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Studies on Cancer of the Prostate Gland, a Search for Aetiological and Prognostic Factors

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The aim of this long study was to try to elucidate the aetiology and prognostic traits in patients suffering from cancer of the prostate gland (CaP) e.g. by medically restoring, in an active but non-invasive way, the normal metabolic balance and mitochondrial control of oncogene transcription in CaP.

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Carcinoma of the prostate is still today potentially an incurable age-linked disease of unknown aetiology. Side effects coupled with deterioration of the life-quality of the cancer patient and his family, pared with expensive treatments without a guarantee of a cure, mar all our present standard therapies. The aim of this long study was to try to elucidate the aetiology and prognostic traits in patients suffering from cancer of the prostate gland (CaP) e.g. by medically restoring, in an active but non-invasive way, the normal metabolic balance and mitochondrial control of oncogene transcription in CaP.[1] The reasoning was that intake of certain metabolic dietary components, by chance, may explain why some patients do not die of CaP, since their diet may lead to what we call their "*latent disease*". To unravel these aetiological and prognostic background factors a wide range of changes in hormonal and biomodulating factors were measured and followed for years, in selected patients during different stages of prostate cancer, while they were receiving various forms of therapy. The biological and pathophysiologic responses were followed-up for over twenty years, which presently seems to result in a better understanding of CaP.

Dietary Habits

Descriptive *epidemiology* has shown that the probable causes of CaP are determined rather on *environmental than genetic factors*, and that *dietary habits* have a pronounced effect on prostate cancer incidence. "Latent disease" may actually be a result of dietary habits and life style. The low incidence of CaP in Japan and Italy (compared to the > tenfold in Northern Europe and USA), may be linked to the intake of *soy* and *parmesan* respectively, which both contain the amino acid Serine (i.e. 0.5% and 0.25%), further supported by the lycopene intake from tomatoes in the Italian diet. Such a dietary change simulating an Italian diet actively administered over a two year period to a patient in stable disease (No 1), which had lasted for over ten years, showed that his DHEA and DHEAS decreased, while the FSH-level stayed normal indicating an incessant favourable prognosis (**Table II a**). Idiopathic, initially increased FSH-levels specify stable disease as well as increased PRL levels found in certain patients (No 2-5) in follow-up for more than eleven years (**Table II b**).

The lowering effect on PSA (a serine protease) *from dietary supplementation with Serine* was detected over a decade ago.[1] Instead of recommending only passive "watchful waiting", which many patients rightly regard as a depressive form of "Russian roulette" they were, with informed consent, offered a dietary supplementation schedule based on epidemiological clues and our empiric findings. This dietary supplementation formed an effort to cause a "*therapeutic bio-modulation*". Patients were fed the natural amino acids (approx. 3-5 g/d); Arg, Asp, Glu, Gly, Lys, and especially Ser, together with the trace-element salts; Cr, Sn, & W, sometimes also Zn (in mg/day), Ca & Manganese, [strontium (Sr) is prescribed for CaP with bone metastases after orchiectomy or total androgen ablation], plus Folic acid, and a prion-free diet containing neurogenic lipids were added. This clinically active - combined formulation was prescribed and administered e.g. mixed in the patients' morning yoghurt, as described in **Table I**.

Contrary to this positive dietary effect 12

Table II a.

Patient No1, Incidentally detected CaP ten years ago with stable disease, in deferred treatment > 10 years. Placed on simulated [Italian / Japanese] diet consisting of; parmesan, soy, lycopene

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA µg/L
1-7#9	2.5-12	50-300	3.0-17.0	0.0-8.0	9-38	~60pg/ml	~500pg/ml	16-253	15-50	<4.0
(1998) 4.8	3.1	155	3.5	0.7	6.6	90.4	700	96	30	< 1
(2001) 4.6	2.4	136	3.7	<0.8				163	43	< 2
(2003)			2.3	0.8	11.0					1.3

observed – trials with *active specific immunotherapy* using autologous vaccines could only for a limited time decrease the PSA-level in patients but *did not arrest CaP*, since PSA seems to be only a metabolite which can be neutralized for a while by the activated antibodies produced, but is not a proper cancer cell marker.

A *negative effect*, seen as an increase in PSA, may result from ingestion of Alanine. Consequently, patients should avoid foods containing high amounts of Ala, but increase the intake of Serine containing food-items. These biological exploits were based on the positive effect obtained with other cancer forms in bio-immunotherapy,[1] in which negative outcome also occasionally were seen, since certain natural metabolic components may act as growth factors for specific cancer cells. The intake of such components should therefore be minimized.

