“Cancer Prevention in the 21st Century”

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“Fortify Your Life”
“Healthy At Home” and
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“God grant me the serenity to accept the things I cannot change; Courage to change the things I can; And wisdom to know the difference.”

Reinhold Niebuhr

Statistics

• In 2010, 1.6 million people were diagnosed with cancer.
• In 2030, estimated to increase to 2.3 million.
• Cancer rates are increasing globally, people being diagnosed at younger and younger ages.
• In US, one in four people will die from cancer.
• But many people survive the disease.
• >12 million people have survived cancer treatment and are looking to prevent cancer recurrence.

https://nccd.cdc.gov/uscs/toptencancers.aspx
Recommendations for Cancer Prevention WCRF/AICR

- Do not smoke or use tobacco products.
- Body Fatness – be as lean as possible within normal range of body wt.
- Physical Activity – be physically active as part of everyday life
- Foods and Drinks that Promote Weight Gain – limit consumption of energy-dense foods. Avoid sugary drinks
- Plant Foods – eat mostly foods of plant origin
- Animal Foods – limit intake of red meat, avoid processed meat
- Alcoholic Drinks – limit 2 serving/d men, 1 serving/d women
- Breastfeeding – mothers to breastfeed, children to be breastfed

Cancer Survivors – follow recommendations above

Alcohol and Cancer

- LACE (Life after Cancer Epidemiology) found women drinking more than half-serving of alcohol/day had 35% increased risk of recurrence and 51% increased risk of death due to breast cancer, especially if postmenopausal and obese.
- Women drinking ~1 serving alcohol/d had increased survival from colorectal cancer compared to non-drinkers.
- Mixed picture. Clear evidence moderate wine consumption has beneficial effects on CVD, longevity.


Diabetes, Inflammation, Cancer

- Poorly regulated blood sugar in diabetic patients is often accompanied by increased levels of chronic inflammatory markers, e.g., interleukin (IL)-1β, IL-6, and TNF-α; emerging evidence has highlighted activation of the immune response in the progression and development of cancer cells.
- Uncontrolled pro-inflammatory responses create a chronic inflammatory state, promoting a tumor-favorable microenvironment and potentially triggering immune over-activation and cancer growth.

Inflammation and Cancer

• Activation of NF-κB is vital for our body's ability to defend itself against infection and is a central mediator of inflammation.
• Many things activate NF-κB and when it is persistently “turned on” it induces genes that are responsible for increasing cell survival, proliferation, migration and invasion. It also turns down growth regulators (e.g., p53) that suppress tumor growth.


Factors That Drive Inflammation and Insulin Resistance

• Sedentary lifestyle, lack of exercise
• Pattern of central obesity
• Western-dietary pattern, high fructose
• Prolonged psychosocial stress
• Environmental exposures (smoke, toxins, chemicals)
• Alterations in oral and gut flora and intestinal permeability
**WCRF/AICR Recommendations to Reduce Cancer Risk**

- Be as lean as possible without becoming underweight.
- Be physically active for at least 30 minutes/d.

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**Obesity and Cancer: What is The Connection?**

- Fat cells, particularly those in the belly, produce and react to hormones and proteins that drive inflammation and insulin resistance, which promote cell growth. The more often cells divide, the more opportunity there is for cancer to develop.
- Waist measurements indicating increased risk:
  - 31.5 inches or more for women
  - 37 inches or more for men
- High risk:
  - 35 inches or more for women
  - 40 inches or more for men

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**Obesity and Insulin Growth Factors**

- Obesity is associated with multiple factors that may cause an increased risk for cancer and cancer-related mortality including insulin resistance, high blood sugar and insulin-growth factors (IGF).
- Elevated insulin increases tumor growth and aggressiveness.
- IGF-1 and IGF-2 have been identified as tumor promoters in multiple studies.


