Integrative Solutions for Prostate Cancer

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From information obtained
in study under
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Incidence and Deaths

- In 2003, 221,000 cases were diagnosed with 28,900 deaths
- 1 patient died for every 8 cases diagnosed that year

Prostate cancer

- Of men who undergo definitive therapy with surgery or radiation, 1/3 will have rising PSAs within 10 years
  - 1/3 of these will develop clinical disease progression within 5 years
  - Salvage radiation in these situations is rarely beneficial

Androgen depression therapy

- Androgen depression therapy is effective for 1-8 years but leads to **many side effects**
- **Intermittent androgen depression** lessens these symptoms and appears to be as effective
  - Strum, SB, Scholz, MC, McDermed, JE: Intermittent androgen deprivation in prostate cancer patients: factors predictive of prolonged time off therapy. Oncologist 2000;5:25-52

Dietary risk factors

- **Total fat** intake, **animal fat** intake, and **red meat** consumption
- Cooking **red meat** at **high temperatures** or on grills
- Excess commercial **dairy** products
- Consuming >2000mg of **calcium** increased metastatic prostate cancer risk by 4.6-fold
- Every 500mg of **calcium** as a supplement increased risk 16%; calcium lowered vitamin D

Other risk factors

- Overweight and obesity
- Family history
- Lack of sunlight
- Smoking
- Pesticide exposure
- Smaller prostates are associated with higher grade, more advanced cancer
- Rotating work shifts increased risk 4-fold

Protective dietary factors

- **Vegetables, fruits, & antioxidant nutrients**
- **Tomatoes** and **cruciferous vegetables**
- Higher blood levels of **selenium**, **vitamin E**, and **lycopene**
- **Omega-3 fatty acids** from oily fish can stop prostate cancer spread

Protective dietary factors

- **Pomegranate juice 8** ounces daily slowed the increase in PSA to 1/4th its usual rate in prostate cancer
    - Clin Cancer Res. 2006Jul1;12(13):4018-4026
- **Flax seeds** are anti-estrogenic and reduce prostate cancer cell proliferation
- **Soy** is associated with less prostate cancer ;
  - fermented soy may be best e.g. tempeh, tamari, miso
  - May be wise to avoid processed or GMO soy

Nutrition

- Consume **omega-3 fish** e.g. wild salmon, sardines
  - Avoid tuna due to mercury content
  - Avoid farm-raised fish except tilapia due to PCB contamination which has xenoestrogen effects
- Consume a lot of **eggs**, preferably omega-3
- Eat organic **fruits** and **vegetables**
- **Eliminate** processed and fast foods
- Drink water, **green tea**, and **pomegranate juice**

Spirituality

- Typically, cancer patients feel **panic** when they are diagnosed
- This can lead to poor **decision-making**
- Panic increases epinephrine and cortisol
- **Epinephrine** increases blood glucose, which facilitates cancer growth
- **Cortisol** suppresses the immune system, increases blood glucose, and increases clotting, all of which promote cancer

Why do systemic therapy before surgery?

- Surgery leaves tumor cells in the blood
- If the tumor can be shrunk or disappears entirely, long-term prognosis is good
- If the tumor has shrunk, surgery is easier, less invasive
- Because cancer is a systemic disease, metastasis is reduced through systemic approaches

Surgery vs. radiation

- **In localized prostate cancer, surgery was superior to radiation** in prolonging overall and disease-specific survival
    - Wong YN, Wan F, Mitra N, et al. Treatment of localized prostate cancer: a survival analysis using SEET-Medicare ata. Program and abstracts of the American Urological Association 2006 Annual Meeting; May 20-25, 2006

Surgery vs. watchful waiting

- A **radical prostatectomy** for **early prostate cancer** offered **no overall survival benefit** over watchful waiting; we know surgery does not improve quality of life
    - Two studies in NewEnglandJMed Sept12, 2002

Casodex following standard care

- **Casodex** 50mg daily, an anti-androgen therapy in patients with early, non-metastatic prostate cancer while reducing disease progression **did not reduce overall survival**

Androgen suppression therapy

- Early prostate cancer is primarily regulated by androgens
- While only 13% of men in 2003 died from prostate cancer relative to those diagnosed, men are **fearful of prostate cancer**
- **Cardiovascular disease should be of equal concern**

Androgen suppression therapy

- Hormone suppressive therapy increases risk of **depression, osteoporosis, diabetes, heart disease, cachexia, weakness**, and **impotence**
- Therefore, hormonal treatment **may worsen quality of life and shorten lifespan**

