BREAST CANCER: 21st CENTURY TREATMENTS FOR THE BODY, MIND AND SPIRIT.

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Integrative Oncology

Conventional treatments (and/or monitoring) by oncologists and other conventional practitioners + Naturopathic treatments + Other treatments (Psychospiritual interventions, nutritional counseling, dietary supplements, acupuncture, manual therapies) = Patient Centered care

Interdependence Integrative Medicine

All participants are emotionally, economically, ecologically and/or morally self-reliant while at the same time responsible to each other. An interdependent relationship can be defined as an entity that depends on two or more cooperative autonomous participants.

Tracy W. Gaudet, M.D., Director, Patient Centered Care and Cultural Transformation for the Veterans Admin.
What is Naturopathic Oncology

- Experts in the emerging field of Integrative and complementary cancer treatment
- Supports patients through surgery, chemotherapy, radiation, post conventional therapies, survival
- Ensures that there are no known herb-drug or nutrient-drug interactions
- Concerned with prevention of recurrence - empowers patients to be proactive through lifestyle changes, botanical medicines (herbs), stress management and supplements
- Assists with end of life care
- Treats the individual

OncANP

- OncANP = Oncology Association of Naturopathic Physicians
  - To advance the philosophy, science and practice of naturopathic oncology
  - Active list serve, continuing education, tumor boards
- FABNO: Fellow Associate to the Board of Naturopathic Oncology
  - Naturopathic physicians who meet standards representative of advanced experience and knowledge in cancer care are eligible for board certification in Naturopathic Oncology.
- Naturopathic oncology
  - is the application of the art and science of naturopathic medicine to the field of cancer care and treatment.
  - www.oncanp.org

Who uses our services?

- 68.7% of cancer patients surveyed had used at least one CAM therapy (not including prayer) [1]
  - A recent study reported 84% of radiotherapy cancer patients used dietary supplements [2]
- Most do not disclose their use of herbs and supplements to their conventional doctors
- Cancer patients are particularly vulnerable to false claims of natural cures for cancer
- Patients often get their information from health food store clerks and well-meaning friends and family

Naturopathic Oncology Goals

1. To provide safe and effective integrative cancer care
2. To avoid herb drug and nutrient drug interactions
3. To keep patients healthy enough to complete their course of care as prescribed by their oncologist
4. To ensure oncologists are aware of everything their patients are taking
5. To ensure no patient receives conflicting advice gets stuck “in the middle”
6. To be a resource for healthcare practitioners and staff’s questions on complementary medicines
7. Survivorship, prevention, decrease risk of recurrence

SEER Fact Sheet Breast Cancer

SEER # New Cases and Deaths

<table>
<thead>
<tr>
<th>Common Types of Cancer</th>
<th>Estimated New Cases 2014</th>
<th>Estimated Deaths 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate Cancer</td>
<td>233,000</td>
<td>29,480</td>
</tr>
<tr>
<td>Breast Cancer (female)</td>
<td>252,679</td>
<td>40,000</td>
</tr>
<tr>
<td>Lung and Bronchus Cancer</td>
<td>224,210</td>
<td>15,300</td>
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<tr>
<td>Colon and Rectum Cancer</td>
<td>138,830</td>
<td>59,310</td>
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<tr>
<td>Melanoma of the Skin</td>
<td>76,100</td>
<td>9,710</td>
</tr>
<tr>
<td>Bladder Cancer</td>
<td>74,830</td>
<td>15,080</td>
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<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>70,800</td>
<td>18,590</td>
</tr>
<tr>
<td>Kidney and Renal Pelvis Cancer</td>
<td>63,620</td>
<td>13,860</td>
</tr>
<tr>
<td>Thyroid Cancer</td>
<td>62,080</td>
<td>1,850</td>
</tr>
<tr>
<td>Endometrial Cancer</td>
<td>52,650</td>
<td>6,550</td>
</tr>
</tbody>
</table>

Breast cancer represents 14.6% of all new cancers in the U.S.
National Cancer Institute: Female Breast Cancer: Mortality 2007-2011

Lower Socioeconomic Status (SES)

- Higher cancer death rates
- Higher cancer incidence rates – Why?
  - Incr. tobacco use, decr physical activity, decr access to healthy foods,
  - Less likely to receive standard treatments. Barriers to health care, inadequate health insurance, financial and structural barriers.
  
  Cancer Facts and Figures 2015 American Cancer Society pg.7

- MNDA has accomplished step 1: Licensure for NDs
- Now it is time to address Step 2: insurance coverage and equal access.

