Cancer: Protocols for Navigating the Biological Terrain

Presented by: Dr. Ronald L. Stram & Dr. Heidi S. Puc
Biological Terrain involves:

- The in-depth study of the micro-cellular environment in the human body, the nutrient-filled environment that bathes and nourishes those cells.
- Testing for nutritional / vitamin optimization
- Genetic predispositions, inflammatory markers, immune status and possible environmental toxic exposure and how they influence acute and chronic disease states.
- Biological Terrain closely monitors cellular environment to gather important information about an individual’s cellular health.
- Appreciating the vital role a healthy biological terrain environment plays in establishing and supporting an individual’s overall state of health, vitality and well-being.
The Healing Powers of the Biological Terrain

- **Oxidation**: Oxidation creates free radicals in the body that damage DNA like unguided missiles. Keeping antioxidant levels in the body at optimal levels helps to minimize and control oxidation.

- **Inflammation**: Inflammation damages cells and organs, fuels pain, stimulates disease progression and weakens the immune system.

- **Immunity**: A surveillance system for assessing harmful bacteria, viruses and mutated cells while assisting in recovery from illness, surgery, or cancer treatment that may harm the body.

- **Circulation**: Thicker blood increases risk of blood clots and encourages development of blood vessels to tumors and distant tumor sites (metastasis). A healthy circulation allows nutrients to circulate, nourishes the body avoiding disease progression.

- **Glycaemias**: Higher blood sugar fuels aberrant cell growth, dampens the immune system and encourages disease progression.
Beta carotene, Vitamin C, E, Selenium

- Anti-oxidants are essential to rebuilding tissue especially lung, gut, skin, and immune cells.
- These do not remove tumor tissue, they are used to assure good normal cell reproduction and protect from toxicity as well as to assure a well functioning immune system.
Antioxidants and Chemotherapy

- Of reviewed studies that reported effects of antioxidants on toxicities, there were 49 separate reports of decreased toxicities (40 significant), 39 reports of no differences and 3 reports of increased toxicity.

- Some antioxidants may have potential to decrease toxicities but this varies by the antioxidant and chemotherapy chosen. Glutathione has the highest number of studies and of positive results.

- Met Breast Cancer – 90 advanced, whole system integrative treatment, chemotherapy combined with aggressive antioxidant therapy

- Median survival: 38 mo’s vs 18 mo’s
Biological Terrain

The Tumor Microenvironment Plays a Key Role in Tumorigenesis and Progression

Bissell and LaBarge (2005)
Tumors as complex tissues

Figure 3. Tumors as Complex Tissues

The field of cancer research has largely been guided by a reductionist focus on cancer cells and the genes within them (left panel)—a focus that has produced an extraordinary body of knowledge. Looking forward in time, we believe that important new inroads will come from regarding tumors as complex tissues in which mutant cancer cells have conscripted and subverted normal cell types to serve as active collaborators in their neoplastic agenda (right panel). The interactions between the genetically altered malignant cells and these supporting coconspirators will prove critical to understanding cancer pathogenesis and to the development of novel, effective therapies.
Chemotaxis and Metastasis

Breast

- Clonal proliferation
- Invasion of local tissue
- Induction of angiogenesis

Blood vessel

- CXCL12
- Tumor
- Binding of CXCL12 and migration to normal tissue with high CXCL12 levels

Target tissue or organ

- CXCL12
- Tumor

Detachment

Migration and entry into circulation
Intratumor heterogeneity can lead to underestimation of the tumor genomics landscape portrayed from single tumor-biopsy samples and may present major challenges to personalized-medicine and biomarker development. Intratumor heterogeneity, associated with heterogeneous protein function, may foster tumor adaptation and therapeutic failure through Darwinian selection. (Funded by the Medical Research Council and others.)
Extrinsic pathway
- Inflammation or infection
  - Transcription factors (NF-κB, STAT3, HIF1α) activated in tumour cells
  - Chemokines, cytokines, prostaglandins (and COX2) produced by tumour cells
  - Inflammatory cells recruited
    - Macrophage
    - Eosinophil
    - Mast cell
    - Neutrophil
    - Myeloid-derived suppressor cell
  - Transcription factors (NF-κB, STAT3, HIF1α) activated in inflammatory cells, stromal cells and tumour cells
  - Chemokines, cytokines, prostaglandins (and COX2) produced
  - Cancer-related inflammation
    - Cell proliferation, cell survival and epithelial-mesenchymal transition
    - Angiogenesis and lymphangiogenesis
    - Tumour-cell migration, invasion and metastasis
    - Inhibition of adaptive immunity
    - Altered response to hormones and chemotherapeutic agents