Aetiological Aspects

The evidence at hand implies that our standard hormone treatments only *activate a feed-back* reaction mediated by the *zona reticularis (ZR) cells of the adrenal gland.* The ZR cells in the adrenal seem to have a central position in the regulatory *physiological cycle, embracing several organs,* controlling normal prostate cells; the hypothalamus - pituitary, healthy prostate gland cells, and epididymis in the testes, a cycle schematically presented in **Figure 1**. Clues pointing to the importance of adrenal ZR cells in CaP are; a) the marked proliferation of ZR cells in orchiectomized patients; b) the lack of ZR cells in male pigs castrated at a young age (eunuchs); c) the marked decreased number of ZR cells in patients succumbing to CaP; d) the conspicuous hormonal effects in patients elicited by intake of extracts made from ZR cells of castrated boars; e) the rapid lethal outcome if patients suffering from CaP are adrenalectomized after orchiectomy [observed already in the forties], since adrenalectomy may eliminate the production of the life-preserving ZR components?

Therefore, to analyse human adrenal (forensic ZR tissue) extracts for biological activities is essential, as it may lead to a biological compensatory treatment, like insulin for diabetics.

Table II b.

Patients with initially high FSH or PRL-levels have remained in stable disease for years.

	FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA µg/L
	1-7#9	2.5-12	50-300	3.0-17.0	0.0-8.0	9-38	~60pg/ml	~500pg/ml	16-253	15-50	<4.0
No 2.	18.6	13.4	242	6.3	3.9	7.6	66	790	133	27	14.4
	18.0	12.8	241	4.0	3.3		83	550	86		13.0
No 3.	27.2	11.8	144	7.8	5.0	16	73	430	38	49	< 0.3
	27.0	11.0	162	5.3	4.2	16			34	49	< 0.4
No 4.	75.0	33.0	224	20.9	2.3	6.7			20	38	29.8
	13.0	0.1	122	2.9	1.5	10.0	(TSH 9.8)		50	34	2.8
No 5.	2.3	3.9	392	3.4	1.1	12.9	187	92	55	46	< 1.0
	2.1	2.4	566	2.8-2.4 <2	<0.8	9.8-8.9			44	37	1.7/29%

The ZR cells seem to produce at least two unknown endocrine factors which cause an increase in FSH- and/or PRL-levels. Increase of these hormone products signal a positive prognostic sign, especially when coupled with decreased DHEAS levels. Stimulation of FSH and PRL appear to form an essential part in the cycle preserving and/or restoring the normal genetranscription of prostate gland cells. They are probably also involved in procuring the mitochondrial regulatory signals, which can retract oncogene transcription in CaP cells (**Fig 2**).

The Benefit of Screening Studies for CaP

With patients diagnosed for CaP in *screening tests* these dietary supportive measures can normalize the PSA-level and halt the disease for years if therapy is started in the early phase of the disease, even without the help of hormone treatment. Using this combined bio-modulating therapy (see Table I), it has been possible to halt progression of CaP for over five years. In the first case progress of CaP had been arrested for six years when he was persuaded to accept prostatectomy. In histopathology at this late incidence his Gleason score had declined from 7-8 to 4 and the tumour had not grown. The positive clinical effect of *dietary bio-modulation* was found to be elicited in a dose-response-linked manner, especially in patients who have not been prostatectomized. The reason is most likely that the physiological cycle regulating prostate gland cells involve also the healthy cells to function properly (excluding also irradiation damage). In an early stage (when PSA is < 12 µg/L) prostatectomy should probably not be performed before one has had time to test whether this biomodulating treatment can halt the malignant process, due to the grave side-effects caused by our invasive treatment modalities. The possibility to biologically stop the progress of CaP for years,

Table I

Dietary bio-modulation schedule for treatment of prostate cancer patients

Supportive dietary measures.

