Food & Cancer Prevention
Diet can stop cancer before it starts

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UMR ENVTV-INRA Xénobiotiques: Aliments & Cancer
Lesson : http://Corpet.net/Denis
Cancers Kill
One Person out of Three

• 100 new colon cancer cases /day in France
  Half of them will survive, half will die But
  Prevention is possible:
  • Lung: 9 out of 10 (at least 90 to 95 %)
  • Colon : 3 out of 4 (60 to 80 %)
  • Breast : 1 out of 2 (35 to 50 %)
Number of Cancer Cases in France
& Survival at 5 Years (%)

Catherine HILL
IGR, 2005

Number of Cases diagnosed in France 2000
(Remontet et al. 2002)
Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective

Full Report Online (pdf)
http://www.dietandcancerreport.org
WCRF/AICR 2007 Report
Food & Prevention Cancer

• 1- Lean : Be lean (within normal BMI range)
• 2- Active : Be physically active (in everyday life)
• 3- Low Fat-Sugar: Limit energy-dense foods, no sugar drink
• 4- High Veggies-Fruits: Eat mostly foods of plant origin
• 5- Beef: little, Proces.meat: no Avoid processed meat,
  Limit red meat intake ( indiv.< 500 g/wk, group < 300 g/wk)
• 6- Low alcohol: Limit alcoholic drinks ( man/woman < 2 / 1 gl/d)
• 7- Low salt, no mould: Limit salt, avoid mouldy cereals
• 8- No Supplements: Meet needs through diet alone
• Mothers to breastfeed / Cancer survivors to follow the above 8s

Five year process: 19 methodologists, PANEL= 21 top-scientists,
100 Systematic Literature Reviewers /9 centers,
82 Peer Reviewers & External Contributors. 200 persons x 5 years!
World Cancer Research Fund
WCRF 2007 Expert Report

• 1- Lean
• 2- Active
• 3- Low Fat-Sugar
• 4- High Veggies-Fruits
• 5- Beef: low, Proc.meat: no
• 6- Low alcohol
• 7- Low salt, no mould
• 8- No Supplements
• Mother: breastfeed
• Cancer “survivors” same recommendations
### Summary of ‘convincing’ and ‘probable’ judgements

<table>
<thead>
<tr>
<th>Foods containing dietary fibre</th>
<th>Aflatoxins</th>
<th>Non-starchy vegetables</th>
<th>Allium vegetables</th>
<th>Garlic</th>
<th>Fruits</th>
<th>Foods containing folate</th>
<th>Foods containing lycopene</th>
<th>Foods containing selenium</th>
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</table>

**KEY**

- **Convincing decreased risk**
- **Probable decreased risk**
- **Probable increased risk**
- **Convincing increased risk**

1. Includes evidence on foods containing carotenoids for mouth, pharynx, larynx, foods containing beta-carotene for oesophagus, foods containing vitamin C for oesophagus.
2. Includes evidence on foods containing carotenoids for mouth, pharynx, larynx, and lung foods containing beta carotene for oesophagus, foods containing vitamin C for oesophagus.
3. Evidence is from milk and studies using supplements for colorectal.
4. Includes “fast foods.”
5. Convincing harm for men and probable harm for women for colorectal.
6. The evidence is derived from studies using supplements for lung.
7. Includes evidence on television viewing.

**FOOD, NUTRITION, PHYSICAL ACTIVITY, AND THE PREVENTION OF CANCER**

**OVERVIEW OF THE PANEL’S KEY JUDGEMENTS**

- **Lung**
- **Stomach**
- **Pancreas**
- **Liver**
- **Colorectum**
- **Bladder, prostate, and pancreas**
- **Ovary**
- **Endometrium**
- **Breast**
- **Kidney**
- **Skin**
- **Lung, breast, skin, and colorectal**
Cancer Mortality - France 1950-2010

Hill C, Doyon F, Jan P

- Men: Lung, Mouth, pharynx, larynx, oesophagus
- Women: Breast, Lung, Stomach, Colon, rectum et grèle

Taux pour 100 000, à âge égal [standard Europe]


Men: Lung, Mouth, pharynx, larynx, oesophagus

Women: 2x enlarged scale!
Cancer Death - Men - USA

*Age-adjusted to the 2000 US standard population.
Cancer Death, Women - USA

Rate Per 100,000


Lung - Poumon
Breast - Sein
Colon & rectum
Stomach
Uterus
Ovary
Pancreas

*Age-adjusted to the 2000 US standard population.
Some Cancers Disappear…

- **Stomach /Refrigerators:** more fruits, less salted meat, more hygiene *Helicobacter pylorii*
- **Head & Neck:** less liquor *bouilleurs de cru* (strong alcohol + cigarette)
- **Cervix (neck of the womb):** hygiene, cervical smear (Pap test) screening, HPV vaccine
Killer №1: Tobacco Smoke

- Cancers #1 (France & USA) are smokers cancers: Lung, throat, and others...

