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Radiation Epidemiology

Discuss the overview of studies of populations exposed to ionizing radiation and its risks later in life. Populations covered will be patients exposed to diagnostic and therapeutic radiation, & workers exposed to ionizing and environmental radiation.

John D. Boice, Jr.
Vanderbilt University
28 July 2008
Outline – Radiation Epidemiology

• Overview
• Medical Exposures
• Environmental: Chernobyl, Hanford
• Radon (Miners, Home)
• Nuclear Workers

10 rad = 10 rem = 100 mSv = 0.1 Sv = 0.1 Gy
Epidemiology is the study of the distribution and determinants of disease in human populations

[ but not all studies are equal ]

(MacMahon and Trichopoulos, 1996)
### Types of Epidemiologic Studies

<table>
<thead>
<tr>
<th>TYPE</th>
<th>Intrinsic Quality</th>
<th>Susceptibility to Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td>Highest</td>
<td>Least</td>
</tr>
<tr>
<td>Cohort (Follow-up)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prospective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case-control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ecologic (Geographic)</td>
<td>Lowest</td>
<td>Most</td>
</tr>
</tbody>
</table>
Human Studies are the Basis for Cancer Risk Estimates

Nominal risk coefficients, radiation detriment, and tissue weighting factors

(A 105)
Radiation risk estimates are derived for incidence data for specific tumour sites when adequate dose response data are available from the Japanese Life Span Study (LSS), pooled analyses of multiple studies, or other sources.
No radiation-induced genetic diseases have so far been demonstrated in humans... estimates of risk have to be based on mouse experiments. United Nations, UNSCEAR 2001
# Sources of Human Data

## JAPANESE ATOMIC BOMB SURVIVORS

### RADIOTHERAPY - CANCER
- Cervical
- Endometrial
- Childhood
- Breast
- Hodgkin Lymphoma

### RADIOTHERAPY - NON-MALIGNANT
- Spondylitis
- Thymus
- Tonsils
- Menstrual Disorders
- Scalp Ringworm

### DIAGNOSTIC
- TB - Fluoroscopy
- Pelvimetry
- Scoliosis
- General

### RADIONUCLIDES
- Thorotrast
- I - 131
- Ra - 224
- Uranium
- P - 32
- Plutonium

### OCCUPATION
- Ra Dial Painters
- Miners (Radon)
- Radiologists
- Technologists
- Nuclear Workers

### ENVIRONMENT
- Chernobyl
- Weapons Fallout
- Natl Background
- Techa River
- Atomic Veterans
Radiation Reports and Committees

International ICRP 2007

United Nations UNSCEAR 2008

IARC-WHO

NAS – BEIR 2006

National NCRP
Limited Evidence Below 100 mSv (10 rem) – Judgment Needed

(ICRP Publ 103, 2007; NCRP Annual Meeting, April 2008).
There are some cancer sites for which there is little evidence for an association with radiation (e.g. pancreatic cancer, cutaneous melanoma, prostate cancer, non-Hodgkin’s lymphoma, Hodgkin’s disease and multiple myeloma),

and others where excess risks have only been seen following very high (radiotherapeutic) doses (e.g. cancers of the small intestine, rectum, uterus and kidney).
Radiation Epidemiology Dates Back 100 Years

- X-Rays Discovered 1895
- Skin/Bone Cancer
- Radium Dial Painters
- Thorotrast Imaging
- Radiologists
- A-Bomb Data
- Duffy Thyroid Cancer
- Medically Treated Populations
- Underground Miners (Radon)
- Nuclear Workers
- Chernobyl
- Cancer Survivors (therapy)
Bone cancer; no leukemia.
Breast cancer?
Bone Sarcoma Incidence in Radium Dial Painters (UNSCEAR 2000)

