Cancer Care for the Whole Person: Nutrition, Exercise, and Genetics

Chris D’Adamo, PhD
Assistant Professor
University of Maryland School of Medicine
Center for Integrative Medicine
Part I: Nutrition and Cancer

• I. ) Reducing Chronic Inflammation

• II. ) Managing Metabolic Influences

• III. ) Enhancing Immune System Function

• IV. ) Maximizing Genetic Protection
Inflammation

• What is inflammation?
  – Response led by immune & vascular systems
  – Production of cytokines, prostaglandins, etc.
    • CRP, IL-6, IL-1β, TNF-α, and many others

• Acute inflammation
  – Short-term response to injury, infection, etc.
  – Characterized by pain, swelling, and redness
  – Beneficial... clears infection/heals tissue & resolves

• Chronic inflammation
  – Chronic response to ongoing injury, infection, & poor lifestyle!
  – Contributes to many chronic diseases
  – Encourages cancer growth
Inflammation & Cancer Survival

• Higher CRP associated with decreased survival
  • CRP (C-reactive protein) inflammatory biomarker
Inflammation & Cancer Prognosis

- Higher CRP also associated with worse outcomes
  - Fatigue and reduced quality of life
  - More toxicity during chemotherapy
  - Weight loss, anorexia/cachexia, and recurrence
Diet Impacts Chronic Inflammation

• Dietary fat has major impact on inflammation
  – Some fats inflammatory & some fats anti-inflammatory
    • “No-fat” and “low-fat” diets… bad advice!

• Inflammatory fats
  – Trans fats
    • Hydrogenated oils
    • Avoid at all costs!
  – Saturated fats
    • Some bad, some neutral, some good (lauric acid [coconut])
    • Avoid saturated fat from grain-fed meat, hydrogenated oils
  – Omega-6 fats
    • Need some (linoleic acid an Essential Fatty Acid)
    • Inflammatory when consume too much!
    • Grain-fed beef & eggs, corn oil, soybean oil, nuts, etc.
Diet Impacts Chronic Inflammation

• Anti-inflammatory fats
  – Omega-3 fats
    • EPA & DHA – oily fish, grass-fed beef, etc.
    • ALA – converted to EPA & DHA – nuts, seeds, etc.
    • American diet low in omega-3, high in omega-6!

• Colorful fruits & vegetables highly anti-inflammatory

• Sugar & refined carbohydrates highly inflammatory… AVOID!
Diet Impacts Chronic Inflammation

- Anti-inflammatory herbs & supplements
  - Many studied in cancer patients!
  - Fish oil
    - Preferable to flax (ALA to EPA/DHA conversion poor)
  - Boswellia
  - Quercetin
  - Zyflamend
Metabolic Syndrome & Cancer

• Common question: “Does sugar feed cancer?”

• High sugar intake → environment where cancer thrives
  – Highly inflammatory
  – Increases risk of abdominal obesity
  – Increases triglycerides
  – Increases blood glucose
  – Increases risk of insulin resistance
  – Contributes to high blood pressure

SUGAR INTAKE A MAJOR METABOLIC SYNDROME RISK FACTOR!!!
Metabolic Syndrome & Cancer

- Metabolic syndrome
  - aka "Syndrome X"
  - Several definitions… cluster of symptoms increase risk and worsen prognosis of heart disease, stroke, diabetes & cancer

<table>
<thead>
<tr>
<th>TABLE 1. ATP III Clinical Identification of the Metabolic Syndrome</th>
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</thead>
<tbody>
<tr>
<td>Risk Factor</td>
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<tr>
<td>---------------------------------</td>
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<tr>
<td>Abdominal obesity, given as waist circumference</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Triglycerides</td>
</tr>
<tr>
<td>HDL cholesterol</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>Fasting glucose</td>
</tr>
</tbody>
</table>
Metabolic Syndrome & Cancer

• Metabolic syndrome increases risk of many cancers
  – Breast, colorectal, prostate, etc.