- We already know: NO smoking = NO Cancer
Cancers: Not Everywhere the Same

- Affluent Countries, 10 to 20 times more cancers (colon, breast, prostate) than southern countries
- Genetic? seldom
- Migrants catch cancers of welcoming land
Eat more fruits & vegetables:
- All epidemiological studies consistent
- Protection is certain, not « magical »
- Stomach cancers: 3 times less
- Colon, mouth: - 20%
- Breast, prostate: little protection
Fruits & Veg., OK, Which, How Much?

- All, and a lot
- At least five a day, that's 400 to 800 g/day
- All of them, varied: Colors & Tastes!

- Lycopen
- B-carotene
- Fолates
- Hesperidine
- Limonen
- Glucosinolates
- Isothiocyanates
- Sulforaphane
- Allyl-sulfides
Phytochemicals against Cancer? 
Evidence in Rodents

Diapo: Laurence Gamet-Payrastre

Anthocyanes des myrtilles diminuent tumeurs du colon

Glucosinolates brocoli diminuent tumeurs mammaires & coliques

Diallylsulfide de l'ail diminue le nombre de tumeurs colique

Polyphénols cacao bloquent carcinogenèse de la protaste

EGCG & caféine du thé diminuent tumeurs colon

Curcumine réduit les tumeurs côlon chez rats et souris

Resvératrol du raisin diminue tumeurs colon

Pectine citron réduit métastases prostate.
Pectine de pomme diminue cancers poumon & colon

Lycopene des tomates diminue les tumeurs coliques
What are the Protective Mechanisms?

1- Carcinogen trapping
2- Help to Detoxify
3- Block Proliferation (cell growth)
   Promote Apoptosis (cell suicide)

Polyphénols, Caroténoïdes, Vitamines C, E

Sulforaphane, Anthocyanes, DiallylSulfide, Flavonoides, Lycopène

- Glucosinolates
- Sulforaphane
- Flavonoïde
- Sulfide

Antioxydant

Elimination dans les urines

Inactivation Cancérigène
• Physical activity protects (breast, colon)
• Obesity & Sedentary increase risk (post-menopausal breast, colon, uterus endometrium)
• Mechanism: hormones (estradiol, insulin)

Recommendations
- Be lean, do not put weight
- Calories: Eaten = Burned
- Physical activity = 5 x 30 min /week (or more)
Body fatness & sedentarity convincing causes of colorectal & breast cancer

• Major hypotheses, mechanisms linked to hormones, growth-factors
• Abdominal fat = **insulin resistance** syndrome
• => insulin and IGF1 blood levels are raised.
• **Insulin & IGF1** = proliferation of cancer cells
  (*true at all cancer sites, promotion well demonstrated in colon cancer*)
FFA
Free fatty acids

IGFBP1 & 2
insulin-like
growth factor
binding proteins

Calle & Kaaks,
Nature Reviews Cancer 2004
Body fatness convincing cause of cancer breast (p.m) & uterus endometrium

• Post-menopause, body fat = major site of steroids aromatisation
• Obese women post-menopause have increased circulating oestrogens (oestradiol)
• Oestradiol promotes the growth of breast cancer cells (and uterus endometrium cells)
E1, oestrone => E2, oestradiol

deltaA4-androstenedione => T, testosterone

SHBG, sex-hormone-binding globulin

Calle & Kaaks
Nature Reviews Cancer 2004
Alcohol

There is *sufficient evidence* in humans for the carcinogenicity of alcohol consumption. Alcohol consumption causes cancers of the oral cavity, pharynx, larynx, oesophagus, colorectum, liver and female breast (IARC Monographs 2011)

- **Mouth, pharynx, larynx, esophagus**: e.g.,
  1.5 L wine per day = 20 times more cancer than 1 glass a day
- **Breast**:
  3 drinks/d = +50% risk
  10 g/d = +7-12% risk
- **Rectum**: beer
Alcohol, a convincing cause of head & neck cancers, colorectal cancer, breast cancer