1. Oral administration of each (2-5 g/day) of respective L-amino acids; Arg, Asp, Glu, Gly, Lys, & Ser, eventually also His, all in connection with meals.
2. Essential trace-element salts prescribed orally as biologically active ions, at dose levels of some milligrams (1-3mg/day); Chromium ($CrCl_2.6H_2O$) 6 mg (= 1.17 mg Cr), Tin ($SnCl_4.5H_2O$) 4 mg (= 1.35 mg Sn), Strontium ($SrCl_2$) 0.1 mg - 7 mg (~2 mg Sr), Vanadine ($Na_2VO_4.4H_2O$), 6 mg (= 2.5 mg V), Wolfram ($Na_2WO_4.2H_2O$), 4 mg (= 2.3 mg W).
3. [Sr supplementation is applied to patients who have been orchiectomized, and the oncogen transcription has been forced to obey normal mitochondrial regulatory function.]
4. Small physiologic amounts of vitamins; A, B, C, D, E, K , folic acid (2 mg/d) and lycopene.
5. To improve lymphopoiesis and the immunedefence of patients a diet containing prion-free neurogenic lipids (equivalent to approx. 50 g of brain) was recommended, (purchased and canned by Neurofood Ltd. Finland).
6. All these dietary ingredients can be mixed together in yoghurt, forming a daily ration, using pre-packed pulvers.
7. Dose-levels are individually adjusted based on clinical response as measured during therapy correlated to; stage, age and the patients´ body weight.

Footnote: This formulation is the intellectual property of The Helsinki Institute of Bio-immunotherapy Ltd.

especially in the early phase of the disease utilizing non-invasive and inexpensive treatment modalities, devoid of side-effects, impart PSA screening a definite rectification, because we may have a positive new therapeutic alternative.

Androgen Deprivation by Intermittent Short Time Cycles

The provoked feedback reaction caused by castration, or standard LHRH treatment, androgen inhibitors etc., except in cases when the hormone therapy is performed intermittently, is depriving the body a chance to produce its biological response-cycle, evidenced as a rise in the patients' testosterone and PSA levels. Unfortunately this is also caused by constantly upheld LHRH-analogue treatment, as well as a natural sequel of orchiectomy. Our standard therapy will therefore ultimately lead to a hormone refractory state, ending in recurrent disease. It is thus understandable that our androgen ablation therapy, which triggers only a feedback reaction, will finally fail, since it does not supply the missing endocrine ZR factors. Nor does it seem to have an effect on crucial enzyme reactions, especially the sulphonation of DHEA to DHEAS. A decreasing level of DHEAS seems to constitute an important part of the biological reactions arresting malignant cell growth in the prostate gland. The 5α-reductase level was found to be decreased in certain patients, but the enzyme does not seem to arrest CaP,[3] and does not materialize to be as important a prognostic factor as the depressed sulphonation of DHEA (or its isomer?).

In order to preserve and prolong the effect of the hormone therapy *intermittent treatment using LHRH analogues administered with short cycle duration* is presently recommended, [e.g. Zoladex®, 3.6 mg injection, *expressly not* 10.8 mg for 3 months duration, since it simulates too much the irreversible effect of orchiectomy]. To achieve total androgen blockade the LHRH analogue injection is combined with Androcur® (50 mg × 2 /day) for 3 days before, and for an additional seven days after the Zoladex injection to prevent a flare-up reaction. This form of intermittent, short time, total androgen ablation is repeated only when the patients PSA-, testosterone and FSH-levels have had time to increase slightly (PSA ~15 µg/L). This schedule seems to effectively *postpone the emergence of the "hormone refractory state"*, now already for 12 years, as it fools the adrenal that it has been able to achieve a biological reaction. Patients respond then as in a primary reaction to the hormone therapy because the response is synergized by the continuous dietary measures as described above (Table II c). There is a typical oscillation in certain laboratory assays caused by the hormone therapy (No 6), especially in the prognostic pattern related to the levels of ; FSH, LH, PRL, ACTH, TSH, DHEA, DHEAS, ferritin, oestrogen and PSA, as followed for more than 12 years with CaP patients. Typically FSH, LH, PRL, Ferritin and PSA-levels decrease as a result of renewed androgen ablation to regain starting levels after individually variable time-intervals (Table II c), marking the individual optimal interval length for the intermittent hormone therapy schedule (these prognostic characteristics, and symptomatic laboratory patterns are presented in detail during the lecture, as well as in the full article in preparation).

The use of a short time cycle is at variance with the established striving to achieve a PSA-nadir, which unfortunately almost all previous trials using intermittent hormone therapy for CaP have tried to reach.[4] To attain a PSA-nadir usually requires over six months of constant androgen ablation. This forced long-time depression of the physiological interplay in this multiple-organ cycle is therefore irreversibly interrupted, as well as the natural inductional control of these organ cells. Consequently, it may lead to transition of the CaP cells into an androgen independent state. This transition is not necessarily the result of emergence of a hormone resistant cell-clone in patients, but rather due to a wrecked hormonal adrenal feedback function, since it is not periodically allowed to react.

