Teratogenic radiation effects

Perinatal mortality and congenital malformations

following Chernobyl

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Teratogenic radiation effects:

Adverse health effects to the fetus after exposure to ionizing radiation:
Congenital malformations, perinatal deaths
(i.e. stillbirths and early neonatal deaths), cognitive impairment

UNSCEAR on teratogenic effects:

- UNSCEAR 2008 (Chernobyl consequences):
  A search in the document finds **no hit** for
  "teratogenic" OR "perinatal" OR "malformation"

- UNSCEAR 2013 (Fukushima consequences)
  (b) Other health effects, F14:
  "Prenatal exposure was not expected to increase .. the incidence of spontaneous abortion, miscarriages, perinatal mortality, congenital effects or cognitive impairment."

ICRP 90 (2003): Biological effects
after prenatal irradiation (embryo and fetus)

- Experimental data on age-dependent patterns of sensitivity to malformation induction re-inforce the view of **maximum sensitivity during major organogenesis, but with a true dose threshold**.
  For practical purposes, risks of induction of **malformation at low doses may therefore be discounted.**

- (44) Induction of malformations [...]
  most pronounced during organogenesis (weeks 3-11 p.c.)

- (60) Most experimental data basically fit
  sigmoid or shoulder-type dose-response curves [...]

ICRP 90, Fig.1.1:
Occurence of lethality and abnormality after prenatal radiation exposure of about 2 Gy

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Shape of the dose-response relationship for stochastic and teratogenic effects

From: http://gd1.med.uni-giessen.de/ugm_2/deu/ugi_nuk/PDF/Rad_V2_Strahlentherapie.pdf

Results of epidemiologial studies

Perinatal mortality in **Germany** and regression line.
Excess rate in 1987: 0.36 per 1000 (*P*=0.018), 317 excess deaths

from: Körblein A, Küchenhoff H.
Perinatal mortality in Germany following the Chernobyl accident. Radiat Environ Biophys. 1997 Feb;36(1):3-7.

Perinatal mortality in **Poland** and regression line.
Excess rate in 1987: 0.57 per 1000 (*P*=0.015), 348 excess deaths

Deviations of perinatal mortality in **Germany** and **Poland** from secular trend (standardized residuals) and range of 2 standard deviations.

Perinatal mortality in Germany

Monthly perinatal mortality rates and trend line.
The vertical line indicates the date of the Chernobyl accident.

Deviations of mortality rates from undisturbed trend line **(standardized residuals)** and 3-month moving average.   After Chernobyl, mortality peaks are found in **February** and **November** 1987

Monthly infant mortality in Poland

Infant mortality rates in Poland
and trend line with seasonal variations

Lower panel:
standardized residuals and 3-month
moving average

Peaks are found in
January , April, and **November** 1987

Early neonatal mortality in oblast Zhytomyr

Upper panel:
monthly rates and regression line

Lower panel:
Standardized residuals and 3-month moving average

Maximum in April 1987

Trend analysis of monthly data

- Logistic regression with linear-quadratic time trend

- Seasonal effect modeled by dummy coding for individual months
  (dummy variables for Feb through Dec, Jan=reference)

- Cesium burden of pregnant women calculated from cesium concentration
  in cow milk (measured), beef, cereals, and pork

- Linear- plus quadratic cesium dependency
  to allow for a curvilinear shape of cesium effect on perinatal mortality

Figure A-IX. The activity concentrations of ¹³⁷Cs in cow milk near Munich following the Chernobyl accident as observed and as simulated by the ECOSYS-87 model [M9]

From: UNCEAR 2008, Annex D, page 95

Measured **cesium-137 concentration in cow milk** (black points)
and calculated cesium concentration in beef, cereals, and pork, semilogarithmic plot

Measured **cesium-137 concentration in cow milk** (black points) and calculated
cesium concentration in beef, cereals, and pork, linear plot

Cesium-137 concentration in cow milk (crosses, left axis)
and **cesium burden in pregnant women** (grey line, right axis),
calculated with a biological half-life of 70 days

Cesium-137 concentration in **cow milk, beef, cereals, and pork** and **cesium burden in pregnant women** (grey line, right axis), calculated with a biological half-life of 70 days

Monthly averages of **cesium burden** in pregant women from ingestion of milk and other foodstuff

Residual sum of squares obtained with regressions of German monthly perinatal mortality rates **as a function of time-lag** between cesium burden and mortality. Horizontal broken line indicates critical chisquare value. Best estimate of **time-lag is 7 ± 1 months**.

Standardized residuals of perinatal mortality in Germany and 3-month moving average.
Lower graph: **cesium burden** of pregnant women, shifted by 7 months

Dose dependency

Increase of **perinatal mortality in Germany** as a function of lagged cesium burden, and regression line. The cesium effect on mortality is significant ($P=0.0016$, F-test).
The dose-response is curvilinear: Linear term <0, quadratic term >0 ($P=0.034$)

Dose dependency

Increase of **infant mortality in Poland** as a function of cesium burden, and regression line. Cesium effect on mortality is significant ($P=0.014$, F-test). Dose-response is curvilinear: Linear term <0, quadratic term >0 ($P=0.016$)

Congenital malformations in Bavaria

- After Chernobyl, a study of congenital malformations in Bavaria was conducted by German Federal Office of Radiation Protection (BfS-ISH)

- The following **isolated malformations** were included:
  - neural tube defects,
  - anophtalamus, microphtalamus, cararact
  - limb anomalies
  - cleft lip and palate
  - atresia of gastrointestinal tract
  - cong. anomalies of the heart, cong. anomalies of abdominal wall
  - diaphragmatic hernia

- Malfomations with likely genetic origin:
  trisomy 21, malformation syndrom (**multiple malformations**)

- Malformation rates in Southern Bavaria (total cesium soil contamination: ~30 kBq/m²) were compared with rates in Northern Bavaria (~10 kBq/m²)

Combined spatial-temporal regression

Method: Cesium burden cs(k, t) is defined as the product of

(1) cesium soil deposition (kBq/m²) in district k (k = 1 to 96) cs(k) and
(2) cesium concentration (Bq/kg) in pregnant women as a function of time t, cs(t)

cs(k, t) = cs(k) * cs(t) [kBq/m² *Bq/kg]

The model allows for a linear time trend and a linear-quadratic dose-response
i.e. a nonlinear dependency of malformation risk on cesium burden.

Result: The association of malformation rates with cesium burden is significant
(*P*=0.014, F-test). The dose-response curve is non-linear: neg. linear term (*P*=0.0092),
pos. quadratic term (*P*=0.0023)

from: Küchenhoff H, Engelhardt A, Körblein A, 2006
available at: http://www.ratical.org/radiation/Chernobyl/chernobylebook.pdf, pp 179-183

Odds ratios (~relative risks) of malformation rates in Bavarian districts as a function of cesium burden, aggregated values and regression line. The error bars are standard deviations.

Summary

- In 1987, perinatal mortality is significantly increased in Poland and in Germany. Effect in Poland is 1.6 times greater than in Germany.

- 317 excess perinatal deaths in Germany and 354 in Poland in 1987

- Significant association of perinatal mortality in Germany and infant mortality in Poland with calculated cesium burden during pregnancy

- Curvilinear dose-response (negative linear, positive quadratic term)

- Significant association of malformation rates in Bavaria with cesium burden

- **No "safe dose" (threshold dose) for teratogenic effects**