10 Gy suggested as a “practical threshold” for bone cancer

Bone Cancer, not Leukemia

1339 cases
No sarcomas

191 cases
46 sarcomas
Mayak Nuclear Weapons Plant
Mayak Nuclear Facility

-- First and largest nuclear weapons facility in the former Soviet Union

-- Began operations in 1948

-- Located in Ozyorsk, Russia near Chelyabinsk (near Urals)

-- Large exposures to both workers and general public, mostly in the 1940’s and 1950’s

Koshurnikova, Radiat Environ Biophys 41: 29, 2002
# Mayak - Plutonium - Bone

<table>
<thead>
<tr>
<th>Body Burden (Bq)</th>
<th>No. Cancers</th>
<th>P-Yrs</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 1480</td>
<td>6</td>
<td>162,540</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>1480 - 7400</td>
<td>1</td>
<td>15,614</td>
<td>0.9</td>
<td>0.1-5.5</td>
</tr>
<tr>
<td>&gt;7400</td>
<td>3</td>
<td>4,410</td>
<td>7.9</td>
<td>1.6-3.2</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiochemical</td>
<td>6</td>
<td>149,878</td>
<td>1.4</td>
<td>0.4-4.7</td>
</tr>
<tr>
<td>Plutonium</td>
<td>7</td>
<td>97,058</td>
<td>4.1</td>
<td>1.2-1.4</td>
</tr>
</tbody>
</table>


Threshold?
Abb. 1 Originalampulle "Thorotrast" (12 ml) der Firma Heyden. Daneben eine 25 ml Ampulle der Firma Fellows Testagar; dieses Präparat wurde nach 1947 nur für Tierversuche hergestellt.

Photo, courtesy of Dr. Gerhard van Kaick.
Thorotrast in Bone Marrow


Leukemia; not bone cancer
Liver Cancer – Thorotrast Patients

Enormous excess of liver cancer reaching a cumulative percent of 70%
# Leukemia

## Radiologists / Technologists

<table>
<thead>
<tr>
<th>Study</th>
<th>Years</th>
<th>Obs No.</th>
<th>Obs/Exp</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>British</td>
<td>1897-79</td>
<td>9</td>
<td>1.9</td>
<td>0.9-3.7</td>
</tr>
<tr>
<td>USA</td>
<td>1915-54</td>
<td>17</td>
<td>2.5</td>
<td>1.3-3.5</td>
</tr>
<tr>
<td>China</td>
<td>1926-85</td>
<td>34</td>
<td>2.4</td>
<td>1.3-4.1</td>
</tr>
<tr>
<td>USA Tech</td>
<td>1926-80</td>
<td>103</td>
<td>0.9</td>
<td>0.8-1.1</td>
</tr>
</tbody>
</table>

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**Early radiation workers**
DU ammunitions used during the Kosovo conflict
### 120,000 Uranium Workers – Cancer Risk

#### The Health Hazards of Depleted Uranium Munitions, Royal Society, London, 2001

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Total number of deaths</th>
<th>O/E (95% CI)</th>
<th>Estimated ratio of observed (O) to expected (E) deaths &amp; 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>33502</td>
<td>0.86 (0.79-0.93)</td>
<td></td>
</tr>
<tr>
<td>All cancers</td>
<td>7442</td>
<td>0.91 (0.85-0.97)</td>
<td></td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>365</td>
<td>0.76 (0.62-0.89)</td>
<td></td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>728</td>
<td>0.91 (0.78-1.04)</td>
<td></td>
</tr>
<tr>
<td>Liver cancer</td>
<td>123</td>
<td>0.84 (0.62-1.07)</td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td>2846</td>
<td>0.94 (0.83-1.05)</td>
<td></td>
</tr>
<tr>
<td>Bone cancer</td>
<td>30</td>
<td>0.93 (0.53-1.33)</td>
<td></td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>490</td>
<td>0.98 (0.89-1.07)</td>
<td></td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>196</td>
<td>0.83 (0.71-0.96)</td>
<td></td>
</tr>
<tr>
<td>Kidney cancer</td>
<td>151</td>
<td>0.78 (0.59-0.96)</td>
<td></td>
</tr>
<tr>
<td>Brain cancer</td>
<td>223</td>
<td>0.91 (0.65-1.17)</td>
<td></td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>7</td>
<td>0.38 (0.00-0.81)</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>266</td>
<td>0.82 (0.71-0.92)</td>
<td></td>
</tr>
<tr>
<td>Hodgkin’s disease</td>
<td>68</td>
<td>0.83 (0.61-1.06)</td>
<td></td>
</tr>
<tr>
<td>Leukaemia</td>
<td>295</td>
<td>0.90 (0.67-1.14)</td>
<td></td>
</tr>
<tr>
<td>All genito-urinary diseases</td>
<td>318</td>
<td>0.70 (0.54-0.87)</td>
<td></td>
</tr>
</tbody>
</table>