The Economics and the Outcomes

UC Project for Global Inequality

5/2/2015
### Change is in the air – Our Expertise is Needed

- **Senator Barbara Mikulski Resolution 221:**
  - "Naturopathic Medicine Week" to recognize the value of naturopathic medicine in providing safe, effective, and affordable health care.
- **ACA: Affordable Care Act**
  - Prevention & Wellness
  - Patient centered Medical Homes
- **Mark Bertolini, C.E.O. Aetna advocate for Naturopathy and prevention:**
  - Dietary changes
  - Food sensitivity testing and elimination
  - Weight loss
  - funding Wholesome Wave: Increases value of food stamps when used at farmers’ market for foods
- **Tracy W. Gaudet, M.D., Dept. Veterans Affairs,**
  - Director, Patient Centered Care and Cultural Transformation

### Importance of a Naturopathic Presence in every State

- **Case study – 45 yo African American female, presents with shoulder pain and deec. ROM**
  - 2 kids
  - Fungating lesion in shoulder
  - Denial, refuses to see oncologist or even PCP
- **Local MD’s need an expert to contact on these topics.**
  - Phone call from local Surgeon: is resveratrol vs Surgery in breast cancer stage 1-2?
  - Advice by an ND with no credentials
  - Patient “Failed chemo” sent home to put her life in order with a 3 months prognosis

### Naturopathic Co-Management of Cancer Patients

- **Side effect management**
  - Prevent long term Sequelae
  - Prevent discontinuation, delay or dose-reduction
  - Maintain Quality of life
- **Maintain nutritional status**
  - Associated with fewer side effects
  - Maintain quality of life
  - Assist the body in rebuilding of the GI tract
- **Increase efficacy of treatment**
Naturopathy and Surgery

- Goals
  - Decrease inflammation
  - Increase healing time
  - Strengthen the immune system
  - Decrease adhesions
    - Bromelain
    - Vitamin C
  - Decrease potential metastasis
  - Decrease cordling (aka Axillary Web Syndrome)
    - Incidence 6-72%, early post operative period (study 31.5% ½ early and ½ up to 24 months out). Breast Cancer Res Treat. 2013 Jul; 140(1): 105–111.
  - Decrease potential metastasis
  - Decrease cording (aka Axillary Web Syndrome)

- Basic Surgery protocol
  - Start 2-4 weeks pre-surgery, continue 4-12 weeks post-surgery
  - homeopathics, nutrients, botanicals, stress management, diet & Lifestyle
  - Foods, herbs and supplements to discontinue prior to surgery

- Contraindications pre surgery
  - Herbs: Ginko, Garlic, feverfew, hydrastis, Kava kava
  - Foods: inflammatory foods, hydrogenated fats
  - Supplements: Fish oil, Vitamin E

- Homeopathics, supplements
  - Anti-inflammatory pre/Post surgery
    - Arnica 30c/200c
    - Anesthesia difficulties
    - Fear of surgery/knife

History of Homeopathy

- Homeopathy is a very different paradigm than conventional medicine and is often misunderstood.
- Homeopathy is a system of medicine developed 200 years ago by German physician Samuel Hahnemann (1755-1843).
- There are around 2000 homeopathic remedies in use today, made from plant, mineral and animal sources. Hahnemann found that the more diluted substances had fewer side effects, and were actually, counter to a layman’s intuition, more powerful.
Foundation of Homeopathy

- **Law of Similars**
  - Homeopathic medicines are called remedies. To cure a patient, Hahnemann found he had to choose the remedy that most closely fit the patient’s symptoms. This means, the task of the homeopathic doctor is to match the symptoms of the sick patient to the homeopathic remedy which has been shown to produce those same symptoms in experiments on healthy people.

- **Homeopathic medicine is highly individualized.** For example, 10 patients with asthma could end up with 10 different homeopathic remedies for each person has a unique set of symptom’s

Homeopathy and Cancer Care

- **Homeopathy is the 2nd most used healing method according to the World Health Organization.**
- **Homeopathy does not interfere with conventional therapies**
  - Does not use CYP450 pathways
- **How Homeopathy works and can be researched – one theory**
  - The Nanoparticle-Allostatic Cross-Adaptation (hormesis)-Sensitization (NPCAS) Model.
  - Testing the nanoparticle-allostatic cross-adaptation-sensitization model for homeopathic remedy effects.

- **Colon Cancer**

- **End of Life, Hospice & Homeopathy**

  - **Aconite 30c**
    - Mental restlessness, shooting pains, fear of death excessive in night - panic attacks
  - **Arsenicum album 30c**
    - Extremely restless, tosses and turns, unable to find comfortable position, weakness, debility, fears being left alone
  - **Ruta graveolens 9C for qol in Advanced Cancers**
Co-Management with Chemo

- Decrease Side effects
  - Maintain Quality of life
  - Prevent discontinuation, delay, or dose reduction
  - Prevent long term sequelae
- Maintain Nutritional Status
  - Maintain quality of life
  - Associated with fewer side effects
- Increase efficacy of treatment

Common Drug Combinations for Breast Cancer

- AC&T: Doxorubicin & cyclophosphamide x4 followed by paclitaxel or docetaxel
- TC: docetaxel & cyclophosphamide
- TAC: docetaxel, doxorubicin & cyclophosphamide
- CAF/FAC: cyclophosphamide, doxorubicin, 5-FU
- FEC/CEF: cyclophosphamide, epirubicin, 5-FU
- CMF: cyclophosphamide, methotrexate & 5-FU

Doxorubicin (Adriamycin), Cyclophosphamide (Cytoxan), Docetaxel (Taxotere)
TIMING

- Conventional Chemo is given in cycles to give the body time to recover from the adverse effects
  - Given at maximum tolerated dose (MTD) every 3 weeks, just below what would cause over 50% of pts to experience severe or dose limiting toxicity.
- Dose-dense chemotherapy
  - Cycles of chemotherapy are given closer together which may help decrease resistance and improve survival
  - Colony stimulating factors (Neupogen, Neulasta) may be needed to help boost WBC
  - Associated with increased adverse effects
- Metronomic chemotherapy
  - Low dose chemotherapy administered more frequently and regularly (weekly or daily)
- Insulin Potentiated chemo (ITP) or insulin-potentiated targeted low-dose therapy (ITLTD)
  - Utilizes standard schemes of chemotherapy in combination with intravenous insulin, 10 times lower doses of chemotherapeutics, and short intervals between the applications.