Intrinsic pathway
- Oncogene activation
Human Microbiome

Systemic effect of the Gut Microbiota

- The human body has \( \sim 100 \) trillion cells; the gut has \( \sim 10 \times \) as many microorganisms with \( \sim 100 \times \) more genes
- Our gut microbiota has a symbiotic relationship
  - fermenting unused energy substrates
  - fending off harmful bacteria
  - training the immune system
  - regulating gut development
  - producing vitamins and hormones.
- Changes in the gut microbiome have been implicated in diseases from obesity to infections to cancer and graft-versus-host disease.

Sun and Chang (2014)
Eat ORGANIC!

Organic Food

Broccoli stimulates the production of phase two detoxification enzymes, glutathione transferase which protect against cancer.
Cruciferous Vegetables

- Isothiocyanate and Sulphoraphame in broccoli sprouts have 50 times the amount than mature plant.

- Extracts are effective in reducing incidence, multiplicity rates and development of breast cancer in animals.
Boost your immune system

1. ↑ intake of foods rich in Beta-Glucans
   - Compounds that can help ↑ your immune system:
     - Onions, garlic, mushrooms, oats, nutritional yeast

2. Limit saturated fat
   - May (-) Natural Killer Cells & T Cells (WBC’s)

3. ↑ Variety of plant based foods in diet

4. ↑ Exercise

5. Get adequate sleep & ↓ stress

http://illustratedbites.wordpress.com/2012/08/03/desktop-wallpaper-download/
The microbial organ: Essential for Health

- Beneficial Functions
  - 1) Gleaning ingredients from food and synthesizing nutritional factors, such as vitamins, anti-inflammatory proteins
  - 2) Detoxifying deleterious pesticides
  - 3) Development of a intestinal immune system
The microbial organ: Essential for Health

4) providing signals for epithelial renewal and maintaining gut integrity
5) secretion of anti-microbial products, which negatively select against pathogenic bacteria through.
The microbial organ: Essential for Health

- Microbes are selected by an inflammatory milieu by the bad micro-bugs ability to survive this environment,
- In contrast the beneficial micro-bugs cannot tolerate an inflammatory environment.
- Thereby allowing invasive bugs to maintain the inflammatory process and prevent the return of the beneficial microorganisms
- Leading to chronic disease.
Inflammation: The Heat

- **Inflammation Panel**

- **C-REACTIVE PROTEIN – HIGHLY SENSITIVE (Optimal: <1.0)**

- CRP is a sensitive marker of systemic inflammation. Researchers call it the “unifying theory” behind the major killers of our times. High levels of inflammation have been linked to increased risk of cardiovascular disease, diabetes, Alzheimer’s, Parkinson’s, and cancer.

- **Treatment:**
  - Omega 3’s, fish oil, bromelain, MSM, curcumin
Immune Support / Anti-inflammatory

- **ZINC (Optimal: 110-150)**
  - Functions as an intracellular signal molecule for immune cells, and helps control inflammation markers. A lack of sufficient zinc in the body has been linked to increased production of pro-inflammatory cytokines and oxidative stress. Normal zinc concentrations have been correlated with a decreased risk of pneumonia, and decreased chance of infection.
  - **If elevated:**
    - Zinc is readily found in animal protein, so reduce animal protein consumption and increase consumption of plant based foods
    - Limit intake to less than 25mg zinc daily
  - **If low:** Several foods contain small amounts of natural zinc, but likely a supplemental form of zinc will also be necessary.
    - Oysters – 13 mg per oyster
    - Pumpkin seeds, hulled – 2.1 mg per ounce
    - Green peas - 1.8 mg per cup
    - Pine nuts – 1.8 mg per ounce
    - Wheat germ – 1.3 mg per tablespoon
    - Pecans – 1.3 mg per ounce
    - Almonds – 1 mg per ounce
Circulation: Angiogenesis = blood vessel growth

- **MMP-9 (Optimal: <984)** Matrix metalloproteinase-9 is a marker that is related to normal tissue and development, such as embryonic development, ovulation, wound healing, etc. Inflammation markers often regulate its expression. MMP-9 is an enzyme that cancer cells use to degrade surrounding connective tissue and spread in the body. Elevated levels have been found to promote tumor growth, progression and angiogenesis.