IARC 2001, UNSCEAR 2008: Uranium not an established human carcinogen
Leukemia in Patients With Cancer of the Cervix Uteri Treated With Radiation: A Report Covering the First 5 Years of an International Study

GEORGE B. HUTCHISON, M.D., Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts 02115

Reprinted from the Journal of the National Cancer Institute
JNCI 40:951, 1968

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
Cervical Cancer

Number: 30,000 women
Dose: 500-1500 rad (Marrow)

Leukemia
  Observed: 13
  Expected: 15.5
Risk: 0


Huge dose but no risk
Large doses to small volumes result in cell killing
But essentially whole body exposure at low doses
SECOND CANCER IN RELATION TO RADIATION TREATMENT FOR CERVICAL CANCER

From the International Radiation Study Group on Cervical Cancer

EDITORS
N.E. DAY and J.D. BOICE, Jr

IARC SCIENTIFIC PUBLICATIONS No. 52

LYON 1969
Characteristic wave-like pattern
Downturn at high doses
Long Minimum Latency

Time Response – Heavily Irradiated Organs

[Graph showing observed/expected ratio over years after cervical cancer treatment for exposed and nonexposed groups.]

Boice, JNCI, 1985;74:955
DOSE COMPONENTS OUTSIDE THERAPY BEAM

1 = HEAD LEAKAGE
2 = COLLIMATOR SCATTER
3 = SCATTER IN PATIENT FROM USEFUL BEAM
## Lightly Irradiation Sites - Cervical Cancer

<table>
<thead>
<tr>
<th>Second Cancer</th>
<th>Number Cases</th>
<th>Organ Dose (ave. GY)</th>
<th>RR at 1 Gy (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>338</td>
<td>2.0</td>
<td>1.69 (1.0 - 3.3)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>211</td>
<td>1.9</td>
<td>1.00 (0.7 - 1.6)</td>
</tr>
<tr>
<td>Liver</td>
<td>19</td>
<td>1.5</td>
<td>1.00 (0.7 - 1.3)</td>
</tr>
<tr>
<td>Kidney</td>
<td>134</td>
<td>2.0</td>
<td>1.71 (1.0 - 3.2)</td>
</tr>
<tr>
<td>Breast</td>
<td>838</td>
<td>0.3</td>
<td>1.03 (0.1 - 2.3)</td>
</tr>
</tbody>
</table>

Boice, JNCI, 1985;74:955
Boice, Radiat Res, 1988;116:3
Kleinerman, Cancer, 1995;76:442
RADIOThERAPY
DOSE TO CONTRALATERAL BREAST
# Breast Radiotherapy for Breast Cancer

## Table

<table>
<thead>
<tr>
<th></th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Subjects*</td>
<td>1.19</td>
<td>0.9-1.5</td>
</tr>
<tr>
<td>Time After Exposure (Yr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-9</td>
<td>0.99</td>
<td>0.7-1.4</td>
</tr>
<tr>
<td>≥10</td>
<td>1.33</td>
<td>1.0-1.8</td>
</tr>
<tr>
<td>Age at Exposure (Yr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td>2.26</td>
<td>0.9-5.7</td>
</tr>
<tr>
<td>35 -</td>
<td>1.46</td>
<td>0.9-2.3</td>
</tr>
<tr>
<td>≥45</td>
<td>1.01</td>
<td>0.8-1.4</td>
</tr>
</tbody>
</table>

*655 Cases, 1189 Controls


Risk after 10 years among young.
Example of age modification.

