Research on thyroid cancer – from Chernobyl to Fukushima

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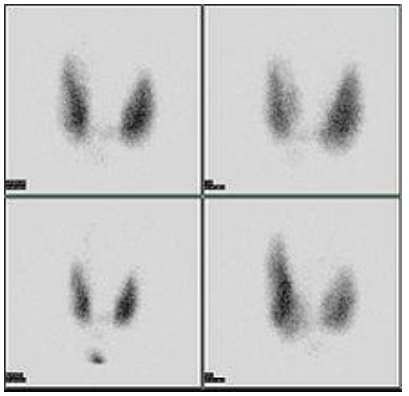
outline

- what have we learned from Chernobyl studies about radiation and thyroid cancer:
  - internal vs. irradiation external
  - latency
  - potential risk modifiers (host and environmental factors)
  - exposure in childhood vs. adulthood
- Fukushima thyroid issues through the prism of increased thyroid surveillance worldwide
- conclusions

Chernobyl: external irradiation vs. internal

- first reports on thyroid cancer increase after Chernobyl were met with scepticism because:
  - susceptibility of thyroid gland to internal exposure from radioactive iodine was less established, compared to external radiation exposure
  - main evidence came from studies of medically exposed populations with underlying thyroid conditions and limited data on childhood exposure



Chernobyl: latency

- very early onset (first cases appeared only 3 to 4 years after the accident) was unexpected based on existing knowledge from externally exposed populations*

* Ron *et al*, 1995; Veiga *et al*, 2016

Caution: the first cases demonstrated very clear clinical symptoms, they were not detected by screening

Photo: http://renaissanceresearch.blogspot.fr/2006_04_01_archive.html

Chernobyl: risks after exposure in childhood and adolescence

summary of most informative analytical studies

Study	Ascertainment period	Number of cases	Number of controls/ size of study population/PY	ERR* at 1 Gy (95% CI)
Chernobyl studies				
Case-control studies				
Astakhova *et al*, 1998	1988-1992	107	214	OR >=1 Gy vs. <0.3Gy: 5.0 (1.5-16.7) to 5.8 (2.0-17.3)
Kopecky *et al*, 2006	1986-1998	66	132	48.7 (4.8-1,151)
Cardis *et al*, 2005	1992-1998	276	1,300	4.5 (2.1-8.5) to 7.4 (3.1-16.3)
Screened cohort study				
Tronko *et al*, 2006	1998-2000	45	13,127	5.25 (1.7-25.5)
Brenner*et al,* 2011	2001-2007	65	12,514	1.91 (0.43–6.34)
Zablotska *et al,* 2010	1996-2004	133 85	11,611	3.16 (1.49 – 6.95) 2.15 (0.81 - 5.47)
Exposure in utero				
Hatch *et al, 2009*	2003-2006	7	2,582	11.7 (NE – 1,982)
External exposures - *Pooled analyses*				
Ron *et al.* 1995		458	1.400.000 PY	7.7 (2.1-28.7)
Veiga *et al,* 2016		927	3.400.000 PY	5.5 (4.1–7.5)

