Basis behind a Dietary Approach to combating Prostate Cancer. By John Mayes

Medical Scientists are doing lots of valuable and important work, in trying to find ways to combat Prostate Cancer. Most of the work is focussing at the level of the cell and using the various techniques and the knowledge base of Molecular Biology to try and find a 'Silver Bullet' that will kill Prostate Cancer cells. Work on how various ligands lock into receptors to trigger CaP growth, alternative pathways for CaP activation when various antagonists are used to 'block' receptors, dealing with kinases that trigger growth, the role of mutated P53 genes and other factors etc. are the foci of much research. One could fill many pages just listing the various approaches and stages of sometimes quite diverse research. None of this important work while interesting, was seen by me as vital to my interests as even if it did eventually come to fruition, it would be far too late to keep me on this mortal coil. In addition I am somewhat sceptical about the search for the 'Holy Grail', the 'Silver Bullet'. I know the various mechanisms of cancer progression are quite diverse and consequently it is unlikely in my view, that any one pharmaceutically produced compound, is likely to be able to effectively deal with the full range of prostate cancer. In addition, despite the confidence of various proponents, it became very clear to me that even the mechanism of cancer initiation, promotion and progression was open to debate and dispute. In the light of this I asked myself if there were any generalisations that could be made about cancer other than the usual ones such as rapid proliferation and the inability to undergo programmed cell death [apoptosis] , its invasive metastatic qualities and its capacity to stimulate angiogenesis etc. Anything that could be said about all cancer cells that would differentiate them from normal cells in a way that was amenable to non-medical intervention. One aspect that did seem promising was that there seemed to be some aspects of cancer cells' nutrition that were significantly different. If so was there anything that one could do about it to interrupt or disrupt the nutrition of cancer cells ? What follows is my attempt to do something about it.

What follows should be understood to be one particular approach of one individual and as I am not qualified medically, should not be seen in any way as a medical prescription. On the other hand, there is no reason why my particularly dietary approach should not be an important adjunct to orthodox medical therapy. In fact I hesitate to use the word diet as such a term tends to imply a 'quick fix'. I would prefer to use the terms life-long, balanced healthy eating. Everyone is different in their levels of self discipline, determination, mind-set, confidence and self image. All of these factors come into play in successfully implementing my particular approach. Only the basic rationale behind the approach is discussed here, not the day to day minutia of implementing it. I have also used various mind/body strategies in my 'fight back', which are beyond the scope of this immediate discussion. I do not see myself as being exceptional in any way. Any success that I have gained in my 'fight back', could I believe, be emulated by many others.

I was diagnosed with CaP more than four years ago. I under went a Radical Prostatectomy and the operation and pathology revealed a poor prognosis – Locally Advanced Prostate Cancer with a Gleason Grading of 8. I have not had any orthodox medical treatment since my operation and at present have no medically detectable PSA. It is 'still early days' but nevertheless an excellent start. This happy state of affairs is due to being given a marvellous start by my Surgeon but is also I believe, due to what I have done myself. What follows is in part the justification for what I have done regarding diet. I believe and am prepared to argue that it is based upon valid science. If any readers think otherwise, I would relish an opportunity for them to engage in public debate with me. – John Mayes.

We start the explanation by looking at one of the fats very common in our diet **Linoleic Acid**. This fatty acid is very common in vegetable fats and is also common in animal fats. It is a polyunsaturated fat, one of the 'family' of Omega 6 Essential fatty acids. The important word is essential. We would not be able to survive without it yet in excess it provides much of the basic 'raw material' for cancer cell stimulus and nutrition. Apparently the excess of **linoleic acid** in our diet was not always the case. In the past – say a century ago, the proportion of Omega 6 fatty acids to the Omega 3 family of fatty acids was in the ratio of perhaps 5 to 1 whereas today the ratio is anything from 20 through to 40 to 1.

With the above comment in mind, it is important to decrease the level of **Linoleic Acid** in one's diet. Today great stress is placed upon lessening saturated fats in the diet and quite rightly so, but polyunsaturated fats tend to be presented publicly as having an unqualified benefit, this as you will see is highly debatable.

The fat component of our modern diet tends to be saturated and polyunsaturated fat with a high proportion of Omega 6 fatty acids and a relatively modest amount of Omega 3 fatty acids as well as an even smaller amount of monounsaturated fats. Medical Oncologist Charles E. Myers M.D. in a Presentation to the Sloan Kettering Medical Centre Prostate Cancer Support Group on April 25, 2002 quoted a study published in the Journal of Urology from the University of Massachusetts in 2001. They took a group of men with 'failed' radical prostatectomies, that is they were exhibiting a rising PSA. "For these men, their PSA was doubling about every six and a half months. They were put on a low fat heart healthy diet, and then their PSA doubled every 18 months. By just taking on the diet and lifestyle change that would be good for heart disease, they effectively tripled their survival for prostate cancer." Just the simple expedient of dramatically cutting your consumption of fat – particularly the saturated and Omega 6 fatty acids is likely to make a positive difference. Better still, if one can increase the proportion of long chain Omega 3 fatty acids while decreasing the Omega 6 fatty acids. One could also hazard a guess that the sample of men quoted by Myers, stuck to the 'orthodox heart healthy diet' pushed by the American Medical Authorities, One that focuses mostly on dramatic reduction of fat consumption and does not consider strategies for controlling Insulin levels or a 'balanced' production of eicosanoids. With these aspects also dealt with, it may be that the reduction in PSA doubling rate could have been even more pronounced.

Linoleic Acid is changed by an enzyme **Delta-6-Desaturase** into **GLA [Gamma Linolenic Acid]** which is then changed by another enzyme **Elongase** into **DGLA [Dihomo Gamma Linolenic Acid]** This brings us to the next stage in the explanation.

Imagine **DGLA** molecules lurking in the cell membranes of a cancer cells, waiting for 'something to do'. The **DGLA** is very much subject to its environment, which includes other cells, a variety of chemicals in our blood and a number of enzymes **COX-1** and **Delta 5-Desaturase** that can be produced by the cancer cells as well as other normal cells. How DGLA is changed by either of two enzymes, **COX-1** or **Delta-5-Desaturase**, will either result in a cascade of reactions that are positive for you as the host of the cancer cells and mostly inhibitory for the cancer cells, or there can be a cascade of reactions that are very helpful to the cancer cells and mostly have a negative impact on you the host.