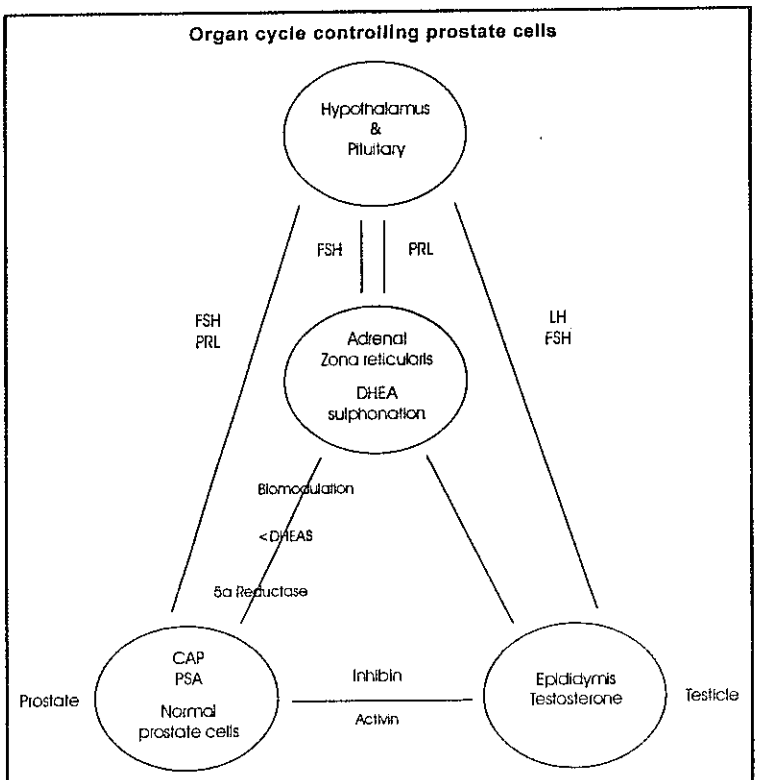

Figure 1.

Initially increased FSH or PRL are good prognostic signs and should always be analysed when CaP is found by screening tests since invasive treatments can be avoided. The human adrenal biological factors harboured in the zona reticularis should be assayed for their stimulatory effect on the pituitary as they could form a biological compensatory, dietary medical treatment for CaP. The effect of hormone therapy for CaP, in recommended intermittent short time pulses combined with metabolic bio-modulation causes a feed-back reaction recorded as characteristic changes in the laboratory response profile, with FSH, LH and/or PRL increase trailed by DHEAS decrease. In this reaction adrenal zona reticularis cells seem to have a central regulatory position. Orchiectomy will cause FSH to increase, further accentuated by prostatectomy. Prostate cancer patients die in a short time if orchiectomy is followed by adrenalectomy. A dramatic rise in activin levels is recorded in a special form of CaP. These cases were diagnosed based on soft tissue metastases. Inhibin is on the contrary remarkably decreased following orchiectomy.

Changed Inhibin and Activin Patterns in CaP, Pregnancy, and in Female Oestrogen Substitution

CaP patients diagnosed from the presence of *soft tissue metastases represent a special form* of prostate cancers (possibly neuroendocrine?). They may have markedly high serum activin-levels ((1850- 2900 pg/ml) paired with low inhibin-levels (25-34 pg/ml). Initially their serum ferritin levels are high (1164-2499 µg/ml), while DHEAS (< 0.8 – 1.8) and DHEA (2.2 - 2.4) are low. FSH-levels are normal or low (1.9 -5.1 IU/L) while LH-levels are undetectable (<0.1 IU/L). Patient No 7 had a PSA-level of 10070 µg/L, while patient No 8 showed a PSA of 246 µg/L. In both patients their PSA decreased to 5.3 µg/L and 2.1 µg/L respectively in half a year, following intermittent short cycle LHRH therapy, in synergy with biomodulating dietary measures (**Table II d**). The high activin levels were not appreciably affected by the therapy, while PSA decreased markedly. *Orchiectomized* CaP patients generate an increase in their FSH-levels to; 40 – 130 IU/L, in some months, but show also a characteristically manifestly depressed serum inhibin level (<7.8 pg/ml) while their activin level (~560 pg/ml) is normal.