Estrogen in prostate cancer

- High doses of **estrogen** in combination with high doses of **androgens** induce malignancy
- **Finasteride** reduced prostate cancer incidence but increased **aggressive** prostate cancer, perhaps because **blocking 5 alpha reductase shifts testosterone metabolism to the aromatase pathway to estrogen**

Blood tests

Obtain monthly in advanced disease

- **White count**
- **Hemoglobin**
- **Albumin** – consider keeping >4.4
- **Platelets** – consider keeping <250,000
- **Dihydrotestosterone**
- **Estradiol**
- **Estrone**

Blood tests

Obtain monthly in advanced disease

- **Vitamin D 25OH**
- **Zinc**
- **Copper**
- **Ceruloplasmin**
- **Fibrinogen**
- **D-dimer**
- **Free T3** – target 300-400
- **Free T4, TSH**

Blood tests

Obtain monthly in advanced disease

- **Glucose**
- **PSA**
- **Prostatic acid phosphatase**
- **ALT**
- **Hemoglobin A1c** – target <5.8
  - Test it initially; can test less regularly if normal

Hypercoagulation in cancer

- 7-fold increased risk of **venous thrombosis**
- **Platelets** can release angiogenic factors such as VEGF
- **Inflammation** has been implicated in **coagulation** and **angiogenesis**

  - Cestari DM, Weine DM, Panageas KS, et al: Neurology 2004Jun*;62(11):2025-30

Hypercoagulation in cancer

- **Emboli** are the most common cause of **stroke**
- In addition to platelets, **D-dimer** and **fibrinogen** also assess clotting risk
- Assisting in **maintaining normal hemodynamic balance**:
  - **Botanicals**: curcuminoids, resveratrol, gingerols
  - **Omega-3** fatty acids
  - **Vitamin D**
  - **Enzymes**: lumbrokinase, nattokinase, bromelain

Prostatic acid phosphatase

- While less sensitive than PSA in initial detection, it is more reliable
- PSA can be altered from causes other than cancer, and has a different scale in each individual

EGFR (Her1) & **Her2 neu**

- **Her2 neu** or **Her1 (EGFR)** causes prostate cancer to progress to an **androgen independent** tumor-type in about 1/4th of prostate cancers

Chemotherapy plus nutrients

- A search of MEDLINE and CANCERLIT from 1965 found 50 peer-reviewed studies involving 8,521 patients; 5,081 received nutrients. They **consistently showed that nutrients did not interfere with therapeutic modalities for cancer**.
- In 47 of these studies, nutrients were found to **protect normal tissues** and **reduce the often serious side effects of chemotherapy and radiation**.
- In fifteen of the studies, 3738 patients had improved survival – a very unusual outcome for cancer studies.
  - *Altern Ther Health Med. 2007;13(2):40-46.*

Adaptogens

- **Rhodiola rosea**, which grows at 11,000 feet in Siberia, was discovered by the Soviets
- Rhodiola made ordinary people **more fit** and **able to adapt** to all forms of stress
- The Soviets utilized Rhodiola in their **soldiers, Olympic athletes**, and **cosmonauts**
- Other herbs have now been recognized to have similar abilities & are called '**adaptogens**'

Adaptogens in cancer

- Restore **immune surveillance**
- Build **bone marrow, blood counts**, reduce **infection**
- **Protect** and **detoxify** organs and cells
- **Inhibit multi-drug resistance**
- **Improve healing** after **surgery, chemotherapy**, and **radiation**

Adaptogens in cancer

- **Inhibit cancer metastasis** and **recurrence**
- Suppress **angiogenesis**
- **Reduce cortisol** levels
- **Reduce** cancer-related **inflammation** e.g NF-kB, COX-2

  – Kupin, VJ: Eleutherococcus and other Biological Active Modifiers in Oncology, Medexport, Moscow, USSR, 1984

Adaptogens in cancer

- **Panax ginseng** –
  - increases **p21** and **p27**,
  - modulates **MAP kinases**,
  - enhances **Taxol**,
  - **heals wounds** despite **suppressing cancer blood vessel growth**

Adaptogens in cancer

- **Ashwagandha**
  - potent **angiogenesis** inhibitor
  - enhances **chemotherapy** & **radiation** therapy
  - inhibits survival of both **androgen-responsive** and **androgen-refractory** prostate cancer cells

Adaptogens in cancer

- **Chinese skullcap**
  - inhibits **NK-kB, COX-2, LOX-5**
  - reduces **PG2**
  - Blocks **androgen receptors**
  - inhibits **beta-glucoronidase**
  - induces **apoptosis**
  - inhibits **angiogenesis** (down-regulates bFGF & MMP-2)
  - 6 studies support specific **prostate cancer** benefit

Curcumin (80% of Turmeric)