Lets just take our exercise in imagination a stage further and imagine that you as the host of those cancer cells, can shift the balance, that is you can simply influence whether you get the cascade of beneficial reactions and products with their consequences or the cascade of reactions, compounds and consequences, that impede your efforts to control and fight your cancer. Obviously you would want to get the cascade of beneficial reactions and consequences if possible. It is possible and it is not just a flight of imagination as you can get the desired outcome through diet. It is based upon long term research and backed by hundreds of references and scientific research papers. The basis for the dietary approach I am advocating was developed by a former researcher and lecturer at the Massachusetts Institute of Technology, Dr. Barry Sears. He holds a Doctor of Philosophy specialising in Biochemistry with his initial research and Thesis dealing with an aspect of Lipid chemistry. He is clearly a man 'with runs on the board' as he holds the patents on 12 Chemotherapeutic Drugs used around the world to combat cancer. He has now changed direction. He left his academic position and researched for 15 years before publishing his first book on a new approach to 'balanced eating'. Fifteen years scarcely indicates a frenzy to get into the Diet book publishing business to reap 'mega-bucks'. Actually his first book was aimed primarily at Cardiologists. Sears' basic approach is to control the level of **Insulin** in one's blood serum as a means of establishing a favourable balance of what are called **Eicosanoids** in the body. This is done by controlling the rate at which carbohydrates are digested, eating sufficient

protein to inhibit a particular enzyme that changes **DGLA** into a 'dangerous' **AA [Arachidonic Acid]** and ingesting sufficient **EPA[Eicosapentaentoic Acid]** either from oily fish or from Fish Oil capsules, to also aid in that inhibition.

I have added a couple of further layers of dietary technique, that attempt to inhibit by use of herbs and spices etc., many of the enzymes that produce the cascade of compounds that are used by cancer cells to grow and spread. These enzymes use the **AA (Arachidonic Acid)** as the raw material. The basic dietary approach focuses on controlling the amount of **AA** produced through the control of **Insulin**. This was not enough for me as I wanted to inhibit the production of the compounds produced from **AA**. I also found that I could arguably boost the anti-oxidant Glutathione resources of normal cells while depleting the Glutathione resources of cancer cells thus hopefully leaving them a bit more vulnerable to other dietary techniques to disrupt their growth and 'food supply'. The research on this latter aspect, can demonstrate what happens, but the exact molecular mechanism for depletion of Glutathione in cancer cells is still a matter of conjecture.

Just in case readers might think that what is being said might apply to combating other cancers but not necessarily Prostate Cancers because they are highly heterogenous and slow growing.
The following Research Abstracts just recently to hand :- 'Clinical, haemodynamic, anthropmetric, metabolic and insulin profile of men with high-stage and high-grade clinical prostate cancer.' Hammarsten J, Hogstedt B. from Dept Urology, Central hospital, Halmstad, Sweden. In – Blood Press. 2004;13(1): 47-55, - 299 men were studied
[See at www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve$db=pub] Also (Abstract 1217) 'Dietary Fat and Carbohydrates : Role in Prevention of Prostate Cancer Progression in TRAMP mice.' This study was undertaken at the University of Alabama by a group led by Ada Elgavish PhD. and released by the 'American Association for Cancer Research' on 27/10/03. - [See listed Abstract under 'Lifestyle changes clinically effective' at www.eurekalert.org/pub_releases/2003-10/aafc-lcc102503.php]Perusal of these cited abstracts just might persuade doubters that high blood sugar from high carbohydrate intake, and high Insulin levels can indeed have an intimate association with Prostate Cancer progression.

Let us first focus on what happens when **COX-1 [Cyclo-oxygenase-1]** or **Delta 5-Desaturase** enzymes interact with **DGLA** to form various compounds and let us deal with **Delta 5-Desaturase** enzyme first as it produces the **AA Arachidonic Acid** which the dietary approach aims to limit.

The first thing to understand is the role of **Insulin**. **Delta 5-Desaturase** is activated by **Insulin**. The higher the level of Insulin the more **DGLA** is preferentially converted into **AA** by **Delta 5-Desaturase** rather than being converted into more benign products by the other enzyme **COX-1**.

Insulin is produced by the Pancreas in response to blood sugar [glucose] levels in the blood. Insulin is essentially a 'storage hormone' in that it drives glucose from our blood into our cells which need them for fuel. If our blood sugar [glucose] concentration rises too quickly or too high, then a greater amount of **Insulin** is produced by our Pancreas. Stress hormones such as Cortisol can also stimulate Insulin release/increase. This piece of information of course, is one part of the jig-saw puzzle of how Stress often has an intimate relationship with the onset of Cancer as well as of course, depressing the activity of the Immune System.

If you eat food that is digested quickly [particularly carbohydrates that may be High Glycaemic Index food.], then there will be a very rapid and high glucose spike in your blood serum. Your Pancreas will release a lot of **Insulin** to drive the glucose into your cells. As the High GI food has produced a higher blood sugar concentration than your body can immediately use, excess glucose will be driven into your adipose cells and stored as fat. Of course the high **Insulin** level will then drop your blood sugar too low and you will become prematurely hungry and want to eat again. Have you ever had a big meal rich in carbohydrates and then felt hungry after a couple of hours ? A balanced appropriate diet even with a restricted calorie intake, should suffice for 5 to 6 hours before you experience hunger pangs. Actually sufficient protein arguably has now been shown to suppress appetite and of course the slow digestion of carbohydrate avoids the blood sugar and accompanying Insulin spike and 'drop and bounce' that prematurely triggers appetite. [i.e. The example midway through this paragraph.].