Surprisingly healthy *pregnant females revealed a similar change* in their inhibin / activin levels, with a correlation value of

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1 70, until parturition when the "growing cell-mass" – the healthy child is borne and the correlation value again becomes normal. Alarmingly, also oestrogen substitution (already 50 µg plasters) in postmenopausal women can show a similar dramatic change in their inhibin / activin correlation values. Such a provoked change in a females serum growth factor levels – usually actively made to *last more than nine months* by their gynaecologists – could easily fool the body that it should produce growing cells. This anomalous change may explain the observed increased breast-cancer and lymphoma incidence generated by oestrogen substitution therapies in otherwise healthy females. The effect of *oestrogen substitution therapy*, prescribed to any female patient, *should therefore obligatory be monitored by inhibin / activin assays*, to see *if it causes a reaction simulating pregnancy*, since such an anomaly may physiologically be misinterpreted by the body, which consequently could generate proliferating (malignant?) cells. With breast cancer patients in bio-immunotherapy, frighteningly many cases have been on oestrogen substitution therapy before the disease was detected.

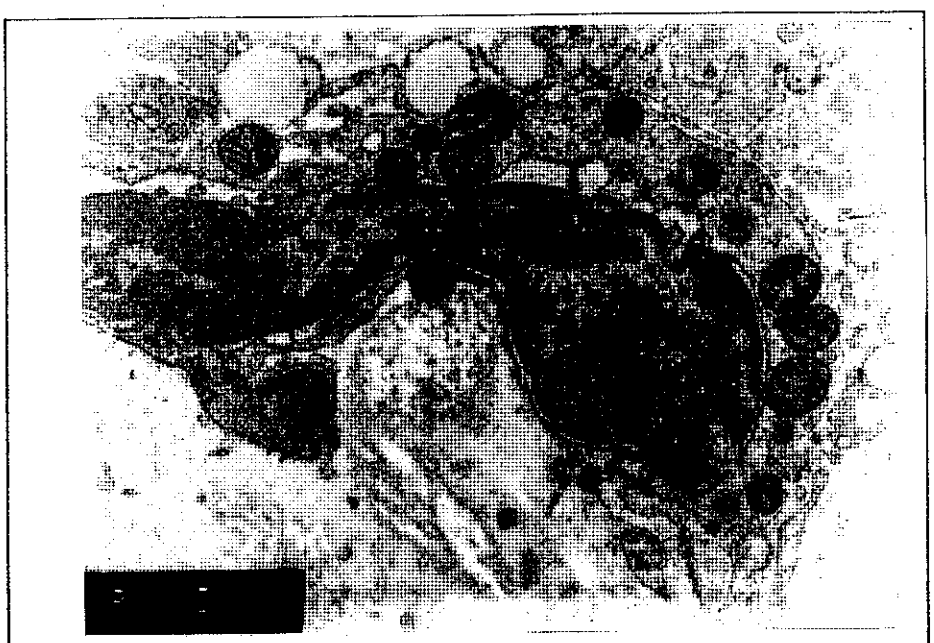

Figure 2.
Electron microscope showing the nucleus of a prostate cancer cell. The mitochondria insert their electron dense material when the tumour cell is forced back into normal healthy function without apoptosis. This is registered as normalisation of the PSA-level, followed by stabilized disease, (reproduced from ref. 2).

Especially, instructive clinical cases:

Orchiectomy combined with dietary bio-modulation.

One patient suffering from multiple bone-metastases, and with PSA 30 µg/L, was initially orchiectomized 12 years ago. He was then prescribed our supportive dietary measures in 1992. His bone-pain subsided in 6 months, the bone-metastases disappeared after four years, and he is now in excellent clinical condition. The laboratory pattern is presented in **(Table II e)**. Recently it was found that, in addition to all the dietary biomodulating components prescribed by me (Table I), he had ingested a daily amount of 7 mg of strontium-oxide, contained in the birch ash he prepared at home and had been taking continuously (No 9). As may be recalled, radioactive Strontium[89] was formerly used to scan bone-metastases. Sr homes into the metastases, although only ~ 10% of the i.v. dose (up to 80 mg $SrCl_2$) may be radioactive ^{89}Sr it is sufficient to localize metastases. Repeated trials to localize bone-metastases were hampered, and the scanning became unreliable. Probably the excess of non-radioactive Sr injected was blocking the cell-receptors. Therefore, presently we use technetium. The strontium content was found to markedly decrease in "activated" mitochondria (in ref. 2., Table II), as it seems to be involved in transporting the mitochondrial regulating code to the genome and reverse the oncogene transcription in tumour cells - without causing apoptosis. Sr could have been a crucial co-factor leading to the disappearance of his bone metastases.

Patients with idiopathic - increased FSH and prolactin-levels.