- **If elevated:**
- Increase foods and supplements which help to inhibit angiogenesis, like green tea and foods rich in omega-3 (cold water fish, flax, walnuts, hemp seed)
- Consume foods rich in vitamin C – vitamin C acts as a natural inhibitor of degradation of connective tissue (MMP-9 is an enzyme that cancer cells use to degrade surrounding connective tissue and spread in the body)
Circulation: Angiogenesis = blood vessel growth

- Hypercoagulation Panel
- **Fibrinogen Antigen (Optimal: <350)**

Fibrinogen can cause increased platelet aggregation, hyper-coagulation, and excessive blood thickening. This increases risk for heart attack and stroke. Fibrinogen is the precursor for fibrin, which cancer cells may use to coat themselves to hide from the immune system. Fibrin also relays a signal to cancer cells to initiate angiogenesis and sets the stage for tumor growth and metastasis.

*If elevated:*
- Achieve and maintain a healthy weight
- Perform daily moderate-intensity aerobic exercise as recommended by your physical therapist
- Consume high omega-3 foods (cold water fish, walnuts, flax, omega-3 fortified eggs)
- Include garlic, onion, olive oil, green tea, and ginger in your diet
- Also include ferment soy (natto, tempeh, miso)
- Don’t drink alcohol
- Quit smoking

Get your homocysteine levels checked. Excessive homocysteine blocks the natural breakdown of fibrinogen by inhibiting the production of tissue plasminogen activator (tPA). Optimal homocysteine is <5.5.
## Cancer Fighting Foods

<table>
<thead>
<tr>
<th>Food</th>
<th>Component</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cruciferous--broccoli, cauliflower, brussel sprouts</td>
<td>Indoles, Isothiocyanates</td>
<td>Help detoxify estrogen in body</td>
</tr>
<tr>
<td>Grape, raspberry, strawberry, pomegranite</td>
<td>Ellagic Acid</td>
<td>Carcinogen scavenger and prevents alteration of DNA</td>
</tr>
<tr>
<td>Orange and yellow fruits and vegetables</td>
<td>Retinol, vit C, carotenoids</td>
<td>Anti-tumor, anti-oxidant</td>
</tr>
<tr>
<td>Green Tea, Berries</td>
<td>Catechins</td>
<td>Immune boosting, anti-oxidant</td>
</tr>
<tr>
<td>Tumeric</td>
<td>Curcuminis</td>
<td>Anti-oxidant, anti-inflammatory, cancer protection</td>
</tr>
</tbody>
</table>
STRATEGIES FOR CANCER PREVENTION
CASE 1: STACEY R.

- 49 perimenopausal white female, abnormal calcifications right breast on routine mammogram. Bx: DCIS, cribriform and papillary, ER+/PR+.
- MD recommends surgery, XRT, hormonal.
- Comes for IM consult, holistically minded, overwhelmed.
- PMHx: borderline HTN, hypercholesterolemia, torn meniscus, two prior nl vaginal deliveries
- All: environmental
- Meds: red yeast rice, mvi, occas xanax
STACEY R.

- FHx: no breast cancer, + heart disease
- SocHx: strained marriage; 2 supportive daughters, past 10 yr smoker, 2 glasses wine qd, stressful real estate business.
- Lifestyle: sedentary/packaged food with little cooking (time constraints), coffee throughout day; sweet tooth; high strung with anxiety.
INTEGRATIVE SUGGESTIONS

- DCIS standard approach: LP +/- XRT +/- hormonal, vs mastectomy; debate on overtreatment, as approaches have not changed survival, have not decreased incidence of invasive BC; wider excision will upstage some patients to invasive ds.

- Oncotype DX for DCIS may help.

- Recommendations: plant-based (crucifers), AI diet, iodine sufficiency, regular vigorous CV activity, minimize ETOH, add fish oil, curcumin, decaff green tea, Asian mushrooms, I3C (if not on Tam), calcium d-glucarate, check vit d and supplement, melatonin, minimize caffeine, mind-body therapies (breath, meditation, yoga, GI/hypnosis, PMR, essential oils); address importance of good sleep.
CASE 2: MONICA B.

