National Cancer Institute

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Post-Chernobyl Thyroid Cancer in Exposed Children

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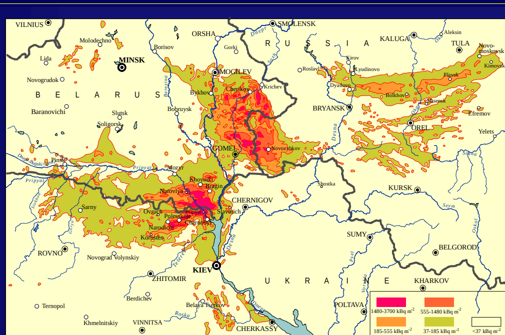
The Chernobyl Accident – 26 April 1986

- 10 days of releases into the atmosphere
- Widespread and spotty fallout due to rain and changing wind directions
- Iodine 131 the principal contaminant
- Over 200,000 evacuated, 5 million living in contaminated regions

Chernobyl Fallout



Contaminated* Areas in European Countries Following the Chernobyl Accident (Izrael et al. 1996)

	Area in deposition-density ranges (km^2)			
Country	37-185 $kBqm^{-2}$	185-555 $kBqm^{-2}$	555-1480 $kBqm^{-2}$	>1480 $kBqm^{-2}$
Russia	49,800	5,700	2,100	300
Belarus	29,900	10,200	4,200	2,200
Ukraine	37,200	4,200	900	600
Sweden	12,000	-	-	-
Finland	11,500	-	-	-
Austria	8,600	-	-	-
Norway	5,200	-	-	-
Bulgaria	4,800	-	-	-
Switzerland	1,300	-	-	-
Greece	1,200	-	-	-
Slovenia	300	-	-	-
Italy	300	-	-	-
Moldova	80	-	-	-

* The contaminated areas are defined as those where the ^{137}Cs deposition density resulting from the Chernobyl accident was greater than 37 $kBqm^{-2}$

Exposure to Radioactive Iodine from Chernobyl

- ^{131} I concentrates in the thyroid (thyroid dose much greater than average body dose)
- Can be inhaled and ingested (mainly in milk)
- Children received the highest doses (small thyroid mass, high milk consumption)

Iodine Deficiency in Contaminated Areas

- Possible risk factor for thyroid cancer
- Increases uptake of radioiodines
- May stimulate thyroid cell proliferation
- May increase effect of radioiodines

Radiation and Thyroid Cancer: What was Known before Chernobyl

- Atomic bomb
  - Biggest increase in children
- X-ray exposures: medical uses
  - Increase following exposure in childhood
- ^{131}I: dx and tx
  - No obvious increase in adults but data sparse in children

Data from Chernobyl will contribute to:

- Understanding of ^{131}I carcinogenesis
- Effective handling of future nuclear events
- Safe use of radioiodines in clinical practice

Exposure in Childhood to Fallout:
Radioiodines from the Nevada Test Site ,1985-1986

- 3545 schoolchildren screened and interviewed, 2473 (2496) analyzed
- Doses based on diet and deposition
- Mean dose=170 (120) mGy
- Significant excess of thyroid neoplasms (n=19, 23)

Kerber R, et al., JAMA 1993; Lyon et al., Epidemiol 2006

Thyroid Disease in Those Exposed as Children to Iodine 131 from the Hanford Nuclear Plant

- 5199 children from contaminated areas (1944-1957), 3440 screened and analyzed
- Thyroid radiation dose estimated through specially designed computer program
- Mean dose 174 mGy
- No dose-response relationship with benign or malignant thyroid disease

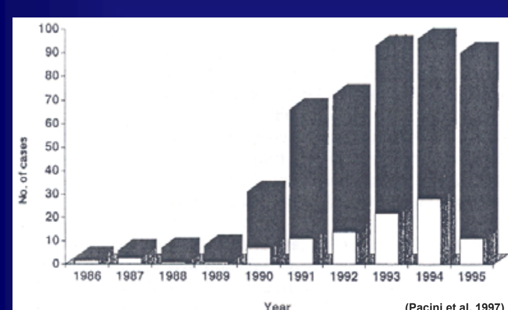
Davis S, et al., JAMA 2004

Thyroid Cancer in Contaminated Areas of Ukraine, 1981-1990

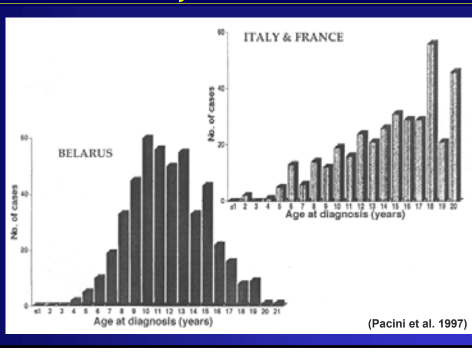
Year	Thyroid Cancer (No.)
1981	0
1982	0
1983	0
1984	0
1985	0
1986	0
1987	0
1988	0
1989	0
1990	3