Cyclophosphamide (Cytoxan)

- Chemotherapeutic class:
  - Alkyating agent, cell cycle non specific
- Mechanism of action
  - Alkylates nucleic acids leading to DNA helix strand breaks thus interfering with DNA replication
  - Cell-cycle non-specific
  - Tumor resistance develops due to the capacity of cells to repair nucleic acid damage and due to inactivation of the drug by conjugation with GSH
- Pharmacology
  - Half-life $T_{1/2}$: 4-12 hours
  - CYP metabolism
    - A pro-drug (inactive) converted to the active alkylating agent phosphoramidate mustard and acrolein via CYP2B6
    - Inactivated by CYP3A4
- AVOID
  - Substances that inhibit CYP3A4 – Metabolite is active form

Adverse Effects of Cytoxan

- Nausea/vomiting
- Myelosuppression (dose-limiting)
- Alopecia
- Mucositis
- Diarrhea
- Anorexia
- Hyperpigmentation skin/nails
- SIADH
- Headache
- Hemorrhagic cystitis (dose-limiting)
- Cardiomyopathy
- Amenorrhea with ovarian failure
- Increased risk of secondary malignancies
Natural Support for Cytoxan: To Reduce Toxicity

**MYELOSUPPRESSION**

- *Withania somnifera* (Ashwagandha)  
  - Immunopharmacol Immunotoxicol. 1999 Nov;21(3):27-35
- *Melatonin*  
  - J Pineal Res. 2005 May;42(4):272-7
- *Astragalus membranaceus*  
  - Zhongguo Zhong Xi Yi Jie He Za Zhi. 2002 Jul;22(7):515-7
- *Coriolus versicolor* (PSK)  

**HEMORRHAGIC CYSTITIS**

- Hydration
- *Withania somnifera*
- *Melatonin*
  - J Pineal Res. 2005 May;42(4):272-7

**NAUSEA**

- *Zingiber officinale*  
  - Integr Cancer Ther. 2012 Sep;11(3):204-11

**OTHER**

- *Fish Oil* (EPA)  
  - In Vivo. 2004 Sep-Oct;18(5):543-7

Drug-Herb Interactions

- Combined use of herb & chemotherapy may increase or decrease the effect of the chemotherapy, potentially leading to greater toxicity or decreased effectiveness

**MECHANISMS**

- Cytochrome P450 (CYP)
- SAPK/JNK pathway
- P-Glycoprotein
- Cell cycle arrest

Common Breast Cancer Chemo metabolized through CYP:

- Epirubicin, doxorubicin
- Cyclophosphamide
- Paclitaxel, docetaxel, ixabepilone
- Vinblastine, vincristine, vinorelbine

5/2/2015
INDUCERS
- Hypericum perforatum
- Echinacea sp.
- Schisandra

INHIBITORS
- Berberine
- Curcumin- Oral Rx
- GTE/EGCG- mild at 800mg EGCG
- Glycyrrhiza glabra- mild not clinically relevant
- Harpagophytum- mild, not clinically relevant
- Polygonum sp.
- Resveratrol
- Sulforaphane
- Tanacetum parthenium
- Trifolium pratense
- Uncaria tomentosa

Drug-Herb Interactions: CYP3A4

- Human PK Studies- 3A4 safe
  - Cimicifuga racemosa
  - Gingko; possible induction at doses >360mg
  - Garlic/allicin
  - Ginseng (Panax, Eleutherococcus)
  - Piper Methysticum
  - Silybum marianum
  - Valerian

Antioxidants during chemotherapy

Research Update - Selenium

- Vital ingredient of the antioxidant enzyme glutathione peroxidase, which works with Vit E and C to prevent free-radical damage to cell membranes
- Stimulates WBCs, NK cells (82% increase in activity), IL-2 and thymus function

Research Update - Melatonin

- Night Shift- Melatonin connection: 60% increased breast cancer risk (melatonin stimulated by darkness and suppressed by light) (Schernhammer E et al. Rotating night shifts and risk of breast cancer in women participating in the Nurses’ Health Study.
- Inhibits several cancers in vitro and in animal studies - increases expression of p53 gene which reduces cell proliferation by inducing apoptosis
- May regulate cell signaling, including interleukins and gamma interferon, which increase NK cells
- Reduces toxicity and enhances efficacy of chemotherapy, including cisplatin, etoposide, interleukin-2, interferon, tamoxifen, and lupon, as well as radiation

- 15 of 24 patients were alive after one year on melatonin 20 mg/d, compared with 7 of 36 on chemo alone. Patients on melatonin also had less neuropathy, cachexia, and myelosuppression (Lissoni P, et al. A randomized study of chemotherapy with cisplatin plus etoposide versus chemoendocrine therapy with cisplatin, tamoxifen and the pineal hormone melatonin as first-line treatment of advanced non-small cell lung cancer in a poor clinical state. J Pineal Res 1997;232:15-19)
- Patients taking melatonin 20 mg/d had significantly less weight loss (9 kg vs. 16 kg) and a lower chance of disease progression (53% vs. 90 %) compared to those treated with supportive care alone (Lissoni P, et al. Is there a role for melatonin in the treatment of neoplastic cachexia. Eur J Cancer 1996;32A:1340-41)
Co-Management during Radiation

