Pregnant Women with High Levels of $^{137}\text{Cs}$ and High Rates of Congenital Anomalies near Chornobyl

Wladimir Wertelecki$^1$, Lyubov Yevtushok$^{1,2}$, Natalia Zymak-Zakutnia$^{1,3}$, Serhiy Lapchenko$^1$, Illya Kuznetsov$^4$, Oleksandr Komov$^5$, Zoriana Sosyniuk$^{1,2}$, Diana Akhmedzhanova$^{1,3}$, and Bogdana Ievtushok$^{1,2}$

$^1$OMNI-Net Ukraine Birth Defects Programs, $^2$Rivne Regional Medical Diagnostic Center, Rivne, Ukraine, $^3$Khmelnytsky Perinatal Center, Khmelnytsky, Ukraine, $^4$Human and Animal Physiology Department, Eastern-European University, Lutsk, Volyn, Ukraine, $^5$Rivne Province State Sanitary-and-Epidemiologic Service, Rivne, Ukraine

Definitions and abbreviations

$^{137}\text{Cs}$$^{137}\text{Cs}$ – among the most abundant and convenient to measure radioactive matter (radionuclides) released by atomic chain reactions – this nuclide is similar to potassium and so are its incorporation and tissue bindings characteristics; $^{90}\text{Sr}$$^{90}\text{Sr}$ – a frequent radionuclide released by atomic chain reactions – its similarity to calcium is conducive to long lasting binding to bones and concentration of IR damage on bone marrow cells resulting in leukemia; ABCC – Atomic Bomb Casualty Commission, established by the U.S.A. government to conduct studies of the impacts of the Hiroshima and Nagasaki atomic bombs explosions; biota – living matter; anencephaly – an early congenital anomaly of the rostral (cephalic) pole of the neural tube from which derives, among other structures, the cerebrum and the retina; anophthalmia – lack of ocular globes; blastula – the earliest stage of a fertilized egg – blastopathies are anomalies of the fertilized egg prior to its implantation in the uterus and the onset of embryonic development; $\text{Bq}$ – or becquerel, a unit of radiation reflecting energy released by disintegrating atoms; $\text{CA}$ – congenital anomalies, in this study comprising, for the most part, visually evident structural anomalies noted by fetal prenatal ultrasonography or clinical examinations detected after birth up to the age of one year; carcinogen - see text; Epigenetics – see text; process that results in the modification of gene expression rather than alteration of the genetic code per-se; FASD – fetal alcohol spectrum disorders; IAEA – International Atomic Energy Agency; ionizing radiation or IR – radiation with sufficient energy which upon impacts with matter can liberate electrons or molecules resulting in positive or negative electric charges denoted by the term “ionizing”; microcephaly – reduced head size, in this study of at least two standard deviations below the average for sex and age; microphthalmia – small ocular globes; IRPA or International Radiation Protection Association; millisievert or mSv – a calculated unit or indirect estimate of biologic impact of ionizing radiation; $\text{mSv}$ – see millisievert; M/M – microcephaly and/or microphthalmia; mutagen – see text; neural tube defects – anomalies resulting from developmental alterations of the neural tube from which derive the brain and spinal cord; non-P or non-Polissia – represents Rivne regions excluding seven counties categorized as Polissia; NTD – see neural tube defects; NPP – nuclear
power plant or complex, which in Ukraine usually includes a “atom-city”; P or Polissia or Prypiat Marshes – name of the flood plains of the eponymous river and two of its tributaries – the soils of the seven counties in Polissia are sandy, a factor that augments the transfer of nuclides from the soil to the food-chain; radionuclide – chemical molecules that contain unstable atoms (nuclides) that decay and emit energy, mainly ionizing radiation; spina bifida – a failure of closure of the distal or caudal pole of the neural tube – a serious anomaly conducive to paralysis of the lower limbs often compatible with survival; teratogen – see text; UNSCEAR – United Nations Scientific Committee on the Effects of Atomic Radiation; WBC – whole body counts of incorporated IR, in this report this measure solely detects incorporated $^{137}\text{Cs}$; WHO – World Health Organization.