[To contrast an alternative approach sometimes confused with the approach advocated -the Atkins High Protein Diet. This diet certainly has allowed followers to lose weight however it has now

been demonstrated that this was because people on the diet actually ate less even though they were allowed to eat as much protein and fat as they liked. The very high Protein level effectively suppressed their appetite. This was beautifully illustrated by two successive weeks of the ABC's 'Catalyst' science programme, that investigated recent research in the US and UK into the Atkins Diet. On the other hand followers of the Atkins Diet missed out on the Fibre, Anti-oxidants, Phyto-nutrients, Enzymes, Vitamins etc. that are such an important part of the balanced Sears' approach as well as generating ketone bodies in the blood with long term bad consequences. Also of course, the Atkins diet really did nothing about controlling the bad eicosanoids emanating from the high fat consumption.]

Meanwhile your high **Insulin** level has really got the **Delta 5-Desaturase** very active producing a lot of **AA** leading to a cascade of products that help your cancer cells grow. In addition the high blood glucose level you have produced will give an added impetuous to your cancer cells as cancer cells tend to have a very inefficient glucose metabolism and need more glucose than normal cells to prosper. Glucose tends to be the preferred base for the anaerobic glycolytic energy pathway for cancer cells

Clearly one needs to avoid the high blood sugar spike and large Insulin release. One can do this by eating slowly digested Low Glycemic Index food, preferably of low density to avoid the over consumption of calories.

All this so far is about stopping **Delta 5-Desaturase** from being activated. It is possible to inhibit Delta 5-Desaturase by consuming **EPA [Eicosapentaenoic Acid]** , either through a high consumption of oily fish and/or taking Fish Oil capsules.

It is also possible to inhibit **Delta 5-Desaturase** by getting your Pancreas to produce another hormone that essentially acts in the opposite way to **Insulin** but also inhibits **Delta 5-Desaturase**. That hormone is **Glucagon** which together with **EPA** will inhibit **Delta 5-Desaturase**. You can trigger the release of **Glucagon** by eating sufficient low fat protein at every meal. Sufficient in the sense of the Protein to Carbohydrate ratio being very close to the ideal 3 to 4 ratio. Don't be alarmed ! it is close enough for you to eat Protein equivalent to no more than the size and thickness of the palm of your hand. Let that protein represent one third of your plate and pile the rest of your plate with low density and colourful vegetables and/or fruit. This is enough ! Forget about a High Glycemic Index dessert.

Quite apart from **Glucagon** inhibiting **Delta 5-Desaturase**, I have already indicated that it acts in the opposite way to Insulin. **Glucagon** is a mobilisation hormone so if you keep your calorie intake restricted and your insulin level low, the **Glucagon** will 'drag out' excess fat out of your adipose cells to be metabolised as fuel elsewhere in your body. **Glucagon**'s primary job is to release stored carbohydrates from the liver to maintain adequate levels of blood sugar for optimal mental performance.

The above outline is the essence of the strategy for decreasing the production of **AA,** not eliminating it completely as our cells do need it under some circumstances and conditions. What is important is to ensure that **AA** in excess of 'normal' cellular/bodily needs is controlled.
Now let us look at what the other enzyme **COX-1** can do in reacting with **DGLA**.

The COX-1 [Cycloxygenase-1] enzyme produces from **DGLA** a number of compounds called **Eicosanoids**. These **Eicosanoids** produced via **COX-1** from **DGLA** are relatively few in number and tend to have a 'good' consequence in one's body under most circumstances.

- For example **PGE-1 [Prostaglandin E-1]** tends to help suppress Insulin release; dilates blood vessels, inhibits blood platelet clumping; increases human growth hormone; increases Lymphokine release; decreases cholesterol production in the liver; decreases histamine; decreases pain; decreases inflammation; decreases sleep needs; decreases gastric HCL; acts as a bronchodilator; and helps protect the lining of the intestinal tract.

- Another usually beneficial eicosanoid is **PGA-1 [Prostaglandin A-1]** This is a powerful suppressor of viral replication, and inhibits nuclear transcription factor (NF Kappa B) necessary for synthesis of a wide variety of pro-inflammatory Cytokines. Clearly if one wants to enjoy good

health, the balance of eicosanoid production in one's body should not be skewed against these 'good' eicosanoids.

On the other hand, it is important to look at what one needs to minimise if one is to successfully fight one's cancer. I have previously indicated that the basic dietary approach focuses on controlling the amount of **AA Arachidonic Acid** produced. I think you need to be very clear that **AA**, one of the **Omega 6 Fatty Acids**, is not all bad. Our body needs it and can manufacture it but only in so far as it is needed for 'normal' bodily processes. Excess **AA** production can lead to problems particularly if you have cancer. The researcher previously alluded to, has ground up various cancers/tumours of varying virulence and found that the level of **AA** in the cancer cells has always been considerably in excess of what is usually the case in 'normal' cells. Moreover, the more aggressive the cancer the greater the concentration of **AA** in the cells. For example, pancreatic cancer cells which are very aggressive, had a level of **AA** 60 times as great a 'normal' cells. Unfortunately Prostate Cancer cells were not tested, however I strongly suspect that if it was possible to isolate sufficient prostate cancer cells moderately differentiated at Gleason 4, and compare them with undifferentiated CaP cells at Gleason 9, the Gleason 9 cells would have a much higher level of **AA** when compared with those of Gleason 4 which in turn would have a significantly higher level of **AA** when compared with 'normal' prostate cells.

[Such a test would be very difficult to do as it would be difficult to separate out the various stages of prostate cells. While a lot of tumours may have cells at different stages, CaP is perhaps the most diverse, it is the most heterogenous of all human cancers and a wide spectrum of cells co-exist together. Theoretically one could culture cells at the one stage in a laboratory but would they all remain at the same stage ?] Obviously as it seems that the concentration of **AA** in cancer cells is usually quite high when compared with normal cells, the high concentration of **AA** quite likely serves an important purpose in terms of the survival and progression of the cancer cells. In these circumstances any dietary strategy that can limit dietary intake of **AA** and also inhibit the production of **AA** within the body, is an important anti-cancer strategy.

What follows is a 'Rogues Gallery' of compounds that can be beneficial to Cancer Cells.

Enzyme COX-2 [cycloxygenase-2] (Same chemical composition as the 'good' **COX-1** but the molecule has a different shape.)
COX-2 *can be **inhibited** to varying degrees and in different ways by :-*
*Constituents of **Ginger**; Polyphenols from **Green Tea**; **Rosemary; Oregano; Basil**; & **Hops**.*

If there is too much available **AA** in the cellular membrane of the cancer or in the cytoplasm itself, the following **eicosanoids** can be produced by **COX-2**.