- **GOAL**
  - Decrease side effects
  - Increase efficacy of therapy
  - Protect organs at risk

Potential Adverse Effects from Radiation to the Breast

**SHORT TERM**
- Local
  - Sunburn like skin changes in the treated area
  - Swelling and heaviness in the breast
- Systemic
  - Fatigue

**LONG TERM**
- Smaller and firmer breast
- Complications with reconstruction surgery
- Problems breastfeeding
- Brachial plexopathy
  - Numbness, pain & weakness in shoulder, arm & hand
- Lymphedema
- Rib fracture
- Damage to heart and lung
- Angiosarcomas

Radiation Induced Side Effects

<table>
<thead>
<tr>
<th>Dermatitis</th>
<th>Pain &amp; Oral Mucositis</th>
</tr>
</thead>
</table>
| **Prevention**
- Topical
  - Calendula officinalis
    - J Clin Oncol. 2004 Apr 15;22(8):1447-51
    - Cochrane Database Syst Rev. 2009 Apr 15;3:CD004845
    - Semin Oncol Nurs. 2011 May;27(2):e1-17
    - Silymarin
      - Strahlenther Onkol. 2011 Aug;185(8):455-91
| **Traumeel S**
- Pain and oral mucositis
Radiosensitization

- Docosahexaenoic Acid
  - Int J Cancer. 2004 Apr;109(3):449-54
  - Prog Lipid Res. 2010 Jan;49(1):76-86
- Green Tea
  - Increases cellular apoptosis in a dose-dependent fashion in irradiated tissues.
- Berberine
- Curcumin
- Withania somnifera
  - At least 5 in-vivo studies have confirmed the radiosensitizing effects of withanone D.
  - Direct intraperitoneal injections of withanone D increases life span and tumor free survival over mice that receive radiation only.
  - It is unclear how this information pertains to oral dosing in humans

Camellia sinensis (green tea)

- All CA types: Incidence unaffected with doses ≤ 5 cups daily.
- All CA types: Incidence decreased, onset delayed and survival increased with ≥ 10 cups daily (Japan).
- Breast: Reduced risk of primary breast cancer. Also, ≥ 5 cups (avg. 8 cups) daily reduced recurrence of stage I and II and induced a longer disease-free interval.
- Pancreatic: 2 of 3 studies report an inverse association.
- Colorectal: 3 of 5 studies report an inverse association.
- Stomach: 6 of 10 studies report an inverse association.
Take Home Message

- Naturopathic co-management with surgery, chemotherapy or radiation therapy requires extensive research & understanding about the therapies in order to understand the adverse effects a patient may face & how to minimize the risk of negative interactions
- Utilizing naturopathic therapies in conjunction with surgery, chemotherapy & radiotherapy can prevent and treat adverse effects, improve quality of life & potentially improve outcomes
- When using supplements concurrently, extreme care must be taken to prevent interfering with the effectiveness of a patient’s conventional treatments

The War on cancer

- The signing of the National Cancer Act of 1971 by then U.S. President Richard Nixon is generally viewed as the beginning of the war on cancer
- Maybe it is not a war??
- The Natural defenses include
  - The bodies ability to correct a DNA mutation (DNA repair)
  - Apoptosis
  - Immune system (NK cells, etc)
  - Spontaneous healing
  - Remission of unknown origin
**Stephany Porter, ND, FABNO**  
www.BodhiClinic.com

**Cell signaling – The new frontier**

- In the 1950s, medical researchers saw cancer as “an extremely complicated process that needed to be described in hundreds, if not thousands of different ways,”
- In the 1970s, the “War on Cancer” reduced it to belief that one could understand a whole disparate group of cancers by studying these mutant genes that seemed to be present in many of them.
- In 2000, unable to distill it down, we began to accumulate once again an overwhelming mass of information that cancer is indeed a highly complex process.

> "It is now clear that cancer isn’t a single disease or even a hundred different diseases. Between everybody that has cancer today, to everybody that’s probably ever had cancer since the beginning of humankind, [each person] has had different molecular alterations in this disease,”

Robert A. Weinberg, MIT Center For Molecular Oncology.

> “The gaping distance between these data sets and a true understanding of cancer biology is illustrated by the amusing fact that two distinct expression array analyses of cells in breast cancers have been found to be equally useful in predicting future clinical behavior of these tumors but contain almost no genes and thus proteins in common (Ein-Dor et al., 2005; Fan et al., 2006)”

> Cancer is multi-dimensional and demands a multi-dimensional approach.

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**Mitochondrial Apoptosis (intrinsic)**

- The crucial next challenge, thus far out of reach, is to decipher exactly how the elaborate networks of signaling molecules that exist inside a cell enable it to make its crucial decisions—a process analogous to cell "thinking" (Alberts, 2010).