Abstract

We report population-based rates of congenital anomalies in the Rivne province of Ukraine. The rates are significantly higher in the northern half of Rivne, a region called Polissia which is polluted by Chernobyl ionizing radiation. In this region of forested wet-lands, also called Prypiat Marshlands, the soils are distinct from those in non-Polissia. The soils in Polissia transfer $^{137}\text{Cs}$ more readily to plants than those in non-Polissia. The rates of some specific female prevalent congenital anomalies and incorporated ionizing radiation levels are higher than in non-Polissia. The elevated rates of congenital anomalies belong to the category of blastopathies, which arise before the uterine implantation of the fertilized egg (blastula) or during the initial stages of embryogenesis. The blastopathies noted are conjoined twins, sacral teratomas (embryonal tumors of the lower spine), neural tube defects (anencephaly and spina bifida among others), and microcephaly-microphthalmia (reduced head size and/or reduced ocular globes). These elevated rates of blastopathies are persistent and are among the highest reported in Europe.

Our measurements of IR are limited to incorporated levels of $^{137}\text{Cs}$. However, we have detected the presence of $^{99}\text{Sr}$ in potato plants grown in P. Other investigations detected high levels of tritium in the Prypiat river which apparently stem from releases by either or both nuclear power plants in the Rivne region. The average $^{137}\text{Cs}$ incorporated by 3,865 pregnant women from Polissia was 40.4 and among those from non-Polissia was 11.3 becquerels per kilogram of body weight respectively. The levels of incorporation of $^{137}\text{Cs}$ have risen significantly over time.

A comprehensive analysis of prenatal exposures to alcohol, another potent cause of congenital anomalies, did not reveal contrasts between Polissia and non-Polissia.

The observations in Rivne stem from descriptive epidemiological investigations seeking to detect associations to guide prospective cause-effect investigations. The concurrence of elevated population-based rates of blastopathies and higher incorporated levels of $^{137}\text{Cs}$ in pregnant women reflect an association, although such is not a proof of causation. The observations in Rivne are sufficiently compelling to justify prospective investigations of specific cause-specific
Incorporated Radiation and Malformations

effect research projects. In our view, concurrent parallel investigations in Rivne and in areas of
Japan impacted by the Fukushima Daiichi disaster are likely to accelerate and broaden the
understanding of IR impacts on human embryos.

Background

**Chornobyl (in Russian, Chernobyl)**
The 1986 disaster at Chornobyl was soon followed by the implosion of the Soviet Union and
Ukrainian independence. An index of the profound social impacts of these events on the
population in Rivne province is evident in a precipitous drop of birth rates in Rivne, which to the
present remain below those prior to the disaster at the Vladimir Lenin nuclear power plant (NPP)
discretely renamed as Chornobyl.

![Birth rates in Rivne and in the Polissia region.](image)

Soviet Union and IAEA (International Atomic Energy Agency) experts defined regions most
impacted by the Chornobyl ionizing radiation (IR) fallout. For unknown reasons, the Polissia (P)
region of the Rivne province in Ukraine was ignored. Five years later, in 1991, during events that
culminated in Ukrainian independence, the error was corrected (Decree 106, 1991). It is now
recognized that the population in P is among the largest and most severely exposed to Chornobyl
IR in Ukraine (Likhtarev et al. 1996, 2000; Zamostian et al. 2002). It also became evident, as
alleged to later, that these experts were unlikely to focus attention on the impacts of IR on
developing human embryos. To address IR on pregnancy outcomes, a group of like-minded
physicians and scientists formed a partnership that evolved into an organization named OMNI-
Incorporated Radiation and Malformations

Net, now registered in Kyiv, Ukraine as an international not-for-profit entity (Wertelecki 2006). Among the goals of OMNI-Net is to sustain nearly identical projects in Rivne and two adjoining provinces - registers of every newborn and every instance of visually detectable congenital anomalies (CA). Prenatal exposures to alcohol and evidence of Fetal Alcohol Spectrum Disorders (FASD) were investigated concurrently (Wertelecki 2006; Mattson et al. 2010, Wertelecki et al. 2014).