Special cases are patients who initially show increased FSH-levels over the normal value (7-9 IU/L) e.g. varying from 19-70 IU/L, with confirmed diagnosis for CaP based on needle biopsies. Sometimes their PSA levels may stay at 20 – 30 µg/ml but the disease is stable for years without any treatment (No 3), or following only the dietary measures (No 2). The LH-level is not as important as it may be slightly elevated or reduced without affecting the prognosis. DHEA and DHEAS levels are normal or slightly downgraded, but as long as the FSH is elevated the prognosis is fair. One patient (No 4) had needle biopsies taken every year, because his PSA was at 30 µg/L for five years without evidence for actual CaP. Finally a biopsy was found showing an aggressive malignancy, of Gleason score 8. The protracted case history was seen to be due to an iatrogenically high FSH-level, of up to 70 IU/L. His disease reacted very well to intermittent LHRH analogue hormone therapy, in synergy with the dietary measures. (Table II b)

Patients showing initially elevated and/or increasing PRL-levels have been followed for years, in deferred treatment, without showing signs of progressive disease (No 5). Prolactin seems to be one of the factors involved in preserving normal prostate cell function. PRL increases also when ZR- extracts, prepared by micromanipulation of ZR cells from castrated pigs are ingested. Unfortunately I was prevented by officials to retrieve and test human forensic adrenal material although they are collected in the same package as kidneys, gathered for transplantation.

Ingestion of strontium in mg amounts, for two weeks (No 11), was found to cause a PRL increase in healthy persons (> 50%) coinciding with a decrease in his DHEAS (~40%), a reaction pattern usually considered as a favourable prognostic sign **(Table II f.)**. To achieve a positive effect may require that the oncogene mitochondrial signal aberration has been restored to normal function before the transport of mitochondrial signals by administration of Sr is improved?

Table II c.

Pat.No6. Lab assay profiles during short pulse intermittent LHRH treatment, Zoladex 3.6mg, + Androcur with three months intervals in synergy with dietary bio-modulation for >11 years.

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA µg/L
1-7#9	2.5-12	50-300	3.0-17.0	0.0-8.0	9-38	~60	~500	16-253	15-50	<4.0
15.2	16.1	993	3.8	2.4	6.4	75	410	1500	45	13.4
4.2	7.3	1490	2.5	1.6	5.8	72	430	1100		2.5
15.2	17.7	1520	2.2	< 0.8		76	500	993		14.5

Patients Succumbing to CaP.

Laboratory values indicating that he will die soon is usually heralded by a marked decrease in FSH at the same time as LH is almost undetectable (< 0.1 IU/L). DHEAS is normal or slightly elevated and PSA can show great variation (e.g. 200 – 3000 µg/L). The lethal outcome is primarily signalled by a marked decrease in pituitary FSH and LH production (<0.1 IU/L), or rather collapse in the vital production of adrenal *feed-back* ZR factors (fictively called "cycloprostatins" since they may be the same which are responsible for normal female ovulation). The pituitary gland proper does not seem to be exhausted since PRL may be grossly elevated (> 1000 mU/L) indicating that the pituitary is largely functional (No 10), In this final situation, usually also the serum ferritin level is pathologically increased (> 2100 µg/L). A pivotal factor seems again to be the DHEA levels and its transition to DHEAS (sulphonation), while SHBG may be markedly elevated (**Table II f.**).

Table II d.

Pat. 7 & 8. CaP was detected from soft tissue metastases and both had also bone metastases. A special characteristic was extremely high activin and PSA-levels.
In No 3. = 10070 µg/L which declined to 5.3 µg/L.
In No 4.PSA was 246 µg/L which declined to 2.3 µg/L in 8 weeks in combined therapy.

	FSH IU/L 1-7#9	LH IU/L 2.5-12	PRL mU/L 50-300	DHEA nmol/L 3.0-17.0	DHEAS µmol/L 0.0-8.0	Testost nmol/L 9-38	Inhibin pg/ml ~60	Activin pg/ml 300-500	S-Ferrit µg/L 16-253	SHBG nmol/L 15-50	PSA µg/L <4.0
No 7.	5.1	<0.1		2.4	1.8	<0.8	25	2900	1164		10070
	6.2	<0.1					22	2650	316		5.3
No 8.	1.9	<0.1	222	4.0	<0.8	1.2	34	1850	2499	165	246
	0.74	<0.1	212	2.2	<0.8	1.2	33	1770	493	151	2.3

One patient in the late state of standard therapy (stage IV) after hormone therapy had been terminated was given biomodulating dietary treatment as a final try. His laboratory values showed a low level of FSH and < 0.1 for LH, very low DHEA and DHEAS (< 0.2 & < 0.8 respectively) but with a high PSA (2800 µg/L). In biotherapy his intense pain subsided in some weeks, and his general condition improved. The remarkably low levels for DHEA & DHEAS led him to demand oral supplementation with DHEA (25 mg/day) regarded by him, and some doctors as a stimulatory agent. The pain reappeared and he died in two weeks.