> QUESTIONS:
- Cell: a machine or a conscious entity?
- How does this affect our treatment protocols?
### Natural Options

| Pro apoptotic (Bax, Bak, Bad), BH-3 only molecules initiate Bax/Bak (Bld), Mcl-1, Bcl-X. Bax & Bak contain BH-1,2,3 domains if activated → MOMP |
| Anti apoptotic (Bcl-2, Bcl-X, Mcl-1 and BH-3 only) maintain mitochondrial integrity, may bind/inhibit pro-apoptotic members |

- Work on the pro apoptotic pathway
  - I3C and DIM,
  - Sulphoraphane (ITC),
  - Beta carotene,
  - Resveratrol,
  - Genistein (polyphenol),
  - diallyl sulhide (garlic),
  - plabagin (plant naphthoquinone),
  - diterpenes (citrus peel)
- Hibiscus sabdariffa L. (Malvaceae) inhibit Bcl-2
- Phytoestrogens, EPA
- Curcumin, Green tea, Ginger, Rosemary

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### Apoptosis

| Kava Kava Flavokawain B (FKB) Piper Methysticum |
| Panax Ginseng Gensenoside Rg3 |
| FKB induced apoptosis, decreases inflammation, regulated the immune system (Th and NK cells), decreased tumor size and metastatic potential in vivo |

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![Apoptosis Diagram](image-url)
Apoptosis the Natural Way

- Dietary agents that alter MMP and trigger cell death:
  - vanilloids, curcumin, capsaicin, baicilin, nordihydroguaiaretic acid (Chapparral, cytotoxic flavonoids and other dietary phenolic compounds, EPGC, beta-carotene, lycopene, resveratrol
  - Iner Cyt C Release:
    - EGCG, ginger, curcumin, resveratrol

- Alantolactone and isoalantolactone, main bioactive compounds that are present in many medicinal plants such as Inula helenium, L. Inula japonica, Aucklandia lappa, Inula racemosa, and Radix inulae:
  - anti-inflammatory, antimicrobial, and anticancer properties, apoptotic, with no significant toxicity.


Triple Negative Breast Cancer (TNBC) - EPGC

- 15-20% of BC is TNBC, overall survival is <50% at 5 years
- TNBC represents a hostile histological subtype of breast cancer with limited medication options, therefore the development of alternative targeted therapies is important to improve the overall survival rates of TNBC patients.
- EGCG inhibits several critical proteins that are involved in cancer cell progression, migration, and induction of apoptosis through the production of reactive oxygen species, induction of cell cycle progression, and inhibition of the NF-κB cell-signaling pathway in genes upregulated and its genes were downregulated in response to the combined treatment of p53 siRNA cells with EGCG.
- Cancer therapy using p53 siRNA specifically triggers apoptotic mechanisms, and increases the efficiency of other therapeutic agents by increasing the sensitivity of cancer cells to apoptosis.

Hormone Therapy

- **aromatase inhibitors:**
  - Arimidex (chemical name: anastrozole)
  - Aromasin (chemical name: exemestane)
  - Femara (chemical name: letrozole)
- **SERMs (selective estrogen receptor modulators):**
  - tamoxifen
  - Evista (chemical name: raloxifene)
  - Fareston (chemical name: toremifene)
- **ERDs (estrogen receptor downregulators):**
  - Faslodex (chemical name: fulvestrant)
- Oophorectomy or ovarian ablation
Dietary Antioxidants

- **Glutathione**
  - Asparagus, spinach, garlic, onion, broccoli, cabbage, kale, collard, bell peppers, radish, carrots, red bell peppers, squash, zucchini, potatoes, melons, grapefruit, strawberries, peaches
- **Selenium**
  - Brazil nuts, meat, seafood
- **Cyanohydroxybutene**
  - Broccoli, cauliflower, Brussels sprouts, cabbage
- **Alpha lipoic acid**
  - Red lentils, organ meats, yeast (esp. Brewer's)
- **Riboflavin**
  - Sunflower seeds, spinach, asparagus
- **Cysteine**
  - Eggs, garlic, whey protein
- **Flavonoids**
  - Turmeric, cinnamon, echinacea
Vitamin C back in the Forefront

- Meta-analysis over 17,000 BC pts
- 15% reduced risk of premature death from any cause and a 13% reduced risk of death from breast cancer
- Those who took 100-1000mg Vit C qd
- In some studies women who took vitamin C during conventional treatment did not decrease the efficacy of chemotherapy or radiation, and in some cases, their risk of death was lower compared to those who did not take vitamin C.

Fat Cells in Breast May Connect Social Stress to Triple-negative Breast Cancer

- Local chemical signals released by fat cells in the mammary gland appear to provide a crucial link between exposure to unrelen9ng social stressors early in life, and the subsequent development of breast cancer. Exposure to stress of social isola9on leads to reprogramming of genes in fat cells in the mammary glands. These fat cells then secrete substances that cause nearby pre-cancerous epithelial cells to proliferate more rapidly, accelerating the development of breast cancer.

Compounds that Inhibit Cellular pathways

- **NF-κB**
  - Anethole, carnosol, caryophyllene, cinnamaldehyde, curcumin, humulene, perillyl alcohol, quercetin, sulforaphane, ursolic acid
- **TNF**
  - Ajoene, allicin, allyl isothiocyanate, apigenin, curcumin, diallyl sulfide, eugenol, gingerol, humulene, kaempferol, paradol, piperine, zingerone
- **Bcl-2**
  - Ajoene, allyl isothiocyanate, b-carotene, b-sitosterol, capsaicin, carnosol, cinnamaldehyde, curcumin, diallyl sulfide, gingerol, limonene, lutein, rosmarinic acid, S-allylcysteine, sulforaphane, ursolic acid

“Besides suppressing inflammatory pathways, spice-derived nutraceuticals can suppress survival, proliferation, invasion, and engagement of tumor cells.”