• Cancer patients with metabolic syndrome suffer:
  – Increased risk of surgical complications
  – Increased risk of infection during cancer treatment
  – Greater risk of colon cancer recurrence
Survival by mean blood glucose among brain tumor (glioblastoma) patients

Metabolic Syndrome: Risk Factors

• Diet high in sugar and refined carbohydrates
  – Refined carbohydrates → increase blood sugar quickly

• Nutrient deficiencies
  – Vitamin D, chromium, magnesium, etc.
    • Cofactors for metabolic enzyme processes

• Physical inactivity
  – Low muscle mass, high fat mass → insulin resistance

• Poor stress management
  – Increases blood sugar, insulin resistance, highly inflammatory
Metabolic Syndrome: Protection
Metabolic Syndrome: Protection

**Herbs & supplements**

- **Cinnamon**

- **Glucommannan**

- **Chromium**

- **Magnesium**
  - Avoid oxide form… choose citrate, orotate, or chelated form
Metabolic Syndrome: Protection
Immune System & Cancer

- Immune system
  - Multiple organs
    - Thymus, bone marrow, spleen, lymph nodes, gut, etc.
  - Many different types of cells
    - T cells, B cells, macrophages, natural killer cells, etc.
  - Fights bacterial, viral, fungal, etc. infections

- Immune system also fights growth of tumor cells
  - Cancer = immune system dysregulation
  - Modulating immune system can improve cancer prognosis
Immune System & Cancer

• Nutritional modulators of immune system
  – Negative
    • Sugar & refined carbohydrates
    • Hydrogenated oils
    • Gluten (protein in wheat, barley, & rye)
    • Food allergies (dairy, soy, corn, eggs most common)
  – Positive
    • Herbs & spices
    • Probiotic-containing foods
    • Garlic, onions, shallots, etc.
    • Zinc, vitamin C, carotenoids… many other nutrients!

• Nutritional modulators of cancer
  – Vitamin D
  – Mushrooms
Vitamin D

• A uniquely important vitamin
  – Hormone-like activity (secosteroid)
  – Controls expression of over 200 genes

• Active in most biological systems
  – Musculoskeletal system
    • Classically emphasized role
  – Endocrine system
  – Nervous system
  – Cardiovascular system
  – Digestive system
  – Immune system
Sources of Vitamin D

• Sun exposure
  – UVB light converted to vitamin D3 in skin
  – D3 transported to liver, metabolized to 25(OH)D
  – 25(OH)D converted to calcitriol in kidneys
  – 10-20,000 IU from 30 minutes sun exposure
    • Only spring and summer if north of Atlanta

• Food and supplements
  – D3 from oily fish, eggs, butter, cheese, fortified milk/cereals
    • Vitamin D is fat-soluble… needs fat for absorption
    • 10-100 IU: depending upon source
  – Supplements deliver much higher doses… 5,000+ IU per pill
Vitamin D & Cancer

• Multiple mechanisms of action against cancer
  – Regulates blood sugar and insulin sensitivity
  – Decreases cancer cell growth
  – Stimulates apoptosis and promotes cellular differentiation
  – Activates expression of cancer protective genes
    • Elevated activated nuclear β-catenin through vitamin D receptor
Vitamin D & Cancer

• High serum vitamin D associated with lower risk of:
  – Breast cancer
  – Colorectal cancer
  – Pancreatic cancer

• Clinical trials
  – 77% risk reduction of all cancers with vitamin D & calcium
    • 1,100 IU vitamin D3 & 1,450 mg calcium
Vitamin D & Cancer

• Need more trials and studies in cancer patients
  – In meanwhile… test serum 25(OH)D!
  – Covered by most health insurance providers

• Vitamin D Council Goal: 40 ng/mL (100 nmol/L)
Mushrooms & Cancer

• Component of Traditional Chinese Medicine
  – Hundreds of medicinal mushrooms
  – Still common cancer treatment in Asia

• Mechanism against cancer
  – Polysaccharide α- and β-glucans stimulate immune system
  – Generally non-specific immune system stimulation
    • Helpful for many other conditions… not recommended in lymphomas