Confirmed in Stovall et al, IJROBP, 2008
Annex A. Epidemiological Studies of Radiation Carcinogenesis

Studies of Radiation-Induced Breast Cancer

Houston Thymic Irradiation Study

Canadian TB Fluoroscopy Study (Nova Scotia)

Stanford Hodgkin’s Disease Study

Massachusetts TB Fluoroscopy Study

Canadian TB Fluoroscopy Study (other provinces)

New York Acute Post-Partum Mastitis Study

UNSCEAR 1994, p. 155

Preston et al. Rad Res 2002
Lung Collapse for TB
## Breast
### TB - Fluoroscopy, Massachusetts

<table>
<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Nonexposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Women</td>
<td>2,573</td>
<td>2,367</td>
</tr>
<tr>
<td>Woman-Years at Risk</td>
<td>58,985</td>
<td>48,919</td>
</tr>
<tr>
<td>Breast Cancer Cases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observed (O)</td>
<td>147</td>
<td>87</td>
</tr>
<tr>
<td>Expected (E)</td>
<td>113.6</td>
<td>100.9</td>
</tr>
<tr>
<td>O/E</td>
<td>1.29</td>
<td>0.86</td>
</tr>
</tbody>
</table>


Lung
TB - Fluoroscopy, Massachusetts

Number Exposed: 6,285
Number Unexposed: 7,100
Lung Dose: 0.84 Gy (84 rad)
Observed Lung Cancer: 69
Expected: 86
RR (95% CI) 0.8 (0.6 - 1.0)

Davis et al, Cancer Res 49:6130, 1989

Not all tissues respond similarly to fractionation
### Heart

**TB – Fluoroscopy, Massachusetts**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number Exposed:</td>
<td>6,285</td>
</tr>
<tr>
<td>Number Unexposed:</td>
<td>7,100</td>
</tr>
<tr>
<td>Heart Dose:</td>
<td>~0.9 Gy (90 rad)</td>
</tr>
<tr>
<td>Observed Heart Disease:</td>
<td>826</td>
</tr>
<tr>
<td>Expected:</td>
<td>908</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>0.9 (0.8-1.0)</td>
</tr>
</tbody>
</table>

*Davis et al, Cancer Res  49:6130, 1989*

Heart not a low dose effect
Radiotherapy for Ringworm
5 treatments, 3-12 minutes each

Fig 1.—Five Treatment fields used in the Adamson-Kienbock treatment were positioned with the aid of a “cap” made from steel bands.
# Thyroid Tinea Capitis - Israel

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number Exposed</td>
<td>10,834</td>
</tr>
<tr>
<td>Number Nonexposed</td>
<td>16,226</td>
</tr>
<tr>
<td>Thyroid Dose (mean)</td>
<td>9 cGy</td>
</tr>
<tr>
<td>Observed Thyroid Cancers</td>
<td>43</td>
</tr>
<tr>
<td>Expected</td>
<td>10.7</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>4.0 (2.3 - 7.9)</td>
</tr>
</tbody>
</table>

Some Uncertainties …

• Effect primarily among immigrants, mainly from Morocco, not Israeli born (Ron, Rad Res 1989)

• “Irradiation for tinea capitis was given to many Jews in Morocco prior to immigration…” (Modan, JNCI 1980)

• Genetic susceptibility & family clustering (4 sisters thyroid disease)

• Wiggle could increase dose x 3

• Immigrants from Morocco came from Atlas Mt region, and diets deficient in stable iodine
Thyroid Cancer & External Radiation Risk
Dose Response by Age at Exposure