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**Estimated Cancers**

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Cancer Site</th>
<th>Cases Per Year</th>
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<tbody>
<tr>
<td>49</td>
<td>Endometrial cancers</td>
<td>21,300</td>
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<tr>
<td>35</td>
<td>Esophageal cancers</td>
<td>5,824</td>
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<tr>
<td>28</td>
<td>Pancreatic cancers</td>
<td>12,079</td>
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<tr>
<td>24</td>
<td>Kidney cancers</td>
<td>13,978</td>
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<tr>
<td>21</td>
<td>Gallbladder cancers</td>
<td>2,050</td>
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<tr>
<td>17</td>
<td>Breast cancers</td>
<td>35,540</td>
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<tr>
<td>9</td>
<td>Colorectal cancers</td>
<td>12,831</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>103,602</td>
</tr>
</tbody>
</table>

"Cancer Prevention in 21st Century"
Tumor Type

• The Women's Healthy Eating and Living (WHEL) trial found carbohydrate restriction associated with a striking five-fold reduction in breast cancer recurrence in 50% of subjects, specifically those whose tumors expressed the IGF-1 receptor.
• Unfortunately, IGF-1 testing of tumors is not yet a routine clinical practice.


Diet and Cancer

• Study > 2000 women confirmed “Western” diet increased breast cancer risk, while Med Diet rich in fruits, vegetables, legumes, oily fish and vegetable oils lowered risk of all breast cancer subtypes, particularly triple-negative tumors.
• Another review found strong evidence of a beneficial role of the Mediterranean diet on oral and pharyngeal cancer.
• High adherence to MD associated with a significant reduction in the risk of overall cancer mortality (10%), colorectal cancer (14%), prostate cancer (4%) and aerodigestive cancer (56%)

Fruits & Vegetables

- Diets rich in fruits and vegetables (5-9 servings/d) lower risk of cancers of the lung, mouth, pharynx, esophagus, stomach, colon, and rectum.
- May reduce risk of cancers of the breast, pancreas, ovaries, larynx, and bladder.

National Cancer Institute

Eat your Broccoli!

- The cruciferous vegetables include broccoli, cauliflower, cabbage, brussels sprouts, bok choy and kale. Rich in glucosinolates, indole-3-carbinol and, especially, isothiocyanates.
- Protective effect is strongest for cancers of the mouth, pharynx, larynx, esophagus, and stomach – though growing body of evidence suggests protection against breast, endometrial and cervical cancer.

Dark Leafy Greens

- Spinach, kale, romaine lettuce, leaf lettuce, mustard greens, collard greens, chicory and Swiss chard are excellent sources of fiber, folate and a wide range of carotenoids such as lutein and zeaxanthin, along with saponins and flavonoids.
- Research has found that the carotenoids in dark green leafy vegetables can inhibit the growth of certain types of breast cancer cells, skin cancer cells, lung cancer and stomach cancer.

The Allium Vegetables

- Garlic belongs to the Allium family, which also includes onions, scallions, leeks and chives.
- In an impressive number of published studies, the consumption of onions and garlic has demonstrated protective effects against stomach, prostate and esophageal cancer.
- For cancer protection, AICR experts suggest including garlic as part of a well-balanced diet.
Tomatoes & Lycopene

- The tomato’s red hue comes chiefly from a phytochemical called lycopene.
- Research has shown substantial and convincing evidence that foods containing lycopene probably protect against prostate cancer.
- In the laboratory, tomato components have stopped the proliferation of several other cancer cells types, including breast, lung, and endometrial.
- Cooked tomatoes are great way to get lycopene in diet.

Omega-6

- Linoleic Acid (LA)
- Arachidonic Acid (AA)
- Cytoskeletons
- Lipoxigenases

Omega-3

- α-Linolenic Acid (ALA)
- Eicosapentaenoic acid (EPA)
- Docosahexaenoic acid (DHA)

Dietary sources and general metabolic pathways for omega-6 and omega-3 polyunsaturated fatty acids, leading to pro-inflammatory and anti-inflammatory products respectively.


Canadians and Omega 3

• The Omega-3 Index indicates the percentage of EPA+DHA in red blood cell fatty acids.
• Canadian government found that the mean Omega-3 Index level of Canadians aged 20-79 was 4.5%.
• Levels higher for women, older adults, Asians and other non-white Canadians, omega-3 supplement users, and fish consumers; levels lower for smokers and people who were obese.
• Fewer than 3% of adults had levels associated with low CHD risk; 43% had levels associated with high risk.


Omega 3 and Prostate Cancer?

• SELECT trial raised concerns about potential link between omega 3s and increased prostate cancer/aggressive cancer.
• European Food Safety (EFSA) concluded, “there is no evidence for a role of EPA and/or DHA intake in the development of prostate cancer.”
• Also, “supplemental intake of EPA and DHA combined at doses up to 5 g/d does not give rise to safety concerns for adults.”