• Shiitake mushroom
  – *Lentinus edodes*
  – Activated Hexose Correlated Compound (AHCC)
    • α-1,4 glucans… innate & adaptive immune activity against cancer
Mushrooms & Cancer

• Maitake mushroom
  – *Grifola frondosa*
  – Contains 1,3 β D-glucans
  – Extract has anti-tumor activity

• Turkey tail mushroom
  – *Trametes versicolor*
  – Commonly used as adjuvant in Asia
    • Accounts for 25% cancer care cost in Japan
  – Antitumor effects in breast cancer
    • Polysaccharide krestin (PSK) extract
Genetic Influences on Cancer

- Many genes involved in cancer
  - Oncogenes
    - Promote cancer growth
  - Tumor suppressive genes
    - Suppress cancer growth

- Diet & lifestyle major impact on cancer gene expression!
  - Activation/inhibition of transcription factors, enzymes, etc.
  - Nuclear Factor-Kappa Beta (NF-κB)
  - Histone Deacetylases (HDAC)

NF-κB

- Nuclear Factor-Kappa Beta (NF-κB)
  - Transcription factor
  - Activated by poor diet, stress, injury, viruses, etc.
  - Regulates expression of hundreds of genes involved in cancer
    - Cancer's "Master Regulator"

Dietary Impact on NF-κB

- Poor diet activates NF-κB
  - Sugar, refined carbohydrates, hydrogenated oils, etc.

- Nutrient-dense foods deactivate NF-κB
  - Colorful vegetables & fruits, omega-3 fats, tea, herbs & spices
  - Especially **turmeric**
    - Contains polyphenol curcumin

- Curcumin potent inhibitor of NF-κB
Dietary Impact on NF-κB

- Curcumin potent anti-cancer effects
  - Hundreds of studies!
HDAC

- Histone Deacetylases (HDAC)
  - Enzymes involved in gene transcription
    - Including many cancer genes
  - Remove acetyl groups from histones that wrap DNA
  - Need balance of HDAC activity
    - When out of balance… promotes cancer growth
# HDAC Inhibiting Drugs

This table lists several HDAC inhibitors that are being tested in clinical trials for lymphoma.

<table>
<thead>
<tr>
<th>HDAC inhibitors</th>
<th>Research Name</th>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Drug Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAHA (suberoylanilide hydroxamic acid)</td>
<td>Vorinostat</td>
<td>Zolinza®</td>
<td>Small molecule</td>
<td></td>
</tr>
<tr>
<td>PXD101</td>
<td>Belinostat</td>
<td>--</td>
<td>Small molecule</td>
<td></td>
</tr>
<tr>
<td>SNDX-275 MS-275</td>
<td>Entinostat</td>
<td>--</td>
<td>Small molecule</td>
<td></td>
</tr>
<tr>
<td>LBH589</td>
<td>Panobinostat</td>
<td>--</td>
<td>Small molecule</td>
<td></td>
</tr>
<tr>
<td>FK228</td>
<td>Romidepsin (also called depsipeptide)</td>
<td>--</td>
<td>Small molecule</td>
<td></td>
</tr>
<tr>
<td>ITF2357</td>
<td>--</td>
<td>--</td>
<td>Small molecule</td>
<td></td>
</tr>
<tr>
<td>PCI-24781</td>
<td>--</td>
<td>--</td>
<td>Small molecule</td>
<td></td>
</tr>
<tr>
<td>Sodium phenylbutyrate</td>
<td>--</td>
<td>--</td>
<td>Small molecule</td>
<td></td>
</tr>
</tbody>
</table>

Dietary Impact on HDAC Expression

**Broccoli Sprouts**
One cup of broccoli sprouts inhibited HDAC by 70%!

**Many other foods inhibit HDAC…**
Brussels sprouts, onions, turmeric, grapes, etc.

- Genetic predisposition to cancer… not genetic fate!
  - Field of *nutrigenomics*… research interest at Center for Integrative Medicine
Antioxidant Supplements?