Prisyazhiuk A, et al., The Lancet 1991

Cases of Childhood (■) and adolescent (□) thyroid carcinoma in Belarus, registered yearly from 1986- 1995

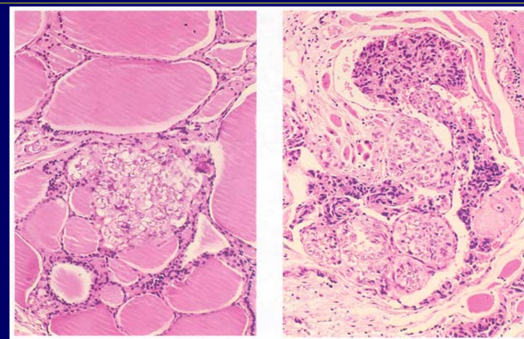


Age Distribution at the time of diagnosis of thyroid cancer patients from Belarus and from Italy and France



(Pacini et al. 1997)

Papillary cancer, solid subtype



Real effect or Screening effect?

Case-Control Study in Belarus

- Belarus, ages 0-16, dx in 1987-1992
- 107 cases, 214 controls (same opportunity for diagnosis)
- exposure assessment ecological

Astakhova L, et al. 1998

Case-Control Study in Belarus

Dose (Gy)	Cases	Controls	OR(95% CI)
< 0.3	64	88	1.00
0.3-0.9	26	15	2.38 (1.2, 4.9)
1 +	17	4	5.84 (2.0, 17.3)

Astakhova L, et al., Radiat Res 1998

Thyroid cancer in Bryansk region of the Russian Federation

- Population-based case-control study (0-19)
- 26 cases, diagnosed before Oct 1, 1997
- 52 matched controls from Russian national registry
- Doses estimated from semi-empirical model

Davis S, et al., 2004

Odds Ratios and 95% Confidence Intervals for Thyroid Cancer by Median Radiation Dose, Russian Federation

Median Dose (mGy)	No. of Cases	No. of Controls	OR (95% CI)
23	4	16	1.00 (ref.)
139	5	14	1.65 (0.32-8.50)
427	4	16	3.05 (0.42-22.1)
1049	13	6	44.7 (3.30-604)

Davis S, et al., Rad Res 2004

Radiation Dose and Iodine Status: Belarus and Russian Federation, 1992- 1998

- Population-based case-control study (<15)
- 276 cases, 1300 matched controls
- Stable iodine status based on settlement soil levels
- Consumption of potassium iodide from interview

Cardis E, et al., JNCI 2005

Risk of Thyroid Cancer at 1 Gy, Belarus and Russian Federation

- Median dose in controls = 245 mGy

OR at 1 Gy (95% CI),	5.5 (3.1, 9.5) -
from different models	8.4 (4.1, 17.3)

Cardis E, et al., JNCI 2005

Radiation Dose and Iodine Status: Belarus and Russian Federation, 1992- 1998

	OR at 1 Gy (95% CI)	
Potassium iodide	Highest two tertiles of soil iodine	Lowest tertiles of soil iodine
No	3.5 (1.8, 7.0)	10.8 (5.6, 20.8)
Yes	1.1 (0.3, 3.6)	3.3 (1.9, 10.6)

Cardis E, et al., JNCI 2005

Joint Effect of Iodine Deficiency and Radiation Dose: Bryansk region of the Russian Federation, 1996

- 3070 individuals in 78 settlements
- 2590 ages 6-18
- Urinary iodine measurements
- 34 histologically confirmed cancers
- Dose estimated from semi-empirical models

Shakhtarin V, et al., IJE 2003

Iodine Levels and Radiation Dose: Bryansk region, Russian Federation, 1996

Urinary Iodine Excretion (µg/dl)	ERR per Gy Estimate	95% CI
< 5.0	24.1	(1.7, 78.31)
5.0 – 7.49	18.3	(10.7, 28.6)
7.5 – 9.99	16.2	(0.8, 49.3)
≥ 10	13.0	(-11.0, 71.2)

