National Cancer Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Health Effects of *In Utero* Exposure to I-131 in Chernobyl Fallout

Maureen Hatch, Ph.D.
Radiation Epidemiology Branch,
Division of Cancer Epidemiology and Genetics

Gilbert W. Beebe Symposium
November 1-2, 2016

Exposure to the Embryo/Fetus

- Iodine-131 readily crosses the placenta
- Once active (10-12 wks), the fetal thyroid rapidly takes up iodine

- By late gestation, levels are many-fold higher than in the maternal thyroid

Prenatal Radiosensitivity

Rationale: rapidly dividing, undifferentiated cells

Radiosensitivity:

- varies as a function of stage
- established for some outcomes
- uncertain for others

Sparse Data on I-131 *In Utero*

- **Thyroid abnormalities but no thyroid neoplasia in 40y f-u of 480 "downwinders" exposed to I-131 *in utero***

  (Lloyd *et al.*, 1996)

- **Sex/age-specific effects on growth in Marshallese children exposed to radioiodines (4 *in utero*)**

  (Sutow *et al.*, 1965)

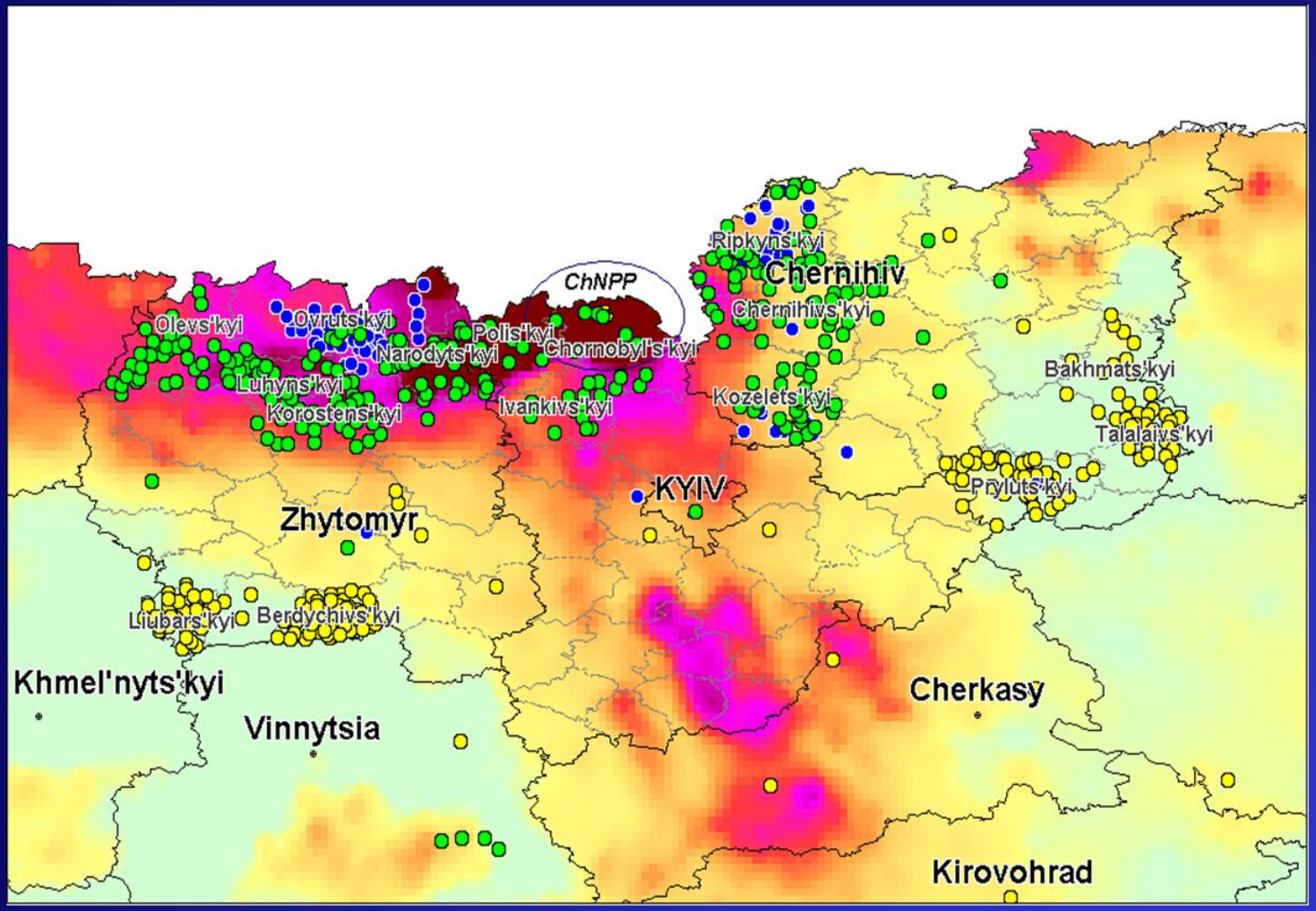
NCI-Ukraine *In Utero* Study

2,582 **children born to women pregnant on April 26, 1986 or the 2 months following**

Most affected northern oblasts

- **-1,494 from contaminated areas**
- **-1,088 from no/low-contaminated areas**

Distribution of Subjects by Level of I-131 Contamination



Estimation of Fetal Thyroid Dose

Prenatal I-131 doses estimated using ICRP 88:
Berkovski's biokinetic model

Mean dose:
72 mGy (0-3,240 mGy)

Likhtarev et al. 2011

Thyroid Screening Examinations

- **Ultrasound, palpation (ultrasonographer)**
- **Palpation, clinical exam (endocrinologist)**
- **Interview with mothers**
  (demog, med hx, resid hx, diet, KI)