Seafood Calculator
www.ewg.org/research/ewg-s-consumer-guide-seafood/seafood-calculator

Dietary Fat and Cancer: Systematic Review

• No associations were found for prostate, esophageal, gastric, renal cell, bladder, lung, skin, or postmenopausal breast cancer by the total intake or types of dietary fat.
• There may be an association between total dietary fat and premenopausal breast cancer.
• Ovarian cancer there was limited suggestive evidence for a positive association with intake of saturated fats.

WCRF/AICR Recommendations to Reduce Cancer Risk

- Limit consumption of red meats (beef, pork, lamb) and avoid processed meats. Aim for no more than 18 ounces per week (10 ounces higher risk)

- Red meat refers to beef, pork and lamb – foods like hamburgers, steak, pork chops and roast lamb.
  
  - Studies show we can eat up to 18 ounces a week of red meat without raising cancer risk.

- Processed meat is red meat that is preserved by smoking, curing, salting or adding other chemical preservatives. Sausage, bacon, ham and lunch meats (such as bologna, salami and corned beef) are processed meats.
  
  - Evidence is convincing that processed meats raise risk of colorectal cancer. For every ounce and half of processed meat eaten per day, risk rises by 21%.

- Traditional Mediterranean diet low in processed foods and fructose.

  - High fructose consumption associated with increased intestinal permeability, elevated toll-like receptor 4, endotoxemia and development of non-alcoholic fatty liver disease.


Intestinal Permeability and Systemic Inflammation

- When lipopolysaccharide (LPS), endotoxin from membrane of gram negative bacteria in intestinal lumen, enters bloodstream it binds Toll-like receptor 4, inflammation is activated, changing insulin signaling and triggering inflammatory mediators.

- Chronic exposure to LPS may contribute to weight gain and type 2 DM. Obese people and diabetics have increased plasma LPS.

Pre and Probiotics

- Regulate/modulate immune functions, reduce risk of intestinal infection.
- Improve intestinal barrier functions, reduce metabolic endotoxemia.
- Induce hypo-responsiveness to food antigens.
- Improve glucose control and reduce inflammatory cytokines.
- Find evidence-based strains and dose:
  - www.usprobioticguide.com
  - www.scienceofprobiotics.ca

Vitamin D

- Necessary for calcium, magnesium, and phosphorus homeostasis; dentin, bony tissue synthesis; mineralization; and bone sufficiency.
- Review of 30 studies show that higher vitamin D status is strongly associated with better breast cancer survival.
- Review ~ 1,000,000 participants found each 10 ng/mL increment in blood 25(OH)D level conferred a 26% reduction in risk for colorectal cancer.
- MANY older individuals have low vitamin D, which leads to muscle weakness and lower back and hip pain.
- Obesity increases the risk of deficiency…

Endocrine Society Guidelines

“For clinical care, it appears that all current (testing) methodologies are adequate if one targets a 25(OH)D value higher than current cut points; for example, a value of 40 ng/ml (100 nmol/L) is without toxicity and virtually ensures that the individual’s true value is greater than 30 ng/ml (75 nmol/L).”


Green Tea
(Camellia sinensis)

- White, green, oolong and black teas contain polyphenols and flavonoids, particularly catechins.
- Dominant catechin in green tea is epigallocatechin gallate (EGCG), which exerts potent anti-inflammatory and antioxidant activity.

Green Tea in Cancer

- Potent inhibitor of NF-κβ and inducer of P53.
- Inhibits every step of carcinogenesis. Stimulates DNA repair and inhibits two proteins that promote tumor cell growth and migration — vascular endothelial growth factor (VEGF) and hepatocyte growth factor (HGF).


Green Tea and Prostate Cancer

- RDBPCT 60 men with high-grade prostate intraepithelial neoplasia given 600 mg of EGCG or placebo for 1 year.
  - 3% in EGCG group converted to prostate cancer versus 30% in placebo group.
- UK study: 199 men (~74 years age) localized prostate cancer, randomized to oral capsule containing pomegranate, green tea, broccoli, turmeric; or identical placebo for 6 months.
  - Median rise in PSA in supplement group was 14.7% as opposed to 78.5% in the placebo group (P=0.0008).

Turmeric
(*Curcuma longa* and others)

- Rhizomes provide bright yellow-orange culinary spice and dye.
- Yellow pigments = curcuminoids, one example is curcumin.
- Long history of medicinal use for respiratory, skin, digestive and inflammatory conditions in India.
- More than 65 clinical trials have shed light on its potential role in CVD, diabetes, cancer, fatty liver, arthritis, neuro/psych disorders.