Shakhtarin V, et al., IJE 2003

Thyroid Cancer Risk in Areas of Ukraine

- Ecological study of 301,907 (1-18) in 1,293 rural settlements
- 24% with individual dose estimates; 76% with ‘individualized’ estimates
- 232 histologically confirmed thyroid cancers through 12/01
- ERR/Gy=8.0 (95% CI 4.6-15)

Likhtarov I et al., Radiat Res 2006

Ukrainian-American Thyroid Study
Belarusian-American Thyroid Study

A collaboration between scientists from Ukraine, Belarus, NCI and Columbia University

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Approach

- Cohort study of 25,000 exposed children
- Biennial screening examinations of the thyroid gland, 1998 - present
  - Palpation
  - Ultrasound
  - Fine Needle Aspiration as indicated
  - Thyroid hormone, thyroid antibody and iodine excretion measurements

Study Endpoints

- Thyroid cancer
- Benign neoplasm
- Diffuse goiter
- Nodular goiter
- Autoimmune thyroiditis (AIT)
- Thyrotoxicosis (hyperthyroidism)
- Hypothyroidism
- Hyperparathyroidism
- Hypoparathyroidism
- Iodine deficiency

Dosimetry

- Direct measurements
- Questionnaire data
- Radioecologic modelling

Mean in Ukraine 0.78 Gy
Median 0.30 Gy

Approximate Mean Doses From Selected Low Dose Radiation Exposures†

Source	Approximate mean individual dose, mGy
Thyroid dose from Chornobyl (Ukraine, <18 y at exposure)	780
Breast dose to scoliosis patients	100
Pediatric CT scan (stomach dose from abdominal scan)	25
Single screening mammogram	3

† Adapted from DJ Brenner et al. 2003

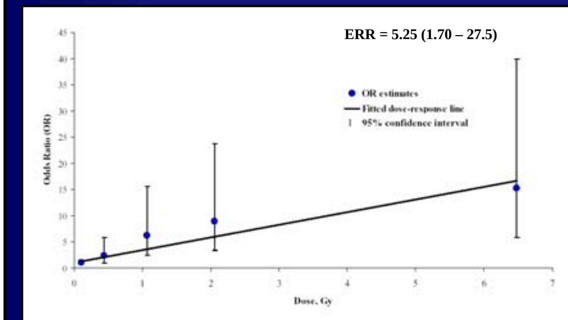
Odds Ratios [a] and 95% Confidence Intervals (95% CI) by Thyroid Dose

Dose Categories (Gy)	Cases (n)	Odds Ratio (95% CI)
0 – 0.24	9	Ref.
0.25 – 0.74	9	2.31 (0.91 – 5.88)
0.75 – 1.49	10	6.25 (2.50 – 15.6)
1.50 – 2.99	8	8.97 (3.39 – 23.7)
3.00+	9	15.30 (5.88 – 40.0)

[a] all odds ratios adjusted for gender, age at screening p (trend) = <0.0001

Tronko M, Howe G, et al., JNCI, 2006

Plot of the Odds Ratio Estimates and the Corresponding 95% Confidence Intervals from the Categorical Analysis and a Fitted Dose-Response Line



Models of Excess Relative Risk per Gray (ERR) and Interactions of Dose, Gender and Age at Exposure

Variable		Parameter and Estimates	
Dose		ERR = 5.25*	
Gender: Male		RR = 2.21	p = 0.14
Female		RR = 16.57	
Dose			
Age at exposure:	0 – 4	RR = 9.08	p = 0. 58
	5 – 9	RR = 7.00	
	10+	RR = 3.39	

* Statistically significant

Conclusions from Cohort Study

- Strong, linear relationship between dose and response
- Not confounded by screening
- Suggestive modification by gender and age at exposure, but not by iodine
- ERR = 5.25 v. ERR = 7.7 (pooled analysis of external radiation)

General Conclusions

- Consistent results from analytic studies (5-6 fold excess overall)
- Strong dose-response
- Magnitude of risk similar to external radiation

Questions Still Remain About....

- Age and gender as modifiers of thyroid cancer risk in children
- Role of iodine deficiency
- Risk of thyroid cancer in exposed adults
- Risk in those exposed in utero
- Specific molecular features
- Changes in tumor characteristics

Thyroid Cancer Morbidity and Mortality Due to Chernobyl

- ~ 5,000 cases of thyroid cancer through 2002
- 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)

Postscript

- Cohort of 110,645 Ukrainian Male Cleanup Workers
- Nested case-control study of leukemia and related disorders
- 70 confirmed, analyzable leukemias, five matched controls (age, residence)
- Individual RADRUE (time and motion-based) dose estimate