- **FNA for large and/or suspicious nodules**

NCI-Ukraine *In Utero* Study: Cycle 1

Initial thyroid screening exam, 2003-2006:

7 cancers, 1 Hurthle cell neoplasm

Prenatal I-131 and Thyroid Cancer

EOR/Gy = 11.66 (P=0.12)

EOR/Gy = 5.35 (P=0.24) neoplasia

Hatch, Brenner et al., 2009

NCI-Ukraine *In Utero* Study: Cycle 1

Initial thyroid screening exam, 2003-2006:

7 cancers, 1 Hurthle cell neoplasm

Prenatal I-131 and Thyroid Cancer

EOR/Gy = 11.66 (P=0.12)

EOR/Gy = 5.35 (P=0.24) neoplasia

Postnatal I-131 and Thyroid Cancer

1-5 yo; n=13 cancers

EOR/Gy = 3.24 (P=0.01)

Hatch, Brenner et al., 2009

NCI-Ukraine *In Utero* Study: Cycle 2

Second cycle of screening, 2012-2015:

2 additional thyroid cancers; n=9

Prenatal I-131 and Thyroid Cancer

EOR/Gy = 4.37 (P=0.25)

Hatch, Brenner et al. (in preparation)

NCI-Ukraine *In Utero* Study: Cycle 2

Cycle 2, Preliminary Findings (age/sex adj.)

Prenatal 1-131 and Thyroid Nodules

EOR/Gy = 1.26 (P=0.036)

(Imaizumi et al., 2008: OR/1Gy=2.78, (0.50, 11.80))

NCI-Ukraine *In Utero* Study: Cycle 2

Prenatal I-131 and Thyroid Nodules

Small Nodules (<10 mm), N=180

EOR/Gy = 0.05 (P=0.94)

Large Nodules (≥10 mm), N=60

EOR/Gy = 4.68 (P<0.001)

Summary of Results: Thyroid Disease

- With 2 new cases (9 overall), there continues to be a suggestion of elevated Thyroid Cancer risk
- The magnitude of risk is similar to that in the main cohort of children exposed at 1-5 years
- There is a significant dose-response association with Thyroid Nodules ≥ 10 mm, statistically compatible with ABS *In Utero*

In Utero Exposed A-Bomb Survivors

ABS studies suggest risk also exists for:

- **small head size (micrcephaly),**
- **IQ, mental retardation**
- **reduced head circumference**
- **reductions in height and weight**

(Wood et al 1967; Blot WJ 1975; Otake and Schull 1993; Nakashima 1994; Lee, Otake, Schull 1999)

NCI/NICHD-Ukraine *In Utero* Study

Retrospective review of cohort members' delivery records at local maternity facilities

Abstraction of records by gynecologists

Record linkage of *in utero* database and IPOG Registry for capture of data on evacuees

NCI/NICHD-Ukraine *In Utero* Study

Cohort members identified:

N= 2,022 (78% of 2,582)

Mean and range of prenatal 1-131 dose:

62 mGy (0-2,263)

NCI/NICHD-Ukraine *In Utero* Study

Preliminary findings, adj. for trimester of exposure, parity, weeks of gestation, gender, maternal height, maternal weight at first visit

- **Fetal dose and Head circumference:**
  -0.89 cm/Gy; (P=0.01*)*
  greater for exposure in 1st trimester

Hatch, Little et al. (in preparation)

NCI/NICHD-Ukraine *In Utero* Study

Preliminary findings, adj. for trimester of exposure, parity, weeks of gestation, gender, maternal height, maternal weight at first visit

- **Fetal dose and Head circumference:**
  -0.89 cm/Gy; (P=0.01*)*
  greater for exposure in 1st trimester

- **Fetal dose and Chest circumference:**
  -0.83 cm/Gy; (P=0.07*)*
  greater for 1st trimester exposure

Hatch, Little et al. (in preparation)

NCI/NICHD-Ukraine *In Utero* Study

No association with neonatal length or BW:

- **Fetal dose and Neonatal Length:**
  -0.37 cm/Gy; (*P=0.37)*

- **Fetal dose and Birthweight:**
  49.66 g/Gy; (*P=0.42)*

Summary of Results: Fetal Growth

- Notable dose-related reduction in head circumference, as seen in ABS *in utero* exposed

- Reduction greatest for those exposed early in gestation
  - when I-131 dose to brain and thyroid is similar
  - when the velocity of head growth is highest

- Decrement at 1 Gy ~1 cm; <1 mm at mean of 62 mGy
  - unlikely to affect cognition, child development

Conclusions, Next Step

Results for thyroid disease and fetal growth among Ukraine *In Utero* cohort exposed to I-131 similar to those for ABS *In Utero* cohort exposed to external radiation

Validate findings in BelAm cohort:

- **~2,500-3,000 Belarusians exposed to Chernobyl fallout *in utero***

Collaborators

NCI

Alina Brenner
Mark Little
Andre Bouville
Vladimir Drozdovitch
Stephen Chanock
Kiyo Mabuchi

NICHD

Paul Albert (now NCI)
Katherine Grantz
Liping Sun

Ukraine

Mykola Tronko
Valery Tereschenko
Ludmyla Chaikovska
Igor Pasteur
Tatiana Bogdanova
Elena Bolshova
Ilya Likhtarev
Victor Shpak

Acknowledgment

With thanks to the late Drs. Gilbert Beebe and Robert Miller, who first encouraged us to follow the disease experience of those exposed to Chernobyl accident fallout *in utero.*