Cardamom, Coriander, Cumin, Dill, Fennel, Ginger, Rosemary, Tamarind, Thyme, Tarragon, Turmeric.
Rosemary

- **BASICS**: Antiviral, antibacterial, antioxidant, anti-inflammatory, immunomodulatory
- Most important AOX constituents are polyphenols: Carnosic acid, caffeic acid and its derivative rosmarinic acid
- Plant content of carnosic acid and rosmarinic acid, leaves highest, flowers next, branches very little.
- Other: caffeic acid, esters (borneol, cineol), terpenes (alpha-pinene, camphene)


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**Rosemary – MDR transporter**

- Inhibition of transmembrane transport pump P-glycoprotein (Pgp), reversal of MDR transporter
  - *Doxorubicin, vinblastine*

- Reversal of P-glycoprotein-mediated multidrug resistance of cancer cells by five schizandrin isolated from the Chinese herb *Fructus Schizandrae*. (*mice*)

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**143 citations for rosemary and cancer**

Blood Sugar and Laughing

- “Negative emotions such as anxiety, fear, and sorrow are known to be factors that elevate the blood glucose level. Conversely, positive emotions such as laughter have been reported to modify the levels of neuroendocrine factors involved in negative emotions and to modulate immune function.”
- These results suggest a significant suppression of the increase in 2-h PPBG by comedy show in patients with diabetes, suggesting that laughter ameliorates the postprandial glucose excursion in the presence of insufficient insulin action.

http://care.diabetesjournals.org/content/26/5/1651.full

- “Our results supported NK cell-mediated improvement in glucose tolerance at the gene-expression level.”


Genetically Modified Foods linked to Infertility and Cancer

- As per the WHO the “three main issues debated are:
  - Allergenicity (tendencies to provoke allergic reaction)
  - Gene transfer (movement of genes from the food to bacteria or human cells)
  - Outcrossing (the transfer of genes from GM crops to organic or native crops).

- US GM Crops:
  - Soy 93%, Corn 86%, Cotton 93%, Canada (Canada) 90%, US papaya 88%, Sugar beet 1%
- Seeds of deception or Genetic Roulette by Jeffrey Smith

Genetically Modified Foods

- US GM crops
  - Soy 95%
  - Corn 86%
  - Cotton 93%
  - Canola 95% (Canada)
- BT toxin in corn: toxic,
  - Govt Australia showed infertility and low birth rate (rats, 11/2008)
- First GM crop: FlavrSavr Tomato
  - Rats refused to eat
  - Animals avoid if given the chance
  - GM Corn after 28 days 77/20 developed Stomach lesions, 7/40 died within two weeks (industry study)
**MIND**

- The National Institutes of Health (NIH) define mind–body therapies as interventions designed to facilitate the mind’s capacity to affect bodily function and symptoms.
- The most researched and frequently used are: relaxation training, guided and interactive guided imagery, meditation, hypnosis, biofeedback, and forms of group social support.
- Mind body approaches have minimal risk, significant benefits, low cost and should be the standard of care with cancer patients.

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**PLACEBO EFFECT**

- Placebo effect can lead to:
  - Increases immune system, even NK cells, apoptosis, etc.
  - Decreases inflammation
  - Placebo and the New Physiology of the Doctor-Patient Relationship. Physiol Rev 2013;93(3):1207-1246
  - 1st placebo controlled trial 1958

- Nocebo (I shall harm) effect can lead to:
  - Increased side effects, death (Voo Doo), etc.

- Administration and effect is directly related to the symbolic significance to the patient and psychosocial context (words by healthcare provider, color/shape/smell medication, belief in the doctor, etc.).
- The ubiquity of the placebo effect suggests that every communication between a doctor and patient can have consequences as potent as a scalpel or cytotoxic agent.

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**CASE STUDY - RK**

- 9/2009 Biopsy of left breast, 74 yu
  - Infiltrating lobular carcinoma well differentiated, Stage II, ER 99%, PR positive 75%, Her 2 Negative by Fish test.
  - Left Femur lesion, required pinning, Metastasis confirmed, upgraded to stage IV.

- Denied radiation, chemotherapy (until later)

- Medications/Supplements
  - Supplement changes over the years: Multi V, Magnesium, Melatonin, Breast blend, Tincture’s, Vitamin D, NAC, Pacific yew, Alpha Lipoe acid, organotherapy, Heavy metal clearing.

- Diagnostics
  - 2/2014 PET/CT stable, no progression in liver, RUL 5mm nodule resolved, new 6mm nodule.
  - Pt still very active and strong vital force.

- 4/2014 first increase in CEA, 6.2 and CA 27-29, 58.1. 9/2014 CEA 19.2, CA 27-29 88.3
Psychoneuroimmunology (PNI)

- From PNI research we now know that there is direct innervation to the thymus gland and lymph nodes, and that lymphocytes not only have receptor sites to all known neurotransmitters, they also produce neurotransmitters that can cause neurological and emotional symptoms. Thus, a biochemical mechanism has been established to explain how depression, anxiety, and related negative or positive emotional states can affect immunity.