Table II e.

Pat 9. CaP was detected 1992 with PSA 30 µg/L with multiple bone metastases, orchiectomy was performed.
Dietary bio-modulation started with Sr. He is now in excellent condition, metastases disappeared 1996.

	FSH IU/L 1-7#9	LH IU/L 2.5-12	PRL mU/L 50-300	DHEA nmol/L 3.0-17.0	DHEAS µmol/L 0.0-8.0	Testost nmol/L 9-38	Inhibin pg/ml ~60	Activin pg/ml 300-500	S-Ferrit µg/L 16-253	SHBG nmol/L 15-50	PSA µg/L <4.0
No 9.	67-30	37-16	159-95	< 2.0	< 0.8	1.0	< 7.8	330-500	109-99	58-61	< 0.1

Good prognostic signs are; a preliminary high FSH-level, and an oscillating level, with rebound of the FSH following short time intermittent LHRH analogue treatment, decreasing DHEA and especially DHEAS-levels, following dietary bio-modulation supported by Strontium supplementation for orchiectomized patients suffering from bone metastases, increasing and high SHBG serum content, a high percentage of free PSA (> 15%), initially increased or increasing serum PRL levels, reduced bone pain following dietary bio-modulation plus by-weekly/ monthly B-vitamin complex injections, supported by the ingestion of prion-free neurogenic lipids (canned by, Neurofood Ltd), normal laboratory blood values, decreased urinary distress and urge, rapid decrease in the size of soft tissue metastases and prostate gland by DRE, normal creatinine values and lack of proteinuria .

Attempts to passively improve the hormone levels linked to a more favourable prognosis.

Although an increase in serum FSH and PRL usually are linked to a better prognosis, injection of FSH, FSH-releasing factor, PRL or HCG to patients does not improve the disease entity, neither active specific immunotherapy. Administration of DHEA is definitely contraindicated since it seems to exacerbate CaP, as ACTH also seems to do. Probably also alanine is contraindicated. Oestrogen may depress FSH-levels. Extracts made from castrated male pig ZR cells, prepared by micromanipulation can cause a positive effect for a short time. Corresponding extracts made from human tissue (forensic samples) should be tested and analysed for their biological activity. Immunotherapy trials using autologous vaccines were ineffective.

Bad prognostic traits are; a FSH-level decreasing to <0.1 IU, high serum ferritin levels, increased DHEAS levels, coupled with normal to high serum DHEA, increasing PSA-levels of high velocity, low SHBG levels, increased alkaline-phosphatase levels (Table II f.), Gleason scores, 8-10 initially.

The LH-level alone does not seem to be ominous although it may stay for years at a level of, < 0.1 IU/L. Bad signs also include; urinary obstruction, progressive neurogenic symptoms, soft tissue and bone metastases, while continuous androgen deprivation, without dietary supportive measures, will usually lead to a hormone refractory state, followed by fatal recurrent disease.

Conclusions

A definite diagnosis of CaP is made usually based on screening tests. Patients in an early phase of the disease are usually devoid of symptoms. A *definitive treatment alternative* to merely "watchful waiting" or active invasive treatments is to recommended assessment for the use of dietary bio-modulation, founded on the results presented. One distinctive motivation is that healthy prostate cells seem to be required in this particular form of biological medical treatment to actually halt the disease. In the organ cycle controlling the prostate gland, adrenal *zona reticularis* (ZR) cells seem to have a central position. In addition, this regulatory cycle entails cooperation with three other organs; the pituitary; testes, as well as normal prostate gland tissue. Detection of an elevated PSA-level should always lead to further assays for; FSH, LH, PRL, DHEA, DHEAS, SHBG, and S-Ferritin to access prognosis and chances for dietary medical treatment modalities. The option is to test if specific biological dietary treatment applied in the early stage of the disease can stop the disease, before invasive treatment modalities have destroyed the normal prostate cells participating in the positive clinical reaction. The aim is to try to avoid our standard invasive treatment modalities, entailed with grave side effects, plus high expense stressing our national health care system. When hormone therapy actually is required, androgen ablation 16

