Chernobyl: 
*Then and Now*

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“Accidents Happen”

- Windscale, UK 1957
- Three Mile Island, USA 1979
- **Chernobyl, USSR 1986**
- Fukushima, Japan 2011
“I want to bear witness…”

We lived in the town of Pripyat. In that town. There you are: a normal person. A little person. You’re just like everyone else – you go to work, you return from work. You get an average salary. Once a year you go on vacation. You’re a normal person! And then one day you’re turned into a Chernobyl person…”

Nikolai Kalugin

“Voices from Chernobyl,” Svetlana Alexievich

Fallout from Chernobyl
Radioactive Iodine (I-131)

• I-131 concentrates in the thyroid (thyroid dose >> doses to other organs)

• Contaminated milk the principal source

• Doses highest in children (small thyroid, high milk consumption)

Pasture-Cow-Milk Pathway
Radiation and Thyroid Cancer: What Was Known Then

• External radiation (gamma, x-ray):
  - effects in exposed children

• I-131 in diagnosis and treatment:
  - no increase in adult patients
  - data on children sparse
  - considered non-carcinogenic

• Hence limited countermeasures against I-131 in fallout

Time Trends Point to a Problem

<table>
<thead>
<tr>
<th>Year</th>
<th>Thyroid Cancer (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1981</td>
<td>0</td>
</tr>
<tr>
<td>1982</td>
<td>0</td>
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<td>1983</td>
<td>0</td>
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<td>1984</td>
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<td>1988</td>
<td>0</td>
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<tr>
<td>1989</td>
<td>0</td>
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<tr>
<td>1990</td>
<td>3</td>
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</tbody>
</table>

Case-Control Study in Belarus

<table>
<thead>
<tr>
<th>Dose (Gy)</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.3</td>
<td>64</td>
<td>88</td>
<td>1.00</td>
</tr>
<tr>
<td>0.3-0.9</td>
<td>26</td>
<td>15</td>
<td>2.38 (1.2, 4.9)</td>
</tr>
<tr>
<td>1+</td>
<td>17</td>
<td>4</td>
<td>5.84 (2.0, 17.3)</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Potassium iodide</th>
<th>Highest two tertiles of soil iodine</th>
<th>Lowest tertiles of soil iodine</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>3.5 (1.8, 7.0)</td>
<td>10.8 (5.6, 20.8)</td>
</tr>
<tr>
<td>Yes</td>
<td>1.1 (0.3, 3.6)</td>
<td>3.3 (1.9, 10.6)</td>
</tr>
</tbody>
</table>

Cardis E, et al., JNCI 2005

NCI Cohort Studies of Exposed Children in Ukraine and Belarus

≈ 13,000 in Ukraine (UkrAm) (mean dose 0.65 Gy)
≈ 12,000 in Belarus (BelAm) (mean dose 0.56 Gy)

Screened serially for thyroid disease using palpation and ultrasound

Tronko et al. 2006; Zablotska et al 2010; Brenner et al. 2011
Thyroid Cancer Prevalence: Ukraine

Conclusions from Analytic Studies of Exposure in Childhood/Adolescence

- Consistent 2-5 fold excess risk; greatest in those 0-4 y at exposure
- Risk remains elevated decades later
- Results similar to external radiation
- Uncertain findings for ID
Characteristic Histology:
Papillary cancer, solid subtype

Exposure to the Fetus

• I-131 readily crosses the placenta

• ~10-12 weeks of gestation, fetal thyroid fully active, rapid uptake from the maternal circulation

• Late in gestation, levels of iodine in fetal thyroid many-fold higher than maternal thyroid
NCI In Utero-Ukraine Study

- 2,682 mother-child pairs
- Mean fetal thyroid I-131 dose = 72 mGy (0-3,240 mGy)
- Screened for thyroid cancer, 2003-2006: 7 cancers, 1 hurthle cell neoplasm

EOR/GY=11.66, (P=0.12); suggestive, needs confirmation

Hatch et al. 2009; Likhtarev et al. 2011

Thyroid Cancer Morbidity and Mortality Due to Chernobyl

In the Most Affected Regions:

- ~ 6,000 cases of thyroid cancer
- 15 thyroid cancer deaths
Thyroid Cancer Morbidity and Mortality Due to Chernobyl

• Variable estimates of lifetime excess
  – 4,000 – 9,000 deaths (WHO, 2005)
  – 30,000-60,000 cancer deaths (Greens/EFA Party, 2006)
  – 93,000 cancer deaths (Greenpeace, 2006)

Infant/Childhood Leukemia

• ↑ reported among in utero exposed at distant sites – 1st in Greece – but subsequent studies found no clear relationship with level of contamination

• Case-control studies of childhood leukemia (serious methodological problems); inconclusive
Leukemia in Cohorts of Exposed Children and Adolescents in Ukraine and Belarus
Hatch et al. 2015; Ostroumova et al. 2016

<table>
<thead>
<tr>
<th>Country</th>
<th>N Observed</th>
<th>N Expected</th>
<th>SIR, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ukraine</td>
<td>5</td>
<td>2.6</td>
<td>1.92 (0.69,4.13)</td>
</tr>
<tr>
<td>Belarus</td>
<td>6</td>
<td>3.4</td>
<td>1.78 (0.71,3.61)</td>
</tr>
</tbody>
</table>

What We Know Now

• I-131 increases risk of PTC among those exposed in early life
• Effect of in utero/early life exposure on hematopoietic processes unclear
• 2 plant workers died in the immediate aftermath of the accident.