*ERR=excess relative risk

Chernobyl: effect modifiers

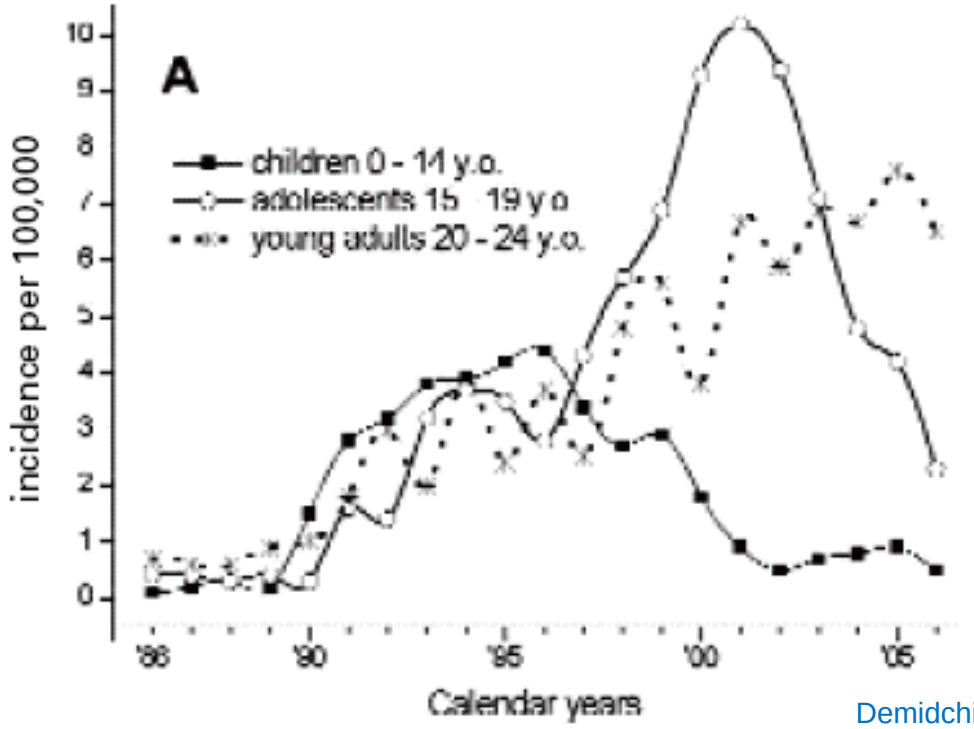
- age at exposure and gender

Reference	Ratio ERR/Gy girls/boys	Age at exposure effect
Cardis *et al*, 2005	0.9 *p=0.9*	NA
Kopecky *et al, 2006*	NA	No monotone trend with increasing age; *p=0.7*
Tronko *et al*, 2006	7.5 *p=0.14*	ERR decreased with increasing age at exposure; *p=0.6*
Brenner *et al*, 2011	2.2 *p=0.9*	ERR decreased with increasing age at exposure; *p=0.4*
Zablotska *et al,* 2010	*3.0* *p=0.13*	No significant effect of age at exposure; *p=0.9*
Ron *et al,* 1995	2 *p=0.07*	ERR decreased with increasing age at exposure; *p=0.004*
Veiga *et al*, 2016	*0.8* *p=0.37*	ERR varied significantly with age at exposure; *p*= 0.001

- overall, risk decreases with increasing age at exp. although trends are not always significant or monotonous

Chernobyl: effect modifiers (2)

- risk pattern over time



Demidchik, Saenko and Yamashita, 2007

- I-131-related risk persisted more than 20 y after exposure, with no evidence of decrease Brenner *et al*, 2011

Chernobyl: effect modifiers (3)

- effect of large scale screening efforts in contaminated areas:
  - *absolute rate of thyroid cancer increases in a screened population*
  - *ERR estimate can be biased upward, if there is a correlation between thyroid dose and frequency of screening*
  - BelAm and UkrAm cohort studies provided an estimate of the risk where confounding effect of screening is unlikely (all subjects were screened, regardless of dose)
- however:
  - ? whether the detection of additional small thyroid cancers affects the excess radiation risks
  - ? whether these small tumours are induced by radiation to the same extent as large tumours

Chernobyl: effect modifiers (4)

- iodine deficiency and iodine supplementation

Consumption of potassium iodide	OR at 1 Gy (95% CI)	
	Highest two tertiles of soil iodine	Lowest tertile of soil iodine
No	3.5 (1.8 to 7.0)	10.8 (5.6 to 20.8)
Yes	1.1 (0.3 to 3.6)	3.3 (1.0 to 10.6)

Cardis *et al*, 2005

- implications potentially important for radiation protection & public health but needs confirmation