- LP, SLNM: 2.8 cm tumor, 3/10 LN+
- 4 cycles AC, 4 cycles T, started H, and XRT
- MD rec. Tam vs Raloxifene prevention.
- Comes for IM consult to decide on hormone, wants “natural remedies”.
- PMHx: NIDDM, obesity, mild HTN
- All: PCN
- Meds: Januvia, Ambien prn, d/c’d OCP
MONICA B.

- FHx: aunt BC in 60’s, father prostate ca; DM
- SocHx: never smoked, occ ETOH, divorced, 3 teens, works nightshift in ER
- Lifestyle: fast food/sweet/salty, no exercise but busy in ER, fragmented daytime sleep
INTEGRATIVE SUGGESTIONS

- Difficult decision on Tam vs Raloxifene for prevention: significant risk vs benefit.

- Address obesity: need to achieve ideal BW if possible, regular CV exercise; discuss metformin’s antibreast cancer evidence, consider switch for DM; similar recommendations as DCIS case (vit d, fish oil, curcumin, DIM/I3C if not on hormone, calcium d glucarate, green tea); flaxseed lignans, ashwagandaha, night shift work correlates with BC risk; consider IV glutathione as detoxifier, could consider IV vitamin C and oral vit c; melatonin if switch to day job.
CASE 3: GWEN P.

- 73 postmenopausal white female librarian, noted worse arthritis pain back and hips, not improving with meds. Bone scan: mets in spine, ribs, hips. Mammo: 1 cm lesion right breast. Body CT -. Bx of bone: ca c/w breast primary, ER/PR strong +, HER2 -, grade 1-2. MD rec Letrozole and Zolendronic acid IV. Wants IM consult to “improve odds of more time with grandkids”.

- PMHx: OA, osteopenia, IBS, hyst. for fibroids, past benign breast bx

- All: none

- Meds: ibuprofen and naprosyn prn, calc plus D 600mg BID, baby asa
GWEN P.

- FHx: mother- BC in 80’s, uncle colon ca 60
- SocHx: widowed x 14 yrs, supportive son and daughter and 7 grandchildren, former librarian, never smoked; one gin/tonic before bed qhs
- Lifestyle: walks daily, eats little meat, tries to eat salad daily, likes breads and likes to bake and eat cookies; plays bridge with girlfriends weekly.
INTEGRATIVE SUGGESTIONS

- I agreed with the need for Letrozole and zolendronic acid. Needed for control of BC and to decrease fracture risk; biphosphonate also assists osteopenia.

- Recommend: AI diet rich in crucifers; high dose IV vitamin C can be given in conjunction (prooxidant effect); consider I3C/calcium d glucarate, curcumin, boswelia (arthritis), vit d, fish oil, green tea, melatonin; acupuncture if hot flashes with AI, as well as consider black cohosh
Curcumin as chemosensitizer: In addition to having direct anticancer effects, turmeric is both a chemo- and radiosensitizer. Extensive preclinical studies have shown that curcumin sensitizes tumors (i.e., makes them more susceptible) to different chemotherapeutic drugs including doxorubicin, 5-FU, paclitaxel, vincristine, cisplatin, vinorelbine, gemcitabine, oxaliplatin, etoposide, etc. This chemosensitization has been observed in cancers of the breast, colon, pancreas, stomach, liver, blood, lung, prostate, bladder, cervix, ovary, head and neck, and brain and in multiple myeloma, leukemia, and lymphoma. It also sensitizes to gamma radiation against a wide range of tumor types, while simultaneously protecting normal tissues from damage.

(Goel A, Aggarwal BB. Curcumin, the golden spice from Indian saffron [sic], is a chemosensitizer and radiosensitizer for tumors and chemoprotector and radioprotector for normal organs. Nutr Cancer. 2010;62:919-930)
GUT PROTOCOL

- One of the most important components to patients' success is a healthy gut
  - Reduces side effects from chemotherapy
  - L glutamine 3 gms
  - Increases patient compliance
  - Promotes healthy lifestyle
  - Improves absorption

- Probiotics are key! (both oral and rectal)

Probiotic Enema Protocol

Supplies Needed:

1 enema bottle - pharmacy OTC
Distilled water – pharmacy OTC
Vaseline or KY lubricating jelly – pharmacy OTC
VSL 3 ½ pack (450 billion) powdered packs – Stram center (or probiotic 225 full pack)
Orthobiotic capsule – Stram center (or Probiomax 30 1 cap)
Enterogenic capsule – refrigerated – Stram center (or Probiomax 100 1 cap – not refrigerated).

Enema Instructions:

The best time for taking an Enema is in the evening, just before bed.