- One study found that when patients with breast cancer used guided imagery to increase an immune response, they significantly increased numbers and aggressiveness of natural killer cells, an effect, which increased with time. Hall, Mumin, and Gross (1995)

- A systematic review of mindfulness-based stress reduction interventions reported significant improvements in anxiety, depression, stress, sexual difficulties, physiological arousal and immune function across the cancer trajectory (Shenan, Payne, & Fenlon, 2011). Integrative Oncology, Oxford Press

- Gruber et all in a 1993 study of Stage I Breast Ca Pts reported reduction in levels of psychological distress, greater use of active coping methods, and significant increases in the percent of large granular lymphocytes and natural killer cells using relaxation, guided meditation and biofeedback training.

Long Term Stress & Cancer Progression and Recurrence Risk

- Clinical and epidemiological studies over the last 30 years have identified psychosocial factors especially stress, chronic depression and feeling of isolation as risk factors for cancer progression.

- Chronicity of negative affect, as manifested by depressed mood or hopelessness/pessimism, appears to have a stronger relationships with outcomes than do stressful events.


- Creating a therapeutic relationship with effective communication
  - Build trust, Rephrasing

- Address the elephant in the room.
Stress Management – Power of Words

- PNS & SNS HPAA axis issues
  
  Buddha’s Brain: The Practical Neuroscience of Happiness, Love, and Wisdom
  
  - acute (first darts) — Chronic (second darts)
  
  - Choose words cautiously as not to create 2nd darts.
  
  - Overstimulation of amygdala and hippocampus = anxiety, altered memories
  
  - DECREASED oxytocin, dopamine, INCREASED: ACTH, NE, Epi.
  
  - DECREASED immune system/activity, increased cancer cell migration, altered DNA repair. Increased viruses and replication, angiogenesis.
  
- Consider Rephrasing
  
  - You have 3 months to live- add “as statistics go and you will be fine”.
  
  - “This is a serious illness, and you may be able to do something about it.”
  
  - Prepare for the worst, expect the best
  
  - “Words are powerful tools in the doctor’s armamentarium, having both healing as well as harming effects. Doctors need to be conscious about the choice of their words.”
  
  - Pulling Weeds Planting Flowers (Buddha’s Brain)

Second Darts

- chronic SNS/ HPAA stimulation disturbs the following systems increasing risks for the health problems (Licinio, Gold, and Wong 1995; Sapolsky 1998; Wolf 1995):
  
  - Gastrointestinal—ulcers, colitis, irritable bowel syndrome, diarrhea, and constipation
  
  - Immune—more frequent colds and flus, slower wound healing, greater vulnerability to serious infections
  
  - Cardiovascular—hardening of the arteries, heart attacks
  
  - Endocrine—type II diabetes, premenstrual syndrome, erectile dysfunction, lowered libido

Brain, Behavior, Immunity

- Cancer diagnosis and treatment induce acute and chronic stress and reduced QoL, which may affect neuroimmune regulation promoting inflammatory processes that could contribute to both symptom exacerbation and metastasis
  
  - Chronic stress, negative affect and social adversity have also been associated with biobehavioral alterations (increased sympathetic nervous system [SNS] signaling, hypothalamic pituitary adrenal [HPA] axis dysregulation, inflammation and decreased cellular immunity)
  
  - Could interact with the tumor microenvironment to promote factors favoring tumor growth (e.g., angiogenesis), invasion (e.g., tissue remodeling and epithelial-mesenchymal transition), and metastatic signaling (e.g., anoikis), during and after cancer treatment

- Psycho-social Intervention Effects on Adaptation, Disease Course and Biobehavioral Processes in Cancer
  
TREATMENTS for Nervous system

- ENCOURAGE more time in the PNS:
- Relaxation
- Meditation
- Breathing (Diaphragm)
- Visualization/Imagery
- Walk in the Woods
- Downtime
- Stop and smell the flowers
- ????

Stress Free Naturopathic Treatment Plans

- A new approach to the “diet”
  - Nutrient dense vs non nutrient dense
  - How much does it offer the body, or take from
  - Foods vs non foods (3 food meals per day).
- Rotational Diets
- Supplement Holidays
- Meet the patient where they are today
  - Financially, emotionally, physically
- Shift Consciousness - Release archetype

“Health was once assessed mainly in terms of disease. Now it is understood to reflect the interaction of complex systems, including nutritional status, spiritual state, stress levels, access to services, educational status, environmental influences, a history of earlier infections, genetics and the like. Promoting good health requires attention to multiple influences on many levels: cell, organ, whole organism (such as human body), family, community, nation, and increasingly, the planet. . . . . Uncontrolled growth in one part of an organism can become cancerous and endanger the whole organism.”

**Spirituality**

“**Spirituality** is a set of beliefs and attitudes that give meaning and purpose to life through a sense of connectedness to self, others, the natural environment, a higher power and/or supernatural forces. These beliefs and attitudes empower and transcend the self and are embodied in feelings, thoughts, experiences and behaviors.”