- **PGE-2 [Prostaglandin E-2]** This helps prostate cancer or any cancer to evade and kill immune system cells such as Natural Killer cells & Cytotoxic T cells. (Clearly one does not want one's Immune system cells being compromised. They often have a hard enough time identifying prostate cancer cells as not belonging and needing to be killed as it is.)
  PGE-2 promotes blood platelet aggregation; vasoconstricts; is pro-inflammatory; promotes cellular proliferation and suppresses the immune system.
  One will never be able to entirely shut down the activity of the COX-2 enzyme which is just as well – we need PGE-2 to help control water/salt balance in our kidneys and it is part of the body's natural response to infection and injury. The trick is to establish an appropriate 'balance through diet'.

- **TxA2 [Thromboxanes]** This eicosanoid causes sticky blood platelets and encourages Angiogenesis (Growth of blood vessels into the tumour so that it can grow .)

Enzyme 5-LO [5 Lipoxygenase] *Can be **inhibited** to some degree and in different ways by :- Ginger- which has 24 different anti-5-LO constituents; Constituents of **Green Tea**; Curcumin from **Turmeric** and **Cumin**; Capsaicin from **chillies** and constituents of **Garlic**.*

If there is too much available **AA** in the cellular membrane of the cancer or in the cytoplasm itself, the following **eicosanoids** can be produced by **5-LO**.

- **LTB4 [Leukotrienes]** These aid the formation of abnormal blood clots: are pro-inflammatory and are a primary mediator of pain. Also promote angiogenesis.

- **5-HETA , 5 HETA Lactone, 5 Hydroxyeicosatetranoids** These stimulate cancer growth and assure the survival of the cancer cells. It has been demonstrated in a laboratory that all lines of Prostate Cancer if deprived of 5-HETA will undergo apoptosis (programmed cells death) within two hours.
  [Ghosh & Myers , Proceedings National Academy of Science. USA, 1998]

Does one need to labour the point more ?

Enzyme 12-LO [12-Lipoxygenase] *Growing evidence that it can be **inhibited** to some degree by **Melatonin** which is a naturally occurring regulatory hormone produced by the Pineal Gland. Ageing tends to result in less efficient Melatonin production however there are some indications that the diet advocated can help restore Melatonin production.*
***Ginger, Scutellaria Baikalensis** and **Feverfew** do contain Melatonin. **Scutellaria** and **Feverfew** apparently contains more than **Ginger**.*

If there is too much available **AA** in the cellular membrane of the cancer or in the cytoplasm itself, the following **eicosanoid** can be produced by **12-LO**.

- **12-HETA [Hydroxylated Fatty Acids]** This encourages the growth of new blood vessels in cancer (angiogenesis) and enhances the ability of the cancer to invade new tissue.

Enzyme 15-LO [15-Lipoxygenase] *At this time there are no known dietary inhibitors.*

15-LO can react with **DGLA** to produce :-

- **15-HETriE** This is a powerful **inhibitor** of the **5-LO** enzyme that produces the dangerous **Leukotrienes & 5-HETA** family of **eicosanoids**. This is great news however it is a mixed blessing – **15-LO** can also interact with **AA** to produce some dangerous products. Obviously the dietary strategy to minimize **AA** production is important here.

If there is too much available **AA** in the cellular membrane of the cancer or in the cytoplasm itself, the following **eicosanoids** can be produced by **15-LO**.

- **15-HETA & Lipoxin A-4** Scientists at present do not yet understand what these do however if one looks at the track record of other products from **AA** it is not reassuring.

- **Lipoxin B-4** This inhibits the action of Natural Killer Cells of our Immune System. As NK cells are part of our front line defence against cancer, this is not good news.

The following is a discussion of the Herbs and Spices that have been shown to have an inhibitory effect on the various Enzymes that produce the cascade of 'harmful' Eicosanoids from Archidonic Acid. Some of the supporting Research is alluded to. It is not in any way exhaustive nor is it elaborated in any detail.
Charles E Myers M.D. who earlier has been mentioned lists a few naturally occurring chemicals able to suppress Prostate Cancer.
Lycopene , Vitamin E, Calcitriol, the active form of Vitamin D, Fish Oils – Omega 3 fatty acids, EPA & DHA, Green Tea Polyphenols, Reservatrol, a Polyphenol from Red Wine, Selenium, Quercetin & Silymarin.

Dietary resources needed to minimise the 'harmful products' of Arachidonic Acid

Green Tea :- [Forget about Tea bags, get the green tea leaf in its various forms. About 10 cups of Green Tea per day is considered to be a therapeutic dose however some commentators indicate that it could be as low as 4 cups per day. I err on the side of the larger figure drinking at least 2.6 litres per day. If you have bladder and/or continence problems, it is possible to get capsules of Green tea extract from Health Food shops. Do consider giving up Coffee drinking in favour of Green Tea. Coffee as a beverage if not drunk to excess will not harm you however on the other hand, it will do nothing for you in your fight against Prostate Cancer. Don't drink any more soft drinks – they send your blood glucose sky rocketing and stimulate a large release of insulin by your Pancreas.]