Ron et al, 1995
Pregnancy and Medical Radiation
### Oxford Prenatal X-ray Survey

<table>
<thead>
<tr>
<th>Cancer</th>
<th>No.</th>
<th>%</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphatic</td>
<td>2,007</td>
<td>14</td>
<td>1.5</td>
</tr>
<tr>
<td>Myeloid</td>
<td>866</td>
<td>14</td>
<td>1.5</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>719</td>
<td>13</td>
<td>1.4</td>
</tr>
<tr>
<td><strong>All Leuk/Lymphoma</strong></td>
<td>4,771</td>
<td>14</td>
<td>1.47</td>
</tr>
<tr>
<td>Wilms</td>
<td>590</td>
<td>15</td>
<td>1.6</td>
</tr>
<tr>
<td>CNS</td>
<td>1,332</td>
<td>13</td>
<td>1.4</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>720</td>
<td>14</td>
<td>1.5</td>
</tr>
<tr>
<td>Bone</td>
<td>244</td>
<td>11</td>
<td>1.1</td>
</tr>
<tr>
<td>Other Solid</td>
<td>856</td>
<td>15</td>
<td>1.6</td>
</tr>
<tr>
<td><strong>All Solid</strong></td>
<td>3,742</td>
<td>14</td>
<td>1.47</td>
</tr>
</tbody>
</table>

Biologically plausible to have same RR?

On the balance of evidence, we conclude that irradiation of the fetus in utero increases the risk of childhood cancer, that an increase in risk is produced by doses of the order of 10 mGy, and that in these circumstances the excess risk is approximately 6% per Gy.

Doll & Wakeford. Br J Radiol (Feb) 1997
It seems likely that the question of the association between fetal irradiation and childhood cancer will fade into medical history unresolved and remain a source of more confusion than enlightenment.

“Although the arguments fall short of being definitive because of the combination of biological and statistical uncertainties involved, they raise a serious question of whether the great consistency in elevated RRIs, including embryonal tumours and lymphomas, may be due to biases in the OSCC study rather than a causal association.”
Grounds for Uncertainty

1. A-bomb *in utero* study of childhood cancer is negative.
2. All cohort studies are negative — only case-control studies are positive and more susceptible to bias.
3. Biological Implausibility; equality of relative risks for leukemia and solid tumors.
4. Twins have lower risk than singletons despite more frequent x-rays.
5. Supporting animal evidence is weak.

Doll and Wakeford *Br J Radiol* 1997
Boice and Miller *Teratology* 1999
UNSCEAR 1994
MacMahon *NEJM* 1985
## Results of Obstetric-Radiation Cohort Studies

<table>
<thead>
<tr>
<th>Study</th>
<th># Irrad. Cancers</th>
<th>Total Cancer: RR (95% CI)</th>
<th>Leukemia: RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edinburgh/London (1)</td>
<td>9</td>
<td>0.86 (0.4-1.6)</td>
<td></td>
</tr>
<tr>
<td>UK National Cohort (2)</td>
<td>12</td>
<td>1.20 (0.6-2.5)</td>
<td></td>
</tr>
<tr>
<td>Chicago (3)</td>
<td>4</td>
<td>1.19 (0.4-4.0)</td>
<td>0.66 (0.1-5.0)</td>
</tr>
<tr>
<td>Baltimore (4)</td>
<td>13</td>
<td>1.05 (0.5-2.1)</td>
<td>1.62 (0.6-4.6)</td>
</tr>
<tr>
<td>US Perinatal Project (5)</td>
<td>7</td>
<td>1.09 (0.5-2.4)</td>
<td></td>
</tr>
<tr>
<td>Rochester, NY (6)</td>
<td>3</td>
<td>0.92 (0.3-3.1)</td>
<td></td>
</tr>
<tr>
<td>Combined Studies</td>
<td>48</td>
<td>1.12 (0.7-1.7)</td>
<td>0.98 (0.6-1.6)</td>
</tr>
</tbody>
</table>

Solid Cancer Incidence in Atomic Bomb Survivors Exposed In Utero or as Young Children

Dale L. Preston, Harry Cullings, Akihiko Suyama, Sachio Funamoto, Nobuo Nishi, Midori Soda, Kiyohiko Mabuchi, Kazunori Kodama, Fumiyoshi Kasagi, Roy E. Shore

Both the in utero and early childhood groups exhibited statistically significant dose-related increases in incidence rates of solid cancers.