Polissia and Polishchuks in Rivne

Nearly one-half of the population of Rivne inhabits wetlands known as P or Prypiat Marshes which are flood plains of the river Prypiat and its tributaries flowing across the lowlands of P (Figures 2, 3, and 4).

![River Prypiat – Flood Plains and Marshes](image)

*Figure 2. Polissia lowlands are conducive to an isolated life style and mineral-poor soils.*

Among Polishchuks, high rates of isonomy of family names are indicative of high rates of endogamy which translates into higher rates of consanguinity of prospective spouses (Colantonio et al. 2003). External exposures to IR in P are minimal. Internal exposures are mostly through inhalation and ingestion. It is unlikely that frequently published estimated exposures to IR in P, usually relying on dietary data collected in other regions, may not be relevant in view of the social circumstances in P as well as its soil characteristics. The wet and boggy soils in P are associated with the highest transfer index of $^{137}$cesium ($^{137}$Cs) from soil to biota in Ukraine. Preliminary investigations in P demonstrated that the daily ingestion of $^{137}$Cs by pregnant women
Incorporated Radiation and Malformations

is above the daily safety limits set by Ukrainian authorities of 3,400 and 14,800 Bq (becquerels) for individuals under the age of 14 years or above, respectively (Dancause et al. 2010). Since 1986, the isolated native population in P continues to be exposed to IR polluted air, smoke and water. Furthermore, Polishchuks and their children virtually have no alternatives but to consume water drawn from shallow wells and locally grown food polluted by IR. Smoke from burning bio-mass, forest fires, and wood burning for cooking and heating is readily evident in P. Smoke is one factor that mobilizes IR and its deposition alters IR soil patterns. In P, approximately 67 percent of households burn local wood for cooking or for heating. The radioactive smoke is inhaled by both adults and their children. Families also use wood ash to fertilize their home garden plots which concentrates $^{137}$Cs in these soils, and the homegrown or locally cultivated food consumed by the family and domestic animals. During harvests, women, among whom many are pregnant, undertake the task of burning plant remnants which results in the mobilization of radionuclides that are then inhaled in smoke. The stems of potato plants grown in P and subject to burning contain $^{137}$Cs as well as $^{90}$Sr. Virtually all infants born in P are exposed to $^{137}$Cs since their conception. A growing proportion of their parents also are exposed to $^{137}$Cs since their conception.

Figure 3. Schematic map of Ukraine and of the Chornobyl impacted regions and Rivne province.
Previous Studies

Most investigations of Chornobyl IR impacts on health in Ukraine as well as elsewhere are focused on adults and on their increased cancer risks. Substantive population-based investigations of CA are rare. EUROCAT, a consortium of CA monitoring systems across regions of Europe, conducted investigations among populations living in European regions distant from the Chornobyl site. The results did not show an impact of Chornobyl IR on rates of CA in these distant regions from the disaster (Dolk & Nichols 1999). Numerous other studies of relatively small series of patients did show increased rates of CA, in particular neural tube defects (NTD), but were dismissed or largely ignored for a variety of reasons. We are unaware of other substantive long term large population-based studies of CA rates in populations living in relative proximity to the Chornobyl site.

Notions inherent in the terms Teratogen, Mutagen, and Carcinogen

The notion “teratogen”, as emphasized in this report, was consolidated after the Hiroshima and Nagasaki events which were followed a few years later by an extensive global rubella epidemic and aggressive marketing of Thalidomide. It became evident that both rubella and Thalidomide were associated with clusters of characteristic CA referred to as “Rubella Fetopathy” and
“Thalidomide Fetopathy”. It also became evident that the prenatal rubella or Thalidomide impacts were neither “genetic” nor “carcinogenic” in nature. In view that IR is also a cause of characteristic CA such as, among others, microcephaly and cataracts as well as genomic mutations and cancer, it could be concluded that IR is teratogenic, mutagenic and carcinogenic. After these seminal events, it became clear that many medications and agents such as alcohol are teratogenic but are not a cause of “genetic” alterations such as gene mutations or carcinogenesis.

