid [129], besides raising patient's capacity to achieve erections [130].
- (e) *Artemisia* (standardized to 25% artemisinin): 500mg three times a day. It can act as an oxidant that selectively destroys cancer cells when it interacts with the mineral iron [131]. Cancer cells contain up to 1,000 times more iron than normal cells. Artemisinin and transferrin (stored iron) might be some 34,000 times more effective in selectively killing cancer cells than normal cells [132].

## 2. BENIGN PROSTATE HYPERPLASIA (BPH)

BPH and prostate cancer are *not* the same condition and they develop in different parts of the prostate gland. However, both conditions produce elevated PSA levels and a variety of urinary problems.

In addition, both are considered hormonally-related disorders. BPH occurs in more than 50% of all men in their 60s and in as many as 90% of men in their 70s and 80s. Like prostate cancer, BPH may be promoted by the relatively increased levels of estradiol (E2) that occur in men as they age. Intake of more than 25 ounces per month of alcohol is correlated with the development of BPH [133] since alcohol is estrogenic. The mean prostate zinc tissue content may be significantly lower in BPH patients [134]. Serenoa repens [135] [136] and soy phytoestrogens [137] are also effective in treating symptoms of BPH.

### 3. DIAGNOSTIC ISSUES

The prostate is a walnut-sized gland located beneath the bladder of males and it surrounds the upper part of the urethra, which is the tube that carries urine from the bladder. The digital rectal examination - once the "gold standard" - is being superseded by techniques such as serum and tissue-based assays [138]. Molecular markers for prostate cancer such as DNA ploidy and nuclear morphometry were considered unnecessary for the patient, who came with full biopsy and other relevant reports issued by reputable hospitals.

While the incidence of prostate cancer in Asians seems to be the lowest [139], it is the most common male malignancy in the Western world but with rather ill-defined risk factors [140]. Some 75% of prostate cancers occur in individuals 55 years of age and older [141]. Other sources confirm that 60% of all prostate cancer cases are diagnosed in men 65 years of age and older [142,143]. Related risk factors include race and geography [144].

Consequently, the patient's family history and dietary/ lifestyle habits could play a crucial role in both the initiation and development stages of his cancer. Indeed, studies found significant association of HPC2 genotypes with prostate cancer [145,146], whereas some studies found no significant association between them [147,148]. A man whose father had prostate cancer may be 230% more likely to develop the disease than if his father never had the disease. A man is also more likely to develop this cancer if his sister or mother develops breast or ovarian cancer. Some 15% of inherited cases may be transmitted through the mother's chromosome. A different gene called HPC1 has been associated with about 30% of all inherited cases of prostate cancer. The highly expressed AP-N in human cancerous prostate probably plays an

important role in the invasion and metastasis of prostate cancer cells [149]. Furthermore, childhood obesity is associated with an increased risk of prostate cancer late in life [150].

Between 50% and 90% of all cancers may be prevented with proper nutrition [151]. However, carcinogens exist in modern diet including those found in fruits and vegetables. Strawberry, for instance, has some of the highest pesticide content compared to other imported fruits. Cadmium toxicity, say from cigarette smoke, as a risk factor could be assessed from the patient's urine [152]. However, urine testing for this heavy metal was unavailable locally.

Adenocarcinoma is the primary type of prostate cancer. Prostate function is regulated by the male hormone testosterone, which can be converted to DHT due to zinc deficiency. Toxic chemicals such as dioxin [153] and pesticides from fruits and vegetables can increase the converting activity of 5-alpha reductase. Blocking this enzyme may diminish the development of prostate cancer [154] since DHT is essential for prostate cell differentiation [155]. Available evidence suggests that prostate cancer could not be considered solely in terms of its response to androgens [156].

There is now a body of research that links prostate cancer to increased exposure to oestrogen [157-159]. In the United States, a link was found between prostate cancer and the oral contraceptive by-products found in drinking water [160]. However, other studies did not find such a clear association [161,162].

Since cancer mortality is directly proportional to disease stage, the detection of stage 2 rather than end-stage prostate cancer offers a longer survival opportunity for the patient [163].

Till his posting to South East Asia, the patient spent mainly indoor with little sunlight exposure. Vitamin D deficiency is an important factor in the development of prostate cancer [164]. Being overweight, the patient would need longer exposure to sunlight compared to non-overweight individuals since most of this fat soluble vitamin could be stored in his adipose tissues and unavailable for his use [165].

Prostate enlargement such as BPH as well as infections can mimic some of the symptoms of cancer. Consequently, prostate cancer can develop with no significant symptoms, particularly in its early stages. As the disease progresses, however, the symptoms might include frequent urination particularly at night, inability

to urinate, painful urination, problems with cessation of urination, blood in urine, pain in ejaculation, and persistent pain in the upper thighs, lower back or hips.

Based on decades' long understanding that cancer cells feed on sugar, the PET imaging offers the potential to detect malignant cells based on their increased glucose metabolism wherever they are located within the body [166]. However, this was considered unnecessary since the adenocarcinoma was adequately documented.

Radioimmunoassay analysis of PSA may be used for diagnosing both localized as well as metastasized stages of the prostate cancer. Though controversial, PSA is nevertheless the most sensitive marker for monitoring this disorder and it is elevated in 25% to 92% of patients with prostate cancer. However, it is also raised in 30% to 50% of men with BPH or prostatitis (inflamed prostate gland). The patient was not offered the newer ultrasound technique using the Doppler, which along with targeted biopsy, seem to have a detection rate some two-fold higher than systematic biopsy [167,168]. It reduces the need for repeated biopsies since the colour Doppler imaging can determine the staging of high-grade prostate cancer [169] and it permits tracking of changing prostate conditions over time [170]. Prostate cancer, if unsuccessfully untreated, can lead to osteoblastic bony metastases. Bone scans or x-rays were considered unnecessary in this case since there was no evidence of the cancer metastasizing.

Malnutrition is a common problem among most cancer patients and any cachexia is associated with rather poor response to further therapy [171]. Extracts from the patient's blood tests and physical statistics for the first three months' therapy during the year 2011 were as follow:

	April*	May	June	July
<b>Serum</b>				
PSA (<4.0µg/L)	9.6	8.1	5.8	3.2
Hs-CRP (<1.0mg/L)	25.3	20.6	13.9	6.4
TG (<200mg/dl)	310	288	237	187
HbA1c (~5%)	6.5	6.2	5.9	5.8
Selenium (ng/mL)	116	118	122	127
25(OH)D (ng/mL)	12	13	18	22

<b>Physical:</b>				
BMI	31.5	29.7	28.4	26.2
Skeletal muscle%	28.9	31.5	31.7	32.6
VFA%	19	17	16	14
Total body fat%	33.5	31.3	29.6	28.2
Total body water%	44.2	47.3	49.1	51.6
Blood pressure (S/D)	142/91	138/88	136/86	131/85

\*date of first consultation.

Although during August 2011 a major private hospital in Singapore declared the patient free from prostate cancer, he continued with his nutritional therapy for another three months. He was advised to recheck his conditions when he returned to San Francisco in November that year.

With dietary and lifestyle modifications, his blood pressure was moderately lowered at the end of his third month of therapy. He was advised not to stop his medication without consultation with his prescribing physician.

## CONCLUSION

The outcome achieved at the end the fourth month strongly suggests that a well-designed, comprehensive nutritional cum phyto-therapy could halt or even reverse prostate cancer especially in its early stages. However, it was unclear if such a natural therapy could reverse or control advanced stage prostate cancer.

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