The apparent difference in EARs between the two groups suggests that lifetime risks following in utero exposure may be considerably lower than for early childhood exposure, but further follow-up is needed.

J Natl Cancer Inst 2008;100:428–436
Conclusion – Prenatal

-- No individual dosimetry

-- Causal association questioned

-- Prudent to assume risk

-- Weak evidence that epidemiology has detected excess cancers at exposures under 100 mSv (10 rem)
RADON AND LUNG CANCER RISK:

A JOINT ANALYSIS OF
11 UNDERGROUND MINERS STUDIES

NATIONAL INSTITUTES OF HEALTH
National Cancer Institute
Lung Cancer Dose Response in Miners

Remarkable consistency
11 UNDERGROUND MINER STUDIES
68,000 MINERS --- 2700 LUNG CANCERS

$RR = 1.0 + 0.0049 \times WLM$

Lubin et al, 1993

1 pCi/l ~ 0.2 WLM / yr.
Underground Miner Extrapolation

Model: \( RR = 1 + 0.0049 \times WLM \)

Concentration: 4 pCi/l (150 Bq m\(^{-3}\))

Exposure period: 30 years

Estimated RR: 1.15
# Domestic Case-Control Radon Studies

## United States
- New Jersey
- Missouri
- Iowa
- Connecticut
- Utah/Idaho

## Canada
- Winnipeg

## Europe
- Southwest England
- Western Germany
- Czech (cohort)

## Nordic Countries
- Sweden
- Finland

## China
- Shenyang
- Gansu

### Pooled
- Lubin (1997, 1999)
- North America (Krewski, 2005)
- Europe (Darby, 2005)
- China (Lubin, 2004)
- World (Darby, in progress)

---

Europe

Ave. home about 0.8 pCi/L or 30 Bq/m³

North America

Ave. home about 0.8 pCi/L or 30 Bq/m³


Krewski et al, *Epidemiology* 16:137, 2005
Indoor Radon Meta-Analysis - Lung Cancer


4 pCi/l = 150 Bq/m³
20,679 Physicians say LUCKIES are less irritating

I too prefer LUCKIES because...

Toasting removes dangerous irritants that cause throat irritation and coughing.

“It’s toasted”

Your Throat Protection—against irritation—against cough.
# Radiation Compared with Smoking

<table>
<thead>
<tr>
<th>RR Lung Ca</th>
<th>Cigarettes Per Day</th>
<th>A-Bomb Dose, Sv</th>
<th>Miners WLM</th>
<th>Radon Indoor Bq/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&lt; 40</td>
</tr>
<tr>
<td>4.6</td>
<td>1-9</td>
<td>3.4</td>
<td>735</td>
<td>4,500</td>
</tr>
<tr>
<td>7.5</td>
<td>10-19</td>
<td>6.1</td>
<td>1,325</td>
<td>8,100</td>
</tr>
<tr>
<td>13.1</td>
<td>20-39</td>
<td>(11.4)</td>
<td>(2,470)</td>
<td>(15,000)</td>
</tr>
<tr>
<td>16.6</td>
<td>40+</td>
<td>(14.7)</td>
<td>(3,180)</td>
<td>(19,600)</td>
</tr>
</tbody>
</table>

Smoking <10 cig / day equivalent to being high dose A-bomb survivor

Risk estimates from studies of radiation workers “are compatible with a range of possibilities, from a reduction of risk at low doses to risks twice those upon which current radiation protection recommendations are based …

Overall, there is no suggestion that the current radiation risk estimates for cancer at low levels of exposure are appreciably in error. Uncertainty regarding the size of this risk remains as indicated by the width of the confidence intervals.”