based on intermittent *short time cycles* should be employed, supported by synergistic active dietary bio-modulation. This approach seems to be able to avoid, or at least postpone, the customary and feared development of a "hormone refractory state" linked to our standard hormone therapies. For older patient's dietary suggestions based on a special food-intake rich in Serine and lycopene, possibly also low physiological doses of Zn, etc. may help to cause "latent disease", as incidentally found in so many elderly men. Presently there is an urgent need to be allowed to study forensic adrenal specimens to delineate the proper human ZR factors, and not only those obtained from pigs. This precious material is now sadly discarded from the samples containing kidneys collected for transplantations. Studies utilizing this human material could assist in defining and producing these vital ZR components. The aim is to be able to biologically compensate this "age-linked" naturally dwindling production of specific essential factors which maintain our normal prostate cell genetranscription. Treatment of CaP by bio-modulation presents also a unique non-toxic physiological method to study the mitochondrial gene-regulatory system[2] using microarray-based expression profiling,[5] to elucidate how oncogene transcription is converted when patients suffering from prostate cancer are cured.

Table II f.

Patient succumbing to CaP -11/96, [T4NxM1 (multiple bone met) -11/94], orchiectomy '94, three years earlier.

Initially PSA 92.6 decreased after orchiectomy 1994 to 5.7; 5.3 (1995) with combined bio-modulation but he stopped the intake of dietary components - and became androgen independent (-96), PSA 119.0 and died 1997 displaying extreme laboratory values, as measured from a blood sample taken the day before exitus.

Patient No 10.

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA µg/L
<0.1	<0.1	1060	7.2	6.8	0.6			2145		364/V 17%

Patient No 11. Healthy male who voluntarily ingested strontium 7mg/ day plus the other trace-element salts as prescribed. He experienced no clinical symptoms during the test.

FSH IU/L	LH IU/L	PRL mU/L	DHEA nmol/L	DHEAS µmol/L	Testost nmol/L	Inhibin pg/ml	Activin pg/ml	S-Ferrit µg/L	SHBG nmol/L	PSA µg/L
15	9.2	201	3.4	3.1						0.5
					two weeks with Sr 7 mg/d					
13		389	9.8	2.3						0.4
					three weeks later without Sr					
11	4.7	152	3.6	2.7					41	0.4

Summary

Carcinoma of the prostate (CaP) is a potentially incurable age-linked disease of unknown aetiology, furthermore impaired by a world-wide increase in incidence. The aim was to try to elucidate the aetiology, prognostic traits, and possibility to medically restore the metabolic balance and mitochondrial control of the oncogene transcription in CaP, by non-invasive means. *Zona reticularis* cells (ZR) of the adrenal seem to have a central position in the feed-back reaction preserving normal prostate gland function, elicited by our standard hormone therapy. This physiological regulatory cycle embraces; normal ZR cells; prostate cells, hypothalamus-pituitary, and epididymis in testes. Descriptive epidemiology indicates that environmental and dietary habits have an effect on incidence and induce latent disease. Supplementation with amino acids; serine, arginine, glycine, glutamate, & lysine, combined with biologically active trace-element ions of Cr, Sn, Sr, W. Sometimes Zn, Ca and Mn plus folic acid and a prion-free diet of neurogenic lipids can arrest CaP for years, without the need for hormone therapy, prostatectomy or brachy-therapy. PSA screening is important since dietary bio-modulation can, in a dose-response-linked manner arrest progress of CaP for years, in the early stage of the disease. This finding rectifies PSA screening since we may have a positive therapeutic alternative to our feared invasive treatment modalities. When hormone treatment is required it should be performed according to a schedule based on short time androgen deprivation. Intermittent LHRH analogue therapy in short pulses, without striving for PSA nadir, can postpone and/or prevent exhaustion of the ZR feed-back cycle whereby CaP can be arrested, already for over a decade. A special form of CaP are patients diagnosed from soft tissue metastases, characterized by markedly increased serum activin- (2900 & 1850 pg/L) and PSA-levels (10070 & 246 µg/L). Clinically they respond to combined dietary and intermittent LHRH analogue treatment. Initially increased FSH and prolactin levels with low and decreasing DHEA and DHEAS are good prognostic signs. When patients succumb to CaP FSH decreases to < 0.1 IU/L, while PRL may rise to 1060 mU/L, and serum ferritin to >2100 µg/L. Transformed electron dense mitochondria seem to restore oncogene transcription back to healthy prostate cells. Treatment of CaP by bio-modulation presents a physiological method to study the gene-regulatory system using microarray-based expression profiling.

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"When your truth unfolds like a flower being born, you will feel it in your heart and know it's true."

Fran Hafey