- Antioxidant supplementation during treatment debate
  - Cons: Interferes with treatment & reduces effect
  - Pros: Reduces side effects & improves treatment effect

- No clear answer in research
  - Systematic reviews: chemo not diminished & potential ↑ survival
  - Glutathione, melatonin, vitamin E, selenium, etc.

- Conservative approach
  - Avoid completely or stop day before, day of, day after treatment

- Antioxidant approach depends upon goal
  - Palliation (continue) or cure (conservative)
Part II: Exercise and Cancer
Exercise Recommendations

• Previous advice
  – Cancer treatment and recovery… REST
  – Rationale: treatment physically & psychologically draining

• Current advice
  – Cancer treatment and recovery… STAY ACTIVE
  – 2010 American College of Sports Medicine cancer guidelines
    • Follow CDC recommendations for healthy adults
      – Moderate-intensity physical activity ≥ 30 minutes ≥ 5 days/week
      – Vigorous-intensity physical activity ≥ 20 minutes ≥ 3 days/week
    • National Cancer Institute, American Cancer Society, etc.
Why Exercise with Cancer?

- Exercise decreases risk of many cancers
  - Colon, breast, lung, etc.

- Exercise improves outcomes & treatment side effects
  - Promotes healthy body composition
    - Prevents GI/brain cancers muscle loss & breast cancer fat gain
  - Increases energy and reduces anxiety
    - Fatigue common side effect of treatment
    - Endorphins improve mood
  - Reduces inflammation
    - Acute increase, but long-term adaptive decrease
  - Improves insulin sensitivity & regulates blood glucose
    - Reduces risk of metabolic syndrome
Why Exercise with Cancer?

- Exercise may reduce expression of oncogenes
  - Represses betaine-homocysteine methyltransferase 2 (BHMT2)
    - Gene involved in colon cancer

- More research needed
  - Only animal models so far
Exercise Improves Cancer Survival

- **Breast cancer**
  - 3-8.9 MET hrs/wk physical activity 20% decrease mortality
  - 9-14.9 MET hrs/wk physical activity 50% decrease mortality
  - MET levels achieved through *brisk walking*

- **Colon cancer**
  - 3 hrs/wk moderate physical activity
  - 63% decrease death risk
Exercise: What Type & How Much?

• No standard answer… varies by individual!
  – Overall health, strength, preferences, etc.

• First obtain medical clearance

• If new or uncomfortable with exercise
  – Seek personal trainer… experience with cancer survivors

• Begin with low-intensity exercise
  – “No pain, no gain”… not true!
  – Gradually increase frequency & intensity to comfortable level
Exercise: What Type & How Much?

• Exercise Intensity: Metabolic Equivalents (METS)
  – 1 MET = Amount of energy (calories) burned at rest

• METS and exercise intensity
  – Low intensity: 1.1–2.9 METS
  – Moderate intensity: 3–6 METS… *ideal range for most!*
  – High intensity: > 6 METS

• List of METS for essentially any physical activity
Exercise: What Type & How Much?

**FORMAL EXERCISE**

- **Intro Pilates class**
  - Level: 3.5
  - Duration: 30 min
  - Calories: 105-131
  - Best for: Lighter workouts and beginners

- **Walking 4.0 mph (very briskly)**
  - Level: 5.0
  - Duration: 30 min
  - Calories: 150-188
  - Best for: Lighter workouts and beginners

- **Weightlifting (vigorou)**
  - Level: 6.0
  - Duration: 30 min
  - Calories: 180-225
  - Best for: Harder workouts and experienced exercisers

- **Swimming front crawl (slow pace)**
  - Level: 8.0
  - Duration: 30 min
  - Calories: 240-300
  - Best for: Harder workouts and experienced exercisers

- **Boot camp / Calisthenics (vigorou)**
  - Level: 8.0
  - Duration: 30 min
  - Calories: 240-300
  - Best for: Harder workouts and experienced exercisers

- **Running 9:00 / mile**
  - Level: 11.0
  - Duration: 30 min
  - Calories: 330-413
  - Best for: Harder workouts and experienced exercisers
Exercise: What Type & How Much?