- Down-regulates **NF-kB, AP-1, STAT-3, & Egr-1**
- Down-regulates **COX-2, LOX-5, NOS**
- Reduces **MMP-2/9, uPA**
- Reduces cancer **cytokines TNF, chemokine**s
- Reduces **CAMs** and **cyclin D1**

Curcumin

- Down-regulates **growth factor receptors** (**EGFR, HER2, bFGF, TGF-B1, VEGF**)
- Inhibits several cancer-inducing pathways (**kinases**)
- Potent **redox cycling agent** – modulator of inflammation
- Can **suppress tumor initiation, promotion**, and **metastasis**
- Down-regulates **androgen receptors**

Green tea extract (GTE)

- In **men at high risk** for prostate cancer after taking GTE for 1 year, 1 of 32 developed cancer vs. 9 of 30 controls
  - GTE mediates clusterins which are important apoptotic genes in prostate cancer
- GTE is **synergistic** with **pomegranate** concentrate
- For 5 days prior to **prostate cancer surgery**, green or black tea significantly **suppressed prostate cancer** cell proliferation

Green Tea in cancer

- **Apoptosis** in a wide range of cancer cell lines
- Inhibits: **NFkB, PG2, COX-2, angiogenesis, protein kinase C, VEGF, VE-cadherin tyrosine phosphorylation, Akt activation, MMP-2** and **9,** and **topoisomerase 1**
- Mediates **MAPKs**

Green Tea in cancer

- Induces **p21** and **p27**
- Protects and improves the **gap junction**
- Modulates **IGF-1**
- Inhibits **aromatase**
- Down-regulates **tNO**

Green Tea in Prostate cancer

- Inhibited development and **metastasis** in models
- Decrease in prostate cancer **growth**
- Synergistic with soy in an **androgen-sensitive** model
- Two studies: 1 year of extract use reduced prostate cancer incidence to **1/9th of non-users in high-risk patients**

Green Tea in Prostate cancer

- Derivative **EGCG** with copper was cytotoxic in a cell culture
- Synergistic with **lycopene** in **dramatically reducing prostate cancer incidence**
- Synergistic with a **COX-2** inhibitor
- **Powdered extract is superior** to the drink
- Use **3-4 grams** of a **95% polyphenol/60% catechin extract**

Milk thistle constituents

- Milk thistle is 80% **silymarin**, which has 4 constituents including **silibin** and **isosilybin**
- **Silibin** inhibits **prostate cancer** through:
  - NFkB, VEGF, EGFR, IGF-1R signaling, cell-cycle regulators including cycoin-dependent kinases, Kip1/p27, Cip/p21, and anti-PCA, and through DHT telmerase inhibition
  - Antiproliferative, pro-apoptotic, anti-angiogeneic
  - Active in hormone-dependent & independent prostate cancer
- **Isosilybin** also suppressed prostate cancer
- **Silymarin** with **lycopene** and **soy** decreased PSA doubling time 2.6 times

Reishi

- Appropriately prepared, it has **radiation** and **chemotherapy-protective** attributes due to stimulating effect on **bone marrow**
- Helps **weakness, dizziness**, and **sleeplessness**
- Inhibited **NFkB, AP-1**
- Down-regulated **jPA, PI 3-kinase & NF-jB**
- Increased **p21** resulting in **apoptosis**
- Inhibited **angiogenesis** by down-regulating **VEGF & TGF-B1**
- Reduced **DHT** by inhibition of **5 alpha reductase**

Rabdosia

- Especially used for **breast** & **esophageal cancers**
  - 6 year survival was **6%** in **moderate or severe esophageal cancer with or without chemotherapy**
- Especially Inhibited NFkB
- Up-regulated p21
- Down-regulated Bcl-2
- Inhibited telomerase
- Anti-angiogenic through VEGF inhibition
- Potent anti-prostate cancer actions

Licorice

- Increases overall **vitality**
- Protects against **carcinogen-induced DNA damage**
- Component glycyrrhizic acid inhibits **LOX, COX**, and **protein kinase C**
- Down-regulates **EGFR** when overactive
- Licorice polyphenols induce **apoptosis** in cancer cells
- **Angiogenesis inhibitor**, has reduced **VEGF**

Licorice

- Derivatives have inhibited **pulmonary metastasis** and inhibited **breast cancer** cell growth
- Effective in **prostate cancer**, especially when combined with **Chinese skullcap** and **rabdosia**
- **Apoptosis** and **inhibition of cancer cell proliferation** have been demonstrated in **prostate cancer** cell lines

Boswellia

- **75% boswellic acids** recommended for cancer
- Inhibited **COX-2**, and **5, 12, and 15-LOX**
- Down-regulates **NFkB**
- Potentiates **apoptosis** induced by **TNF** and **chemotherapy**
- Inhibited **topoiserase I and II**
- **p21** is increased