- Less anxiety and depression
  

**Consciousness of healing vs unconscious healing**

- Consciousness is widely considered to be the greatest challenge for modern science. At present, “Not only have we so far no good theory of consciousness, we lack even a clear and uncontroversial pre-theoretical description of the presumed phenomenon” (Dennett, 1987; p.160).
- This line of reasoning has led us to theoretically formulate the possible relationships between mind, cellular activity (both neuronal and non-neuronal), and the universe, working with the categories of consciousness, self-consciousness, and unconsciousness.
- Something decided at the cellular level about enzyme production is not the same level as the consciousness to move your arm at organismic level. A conscious decision at the cellular level can be an unconscious decision elsewhere.
- On the basis of our results, it seems that contrary to the general view, evolution is primarily the evolution of tacit consciousness, not the information processing of self-consciousness.

*NeuroQuantology* 2013 V11 4 607-617 607
Grandpierre, Chopra, A et al., Multidisciplinary approach to mind and consciousness.

**How to decrease Fear and instill Hope**

- Cancer diagnosis and its prolonged and invasive treatments take the ability away from the patients to enjoy life[3,4] and increase their spiritual needs.[5] Spirituality is associated with both culture and religion and influences our understanding of health and disease.[6] In the case of a life crisis, spirituality arises as a serious issue for both patients and their families.[7] In other words, spirituality is a dimension through which cancer patients can fight the sense of fear and loneliness throughout their disease.[8] because spiritual and religious faith creates a kind of world view which is associated with optimism and hope.
- Importance of addressing this in the oncology and hospital setting whether through nurse training or available clergyman.

Experiences of patients with cancer and their nurses on the conditions of spiritual care and spiritual interventions in oncology units
Relaxation Response – Changes Gene Expression

- Reduced cortisol, increased QoL, increased natural killer cell activity and decreased interleukin secretion in women recently diagnosed with early stage breast cancer (Witek-Janusek et al., 2008)
- "Relaxation causes multiple gene-expression changes that create mitochondrial resilience by stabilizing key cellular processes during the adaptation to oxidative stress, enhancing cell survival and function.
- Increased benefit seen in long term practitioners
  - Meditation Benefits Genes (Bhasin MK et al. PLoS ONE 2013 May 1)
- Meditators Show a range of genetic and molecular changes (Epigenetics)
  - Altered levels of gene regulating machinery
  - Reduced levels of pro-inflammatory genes
  - Faster physical recovery from a stressful situation
  - Changes observed in genes that are the current targets of anti-inflammatory and analgesic drugs (Histone Acetylation and Cox inhibition)
  - Rapid Change in Histone Acetylation and Inflammatory gene Expression in Expert Meditators (Psychoneuroendocrinology, 2014;40:96)

Meditation continued

- "Our analyses might suggest that a relationship exists between the total number of MBSR teachers per state and the total number of years of general meditation practice per state, and colorectal and cervical cancer incidence"
- This descriptive study represents a first step in an important line of research exploring the potential relationship between long-term meditation, stress, and cancer incidence. Despite its limitations, this study is an important addition to the literature on meditation and health, as it is the first to examine the relationship between meditation and cancer from a geographic perspective.
  - Breast vs cervical cancer
  - BMC Complement Altern Med. 2015; 15: 24

SPIRITUALITY – SPONTANEOUS HEALING

- Dying To Be Me, Anita Morjani
  - "I decided to return when I realized that heaven – or nirvana – is a state and not a place. I now know that I can experience Heaven right here and right now."
- Radical remission, Kelly Turner, Ph.D.
  - Most common hypotheses for why radical remission might occur
    - Radically changing their diet
    - Taking control of your health
    - Following your intuition
    - Using herbs and supplements
    - Releasing suppressed emotions
    - Increasing positive emotions
    - Embracing social support
    - Deepening your spiritual connection
    - Having strong reasons for living
Vibrational Healing

  - “In every culture, in every corner of the globe, the ancients told stories of sound and song and the spoken word to explain how humankind was delivered into existence.”
  - “It’s amazing to think of our glands, organs, tissues and cells as storage places for emotion and memory. Candace famously stated that “Your body is your subconscious mind. Our physical body can be changed by the emotions we experience.”

Candace Pert, pHD

- We’re not static beings, we’re always making new cells, even as we’re just sitting here. At any time, no matter how much old training and programming you may have, you always have the potential to literally change your mind.
- Each cell in our body is constantly vibrating, often in several different shapes, and our receptors vibrate as well. It’s a dance that’s constantly taking place in our bodies, and every cell is talking to every other cell in a rhythmic, ongoing way. In fact, the frequencies of your cells are even in sync with the audible sounds around you, which is why music and words can be very healing. Every cell is a mirror. One great way of feeling good is to eliminate the excess static in your life, and the antidote for negativity in our lives is positive affirmations. Research has shown that neurons are strengthened by repeated phrases and empowering words.

Spirituality - Conclusion

- The Divine Principle of Love may be used to eliminate every sorrow, every infirmity, every harsh condition, and every lack that harasses humanity. With the right understanding and use of the subtle and illimitable influence of love, the world may be healed of its wounds and the sweet mantle of its heavenly compassion may cover all inharmony, ignorance and all mistakes of mankind.
CONCLUSION

- The healing Power of Nature
  (Via Medicatrix Naturae)
- Doctor as Teacher
  (Docere)
- Treat the Whole Person
- First do no harm
  (Primum Non Nocere)
- Identify and Treat the Cause
  (Tolle Causam)
- Prevention