Fill the fleet bottle so that there’s about 30-50ml (1-2 ounces) of distilled water in it. Into the 30-50ml (1-2 ounces) of fluid combine:

- Half a pack of VSL 3 or full pack of probiotic 225
- One (1) Orthobiotic/Probiomax 30 capsule opened
- One (1) Enterogenic intensive/Probiomax 100 capsule opened

Once mixed well, apply lubricant to the tip of the enema catheter for lubrication. (If not pre-lubricated).

Follow the posture recommended in the enema instruction booklet, and slowly insert the lubricated Enema catheter approx. ½ - ¾ of its length into the rectum and squeeze the bottle until all the liquid has been instilled. Try to retain for at least 20 mins.

Frequency:
Do once per day for 5 days (unless otherwise instructed by your practitioner).
Omega 3 fatty acids

- Weight gain and improved survival in severely ill patients with generalized malignancy.
- May have an inhibitory effect on breast & prostate cancer through reduction of cytokine production such as TNF.

- Cancer 82:395-402, 1998 Dietary omega 3 PUFA plus Vit E restore immunodeficiency and prolong survival for severely ill patients with generalized malignancy.
Melatonin

- Helpful in solid tumors.
- With cisplatin in NSC lung cancer used 10mg daily at 7pm. Improved one year survival.
- With tamoxifen in metastisized breast cancer 20mg daily at noon.
- With interleukin-2 in several types of solid tumors used 40mg melatonin.
- May modulate estrogen receptor expression
Mushrooms

Maitake, Reishi, Cordyceps

- Increase T and B cells and enhance phagocytosis (digesting) of tumor necrosis factor
- Increase NK cell function and stimulate other immune surveillance production
- Show anti-carcinogenic activity
- Can reduce adverse effects of radiotherapy and chemotherapy
Glutathione: Our Body’s Healing Agent

- Tri-peptide: glutamate, cysteine and glycine
- Primarily synthesized in the liver
- It is involved in DNA synthesis and repair
- Metabolism of toxins
- Immune system function
- Prevention of oxidative cell damage
- Intravenous Glutathione seems to help prevent chemotherapy toxicity
Anti-Oxidants

- **VITAMIN C (Optimal: >1.2)**
  - Vitamin C is a highly effective antioxidant that protects proteins, lipids, carbohydrates, and DNA from damage by free radicals that can be generated through exposure to toxins and pollutants. Vitamin C may also be able to regenerate other antioxidants such as vitamin E.

- *If low:* Consume plenty of good sources of vitamin C:
  - Acerola cherry juice – 1936 mg per ½ cup
  - Red bell peppers – 190 mg per cup
  - Guava – 189 mg per ½ cup
  - Kale, raw – 86 mg per cup
  - Orange – 83 mg per medium-sized fruit
  - Kiwi – 71 mg per medium-sized fruit
  - Broccoli, raw – 66 mg per cup
  - Papaya – 43 mg per ½ cup
Intravenous Vitamin C

- High dose (Ascorbate) Vitamin C used in conjunction with chemotherapy or radiation, reduces cancer cells in the early stages of cancer. For those in the later stages of cancer, the intravenous vitamin C protocol may improve the quality of life.

- Does oral vitamin C (ascorbate) provide the same results? **No.** Oral vitamin C is an antioxidant with controlled absorption. Intravenous vitamin C is a pro-oxidant drug that helps produce peroxide, which targets neoplastic cells while leaving normal cells unharmed. With IV dosing plasma and tissue levels are many times above that of oral dosing.
Intravenous Vitamin C

- **Safe Vitamin C Infusion and G6PD deficiency:** Patients must have a G6PD test before any infusions are given. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an inherited condition in which a person's body doesn't have enough of the G6PD enzyme. G6PD helps red blood cells function normally. Patients with this deficiency should not receive vitamin C infusions because it can cause hemolytic anemia.

- The protocol should NOT be administered in conjunction with methotrexate chemotherapy because of urine pH requirements.
IV Vitamin C: In Practice

- IV suite
Glutathione Use: In Practice

- Used as a treatment and as a diagnostic tool to establish active infection versus need for detoxification

- Under our current protocol, we initiate IV antibiotic treatment followed by glutathione and further detoxify with infrared sauna treatment.
www.Stramcenter.com
90 Adams Place Delmar, NY
518.689.2244
530 Main Street, Bennington, VT
802.445.3152