- indicators of past stable iodine intake are difficult to reconstruct

Chernobyl: thyroid exposure in adulthood

- effect of exposure as an adult – *uncertain:*
  - ❖ recent descriptive studies of clean-up workers:
    - ✓ Russia (Ivanov *et al.* 2007) - SIR 3.39 (95% CI 2.73-4.16),
    - ✓ Ukraine (Ostroumova *et al,* 2014) - SIR 3.86 (95 % CI 3.26–4.57)
    - ✓ Baltic cohort (Rahu *et al,* 2013) – PIR 2.76 (95% CI 1.63-4.36)
  - ❖ recent studies of residents of contaminated territories >18 y at the time of accident:
    - ✓ Russia - no dose-response relationship found in exposed adults (Ivanov *et al,* 2012)
    - ✓ Ukraine - excess of radiation-induced thyroid cancers in exposed adults in contaminated vs. non-contaminated regions (Fuzik *et al*, 2011)

- caution:
  - ❖ possible surveillance bias
  - ❖ no individual dosimetry

Photo: http://www.longshadowofchernobyl.com/photos/chernobyl-victims/

Chernobyl: thyroid exposure in adulthood (2)

- 146,000 Chernobyl clean-up workers (liquidators) from Belarus, Estonia, Latvia, Lithuania and Russia
- 107 cases/423 controls
- individual reconstructed doses, including uncertainty:
  - external – RADRUE method (Kryuchkov et al, 2009)
  - internal – environmental model validated on available direct thyroid measurements
- overall median dose – 69mGy
- ERR/100mGy 0.38 (95% CI 0.1-1.09)
  - similar risks found for external and internal exposures
  - risk remains significant after excluding tumours Ø1cm or less
  - **impact of uncertainties in doses had modest effect on risk**

Kesminiene *et al*, 2012

Chernobyl: role of uncertainties in dose estimates on risk

- dose-error adjustments reported so far had modest effect on risk estimates:
  - Little *et al*, 2014
  - IOP Publishing | Society for Radiological Protection — Journal of Radiological Protection
J. Radiol. Prot. **36** (2016) R36–R73 — doi:10.1088/0952-4746/36/3/R36

Doses for post-Chernobyl epidemiological studies: are they reliable?

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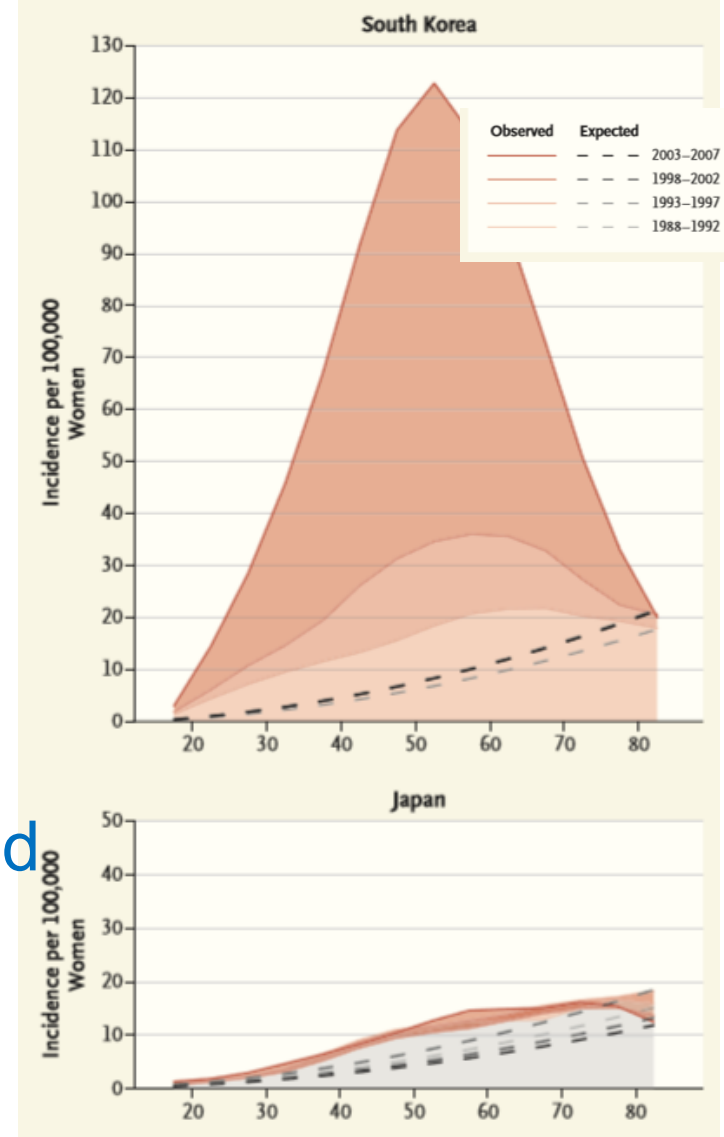
worldwide: rise in thyroid cancer incidence