Boswellic acids

- Inhibited **glioblastoma**, **melanoma**, **colon** and **prostate cancers**, and several **leukemias**
- Re-sensitized drug therapies by inhibiting **Pgp**
- *Effectively crosses the **blood-brain barrier***
- Inhibited **androgen independent prostate cancer** by inhibiting **NFkB**

Boswellic acids

- Inhibited **chemotherapy-resistant** human PC-3 **prostate cancer** cells
- **5-LOX** is fuel for cancer cell growth by stimulating EGF, VEGF, and other growth factors
- **5-LOX** inhibition induces **cancer cell apoptosis**

Nutrient support

- **Nettles** - nutritive; increases **androgen binding** to **sex hormone binding globulin**; anti-proliferative against **prostate** epithelial & stromal cells
- **Pygeum** – inhibits **prostate cancer** by blocking **EGF**, down-regulating **bFGF, EGF**, and **IGF-1**
- **Red clover** – isoflavones (phytoestrogens) have inhibited prostate cancer in animals & are apoptotic in low-moderate grade prostate cancer

Saw Palmetto

- **Dual** inhibitor of **5 alpha reductase**,
- Inhibited **prostate cancer** in an animal model
- Suppresses **COX-2**
- **Anabolic** & **nutritive** helping to prevent **cachexia**

Feverfew

- Regulates **LOX, COX-2**, and **NFkB**
- Active compound **parthenolide**
  - can trigger apoptosis in **acute myeloid leukemia** and **chronic myelogenous leukemia** cells; it is more specific than chemotherapy drug Ara-C
  - it down-regulates **Bcl-2**, **TRAF 1** and **2**, & promoted sustained activation of **JNK**
  - inhibits **NFkB**, enhances **Taxol** in breast cancer cells, & stabilizes **microtubules**
  - Augmented **docetaxel** & restored sensitivity to **anti-androgen** therapy
  - In summary, it is **anti-tumor, anti-angiogenic**, augments **chemotherapy** & **hormonal therapy**

5 alpha reductase inhibitors

- Zinc
- Pumpkin seeds
- Saw palmetto
- Pygeum
- Nettles
- Green tea
- Reishi
- Lycopene

Resveratrol

- In peanuts & grapes
- Japanese knotwood is the richest source
  - Increased white count in radiation patients
  - Pretreatment enhanced radiation effects in a dose-dependent manner
  - Cardioprotective

Resveratrol

- Suppressed proliferation in cancers including:
  - **Lymphoid and Myeloid leukemias**
  - **Multiple myeloma**
  - **Breast**
  - **Ovarian**
  - **Cervical**
  - **Prostate**

Resveratrol

- Also:
  - **Stomach**
  - **Colon**
  - **Pancreas**
  - **Thyroid**
  - **Melanoma**
  - **Head & neck squamous cell carcinoma**

Resveratrol

- Inhibits growth through **cell cycle arrest**
- Up-regulated **p21Cip1/WAF1**, **p53**, and **Bax**
- Down-regulated of **survivin, cyclin D1, cyclin E, Bcl-2, Bcl-xL**, and **cIAPs**
- Activated **capase**
- Suppressed **transcription factors** including **NFkB, AP-1, Egr-1**

Resveratrol

- Inhibited **protein kinases 1kappaBalpha kinase, JNK, MAPK, Akt, PKC, PKD**, and **casein kinase II**
- Down-regulated **COX-2, 5-LOX, EGFR, VEGF, IL-1, IL-6, IL-8, AR**, and **PSA**
- These are its **anti-angiogenic** mechanisms
- It binds **estrogen alpha & beta receptors** equally unlike **phytoestrogens** which have greater **beta** affinity
- It is an **aromatase** inhibitor

Resveratrol

- It is **cytotoxic** to **adriamycin-resistant breast cancer** cells
- Increased the effectiveness of chemotherapy (**taxanes**)
- Inhibited **cancer metastasis**
- GSH (**glutathione**)levels are increased
- **Blood clotting** inhibited via **PAF modulating effects, platelet aggregation inhibition**, and altered **platelet adhesion to fibrinogen**
- Acts through different mechanisms on **androgen or estrogen receptor cell status**

Resveratrol

- **Grape** consumption or **red wine** 4-7 glasses/ week reduced **prostate cancer** >50%
- It is **more effective** in **aggressive prostate cancer**
- Active in **androgen-sensitive and insensitive prostate cancer**
- Dose: **400-500mg** daily
- It is **more effective** with native cofactors e.g. as **Japanese knotwood** or **grape seed extract**