- **Solvent** for tobacco smoke carcinogens
  potent synergy between cigarette smoking & strong spirit drinking

- Oxidized to carcinogenic **acetaldehyde**
  - Alcohol Dehydrogenase (genetic variability)
  - Gut bacteria A.D.ase : acetaldehyde level x1000/blood

- Induces folate deficiency, perturbs –CH₃ metabolism
- Induces lipid peroxides, free-radicals oxygen species
- Interferes with estrogen pathways and reduces immunity
Seitz & Stickel, Nature Reviews Cancer 2007
Fruits & vegs, physical activity, obesity, alcohol, tobacco: Known effects

& may be …

- Processed meat favors colorectal cancers
- Red meat too, but smaller effect

RR=1.25 for 125 g/d

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Red Meat, it is « good » because it is

- Grilled
- Fatty
- Protein (Nitrogen)
- Red
- Veg.deficient

Aloyau provencal, «l’art culinaire français», Flamarion 1976
Processed meat, more tasty and stable than fresh meat, also contains

- Salt - NaCl
- Nitrite - NaNO\textsubscript{2} & other additives
- Nitrosylated haem & other neoformed compounds
Five Hypotheses / Cancer Red & Processed Meat

• **H1- Red** myoglobin (with haem iron)  
  Red/Pink: free **Haem** & nitrosyl haem

• **H2- Nitrogen & Nitrite** =  
  endogenous amines, ammonia, &  
  N-nitrosated compounds (NOC)

• **H3- Cooking** ⇒ **Heterocyclic Aromatic Amines**  
  (HAA) & Polycyclic Aromatic Hydrocarbons (PAH)

• **H4- Fat** = too many calories, secondary bile acids

• **H5- Deficient** = not enough protecting agents  
  (calcium, phytochemicals)
H1: Red Meat contains
Myoglobin contains
Haem contains Iron
Haem iron
USA: heme, Fr: hème

- **Red meat** contains **myoglobin** (blood haemoglobin)
- **Haemin** induces hyperproliferation & cytotoxicity in rat, inhibited by calcium *(Sesink & van der Meer, 1999)*
- **Haem** induces PUFA oils peroxidation *(Sawa, 1998)*
- Haem loaded foods induces **NOC** formation in volunteers *(Cross & Bingham, 2002)*
- **Iron** (inorganic): No consistent effect on carcinogenesis
Vegetarian? No! (1)

• Fish protects?

Poultry beneficial?
Vegetarian? No (2)

- Red meat is **useful**: It brings iron and vitamin B12 (prevent anemia)
- But do not eat "only" meat, nor too much meat: inverse the meat/vegs ratio

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Blessed Fibers?

Fibers would protect

BUT

• Volunteers studies show NO effect of wheat bran supplements!

Fat would promote MAIS

• Volunteers studies show NO effect of low-fat diet!

Five randomized double-blind placebo-control studies, many years in hundreds of volunteers:

No effect of high-fiber low-fat diets

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Clinical Trials
Randomized, Placebo, Double-Blinded
Several Null Interventions

• Beta-Carotene & Alpha-Tocopherol (Vit. E): More Lung Cancers in B-caroten users for 3 years (+25% & +18%) CARET (USA) & ATBC (Finland)

• Low-fat & high-fiber diets:
  No effect on polyp recurrence 5 years later (Toronto, Brisbane, Alberts, Schatzkin….)

• Vitamin C & E: often tested, no effects!
Intervention Studies: Seldom Positives, but …

John Baron, 1999
- **Calcium**
  reduces intestinal polyp recurrence
  (2 g/d carbonate Ca++)
- Modest effect (-15%)

Larry Clark, 1996
- **Selenium**
  reduces several cancers incidence (200µg/j selenized yeast)
- Clear effect (-50%) but study not « on purpose »
- But SELECT 2009 contrasts!
  (purified selenomethionine 35500 men Se/vit.E)
Serge Hercberg's 2004
SUVIMAX Intervention Study

13,000 volunteers

- Daily pill with nutritional levels of vitamin C + vit. E + beta-Carotene + Zinc + Selenium
- One third less cancers in men
- Male mortality – 37%!
Carcinogen Potential of Foods
Can we rank carcinogens by potency?