**AT HOME ACTIVITIES**

- **Sweeping carpet**
  - Calories: 99-124 cal
  - Duration: 30 min
  - Level: Better for lighter workouts and beginners

- **Gardening**
  - Calories: 120-150 cal
  - Duration: 4.0

- **Playing with dog (moderate)**
  - Calories: 120-150 cal
  - Duration: 4.0

- **Wash & wax car**
  - Calories: 135-168 cal
  - Duration: 4.5

- **Playing with Kids (vigorous)**
  - Calories: 150-188 cal
  - Duration: 5.0

- **Moving furniture**
  - Calories: 180-225 cal
  - Duration: 6.0
Exercise: What Type & How Much?

- Exercise Intensity: BORG Perceived Exertion
  - Based upon individual perception

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Nothing at all</td>
</tr>
<tr>
<td>1</td>
<td>How you feel sitting or simply standing</td>
</tr>
<tr>
<td>2</td>
<td>Weak</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>Exercise goal: How you feel when you walk or exercise</td>
</tr>
<tr>
<td>5</td>
<td>Strong</td>
</tr>
<tr>
<td>6</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Very Strong</td>
</tr>
<tr>
<td>8</td>
<td>How you feel when you really push yourself</td>
</tr>
<tr>
<td>9</td>
<td>Extremely Strong</td>
</tr>
<tr>
<td>10</td>
<td>All-out effort</td>
</tr>
<tr>
<td></td>
<td>You’re unable to go on</td>
</tr>
</tbody>
</table>
Exercise: What Type & How Much?

• Walking
  – Low impact, easy on joints, enjoy nature, socialize with partner
  – During winter… treadmill or mall
    • Walk on incline/stairs for added challenge!

• Swimming and water exercise
  – Low impact, easy on joints, improves strength and cardiovascular fitness
  – Start slowly… gradually increase intensity
  – Avoid if chlorine-sensitive
Exercise: What Type & How Much?

• Yoga or pilates
  – Strengthen muscles, improve flexibility, low impact, reduces stress
  – Classes available for beginners

• Group exercise
  – Start with gentle, low intensity
    • BodyFlow, etc.
  – If safe and comfortable, higher intensity
    • Zumba, etc.
  – Social element can be beneficial
Exercise: What Type & How Much?

- **Resistance Training**
  - Can use weights… but don’t need them!
  - Bodyweight resistance exercise many benefits
    - Safely build strength, improves flexibility, enhances mood, etc.
  - Hundreds of choices! Personal trainer can provide guidance
    - Choose personal trainer with experience training cancer patients

- Chair Squat
- Wall Push-Up
- Plank
Exercise Precautions with Cancer

- **Bone cancers**
  - Weight-bearing exercise more painful
  - Avoid
    - High impact exercises... jumping, step class, etc.
    - Obtain medical clearance for weight-training... light/moderate

- **Brain cancers**
  - Be vigilant of seizures, dizziness, etc.
  - Avoid
    - Very strenuous exercise
    - Valsava maneuver... holding breath ↑ intracranial pressure
Exercise Precautions with Cancer

• Peripheral neuropathy
  – Compromised balance & feeling in extremities
    • Consider seated exercise program
    • Make sure shoes fit well

• Low blood cell counts
  – Low white blood cells
    • ↑ infection risk… avoid crowded gyms or exercise when sick
  – Low red blood cells (anemia)
    • Avoid vigorous exercise… moderate/low intensity preferable
  – Low platelets
    • ↑ bleeding risk… noValsava, moderate/low intensity exercise
Exercise Precautions with Cancer

Concentrate on breathing… exhale when exert!
Summary: Nutrition, Exercise & Cancer

- **Nutrition**
  - Not just prevention… improves healthy survival!
    - ↓ inflammation & metabolic syndrome
    - ↑ increase immune function

- **Exercise**
  - Days of rest after diagnosis over… stay active!
    - Exercise increases survival & reduces treatment side effects

- **Mechanism**
  - Healthy lifestyle improves cancer gene expression
    - “Turns off” oncogenes and “turns on” tumor suppressing genes
Thank you! Questions?

Contact information: cdadamo@compmed.umm.edu