Good inhibitor of COX-2. NAPRALERT Database indicates 51 anti-inflamatory compounds and 15 compounds that also prevent ulcers. Recent study Mayo Clinic showed that CaP exposed to Green Tea began to show nuclei fragmentation and other signs of apoptosis. The poly-phenolic fraction EGCG [epigallocatechin gallate] seemed to be the most potent however Green Tea is very complex and researchers could not identify every aspect that seemed to be causing a reduction in CaP. A broad spectrum of the Green Tea seems to be effective. Japanese medical researchers in 1998 noted that the non-phenolic fraction has potent suppressive activities against tumour promotion. Two recent studies from Rutgers University noted that the small amounts of caffeine in GT somehow played a role in activating the herb's anti-tumour properties. (Jankun et al., Nature,1997) found that EGCG acts against urokinase, an enzyme often found in large amounts in human cancers. Urokinase breaks down the basement membrane of cell junctions, which may be a key step in the process of tumour cell metastasis, as well as tumour growth. EGCG also inhibits ornithine decarboxylase (ODC), resulting in a decrease in polyamine synthesis and cell growth (Carlin et al.,J.Urol.,1996) It is also an inhibitor of 5-alpha-reductase Type 1. Which can be important in the formation of 5-alpha-dihydrotestosterone which is up to 10 times as active as Testosterone. [Unfortunately CaP tends to produce much more of Type 2, 5-alpha-reductase which is inhibited by the drug Proscar. On the other hand Type 1 is prominent in Colon cancers and Skin Cancers.] (Liao et al., Cancer lett.,1995) reported that on CaP lines PC-3 & LnCaP, EGCG in in vivo experiments on mice markedly inhibited tumour growth. Apart from GT constituents being excellent Free-radical scavengers and potent anti-oxidants, the complex compounds of GT can work in synergy with other herbs and spices to enhance anti-tumour activity. For example the EGCG from GT with the curcumoids from Turmeric and Ginger have been shown in one study on oral cancer, to increase the anti-tumour effect of curcumin by a factor of 3 and that of EGCG by a factor of 8. Now clearly such an effect with oral cancer does not necessarily mean a similar effect on CaP, however as we already know that GT can have an impact on CaP, to me it is foolish to not include turmeric together with GT in one's strategy. Green tea has been shown to inhibit to some extent **COX-2, and 5-LO** (Ghosh and Myers, Proc.Natl. Acad. Sci. USA, 1998) showed that 5-LO enzyme produces 5-HETA from Arachidonic Acid and that CaP will if deprived of 5-HETA, undergo apoptosis [programmed cell death within two hours] and this apparently applies to all Prostate Cancer cell lines. Obviously if one can knock out some of the activity of the enzyme that produces 5-HETA, then one is well ahead in one's battle. If one uses multiple weapons then better still**. A good many constituents of ginger as well as the curcumin from ginger and turmeric also have an inhibitory effect on 5-LO as well as Capsaicin from chillies and some of the constituents of Garlic**. It may well be that some of these constituents inhibit **5-LO** in different ways. Better still ! Lastly you should realise that the cornerstone of my anti-cancer diet and approach is controlling Insulin levels. It is now known that Green Tea increases the effectiveness of insulin in driving blood glucose into one's cells by a factor of 16. Thus one's Pancreas does not need to produce as much Insulin to control blood sugar levels and this is exactly what we want as we do not want the Delta 5 Desaturase enzyme being activated by our insulin to produce more Arachidonic Acid than is absolutely necessary. In addition, Green Tea consumed with food, slows down the action of the enzyme Amylase in your saliva in converting starch in your food into glucose. This in effect artificially lowers the Glycemic Index of the starchy food that you may be eating.

The Polyphenols from Green Tea have been found in blood serum within 30 minutes of consumption. The useful compounds from Black Tea were not detectable in blood serum until 80 minutes after consumption. Clearly some Green Tea Phytonutrients are digested very quickly and easily.

Basil :- [Grow it yourself ! It really complements the use of tomatoes in meals.]

There are different varieties of Basil that will vary in terms of concentration of beneficial constituents. The most 'effective' variety is Ocimum Sanctum or Holy Basil. If this variety cannot be found, other less potent varieties could also be used.

Constituent – Ursolic Acid – **COX-2 inhibitor** also inhibits **5-LO**.

Oleanolic Acid also a **COX-2 inhibitor**.

The whole herb seems to be anti-mutagenic, radiation-protective and have an anti-tumour effect re. skin cancers. It increases key detox enzyme – glutathione S-transferase activity.

Turmeric :- [Used as ground turmeric. Any form of Curry powder has turmeric plus a host of other useful anti-cancer and anti-inflammatory herbs and spices. Use curry often !]

Has extraordinary anti-inflammatory properties, extraordinarily anti-oxidative, anti-tumour. (Researchers at New York Presbyterian Hospital & Weill Medical College of Cornell University 1999, Cancer Research.) Curcumin directly **inhibited COX-2** . Vanderbilt University 1999, reported that Curcumin **inhibits TxA2** . Oct.1999 Issue of Oncogene , Univ. Leicester, England reports that in human colon cancer cells curcumin **inhibited COX-2** induction by preventing { for those who understand a little of molecular biology } the "phosphorylation of IKappa B by inhibiting the activity of the IKKs"

More DNA protective than Vit E & betacarotene. Stimulates glutathione S-transferase, a detoxifying enzyme that protects against cancer. Curcumin modulates nitric oxide and is associated with its anti-cancer and anti-inflammatory activities.

Intensifies the anti-cancer activity of other phytonutrients.

Inhibits the growth of multiple breast cancer cell lines. Suppresses colon cancer and inhibits precancerous colon lesions.

In 1988 it was observed that a curcumin free extract of turmeric also exhibited anti-mutagenic activities. A research Abstract just to hand – full article to be published in 'Prostate'. 2004 Jun 15; 60(1):1-17. "Therapeutic potential of curcumin in prostate cancer-1V: Interference with the osteomimetic properties of hormone refractory C4-2B prostate cancer cells." By DoraiT, DutcherJP, Dempster DW, Wiernik PH. **Curcumin** was able to interfere with the osteoblastic component as well as the osteoclastic component of C4-2B prostate cancer cell line, by interfering with the growth factor receptor pathways and inhibiting the NF-kappaB activation process. Curcumin may be able to prevent the establishment of bony metastases.

[See at www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pub]

[Obviously if one has Locally Advanced Prostate Cancer or Advanced Prostate Cancer or Androgen Independent Prostate Cancer after 'Hormone Therapy', then **Curcumin** arguably should be an important part of dietary adjunct strategies to complement any Orthodox Medical Strategies being undertaken. It should not be used therapeutically if you have excessive stomach acid, gall stones or bile duct obstruction. – I consume at least 4 grams of ground turmeric daily and at least 6 grams of ground ginger (which also contains Curcumin among other things) daily. Remember it is not a 'silver bullet' but only part of a comprehensive integrated anti-cancer strategy.]

Resveratrol :- Red Wine, Richest source – Hu Zhang or Japanese Knotweed.