National Research Council, BEIR VII 2006, p. 320
81. … there are a number of studies of occupationally exposed persons, who generally receive low doses of ionizing radiation at low dose rates. For example, in the IARC 15-country study, average cumulative doses were 19.4 mSv, and fewer than 5% of workers received cumulative doses exceeding 100 mSv.

Fig 2 Excess relative risks per Sv for all cancer excluding leukaemia in cohorts with more than 100 deaths (NPP=nuclear power plants, ORNL=Oak Ridge National Laboratory)
113. The ERR for Canadian workers in the latter study appears to be unusually high and the lower confidence bound does not include the combined estimate; reviews of historic dose records have raised possible concerns about the completeness of dose records in one Canadian facility (AECL) that may have biased the Canadian ERR. This is currently being evaluated.

It should be stressed that there are substantial uncertainties in the risk estimates derived from the 15-country study.
ERR per Gy for 15-Country Study

Smoking a likely confounder

<table>
<thead>
<tr>
<th>CANCER</th>
<th>ERR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer **</td>
<td>1.85 ( 0.26, 4.0) **</td>
</tr>
</tbody>
</table>

** ERR 0.47 for Male A-bomb survivors

Exceptionally high risk for lung cancer at low doses suggests distortion by smoking as does increase in nonmalignant respiratory conditions (Wakeford JRP 2005)
Uncertainties – Recent Worker Study

-- Heterogeneity (significance depends on one country, Canada)

-- Lung cancer excess is very high & dominates cancer risk

-- Smoking confounding likely (Wakeford JRP 2005)

-- Leukemia risk no longer significant despite increase in study size of a factor of 4

-- Exclusions not clear: 25% because of monitoring (not detection) for internal radiation and others excluded because of SES (Japan, INEL, France) – not all monitored were excluded.
Figure 4.2.9 Distribution of surface ground contamination by Caesium-137 released in the Chernobyl accident (December 1989)
Thyroid Cancers in Children in Belarus

Some doses > 10 Gy; Shinkarev et al H Physics 2008
“Such a high incidence and short induction period have not been experienced in other exposed populations, and other factors have almost certainly affected the reported increase. These include screening bias, iodine deficiency and supplementation, both at the time of the accident and in following years, a possible genetic predisposition and the role of short-lived isotopes of iodine.”
Thyroid Cancer and Chernobyl
Mixed Radioiodines: High Dose, Low and High Rates

-- Increased thyroid cancer in children
-- Intense screening
-- Short-lived radioiodine exposures
-- Limited individual dosimetry
-- Diets deficient in iodine [associated with more active thyroid glands (mild goiter)] – enhance risk
-- K-Iodine supplementation
-- Caution in generalizing to other populations

United nations, 2000; IARC, 2001; Boice JNCI 2005, Boice Jama 2006
Hanford Thyroid Disease Study

-- Exposure 1944-1957 ("pure" I-131)
-- About 5,200 births in 1940-1946 selected
-- 3,440 examined 1992-97
-- Comprehensive dosimetry
  (17.4 rad ave.; <1-100+ rad range)

Davis et al. Final Report, 2002; JAMA 292:2600, 2004
The percentage of people with thyroid disease is the same, regardless of dose.
Yangjiang County, Guangdong Province, bordering on South China Sea, two regions with thorium-containing monazites.
## Natural Background