Mutagens, defined briefly, are agents that alter the genetic code of cells conducive to cell death, teratogenic alterations, sterility, heritable disorders, and in some instances to carcinogenesis.

An additional perspective is rapidly arising under the eponym “Epi-Genetics”. In essence, in the context of IR impacts, this notion concerns heritable alterations not due to mutations of the genomic code but reflecting impacts on regulatory mechanisms of gene expression.

Arguably, it cannot be taken for granted that the teratogenic, mutagenic, and epi-genetic impacts by acute, intense, and brief external IR exposures in Hiroshima-Nagasaki are equivalent or even similar to those in Rivne as implied in assertions by the IAEA with concurrence by the WHO (World Health Organization). As elaborated upon later, these agencies assert that IR exposures in Rivne are too low to cause detectable impacts on CA rates. Irrespective of such Hiroshima-Nagasaki to Chornobyl and more recently to Fukushima Daichi extrapolations, in Rivne, the rates of CA are among the highest in Europe. Regarding nuclides released by the Chornobyl explosion, their variety and diverse chemical nature translate into a variety of modes of their incorporation by pregnant women and their embryos. The exposures in Hiroshima-Nagasaki were external, often intense and brief. In Rivne the IR are chronic, of low overall intensity or high intensity in particular embryonic sites. Furthermore, the sensitivity of embryonal tissues to IR teratogenic is variable, a reflection their developmental stage. Virtually all pregnant women born in P after the 1986 Chornobyl disaster and all their embryos are exposed to nuclides since their own conceptions.

Introduction

The 1986 Chornobyl disaster is among the largest man-made disasters and the released ionizing radiation (IR) continues to have negative impacts on the ecologic integrity, social welfare, and human health in vast regions of Europe. The scope and impacts of the Fukushima Daiichi disaster in Japan are equally enormous. The observations reported here are likely to be relevant, at least in part, to studies of IR radiation impacts in Japan.

Most investigations of Chornobyl IR impacts, including this report, are limited to measurements of $^{137}\text{Cs}$. IR impacts from other nuclides remain largely unaccounted for. This deficit is illustrated by our observation of significant levels of $^{90}\text{Sr}$ in stems of potato from P. The potential of releases of nuclides by two NPP in proximity of populations in Rivne is also a factor to be taken into consideration (Figures 1 and 2).
Another prevalent teratogen in Rivne in addition to IR is alcohol. We conduct an ongoing investigation of maternal consumption of alcohol and its impact on embryonic development (Wertelecki et al. 2014).

The CA monitoring program in Rivne is a full partner of EUROCAT, a network of programs sharing goals and methodologies (EUROCAT Guide 1.4 and reference documents 2013). This network facilitates comparisons of patterns and rates of CA in Rivne with those noted elsewhere in Europe.

**Methods and Population**

To assess IR exposures, we computed whole-body counts (WBC) as becquerels (Bq) emanating from incorporated $^{137}$Cs. We analyzed 44,438 WBC obtained between 2001 and 2013 from outpatients who volunteered to undergo the procedure. This group includes individuals of at least 20 years of age and pregnant women of any age. There were 6,425 pregnant women of any age and of known body weight. The officially set upper norms for WBC in Ukraine are 3,700 Bq and 14,800 Bq for individuals under the age of 15 years and for adults, respectively. Additional information on the subject is summarized in Table 1.

A population-based CA monitoring was initiated in 2000. Every infant born in Rivne and those with evident CA at birth or during the first year of life are registered in a neonatal registry and if appropriate in the CA registry.

![Early anomalies or blastopathies (arising prior to the implantation of the fertilized egg or early embryogenesis). Illustrated are conjoined twins (left); sacral teratoma (upper center); anencephaly (lower center); and an association anencephaly-iniencephaly-omphalocele (lower right). These blastopathies are prevalent among females (see text).](image)
Whole body counts of incorporated $^{137}$Cs were obtained by a single device, a spectrometer incorporated into a chair and calibrated yearly by the Kyiv Metrology Center (Kyiv Metrology Center reference); recording methods were defined by the Kyiv Ecology Institute (SVITCH-M3 “SKRINNER” User Manual 1992); counts were recorded as total Bq; recordings below the detection limit of 100 Bq were excluded from analyses; repeated measurements of some individuals were included. Analyses of WBC radiation measurements and CA rates were focused on determining contrasts between those in P and the rest of Rivne or non-Polissia (non-P). Additional analyses were focused on two counties proximal to nuclear power plants (NPP). The first is Volodymyrets County in P which includes Kuznetsovsk City as an integral component of the Rivne NPP. The second is Ostroh County in non-P, which is adjacent to the Khmelnytsky NPP. Further descriptions of WBC analyses are given elsewhere (in press).