Resveratrol – research at Memorial Sloan Kettering Cancer Centre in 1998 showed Resveratrol to be a powerful **COX-2 inhibitor** and an inhibitor of cancer promotion. MSK and Cornell Medical Centre later noted that in human breast cancer cells and malignant oral tissue, resveratrol worked in a two fold way – it **inhibited the cellular expression of the COX-2 gene** and also **inhibited the actual enzyme activity of COX-2**. As breast cancer cells and usually prostate cancer cells are hormone dependent, it is possible that resveratrol could have a similar impact on CaP. A report from the New York Medical College indicated that resveratrol triggered apoptosis [programmed cell death] in Prostate Cancer cells. Unfortunately my 'source' did not indicate whether the study was in vitro or in vivo. University of Illinois researchers reported in 'Science' that resveratrol stops cancer Initiation and Promotion and in Leukaemia it promotes differentiation. National Univ. of Taiwan researchers found that resveratrol stops production of NFkB which inflames tissues surrounding the tumour.

Problem for men getting stuck into the red wine is that the alcohol provides a lot of calories – not what you need if you are trying to restrict calories to stimulate one's immune system. The alcohol also creates a lot of free-radicals that can nullify other cancer fighting anti-oxidants that one might be taking. On the other hand as one ages, the portals in the blood vessels through the liver tend to close up making it more difficult for large fat molecules to get through for processing in the liver. Apparently a

small amount of alcohol regularly consumed can open up these portals . The strategy should be no more than two standard glasses of red wine per day and not just at one time. Spread the wine consumption. It is possible to obtain powdered red wine marc that has the resveratrol and the other polyphenols but no alcohol. ['The Red Wine Affair' produced by Hilde Hemmes – Herbal Supplies Limited, Ridgehaven, can be obtained through Health Shops – powder equivalent to 74 glasses of wine for about $25.] On the other hand, men who have forms of heart disease that include significant numbers of weakened heart cells, should think twice about consuming significant amounts of resveratrol. University of Minnesota researchers noted that resveratrol tends to activate the p53 gene which acts as a sort of 'molecular patrolman' telling cells to self destruct when things go wrong. This is great for CaP if you have a cancer where p53 is mutated so that it does not operate properly. Unfortunately this also just might 'gee up' the p53 genes in the weakened cells in your heart condition leading to the destruction of the cells and a massive heart attack.

Rosemary :- [Grow it yourself and use frequently in cooking. I have used it raw cut up finely as a potent flavouring in a savoury sandwich or dish.]

In 1992 researchers at the Faculte de Medicine Universite de Limoges, France found that the Ursolic Acid – one of the constituents of Rosemary and Basil { see earlier note }, **inhibited Arachidonic Acid metabolism** in human platelet and leukaemia cells. In 1994 researchers at Rutgers University found that **Rosemary extracts inhibit processes that fuel the growth of tumours**. The Rosemary extracts had a 99% success rate. Individually Ursolic Acid and another compound Carnosol also from Rosemary had an inhibitory effect on tumours but extracts from the 'whole plant' displayed greater inhibition.
Apigenin [also found in Green tea] was found by researchers in 1999 at the National University of Taiwan, to be a markedly **active inhibitor of COX-2**. Also in 1995 it was noted in Japan that rosmanol and epirosmanol from Rosemary protected against oxidative stress.

Ginger :- [Ginger can be consumed in multiple forms, as a ground powder, as glace ginger or as fresh ginger tuber which can be grated up to eat with food and in cooking or brewed up with a pot of green tea. If I encounter an inflammation problem, I grate up about 30 grams per pot of tea.]

Has multiple constituents that inhibit COX-2 and 5-LO, it has compounds that dilate arteries and **inhibit the formation of Thromboxanes (TxA2)**. In 1992 Japanese researchers noted that 8 constituents of the gingerol family were **active against 5-LO**. Also it was noted in 1986 that capsaicin and gingerdione were **potent inhibitors of 5-HETA** biosynthesis. Also curcumin was noted as a potent **inhibitor of 5-HETA production**. The 1999 edition of the USDA Phytochemical database notes that **Ginger has more 5-LO inhibitors (24) than any other botanical source**. There is also growing evidence that Melatonin from Ginger and from other sources such as Feverfew and a variety of Skullcap –Scutellaria Baikalensis, can inhibit the 12-LO enzyme (see chart).

Oregano :- [Why not grow it yourself ?]

A rich source of Apigenin (GT & Rosemary), Kaempherol (Ginger), Ursolic Acid (Rosemary and Basil), Oleanolic Acid (Rosemary) , Rosmarinic Acid – inhibits platelet aggregation. All the above have potent anti-cancer effects. The USDA Phytochemical Database indicates that Oregano has 31 different anti-inflammatory compounds.

Feverfew :- [Can be purchased at 'Perfect Cup' on Grange rd. Flinders Park or at the Central market. Feverfew can be consumed as an infusion/tea.]

This is a rich source of Melatonin as well as Apigenin which also has an inhibitory effect upon tumours. Of course Ginger and Baikal Skullcap also contain Melatonin. Melatonin is a hormone that is naturally produced by the Pineal Gland in the brain, as well as having a powerful anti-oxidant effect it also plays a vital regulatory function in the body affecting other hormones and the immune system. Unfortunately with ageing, the Pineal Gland tends to become less efficient and in some cases even atrophies. This has a disastrous impact on overall health. The Pineal Gland produces melatonin in response to darkness on a relatively stable daily pattern. If you have experienced 'Jetlag' after International Air Travel, this is because that diurnal pattern of melatonin production has been disrupted. (Note the role of Melatonin in **inhibition of 12-LO** !)

Feverfew also contains parthenolide which apparently contains a variant of methylene-gamma-lactone. A compound that interacts with human immune system cells called macrophages in a way to suppress a critical protein process, this in turn inhibited COX-2 expression. [I'm not so sure about this piece of information as it seems to me that 'suppressing a critical protein process' in macrophages might not be necessarily a good thing, The information source was not sufficiently explicit !]

Garlic :- [Use garlic in its various forms as often as possible.]