Bruce Ames (Ames' test inventor)
& Lois Gold (Science 1992, La Recherche 1999)

- Data Base with ALL known rodents' carcinogens
  http://potency.berkeley.edu

- Dose-Effect TD$_{50}$: Tumor Dose 50% =
daily dose yielding a cancer in 50% rats or mice

- Can we extrapolate rodents data to humans?
  Compare eaten DOSE (in food),
  with carcinogenic dose (in rats)

- HE/RP: Human Exposure / Rodent Potency
## Carcinogen Potential of Foods

*Bruce Ames & Lois Gold (Science 1992, La Recherche 1999)*

**HE/RP:** Human Exposure/Rodent Potency, TD$_{50}$: Tumor Dose 50%

<table>
<thead>
<tr>
<th>Relative Risk</th>
<th>Daily Food</th>
<th>Carcinogen</th>
<th>TD$_{50}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HE/RP</td>
<td>intake g/d</td>
<td>intake /day</td>
<td>mg/kg/d</td>
</tr>
<tr>
<td>4,7</td>
<td>Wine (250ml)</td>
<td>Alcohol 30ml</td>
<td>9000</td>
</tr>
<tr>
<td>0,1</td>
<td>Mushroom (15g)</td>
<td>Hydrazines 10mg</td>
<td>200000</td>
</tr>
<tr>
<td>0,1</td>
<td>Apple (230g)</td>
<td>Cafeic acid 25mg</td>
<td>300</td>
</tr>
<tr>
<td>0,07</td>
<td>Mustard (5g)</td>
<td>Isothiocyanate 4,6mg</td>
<td>100</td>
</tr>
<tr>
<td>0,03</td>
<td>Spices</td>
<td>Safrole 1.2mg</td>
<td>60</td>
</tr>
<tr>
<td>0,03</td>
<td>Peanut butter (32g)</td>
<td>Aflatoxin 64ng</td>
<td>0,003</td>
</tr>
<tr>
<td>0,006</td>
<td>Fried bacon (85g)</td>
<td>diethylNitrosamine 85ng</td>
<td>0,02</td>
</tr>
<tr>
<td>0,005</td>
<td>Coffee (4g sec)</td>
<td>Furfural 630µg</td>
<td>200</td>
</tr>
<tr>
<td>0,002</td>
<td>AntiOxidant <em>(additive)</em></td>
<td>BHA 700 µg</td>
<td>600</td>
</tr>
<tr>
<td>0,001</td>
<td>Tap water (1l)</td>
<td>Chloroforme 83µg</td>
<td>90</td>
</tr>
<tr>
<td>0,0003</td>
<td>Carbaryl <em>(pesticide)</em></td>
<td>Carbaryl 2,6µg</td>
<td>14</td>
</tr>
<tr>
<td>0,0001</td>
<td>Fried Salmon (85g)</td>
<td>MelIQx 111ng</td>
<td>2</td>
</tr>
<tr>
<td>0,00008</td>
<td>DDE/DDT <em>(pesticide)</em></td>
<td>DDE 659ng</td>
<td>12</td>
</tr>
<tr>
<td>0,00006</td>
<td>Fried Hamburger (85g)</td>
<td>PhIP 176ng</td>
<td>4</td>
</tr>
<tr>
<td>0,000001</td>
<td>Lindane <em>(pesticide)</em></td>
<td>Lindane 32ng</td>
<td>31</td>
</tr>
</tbody>
</table>
### Natural Carcinogens, plants

- Ethyl alcohol, 30 ml
- Caffeic acid, 66.3 mg
- Mix of hydrazines, etc.
- Estragole, 3.8 mg
- 8-Methoxypsoralen, 1.28 mg
- Safrone, 1.2 mg
- Aflatoxin, 64 ng
- Symphytine, 38 μg
- Diethylnitrosamine, 85 ng
- Furfural, 630 μg
- Glutamyl p-hydrazino-benzoate, 630 μg
- N-nitrosopyrrolidone, 1.45 μg
- UDMH, 5.89μg (from Alar, 1988)
- Dimethylnitrosamine, 255 ng
- Hydroquinone, 160 μg
- Zinc, 487

### Processed-food Carcinogens, meat cooking

- Carbaryl: daily dietary avg
- Toxaphene: daily dietary avg
- Salmon, baked (3 oz; 85 g)
- Salmon, baked (3 oz; 85 g)
- DDE/DDT: daily dietary avg
- Hamburger, pan fried (3 oz; 85 g)
- Whole wheat toast, 2 slices (45 g)
- Hamburger, pan fried (3 oz; 85 g)
- Decofol: daily dietary avg
- Cocoa (4 g)
- Hamburger, 1
- Lindane: daily dietary avg
- PCNB: daily dietary avg
- Chlorobenzilate: daily dietary avg
- Chlorothalonil: daily dietary avg
- Folpet: daily dietary avg
- Captan: daily dietary avg