- estimated number of cases attributable to increased thyroid-gland surveillance:
  - ❖ in women:
    - ✓ 90% in South Korea;
    - ✓ 50% in Japan
  - ❖ in men:
    - ✓ 70% in South Korea;
    - ✓ less than 25% in Japan



"careful data interpretation needed in the context of screening after radiation exposure"

Vaccarella *et al*, 2016

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from Chernobyl to Fukushima

- joint IARC/FMU workshop Oct 2013 recommendations:
  - ❖ importance of population based cancer registry for monitoring population
  - ❖ although thyroid ultrasound screening program benefits from an assessment of baseline thyroid health before any radiation-effect would be expected:
    - ✓ population concerns need to be adequately addressed
    - ✓ incidence of thyroid cancer is predicted to increase substantially as a function of introducing screening into the population
    - ✓ further challenges may remain to disentangle a screening effect from that of radiation, particularly if adherence to the screening is dependent on the level of radiation exposure received

IARC/FMU workshop recommendations (2)

- estimating individual radiation doses among clean-up workers (on-site and off-site) and the general population is essential for studies of the long-term health effects
- it is indispensable to link results of the clean-up workers' dose monitoring to their health check-up data so that it can be used for further follow-up studies
- longitudinal studies of lifestyle and behavioural factors can establish whether there are changes in these factors and whether they are associated with long-term risks
- coordinated data collection between different institutes and disciplines can both reduce the burden on the population and facilitate efforts to examine the inter-relationships between the many factors at play

from Chernobyl to Fukushima

SHAMISEN
Nuclear Emergency Situations Improvement of Medical and Health Surveillance

- subtask 1.2: Critical review of long-term medical surveillance programmes

→ to provide a set of lessons learned from medical surveillance on physical and mental health of populations exposed to fallout from the Chernobyl and Fukushima accidents

→ recommendations for setting up criteria to:

  – justify long-term medical surveillance programmes of affected populations
  – evaluate their effectiveness

International Agency for Research on Cancer

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OPERA OPEN PROJECT FOR EUROPEAN RADIATION RESEARCH AREA

conclusions

- thyroid gland has been proven to be one of the most radiosensitive organs with latency period less than 5y
- sensitivity to I-131 in children is much grater compared to adults
- I-131-related risk persists nearly 3 decades after Chernobyl accident
- there is more to be learned about the impact of:
  - gender,
  - age at exposure, including in adulthood,
  - stable iodine intake
  - increased surveillance
  - uncertainties in doses on risk estimates…
- there is a need for studies to better understand natural history of thyroid cancer (progression and regression of thyroid tumours over life span)
- **importance of international cooperation in science is explicitly recognised and has been proven after Chernobyl**

CO-CHER: setting the scene for future research on Chernobyl

- development of a long-term research programme with agreed research priorities
- Chernobyl Research Programme highlights:
  - establishment of Chernobyl Life Span cohort
  - convening a multinational body - International Chernobyl Research Committee
  - conducting prioritized multidisciplinary studies
  - **more info: http://co-cher.iarc.fr/**


ありがとうございました
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