Ellagic Acid - Pomegranate

- **Pomegranates** are the **richest source** of **ellagic acid**
- Suppressed **VEGFR-2** and **PDGF** receptors indicating **anti-angiogenic** activity
- A **pomegranate extract** inhibited **aromatase 60-80%**
  - **BreastCancerResearch&Treatment2002Feb;71(3):203-217**
- **Pomegranate extract** had **anti-leukemic** effects

Ellagic Acid

- **Synergistic** with **quercetin** & **resveratrol** in inducing **apoptosis** by **caspase 3** induction
- **Ellagic acid** down-regulated **IGF-11**, activation of **p21(waf1/Cip1)**, & prevented **p53** gene destruction
- **8 ounces** of **pomegranate juice** increased **prostate cancer stability 4-fold**

Cruciferous vegetable derivatives

- **Isothiocyanates** (from crucifers e.g. broccoli, cabbage, Brussels sprouts)
  - In **prostate cancer** cell line, inhibited via **AP-1** and **MAPK** suppression
- **Sulforaphane** (from crucifers)
  - Stimulated apoptosis via **p53**-independent means, **Bcl-2** modulation, **ROS** and **JNK**-mediated G2/M arrest, **autophagy** induction, **histone deacetylase** inhibition, **HDA** inhibition
  - Stabilized **p53**, suppressed **apoptosis inhibitors**, increased **BAX** activation

Isothiocyanate and Sulforaphane

- In combination with other isothiocyanate-related compounds
  - Suppressed **prostate cancer** via **NFkB** inhibition & **VEGF** expression regulation
  - Regulated **AP-1**
  - **ROS-dependent disruption**
  - **Angiogenesis** inhibition by down-regulated VEGF
  - Activated detoxifying **glutathione S-transferase** which is usually deactivated in prostate cancer
  - Regulated the **androgen receptors**
  - Inhibited **EGFR** signaling

Wasabi

- **Wasabi** contains many unique isothiocyanates
- Extracts have shown repeated benefit in:
  - **Melanoma**
  - **Stomach cancer**
  - **Breast cancer**
  - **Prostate cancer**
  - **Colon cancer**

DIM (a crucifer derivative)

- A dimer of **indole-3 carbinol (I3C)** that is **more stable** and has **greater anti-cancer effects**
- Altered **estrogen** metabolism away from **16- hydroxylation** toward favorable **2-hydroxylation**
- Blocks **estrogen receptors** from more stimulating estrogens
- Induced **phase I** and **phase II** carcinogen metabolism

DIM

- **I3C**, unlike DIM, can be metabolized unfavorably to the **4-hydroxy metabolite**
- Inhibited expression of **cyclin-dependent kinase-6**
- Induced a **G1 cell cycle arrest** in **ER negative breast cancer**
- Inhibited **MDR**

DIM

- Induced **apoptosis** in **breast cancer** cells independent of estrogen receptor status via **Bax/Bcl-2** apoptotic factors & **NFkB** pathways
- Induced **G1 cell cycle arrest** via selective inhibition of **cyclin-dependent kinase 6** expression and **p21** (Waf1/Cip1) stimulation
- Greatly reduced **EGFR**

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Quercetin

- Inhibited cell growth in cancer cell lines of:
  - **Breast**
  - **Prostate**
  - **Ovarian**
  - **Squamous cell**
  - **Cervical**

Quercetin

- **Bladder**
- **Gastric**
- **Acute myeloid** and **acute lymphocytic leukemia**
- Some **lymphomas**

Quercetin

- **Redox/antioxidative**
- Modulates **COX** and **LOX**, inhibiting PGE-2
- Inhibits cancer **angiogenesis**
- Down-regulated tumor promoters **EGF & HER2-neu**
- Activates **PTEN**
- Inhibits mutation of **p53**

Quercetin

- Inhibited mutation of **p53**
- Activated **caspase-3, Bax**, and **Bak**
- Elevated **p21** and **p27**
- Down-regulated **estrogen binding**
- Reduced circulating **IGF**, increasing IGFBP

Quercetin

- Down-regulated **NFkB, AP-1, Bcl-2, TNF-alpha, MMP-2** and **9, cyclin D** and **E**
- Down-regulated expression of **heat shock protein 70**
- Improved **chemotherapy** effectiveness
- Improved **radiation therapy** effectiveness

Quercetin in prostate cancer

- Inhibited **oncogenes**
- Up-regulated **tumor suppressor genes**
- Down-regulated **HER2-neu**
- Inhibited **metastasis;** down-regulated **MMP-9**
- Inhibited **AR binding**