A study investigated aged garlic extract (AGE)- Kyolic Garlic to see if it could inhibit proliferation of cancer cells. The proliferation and viability of erythroleukemia and hormone responsive breast and prostate cancer cell lines were evaluated. The erythroleukemia cells were not significantly affected by the garlic extract, but the **breast and prostate cancer cell lines clearly were susceptible to the growth inhibitory influence of aged garlic extract**. The anti-proliferative effect was limited to actively growing cells. (LEF.P.131) Page 158 in 'The Super Anti-Oxidants' by Urologist James F. Balch, quotes research by a Dr. Tariq Abdullah showed that when the Natural Killer cells of patients who ate raw garlic were harvested and tested against tumour cells in laboratory cultures, the NK cells killed 139% more tumour cells than what was considered 'normal'. When the NK cells of those who used Kyolic Garlic capsules were tested, the kill rate increased to 159%.

Hops :- [Obviously some of us like it in beer but this is not the anti-cancer way.]

Research at Dept. of Biochemistry, School of Medicine, The University of Tokushima Jan 14, 2000, found that humulone from hops **significantly inhibited COX-2**, it also inhibited the body's re-sorption of bone. Take note those of you on hormone therapy and who are concerned about osteoporosis. The humulone "blocked cyclooxygenase-2 expression mediated by NF Kappa B & NF-IL6 …..The catalytic activity of Cox-2 was inhibited …[moreover] These results showed that humulone suppressed cyclo-oxygenase induction at the step of transcription." That is before it was produced . This makes it easier than trying to inhibit it once it is in the cellular membrane.

In other words it **disrupted the genetic expression of COX-2** which is great as it means that one can stop COX-2 being produced and avoids the problem of inhibiting its action.
I have obtained Hops from the Perfect Cup. [previously mentioned.] It makes a rather bitter infusion or tea.

Chillies :- [Used fresh in cooking or as a Chilli Sauce. Sweet Chilli Sauce has chilli and garlic however it also has a lot of sugar – not such a good idea ! Something like Tabasco Sauce is a better approach.]

The Capsaicin in Chillies is a **potent COX-2 inhibitor** and the 'hotter' the chilli the more Capsaicin. Ginger also contains capsaicin but in much smaller concentrations.

Cautionary Comment :-
Feverfew and Hops can be consumed as an infusion or tea. In each case I suggest that no more than one cup of tea per day be consumed as concentrations of active ingredients are not known. As far as Hops is concerned, humulone significantly inhibited COX-2 however the concentrations required to have a significant impact on bone density is not indicated. Daily sensible mild load-bearing exercise, exercising as many muscle groups as possible and involving as much of your skeletal frame as possible as well as following the diet indicated, is much more likely to have an effect of lessening or halting the onset of osteoporosis. There is a lot of evidence that just the exercise regime itself as indicated can make a difference. As far as the other 'dietary resources' listed, use as many and as a often as you conveniently can.

Earlier I quoted a listing from Charles E Myers M.D. of naturally occurring chemicals that are able to suppress Prostate Cancer. What follows is a further discussion of the chemicals in that listing.

Lycopene
Lycopene acts as a powerful antioxidant. Found in its most accessible form in tomato products, particularly tomato paste where the cellular walls within the tomato have been pulverised. It is most easily absorbed in one's diet if the tomato paste is consumed with a little oil such as Olive oil or Macadamia oil which is very high in mono-unsaturated fats. The lycopene is soluble in fat, not water.

A high level of lycopene in the diet has been shown to be associated with low levels of CaP and newly diagosed CaP patients have been shown to often have below normal levels of lycopene in their blood serum and prostatic tissue. There is also some evidence that lycopene can have a beneficial impact upon active CaP. Life Extension Foundation sources recommend 30 mg of lycopene per day for active CaP. Recent research suggests that the whole tomato rather than just extracted lycopene, is even more effective. Lycopene unlike the other carotenoids, is not eventually changed into Vitamin A in the body and as such is not used up at the same high rate as other carotenoids. Because of this, a heaped dessert spoonful of tomato paste taken with a little appropriate oil, every second or third day, should keep your blood serum concentration of lycopene sufficiently high. Of course by all means add tomatoes and tomato products to your normal diet.

Vitamin E
Studies seem to indicate that Vitamin E can suppress the growth and spread of Prostate Cancer. Natural Vitamin E - d-alpha-tocopherol is said to be the type to take however Moyad et al. In 1999 reported evidence indicating that the gamma-tocopherol is more effective in fighting Prostate Cancer. You can get this from Sesame Seed for example ground up Sesame Seed – Tahini. One problem with the Gamma-Tocopherol is determining exactly what one's intake is. Myer in his book 'Eating Your Way to better Health', mentioned at least one study that suggests that intakes more than 400 IU of Vitamin E per day might suppress immune function. And he points out that doses above 1000 IU have been associated with increased risk of bleeding. [A particular problem if you are on blood thinners.] At present I take more than 1000 IU being fully aware of the risks. I would take less if I was not taking what would be considered a mega-dose of Vitamin C per day. Vit C, Vit E and Selenium all tend to act synergistically in helping to metabolically recycle each other.

Calcitriol active form of **Vit. D**
One's body can manufacture the necessary Vitamin D. It is triggered by sunlight. If you ensure that you get about 20 minutes of sunlight exposure per day – say on your face and arms and ideally during a walk (as vigorous as you can manage) which also gives your cardio-vascular system a work out and stimulates your immune system, then you should be well on your way to getting enough Vitamin D. I take supplemental Vit D however this needs to be in conjunction with a good calcium intake as well as a good intake of magnesium to be effective. Unfortunately as one gets older our bodies do not make the active form of Vitamin D as efficiently as in one's youth. Interestingly, as one progresses towards the higher latitudes in the USA /Canada [where statistics are available], the incidence of Prostate Cancer increases and it is hypothesised that this might be because of less sun exposure in the winters.