**Curcumin**

- Beneficial effects on almost every known target or molecule involved in carcinogenesis.
- May prevent and be beneficial adjunctive treatment for colorectal cancer.
- Acts alone and synergistically with EGCG (green tea) to inhibit malignant changes in oral epithelium.


Mouthwash

- Turmeric mouthwash significantly reduced levels of radiation-induced oral mucositis at all time points.
- Lesser incidence of treatment breaks in first half of treatment schedule (P < 0.01) and reduced change in body weight (P < 0.001).

Absorption and Safety Issues

- Low aqueous solubility and rapid metabolism and elimination of curcumin have constituted major obstacles to clinical use.
- Nanoencapsulation, curcumin complexed with phosphatidylcholine, and inclusion of the black pepper alkaloid, piperine, enhance tissue distribution and bioavailability.
- Note: Piperine causes inhibition of CYP3A4 and at doses of 20 mg can cause clinically relevant drug interactions especially for drugs with narrow therapeutic indices.
- Dose generally 1200-1500 mg per day of turmeric extract standardized to 95% curcumin, taken in divided doses.


Curcumin Bound to Phytosome: Safer If Taking Medications

<table>
<thead>
<tr>
<th>Serving Size: Two Capsules</th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Servings Per Container: 60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two Capsules Contain:</td>
<td>Amount Per Serving</td>
<td>% DV</td>
</tr>
<tr>
<td>Curcumin Phytosome (Curcuma longa extract (root) / Phosphatidylycholine complex)</td>
<td>500 mg</td>
<td>*</td>
</tr>
</tbody>
</table>

Read the Labels Carefully

Ginseng
(Panax ginseng)
P(X Panax quinquefolius)

- Human studies in healthy people and clinical studies in patients with fatigue confirm the antifatigue property of P. ginseng.
- Most studies (both species) show positive influences on intellectual work capacity in normal subjects and those with decreased cognitive functions.
- Considerable variation in quality of product and dose recommendations. P. ginseng often standardized to ginsenoside levels (4-10%).

Cancer Related Fatigue

- *P. quinquefolius* may reduce the risk of moderate-severe respiratory infections in patients with CLL.
- Four RCT show that both species improve cancer-related fatigue. Largest study: 364 participants from 40 institutions.
- Randomized to receive placebo or 2000 mg/d of American ginseng for 8 weeks to determine effect on fatigue.
- *Ginseng* reduced fatigue by almost double that of placebo in those undergoing active cancer treatment. No discernible toxicities.
- Some experts recommend taking breaks every 12 weeks. Unclear if any clinical benefit or enhanced safety.

Herb-Drug Interactions

- No clinically significant drug interactions observed using approved CYP probe drugs and *P. ginseng* administered for 2 weeks in healthy volunteers.
- *P. quinquefolius* did not interact with indinavir (CYP3A4) in human volunteers.
- *P. ginseng* 1 gram/d for 6 weeks, no significant change in INR in patients on warfarin.

Supplement Facts

- **Serving Size:** 2 capsules
- **Serving Per Container:** 25
- **Amount Per Serving**
  - American Ginseng root (Panax quinquefolius)
  - 1000 mg*
- **Daily Value not established**

Benefits of Physical Activity

- Maintain healthy body weight and muscle tone.
- Reduces risk of heart disease and depression.
- Lowers risk of diabetes by enhancing skeletal uptake of blood sugar.
- American Cancer Society, *exercise may reduce risk of cancer by reducing insulin and insulin-like growth factors levels, associated with increased cell/tumor growth."
- Review of 73 studies found 25% average risk reduction for breast cancer amongst physically active women.
### Activity and Movement

<table>
<thead>
<tr>
<th>Activity</th>
<th>In 1 hour</th>
<th>In 30 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Running (1 mile in 12 minutes or 5 miles/hour)</td>
<td>560</td>
<td>295</td>
</tr>
<tr>
<td>Swimming (slow freestyle laps)</td>
<td>510</td>
<td>295</td>
</tr>
<tr>
<td>Walking (1 mile in 13 minutes)</td>
<td>460</td>
<td>220</td>
</tr>
<tr>
<td>Playing basketball</td>
<td>440</td>
<td>220</td>
</tr>
<tr>
<td>Weight lifting (vigorous effort)</td>
<td>440</td>
<td>220</td>
</tr>
<tr>
<td>Heavy yard work (chopping wood or clearing brush)</td>
<td>440</td>
<td>220</td>
</tr>
<tr>
<td>Swimming (slow freestyle laps)</td>
<td>510</td>
<td>295</td>
</tr>
<tr>
<td>Walking (1 mile in 17 minutes)</td>
<td>280</td>
<td>140</td>
</tr>
<tr>
<td>Weight lifting (general light workout)</td>
<td>220</td>
<td>110</td>
</tr>
</tbody>
</table>