Quercetin in prostate cancer

- Reduced over-expression of **c-Jun**
- Potentiated & sensitized **TNF-related apoptosis-inducing ligand (TRAIL)**
- Inhibited **Akt**
- Inhibited **AR expression**
- Down-regulated **c-Jun**
- Inhibited **Benzo(a)pyrene** toxicity

Modified citrus pectin

- Inhibited **prostate cancer metastasis** in a rat model
- 4 of 7 patients experienced a **lengthening of the PSA doubling time of over 30%** at 15 grams/day in 3 doses
- Usual dose 10-30 grams daily in divided doses

Lycopene

- Scavenger of **oxidative damage**
- Enhanced **Gap-junction** communication
- Inhibited **IGF-1**, increased IGF-BP-2
- Inhibited **HMG CO-enzyme A reductase**
- Down-regulated **5-alpha reductase**, reducing **DHT**
- Inhibited **inflammatory cytokine IL-6**
- **G0/G1 cell cycle arrest**
- **Dose: Lycopene-rich diet** or 30mg daily

Grape seed extract

- **Proanthocyanidins** 20X antioxidant power of vitamin E and 50X vitamin C
- Down-regulated **NFkB** for both **androgen-sensitive** and **insensitive prostate cancer**
- Increased **Cip1/p21**
- **Anti-angiogenic** via **VEGF** inhibition
- Upregulated **IGF binding protein-3**

Grape seed extract

- Inhibited **IGF-II**, **MMP-2** and **9**
- Down-regulated **Bcl-2** and **oncogene c-myc**
- Inhibited **tNOX** (with green tea)
- **Chemotherapy** sensitizer
- Potent **aromatase** inhibitor
- Dose **200-800mg** daily

Lumbrokinase

- Degrades **fibrin** and activates **plasminogen** (which is how tPA works)
- It is **safe, non-toxic**, and **without obvious side effects** except that it **could worsen bleeding**
- It is being utilized to **dissolve cancer-induced fibrin**
- It supports normal **fibrinogen** levels (**bromelain** is less powerful, more affordable)

Cocoa polyphenol extracts (CPE)

- Contains **beta-sitosterol** which is **cancer-protective**
- At the highest concentration, CPE induced **complete remission in metastatic and nonmetastatic prostate cancer cell lines**
  - CPE "have an **anti-proliferative effect** on **prostate cancer** cell growth but **not on normal cells**"
- CPE was **more active** & **faster** than **beta-sitosterol**
- Eat a small amount of 70% cocoa organic chocolate sweetened with whole raw sugar

Essential fatty acids (EFAs)

- **EFAs (omega-3)** come from **fish oil** and **gamma linolenic acid (GLA)**
- EFAs are vital for **cell membranes**
- Effective for **malnutrition** and inhibiting **cachexia**
- Improve **immune function**, improve the **quality** and **prolong the life** of cancer patients

Essential fatty acids

- Induce **apoptosis**
- **Anti-inflammatory**
- Can sometimes prevent **immunosuppression**
- Block **angiogenesis**
- **Chemotherapy** protective
- Inhibit **cachexia**

Essential fatty acids

- Derivatives EPA and DHA are related to **lower prostate cancer risk** and **advanced prostate cancer risk**
- Down-regulates **PG2, COX-2, VEGF** in **prostate** cells in mice
- **DHA** with **celecoxib** induced a COX-2 independent **suppression of prostate cancer**
- **GLA** suppressed **PGE2** and **5S-HETE**

Sea buckthorn oil

- Contains a **broad array of nutrients** including unique omega-7 fatty acids
- **Anti-carcinogenic** effects documented in many studies

Selenium

- **200 mcg** reduced **prostate cancer incidence** by **63%** in one study
- **52% reduction** in prostate cancer occurrence over 7.5 years with the strongest effect in those with PSA <4
- In Brazil nuts and sunflower seeds
- **Preventive**: 200mcg
- **Treatment**: larger doses may be cytotoxic; up to 800mcg are being used

Copper

- Elevated **copper** and **ceruloplasmin** levels are associated with the **risk of cancer** and **cardiovascular mortality**
- Copper promotes cancer through **inflammation** and **angiogenesis**
- Serum copper correlates with **tumor incidence, burden, progression**, & **recurrence** in **lymphoma, sarcoma, leukemia, cancer of the cervix, pancreas, breast, prostate, liver, lung**, and **brain**

Copper

- Reducing copper levels reduced the following **angiogenic mediators**:
  - **Vascular endothelial growth factor (VEGF)**
  - **Fibroblast growth factor 2(FGF-2)/basic fibroblast growth factor(bFGF)**
  - **Interleukin-1alpha**
  - **IL-6**
  - **IL-8**
  - **NFkB** levels and transcriptional activity