• High radiation doses to 134 plant and emergency personnel resulted in acute radiation syndrome (ARS), 28 near-term deaths.
Liquidators in Ukraine: NCI and RCRM

• Cohort of ~110,000 clean-up workers, 1986-1990

• Sent by various military and civilian organizations, for a variety of tasks

• Exposed mainly to low dose-rate external radiation (mean ~ 100 mGy)
Focus on Leukemia

• Bone marrow very radiosensitive

• Highest risk per unit dose of radiation among all radiation-induced cancers

• Shortest latency (2-5 y)

Leukemia Case-Control Study

• 137 cases, 866 controls

• Official dosimetry records poor, missing for 60% of subjects

• New time-and-motion method developed – RADRUE (Realistic Analytical Dose Reconstruction with Uncertainty Estimation)
Time-and-motion method (RADRUE)

Database of exposure rates (time and location)

Questionnaire:
-what did you do?
-when? and where?

Radiation exposure

Bone-marrow doses and uncertainties

Dose-Response Results

- All Leukemias:
  ERR/Gy = 1.26 (95% CI: 0.03, 3.58)
  Significant linear dose-response

- Non-significant positive dose-response:
  -CLL: ERR/Gy = 0.76
  -Non-CLL: ERR/Gy = 1.87

Zablotska et al. 2013
What We Know Now

- Risk from low dose/low dose rate exposure to external radiation comparable to A-bomb survivors with acute exposure
- Elevated risk for both CLL (previously considered nonradiogenic) and non-CLL, consistent with IARC study

Romanenko et al., 2008; Zablotska et al., EHP 2013

Thyroid Cancer in Early Liquidators

- Reports of increased risk of thyroid cancer in early cleanup workers, exposed to I-131:
  - 8-fold ↑ in male recovery workers
  - ERR/100mGy=1.38 in males, higher in females
  - SIR=350 for 1st cleanup mission in 1986

Prysyazknyuk A et al., 2007; Kesminiene A et al., 2012; Ostroumova E et al. 2014

- NCI/RCRM study in progress
Non-Cancer Effects in Liquidators

- Cataracts at 1Gy
  
  Worgul BV et al. 2007

- ? Cerebrovascular Disease
  (↑ at >150 mGy)
  
  Ivanov VK et al. 2006

Breast Cancer in Belarus and Ukraine

E Pukkala et al. 2006

<table>
<thead>
<tr>
<th>Period</th>
<th>Dose (mSv)</th>
<th>All women (3,255)</th>
<th>Women &lt;45 (759)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR, 95% CI</td>
<td>P-value</td>
<td>RR, 95% CI</td>
</tr>
<tr>
<td>1997-2001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5.0</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>5.0-19.9</td>
<td>1.14 (1.04,1.25)</td>
<td>0.005</td>
<td>1.16 (1.00,1.36)</td>
</tr>
<tr>
<td>20.0-39.9</td>
<td>1.17 (0.98,1.40)</td>
<td>0.08</td>
<td>1.01 (0.72-1.41)</td>
</tr>
<tr>
<td>40.0+</td>
<td>2.24 (1.51,3.32)</td>
<td>&lt;0.0001</td>
<td>3.33 (1.71,6.50)</td>
</tr>
</tbody>
</table>
Psychological Consequences

- In liquidators, depression and PTSD still elevated decades later

- Mothers of young children a high-risk group for depression, anxiety, PTSD

- Findings on cognitive/neuropsych effects in exposed children inconsistent, needs follow-up

* Bromet, Havenaar, 2011

Further Research Needed on:

- Leukemia in those exposed in early life
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- Thyroid cancer in exposed adults

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- Other solid cancers with long latency
- CVD (a major concern in radiation protection)
- Transgenerational effects
- Mental Health/Well-being
Post-Chernobyl: Some Lessons Learned

• Safer use of I-131 in dx and tx
• Need for multidisciplinary studies
• Risk communication important
• Prompt countermeasures (e.g., food restriction) critical

Fukushima: Reduction of Doses from I-131
Chernobyl: Sociopsychological Impact

- Radiation an invisible enemy
- Misinformation, mismanagement
- Ecological and socioeconomic disruption
- Restrictions on social/cultural practices
- Chernobyl “victims”

“I started wondering what’s better – to remember or to forget.”

I’ve wondered why everyone was silent about Chernobyl, why our writers weren’t writing much about it – they write about the war, or the camps, but here they’re silent…If we’d beaten Chernobyl, people would talk about it and write about it more. Or if we’d understood Chernobyl. But we don’t know how to capture any meaning from it….We can’t place it in our human experience or our human time-frame.

So what’s better, to remember or to forget?”

Yevgeniy Brovkin

“Voices from Chernobyl”
Thank you for your attention

Genomics of Thyroid Cancer After Radiation Exposure

Survey of genetic changes using WGS
- *de novo* mutations
- minisatellites

Radiation and somatic genetic events
- fusion-type mutations