### Contaminant Carcinogens, pesticides

- PCNB (Quintozone), 19.2 ng (1990)*
- Chlorobenzilate, 6.4 ng (1989)*
- Chlorothalonil, <6.4 ng (1990)*
- Folpet, 12.8 ng (1990)*
- Captan, 11.5 ng (1990)*

### Ranking possible carcinogenic hazards: rodent carcinogens in the American diet (heterocyclic amines in italics)

<table>
<thead>
<tr>
<th>Possible hazard:</th>
<th>Daily human exposure</th>
<th>Human dose of rodent carcinogen</th>
<th>TD50 (mg/kg)</th>
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</thead>
<tbody>
<tr>
<td>HERP (%)</td>
<td></td>
<td></td>
<td>Rats</td>
</tr>
<tr>
<td>4.7</td>
<td>Wine (250 ml)</td>
<td>Ethyl alcohol, 30 ml</td>
<td>9110</td>
</tr>
<tr>
<td>0.3</td>
<td>Lettuce, 1/8 head (125 g)</td>
<td>Caffeic acid, 66.3 mg</td>
<td>284 (4970)</td>
</tr>
<tr>
<td>0.1</td>
<td>1 Mushroom (15 g)</td>
<td>Mix of hydrazines, etc.</td>
<td>20,300</td>
</tr>
<tr>
<td>0.1</td>
<td>Basil (1 g of dried leaf)</td>
<td></td>
<td>(29)</td>
</tr>
<tr>
<td>0.07</td>
<td>Mango, 1 whole (243 g; pitted)</td>
<td></td>
<td>(52)</td>
</tr>
<tr>
<td>0.07</td>
<td>Brown mustard (5 g)</td>
<td></td>
<td>(32)</td>
</tr>
<tr>
<td>0.06</td>
<td>Diet cola (12 oz; 354 ml)</td>
<td></td>
<td>(3)</td>
</tr>
<tr>
<td>0.06</td>
<td>Parsnip, 1/4 (40 g)</td>
<td></td>
<td>(17)</td>
</tr>
<tr>
<td>0.03</td>
<td>Saffrole: US avg from spices</td>
<td></td>
<td>(36)</td>
</tr>
<tr>
<td>0.03</td>
<td>Peanut butter (32 g; 1 sandwich)</td>
<td></td>
<td>(10)</td>
</tr>
<tr>
<td>0.03</td>
<td>Comfrey herb tea (1.5 g)</td>
<td></td>
<td>(49)</td>
</tr>
<tr>
<td>0.06</td>
<td>Bacon, pan fried (85 g)</td>
<td></td>
<td>(5)</td>
</tr>
<tr>
<td>0.05</td>
<td>Coffee, 1 cup (4 g)</td>
<td></td>
<td>(77)</td>
</tr>
<tr>
<td>0.03</td>
<td>1 Mushroom (15 g)</td>
<td></td>
<td>(2)</td>
</tr>
<tr>
<td>0.03</td>
<td>Bacon, pan fried (85 g)</td>
<td></td>
<td>(2)</td>
</tr>
<tr>
<td>0.02</td>
<td>Apple juice (6 oz; 177 ml)</td>
<td></td>
<td>(77)</td>
</tr>
<tr>
<td>0.02</td>
<td>Bacon, pan fried (85 g)</td>
<td></td>
<td>(2)</td>
</tr>
<tr>
<td>0.02</td>
<td>Coffee, 1 cup (4 g)</td>
<td></td>
<td>(77)</td>
</tr>
</tbody>
</table>

**/herp.html**

http://potency.berkeley.edu/herp.html

* /Google: Ames Gold HERP
Same carcinogen potency

One glass of wine
contains 13 g alcohol

150 bread baguettes
contains 200 mg furfural (weak carcinogen in crust)

7000 grilled beef steaks
contains 1 mg PhIP (potent carcinogen)

25 million apples pesticide-treated
contains 3 g Captan (pesticide in fruit skin)

Conclusions

• Yes, Fruits & vegetables, physical activity, protect against cancers.

• Yes, it is better not to gain weight, to eat little (processed) meat, to drink little alcohol, and to do not smoke at all

• This **halves cancer risk**: hard to believe but true!

• And everything else that you may read or be talked might be true, but is **not demonstrated yet!**
Conference is online
http://Corpet.net/Denis/

Bon appétit !

Denis E. Corpet
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