Copper and prostate cancer

- In mice rendered **copper deficient**:
- Optimal range of **ceruloplasmin** clinically appears to be in the lower 10-20% of normal
- (**20-25**)
  - the **primary prostate tumor shrunk**
  - **fewer metastases occurred**
  - **survival was improved**
  - there was **excellent tolerability**

Copper

- **Zinc** is the most effective way to lower copper - 30mg 1 to 4 times daily
  - J Lab Clin Med 2005Mar;145(3):139-43
- Clinically other nutrients have helped:
  - **Molybdenum (1-6mg)**
  - **Green tea extract**
  - **Grape seed extract**
  - **Isothiocynates**
  - **N-acetyl cysteine**
  - **Cilantro**

Zinc

- **Deficiency is common** in cancer
- Zinc is important for the **immune system**
  - **T-cell function** and regulation
  - **Prostaglandin** regulation
- **Cancerous prostate cells** contain less zinc

Zinc

- **Blocked copper** intestinal absorption and promoted excretion
- Excess zinc is **not stored**
- **Avoid** taking zinc with **soy** or **pasta** due to phytic acid
- Whole food zinc or liquid zinc sulfate my be better

Vitamin D

- Deficiency is **widespread**
- **Vitamin D3** is more stable and twice as powerful as vitamin D2 (which should no longer be used)
- Is involved with **20 genes** that determine cell **proliferation, differentiation**, and **apoptosis** (normal cell death)
- Research has identified **18 cancers** so far that it may help prevent, especially hormonal cancer

Vitamin D

- It may be able to **arrest cancer**
  - 1179 post-menopausal women receiving **1100IU of vitamin D3** in combination with 1500mg of calcium daily
  - **60% decline** in cancer incidence the first year
  - **77% decline** in cancer incidence in years 2-4

    - Amer Jour Clin Nutrition June 2007

Vitamin D

- Enhances **radiation** and **chemotherapy**
- **Optimal dosing**: 2000-5000IU daily
- Treatment of **deficiency**: 5000-10,000IU daily
  - Monitor levels monthly
  - Up to 40,000IU daily was recently shown to have no adverse effects on calcium homeostasis in multiple sclerosis patients
  - Target blood levels of 60-80ng in early cancer
  - Target blood levels of 80-100ng in advanced cases

Immunonutrition

- **Important for bolstering the immune system:**
- **L-arginine** – may increase WBCs, NK cells
- **Glutamine** – multiple potential benefits
- **Whey protein** – highest biological value of any protein
- **Magnesium creatine chelate**
- **Omega-3 fatty acids**
- **Branched chain amino acids**

Vitamin E

- **Alpha tocopherol succinate** (dry vitamin E) reduced the abundance of **androgen receptors** in **prostate cancer** cells
- Consider **200-400IU**

Boron

- A diet high in boron resulted in 64% less p**rostate cancer**
- **Boron** lowered IGF-1
- In an animal study, boron 1.7mg/kg reduced prostate tumor size 38% and PSA 88.6%
- **Boron-rich foods**: plums, grapes, prunes, avocados, nuts including almonds & peanuts

Pain control

- The **COX-2** activity of **curcumin, fish oil, ginger,** & others augment the **cancer-fighting** and **pain-relieving** COX-2 activity of **celecoxib**
- **Celecoxib** with the herb **corydalis** are good choices for **pain** when used with **nutrients** which protect against **myocardial infarction** and **intestinal ulceration**

Estrogen in cancer

- **Estrogen receptors** are **commonly present** in cancer
- Besides uterine, ovarian, breast, & prostate, **estrogen receptors** are present in cancers including **thyroid, colon, lung, & melanomas**
- Blocking **aromatase** and promoting **estrogen metabolism** are being utilized in controlling these cancers
- Aromatase blockers include **pomegranate juice, zinc, broccoli/DIM, resveratrol with grape seed extract**, and **green tea**

Case Study #1

- A roughly 60 year old man with prostate cancer had **failed chemotherapy, radiation, and hormone suppression therapy**; he was told by his oncologist that he had 4-6 months to live
- His **PSA** was 128.6, **vitamin D 25OH** was 17, and though his TSH and free T4 were normal, his **free T3** was low at 2.2 (N 2.4 – 4.2). **Zinc** was low normal & **copper** high normal.