China, Thyroid

<table>
<thead>
<tr>
<th></th>
<th>High Background</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number examined</td>
<td>1,001</td>
<td>1,005</td>
</tr>
<tr>
<td>Thyroid dose (cGy)</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>Nodular disease</td>
<td>9.5%</td>
<td>9.3%</td>
</tr>
<tr>
<td>Single nodules</td>
<td>7.4%</td>
<td>6.6%</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>1.13 (0.8-1.6)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Thyroid Cancer</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Swedish Diagnostic I-131 (Scans)</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Number Exposed:</strong></th>
<th>24,010</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Years of Scans:</strong></td>
<td>1952-69</td>
</tr>
<tr>
<td><strong>Thyroid Dose:</strong></td>
<td>0.94 Gy (94 rad)</td>
</tr>
<tr>
<td><strong>Observed Thyroid Cancer:</strong></td>
<td>36</td>
</tr>
<tr>
<td><strong>Expected:</strong></td>
<td>39.5</td>
</tr>
<tr>
<td><strong>RR (95% CI):</strong></td>
<td>0.9 (0.6 - 1.3)</td>
</tr>
</tbody>
</table>


Study of Children Given Diagnostic Doses of I$^{131}$ (avg. 1 Gy)

Internal I$^{131}$: High Dose, Low Dose Rate

<table>
<thead>
<tr>
<th>County</th>
<th>No.</th>
<th>Observed</th>
<th>Expected</th>
<th>ERR/Gy</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>2,367</td>
<td>3</td>
<td>3.0</td>
<td>0.01</td>
<td>(−0.8, 1.9)</td>
</tr>
<tr>
<td>Germany</td>
<td>789</td>
<td>2</td>
<td>2.4</td>
<td>−0.14</td>
<td>(−0.9, 4.1)</td>
</tr>
<tr>
<td>USA</td>
<td>3,503</td>
<td>4</td>
<td>3.7</td>
<td>0.08</td>
<td>(−0.7, 1.8)</td>
</tr>
<tr>
<td>Total</td>
<td>6,659</td>
<td>9</td>
<td>9.0</td>
<td>0.00</td>
<td>(−0.6, 1.0)</td>
</tr>
</tbody>
</table>

All under 20 y; 1200 under age 5, expected excess ~40

Boice, JNCI, 97:703, 2005
Boice et al., H Phys, 90:431, 2006
## Comparisons of Thyroid Cancer Risk Estimates - Children

<table>
<thead>
<tr>
<th>Study</th>
<th>RR at 100 rad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical External (X-ray)</td>
<td>8.7</td>
</tr>
<tr>
<td>Medical Internal (I-131)</td>
<td>1.0</td>
</tr>
<tr>
<td>HTDS Internal (I-131)</td>
<td>1.7 (ns)</td>
</tr>
</tbody>
</table>

The non-significant (ns) estimate of I-131 risk for the Hanford population is 11 times lower than seen in childhood studies of external radiation

\[
\frac{(8.7-1)}{(1.7-1)} = 11
\]

I-131 may be 11 times less effective because…
## Overall Relative Risk

<table>
<thead>
<tr>
<th>Disease</th>
<th>Before Startup</th>
<th>After Startup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood</td>
<td>1.08</td>
<td>1.03</td>
</tr>
<tr>
<td>All Ages</td>
<td>1.02</td>
<td>0.98</td>
</tr>
</tbody>
</table>

A SINGLE RADIATION EXPOSURE OF SUFFICIENT SIZE IS SUFFICIENT TO ELEVATE CANCER INCIDENCE

THERE IS NO UNIQUE RADIOPHORENIC CANCER

MOST CANCERS ARE INCREASED, BUT THERE ARE NOTABLE EXCEPTIONS
ORGANS VARY IN SENSITIVITY

PERCENT INCREASE PER RAD DIFFERS

LEUKEMIA IS MOST PROMINENT
SHORT LATENT PERIOD
WAVE-LIKE PATTERN OVER TIME
SOLID TUMORS

LONG LATENT PERIOD
TEMPORAL PATTERN MAY FOLLOW NATURAL INCIDENCE (?)

AGE – THE MOST IMPORTANT HOST FACTOR

DOSE RATE INFLUENCES RISK