Fish Oils Long chain Omega 3 fatty acids **EPA & DHA**
EPA [Eicosapentaenoic Acid] has already been discussed as being a potent inhibitor of the Delta-5-Desaturase enzyme. DHA [Docosahexaenoic Acid] is also an important component of Oily Fish and Fish Oil Capsules made from deep sea Salmon. DHA and EPA are long chain Omega 3 polyunsaturated fatty acids. Unfortunately many people who purport to be experts, knowing that Omega 3 fatty acids such as EPA and DHA are very good for you, tend to think that all Omega 3 fatty acids are good for you. It is not so. A distinction has to be made between the long chain Omega 3 fatty acids such as EPA & DHA and short chain Omega 3 fatty acids such as Alpha-Linolenic Acid. Flax/Linseed has a very high proportion of this ALA in its fat composition 54 %, Walnuts have 10 % of their oil as ALA. Unfortunately ALA to be changed into the desirable and useable long chain Omega 3 s such as EPA and DHA, has to go through a slow and relatively difficult metabolic process. For a start if there is a lot of Omega 6 Linoleic Acid in your diet [remember the modern diet has a ratio of Omega 6 to Omega 3 of anything from 20 to 1 to 40 to 1], Linoleic Acid which is transformed to Arachidonic Acid [for cancer patients, the 'bad' Omega 6] competes for the same enzymes that are needed to transform ALA into EPA and DHA. To make matters worse, ALA tends to suppress the activity of the enzyme Delta-6-Desaturase which is needed for the first step in the conversion process and when it comes to the last step in the process to create EPA, the Delta-5-Destaurase enzyme is needed and as we already know that EPA inhibits the action of Delta-5-Desaturase [remember we want to use this strategy to inhibit it to stop the conversion of GLA into Arachidonic Acid], then any EPA already produced or ingested from food sources is likely to severely slow or stop the process. As an added warning, Charles E. Myers M.D. comments that an association has been observed between consumption of flax seed oil and "dramatically increased risk of metastatic prostate cancer." P.6

'Eating Your way to better Health'. He does not indicate why. My comments regarding the impaired metabolic process for ALA might be the start of an explanation.
Readers may wonder what the significance of DHA is in Fish Oil etc. DHA is important for nerve synapses to transfer information throughout the brain, and for the brain's mitochondria to produce optimal amounts of energy. It is the critical long-chain omega 3 fatty acid required for the building of neural tissue. Furthermore, it appears that only DHA can stimulate the growth of nerve cells. It has been observed that depressed people tend to have low levels of DHA while dramatically increasing intake of DHA can relieve depression .
EPA controls our health by modulating the balance of 'good' and 'bad' eicosanoids. DHA is the key fat for the brain.

Green Tea Polyphenols.
See previous comments above. Above comments focus primarily on effect on cancer however very extensive citing of research papers could be made in terms of Green Teas' impact on Cardio-Vascular disease and other chronic conditions.

Reservatrol
See previous comments above.

Selenium
See short paper by Graham Lyons on this Site or access the paper on www.psaadelaide.org
Brazil Nuts will give you between 100 to 120 micrograms of Seleniumper nut. Problem is that for every 28.4 grams of nuts there is 5 grams of saturated fat, and 7 grams of the undesirable Linoleic Acid. There is also 7 grams of 'good' monounsaturated fat. Eating Brazil nuts to get your Selenium is OK if you are prepared to be extremely rigorous in dramatically reducing the intake of the Omega 6 Linoleic Acid elsewhere in your diet.

Quercetin
Helps prevent multiplication of cells that secrete Histamine – a chemical that causes inflammation and swelling. Helps stop transport of Arachidonic Acid into cancer cells. Stops release of inflammatory chemicals that start growth of blood vessels etc. into tumour. Reduces the activity of mast cells which release inflammatory hormones. Binds to estrogen receptor sites more comp letely than anti-cancer drug Tamoxifen (Nolvadex), therefore deactivates enzymes that trigger the multiplication of bladder, breast, colorectal and ovarian cancer cells. Stops multiplication of neutrophils – immune cells involved in the production of inflammatory causing hormones and prevents the release of inflammation causing Leukotrienes. Quercetin like the polyphenols from Green Tea have an anti-cancer effect because among other things, it stops the mitotic spindle in cancer cells functioning properly which is critical for cell division. In addition Quercetin reduces the amount of bcl2 in cancer cells which tend to up regulate the production of bcl2 as a means of surviving radiation therapy, hormonal therapy and chemotherapy. All vegetables of the allium family [onions, garlic etc] contain quercetin. It is also is found in apples and Green Tea.

Silymarin
Centre of Cancer Causation & Prevention in Denver, Colorado, reported that Silibinin, a component of Silymarin, causes differentiation of prostate cancer cells, influencing them to return to a 'normal' life cycle. This effect is independent of the action of genes that 'patrol' for and destroy cancer cells and may slow the growth of hormone independent strains. Silymarin stimulates the Liver so that it can take excessive amounts of insulin out of the bloodstream quickly. [Just what we want !] Silymarin has been shown to have an anti- PC effect by virtue of it increasing the levels of p27. [Zi et al ., Cancer Res., 1998; & Gali et al., Proc. Annu. Meet. Am. Assoc. Cancer Research, 1994.] Milkthistle which is the only botanical source of Silymarin also contains Quercetin. [see above]

Obviously the above explanations while giving the justification for a particular approach to balanced healthy eating, does not give the detailed specifics of the dietary strategies needed, in order to implement the approach. It requires a considerable and life-long commitment and there

are no short-cuts. In some senses it requires one to become a different person to establish a life-style and culinary regime that is quite different from the habits of a life time. Habits that have helped to produce the physiological and metabolic environment that established the conditions for your Prostate Cancer to be initiated, promoted and to progress. .

If you are on various medications for other medical conditions as well as Prostate Cancer, it is important to be aware that the herbs and spices mentioned may interfere with the activity of some of those medications. First port of call would be your Medical Advisers. Unfortunately some of them may not have the knowledge to advise you or will err on the side of caution if they do not know. You will need to do your own research and start taking responsibility for your actions. For example Green tea contains some Vitamin K and if drunk in large quantities, may interfere with blood thinners such as Warfarin. Similarly the activity of Green tea in increasing the efficacy of Insulin in the body may require a re-calculation of the quantities of Insulin or medication in the case of Type 1 and Type 2 Diabetes. Fish Oil, Turmeric, Vitamin E, Garlic etc. thins the blood to varying degrees and may increase a tendency for bleeding. You must be aware that all food to varying degrees and certainly herbs and spices, can act as powerful drugs in one's body.