Case Study #1

- He started an **integrative protocol**, though he only used half of the recommended doses
- **Vitamin D3** 6000IU, **zinc** 30mg TID, & **Armour Thyroid** were also started
- The next month his **PSA dropped to 82**
- **Peripheral neuropathy** from his Taxotere **resolved quickly** on the protocol

Case Study #1

- Over the subsequent 3 months his condition slowly deteriorated with his PSA rising to 225
- His dose of vitamin D was progressively increased and he did not start to stabilize until his vitamin D 25OH blood level reached the mid-range of normal on 50,000IU of vitamin D
- Also the patient agreed to do full, instead of 2/3rds, doses of his protocol supplements
- His vitamin D level peaked at 115 on 70,000IU of vitamin D

Case Study #1

- At that point, 4 months after initiating the integrative approach, he started improving
- In the subsequent 3 months his PSA dropped 5-10 points a month
- The prostatic acid phosphatase also dropped
- His weight climbed 7 pounds in that period
- The patient continued to drive, get out & about, and looked better

Case Study #1

- He then chose to go to an out-of-state doctor who promised a 50% chance of cure
- The patient stopped his protocol except for vitamin D and zinc
- New chemotherapy was recommended but it was too expensive & not covered by insurance
- In the two weeks off protocol, the patient lost 7 pounds, looked worse, & PSA rose to >300

Case Study #1

- After restarting the protocol, his PSA stabilized but he had difficulty walking & urinary retention
- A scan showed bilateral avascular necrosis of the hips, a side effect of cortisone that Hospice had placed the pt. on months before for pain relief
- Under hospice inpatient care, a TURP was performed but the surgery was too debilitating and he subsequently died

Case Study #1

- His last CT scan showed only prostate and bony involvement which, except for the avascular necrosis, was unchanged from a scan 3 months before
- He lived 11 months from when he was told he had 4-6 months to live and there was nothing more to be done

Case Study #2

- A roughly 70 year old one pack a day smoker had **Gleason's 6** prostate cancer with a **PSA of 6.2**
- Blood revealed **vitamin D 25OH** was low, **zinc** low normal, **albumin** suboptimal, **d-dimer** was elevated, & **estradiol** was high-normal.
- Copper, fibrinogen, dihydrotestosterone, free T3, & prostatic acid phosphatase were normal.

Case Study #2

- He **initiated** the integrative protocol **whole-heartedly** except that he **would not stop smoking**
- He ate **2 eggs** extra daily to support **protein**
- He took **zinc** 30mg twice daily & **vitamin D3** 6000IU daily
- **Fish oil** 5000 EPA+DHA daily and **bromelain** 2400GDU twice daily to support normal blood coagulation
- Natural **aromatase inhibitors** were started

Case Study #2

- One month later his **PSA** has dropped to **3.0**
- Follow-up **blood work will be monitored** to assure optimal vitamin D 25OH, zinc, d-dimer, and albumin
- As importantly, he feels a **new vitality** and is substantially **stronger**, taking the short trail to the top of Natural Bridge

Case Study #3

- A 70 year old physician after prostatectomy for prostate cancer developed a rising PSA
- A bone scan performed at UK showed bony involvement in the pelvis
- He was started on an integrative protocol (no Rx)
- His PSA level dropped and stabilized
- A repeat bone scan after a three months showed regression in bone involvement
- He is happy, pain free, and doing well

Nutrient support program

- Quality **combination nutrient products** designed for cancer support are available
- Nearly all of the nutrients mentioned can be obtained in roughly **twelve products**
- Specific supportive **protocols** utilizing these combinations are being utilized successfully

Can integrative solutions succeed?

- One integrative setting is reporting **great success in prostate cancer control**
- **1200 references** support their approach
- Successful support is also being achieved in other cancers including **metastatic melanoma, glioblastoma, pancreatic cancer, hepatic cell carcinoma,** and **chronic lymphocytic leukemia**

References – Copy of Talk

- **E-mail** me at **jproach@aol.com** for **1200 references** including all of the ones used in this talk that were not cited

- **E-mail** me for a copy of this **power point presentation**

Training, Product Sources, and Protocols

- **Opportunities for training** in integrative cancer approaches are available
- **Information** on **combination product** sources can be e-mailed
- **Specific protocols** will be available in the near future

Summary

- To be fully successful it is essential to **optimize**:
- 1) **Nutrition**
- 2) **Spiritual vision**
- 3) **Supportive home/work/social environment**
- 4) **Blood test parameters**
- 5) **Optimal nutrient support**
- 6) **Targeted chemotherapy** when necessary
- 7) **Pulsed hormonal suppression** when needed

MIDWAY FOUNDATION for Integrative Medicine

- To support **education** of integrative medicine concepts
- To support **medical education** of integrative concepts
- To be a resource in **cancer, autoimmune & thyroid disorders, chronic fatigue-fibromyalgia,** and **hormonal imbalance**
- Our focus includes **longevity, optimal brain health, wellness, optimal nutrition, & student health**
- **Your support** would be **very valuable**