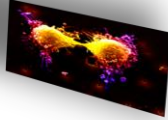


Cancer and nutrition



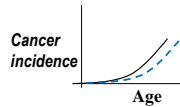
- Part 1: Dietary factors in possible cancer **prevention**
—a major cause of death in Canada & other developing countries after CVD
- Part 2: Dietary changes to moderate the **effects of therapy**

◆ **Cancer involves genetic and epigenetic changes that influence gene expression programs controlling cell growth, death, differentiation**

◆ **Some of these changes that lead to genomic instability can be influenced by diet and other environmental factors**

Generally speaking in this context, what is a **genoprotective diet**?

- low in harmful dietary factors
—substances that may cause cancer—carcinogens
- sufficient in protective dietary factors
—some vitamins, minerals, phytochemicals, e.g., folate (...T...DNA)

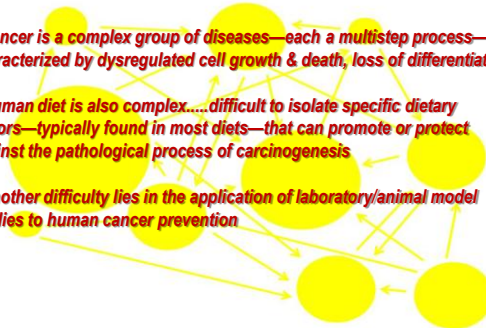


The role of nutrition in the etiology of cancers is not well understood; and some of the related studies are difficult to interpret...

...cancer is a complex group of diseases—each a multistep process—characterized by dysregulated cell growth & death, loss of differentiation

...human diet is also complex....difficult to isolate specific dietary factors—typically found in most diets—that can promote or protect against the pathological process of carcinogenesis

...another difficulty lies in the application of laboratory/animal model studies to human cancer prevention



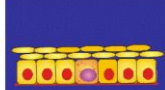
Carcinogenesis

• Stages

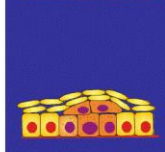
- **Initiation...**
DNA mutation
- **Promotion...**
mut. established & passed on...growth promotion of mutant cells
- **Progression...**
e.g., metastasis

MULTISTAGE PROCESS OF CARCINOGENESIS

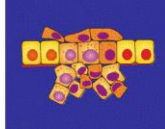
- INITIATION**
- damage of DNA
 - mutation induction in critical target genes
 - activation of proto-oncogenes
 - inactivation of tumor suppressor genes
 - cell replication and fixation of mutation



- PROMOTION**
- clonal expansion of initiated stem cells
 - development of benign tumor



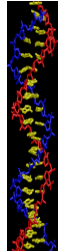
- PROGRESSION**
- altered expression of enzymes
 - proteolysis
 - adhesion & deadhesion
 - invasion
 - migration
 - metastasis

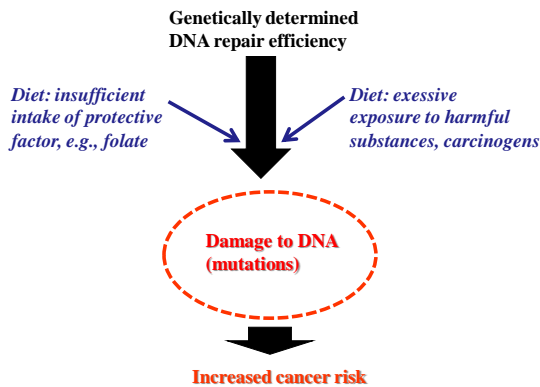


Some specific cancer-promoting events...bases for cancer

- **Damage to DNA (mutations)**
 - reactive chemical species, oxidative damage
 - non-oxidative, e.g., folate deficiency, or decr. efficiency of repair enzymes
- **Expression of cancer-promoting genes**
 - e.g., incr. oncogene exp. or decr. tumor suppressor gene exp.
- **Suppressed immunity**

- **Diet can have a role in all of these events**
 - e.g., deficiencies in antiox vitamins, folate, vitamin A, zinc, etc





- ~ 2/3 of cancers may be caused by environmental factors (?)...but not for many early-onset cancers
 - **dietary** (nutrient deficiencies, food carcinogens) & **non-dietary** (e.g., smoking)
 - main global causes: smoking, obesity, alcohol, infections, sunlight....

- **Dietary studies related to cancer: complex interpretations**
 - many chemicals in foods...some show (+) effects, others (-), when tested, often isolation (outside food context)
 - chronic nature of cancer development...long latency period, multi-step pathological process
 - applicability of animal/model studies ...purified chemicals often tested at relatively high (non-food) concentrations; animals may have different metabolism for chemical



- **Example study: cancers and human migration ...importance of environmental component**

- Japan relative to USA:
 - ↓ colon, ↑ stomach (↓ breast, ↓ prostate)
- Japanese after 2 generations in USA:
 - ↑ colon, ↓ stomach (↑ breast, ↑ prostate)



Grading system for estimating contribution of dietary (and other factors) to cancer prevention (from ACS):

- A1, best established (convincing evidence)**
- A2, probable benefit....A3...B...C...D**