Source: USDA, www.mypyramid.gov

### BPA and Estradiol

- BPA is an environmental estrogen used in the manufacture of polycarbonate plastics and epoxy resins used to make food and beverage packaging.
- BPA associated with increases in developmental disorders of the brain and nervous system in animals.
- FDA banned BPA in baby bottles and children’s cups in 2012.
- Bisphenol A may increase risk of uterine, breast and prostate cancer.

Canned Goods

- Canned goods are a significant source of BPA.
- Researchers at the Harvard School of Public Health found that volunteers consuming one serving of canned soup each day for five days had a more than 1,000% increase in urinary BPA concentrations compared with when the same individuals consumed fresh soup daily for five days.
- When possible, choose fresh, frozen or in glass.


Insecticides and Cancer

- Meta-analysis of 16 studies found childhood exposure to indoor residential insecticides associated with a significant increased risk of childhood leukemia and lymphomas.
- Positive but not statistically significant association also found for childhood brain tumors.
- Use integrated pest management.


Hormone Therapy for Women

- Benefits likely outweigh risks for symptomatic women before the age of 60 years or within 10 years after menopause.
- Symptom control is used to determine the minimum required dose for each woman (not hormone testing!)
- When balancing benefits and risks, dose, type and route of administration need to be considered.


Route and Type

- **Transdermal estradiol** has least effect on lipids and renin as it avoids first pass effect on the liver, permitting lower doses to be used.
- **Unopposed estrogen** does not significantly increase risk of breast CA.
- **Progesterone** or dydrogesterone is associated with lower risk of breast cancer and venous thrombosis compared to synthetic progestogens.
- If symptoms primarily urogenital, vaginal estrogen can be used with minimal systemic absorption.

HPV Vaccine

- An estimated 24,600 newly diagnosed cancers are attributable to the two high-risk HPV types targeted by all currently licensed HPV vaccines.
- Routine HPV vaccination at age 11 or 12 years; and vaccination for females through age 26 years and males through age 21 who were not adequately vaccinated previously.
- 2 doses if before 15th birthday, 3 doses if after.
- CDC, from June 2006-March 2014, ~67 million doses of HPV vaccines distributed and ~ 25,000 adverse events were reported; 92% were classified as non-serious.
- After careful review, none of these adverse events were any more common after HPV vaccination than among comparison groups.

www.cdc.gov/vaccinesafety/vaccines/HPV/index.html
https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm

Stress and Cancer

- While stress does not cause cancer, there is growing evidence that chronic stress can promote the growth of tumors that are already present.
- Studies clearly demonstrate that social isolation and depression promote tumor growth.
- Excess sympathetic tone caused by emotional stress, can decrease cancer survival.


Loneliness, Social Isolation & Your Health

- 148 studies on the effects of social isolation on health found it is:
  - As bad as smoking 15 cigarettes a day.
  - As dangerous as being an alcoholic.
  - As harmful as never exercising.
  - Twice as dangerous as obesity.

Call it a clan, call it a network, call it a tribe, call it a family. Whatever you call it, whoever you are, you need one.  
~ Jane Howard

Neuroplasticity

- Brain's ability to change its structure and function; regularly used neural circuits are strengthened and expanded, those rarely engaged are weakened and contract.
- Long-time meditators have greater activation of areas responsible for sustaining attention, processing empathy, integrating emotion and cognition, and perceiving the mental and emotional state of others.

Mindfulness Meditation Systematic Review

- A review of 47 clinical trials (n=3515) found that mindfulness meditation improved:
  - Anxiety
  - Depression
  - Pain

“There are voices which we hear in solitude …

but they grow faint and inaudible as we enter into the world.”

Ralph Waldo Emerson

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Letting Go…..

“Healing may not so much be about getting better, but about letting go, of all the expectations, all of the beliefs, and becoming who you are.”

— Rachel Naomi Remen, M.D.