Examples:

A1: avoiding overweight for colorectal, breast cancers; limiting alcohol for oral and esophageal cancer

A2: increasing fruit/veg intake for colorectal, lung, oral/esophageal cancers; limiting red meats for colorectal cancer



Energy balance

- ↓ **calories:**
 - ↓ *progression (experimental animals)*
- ↑ **BMI (obesity):**
 - ↑ *breast, colon, endometrial cancer risk*
- ↑ **exercise:**
 - ↓ *breast and colon cancer risk*
 - *is it the exercise itself...?*

Fat

- ↑ **dietary fat:**
 - ↑ *colon, breast, prostate cancer risk ?*
 - *is it fat directly or coincidentals?*

Protein

- ↑ **dietary protein**
 - ↑ *colon cancer risk with high red-meat consumption*
 - (*is it protein directly or other component of red meat or other coincidental?*)



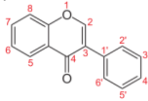
Fruits & Vegetables

--over 150 studies provide evidence for protective effects
 --high fruit & vegetable consumption: ↓ risk of many cancers by up to 2x ...why?

- **high fiber** (...controversy with colon cancer)
- **high nutrient density for vitamins/minerals**
- **phytochemicals**
- **coincidentals...?**



Some Phytochemicals...



- *Affect hormone action/metabolism/levels*
- *Decrease formation/ Increase elimination of carcinogens*
- *Prevent oxidative damage*
- **(Some phytochemicals may also promote carcinogenesis**
e.g., aflatoxins, furans, hydrazines, psoralens)



PHYTOESTROGENS

highest intake populations typically have lowest breast and prostate cancer risk

(is it the phytoestrogens directly or other aspects of high pe diets?)

*Note: phytoestrogen-rich foods **not** recommended for those with breast cancer...may promote growth*

Carcinogens and cancer promoters

...some examples and principles

When considering estimates of possible carcinogen risk for dietary compounds, should keep in mind...

- *Risk is not equal for everyone*
- *Risk is often determined in experimental systems that may not be fully relevant to human metabolism*
- *Risk is often determined using purified compound (out of food context)*



Alcohol

- **↑ alcohol:**
 - *↑ mouth/throat/esophagus cancer risk...also breast...*
 - *often synergistic with tobacco*
 - *consider also that malnutrition is common in heavy drinkers*

Possible food carcinogens may arise from

- Industrial chemicals used to treat foods, e.g., pesticides
- Environmental contaminants from air, soil, etc
- Food processing, e.g., colours, flavours
- Cooking, depending on method....

Cooking method

- smoke, grill, fry
 - (time...temperature...)
 - ↑ in potential carcinogens (PAHs, nitrites, heterocyclic aromatic amines, acrylamide, etc)



Major cancer-preventive recommendations for diet

- ↑ fruits/vegetables
- ↓ alcohol
- ↓ fat

Others...

- Healthy body weight
- Regular physical activity (protection from ox. stress?)
- Limit animal products such as red meats/nitrite-preserved meats/burnt or smoked or fried animal products

Cancer chemoprevention....phytochemicals, vitamins, minerals, etc....?

Nutrition and the Cancer Patient

Dietary management of the side effects of cancer and of its therapy



Some common side effects of chemotherapy and radiation:

- Nausea and vomiting
- Inflammation of tissues mouth and GI tract
- Taste alterations

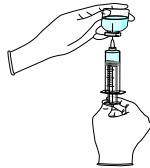
Cancer cachexia (wasting disease)

- ↓ weight & muscle mass
 - muscle protein breakdown
- also anorexia, anemia...
- not very responsive to extra nutritional support
- (role of TNF)



Nutritional care of cancer patient

- At time of diagnosis,
 - ~1/2 of patients exhibit weight loss, poor nutritional status
- Goal: correct nutritional deficiencies (vitamins, minerals, etc)
- Slow or prevent weight loss
- Does enhanced nutritional support ↑ survival?
- Another major goal...manage nutritional effects of cancer therapies



Some recommendations related to food intake and side effects of cancer therapy

- Nausea and vomiting: light, low-fat foods, cold liquids
- Mouth inflammation (stomatitis): liquid, soft, non-acidic foods
- Xerostomia, low salivation: high-moisture foods, broths
- Taste alterations: (a) hypogeusia: spicy or foods with strong flavour
 - (b) dysgeusia: assess bad-tasting foods on individual basis
- Early satiety: calorie-dense foods
- Immunodeficiency: safe (well cooked) foods

Also, uncommon foods given after chemotherapy may help prevent aversion to more common foods...

• **Implementation of nutritional management goals**

- **ORAL NUTRITION**....if able to eat (*PO, per os*)
 - use flavors/textures which the patient likes
 - identify and avoid foods not well digested by patient
 - choose best intake time
 - if possible, deal with emesis (*anticipatory, delayed, acute*)

- **ENTRAL** (tube in gut)
 - milk-based diets
 - soya-based diets
 - elemental/predigested-food diets

- **PARENTRAL** (i.v.)
 - used with nonfunctional GI
 - used with more aggressive chemotherapy, GI surgery