Population-based congenital anomalies surveillance, classification and coding adhered to methods developed by EUROCAT (EUROCAT Guide 2013). Every infant born in Rivne is registered in a neonatal registry and CA among stillborn or live born detected up to one year of age are recorded in a separate registry. The microcephaly category includes instances of at-birth occipito-frontal circumferences at least three standard deviations below normal for age and sex and excludes instances of holoprosencephaly. Microphthalmia and anophthalmia are reported jointly. Instances of Down syndrome include individuals solely diagnosed clinically. Population-based rates are calculated per 10,000 live births of CA detected prenatally or before one year of age. Finally, statistical software R (http://www.r-project.org/) was used for analyses and graphing.

**Results**

*Whole Body Counts*

The number and residence of individuals who underwent WBC recordings are shown in Table 1. The WBC’s of males are higher than those of females in general. The body weights of women of similar ages are similar in Polissia and non-Polissia. Although the averages of WBC in Polissia and non-Polissia differ significantly, within P and within non-P the ranges are quite similar. The WBC’s of pregnant women are higher than those of females in general and often approach or exceed those of males. The WBC from Volodymyrets County are among the highest in Polissia and those from Ostroh in non-Polissia are the lowest in Rivne. In Kuznetsovsk City in Volodymyrets County, the average WBC of men, women, and pregnant women is much lower than in the rest of this county. A Poisson regression of all WBC data from Volodymyrets County, with dummy coding for Kuznetsovsk City, yields a highly significant 60% lower mean WBC in Kuznetsovsk than in the rest of Volodymyrets County (P<0.0001) (Table 1).

*Table 1.* $^{137}$Cs Whole Body Counts in Rivne regions.
### Table: WBC (≥100 Bq $^{137}$Cs)

<table>
<thead>
<tr>
<th>Category</th>
<th>Polissia</th>
<th>Non-Polissia</th>
<th>Kuznetsovsk City</th>
<th>Volodymyrets County</th>
<th>Ostroh County</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Males $^{(1)}$ (2001-2013)</td>
<td>6520</td>
<td>3266</td>
<td>825</td>
<td>432</td>
<td>268</td>
</tr>
<tr>
<td>Median Bq</td>
<td>1516</td>
<td>379</td>
<td>1250</td>
<td>2918</td>
<td>307</td>
</tr>
<tr>
<td>Mean Bq</td>
<td>2663</td>
<td>519</td>
<td>1391</td>
<td>3414</td>
<td>413</td>
</tr>
<tr>
<td>Number of Females $^{(2)}$ (2001-2013)</td>
<td>23628</td>
<td>11024</td>
<td>2013</td>
<td>2163</td>
<td>1207</td>
</tr>
<tr>
<td>Median Bq</td>
<td>1486</td>
<td>404</td>
<td>1117</td>
<td>2425</td>
<td>341</td>
</tr>
<tr>
<td>Mean Bq</td>
<td>2352</td>
<td>523</td>
<td>1164</td>
<td>2918 $^{(5)}$</td>
<td>493</td>
</tr>
<tr>
<td>Pregnant $^{(3)}$ Females (2011-2013)</td>
<td>3865</td>
<td>2560</td>
<td>90</td>
<td>507</td>
<td>377</td>
</tr>
<tr>
<td>Median Bq</td>
<td>1942</td>
<td>594</td>
<td>1428</td>
<td>2197</td>
<td>507</td>
</tr>
<tr>
<td>Mean Bq</td>
<td>2655</td>
<td>744</td>
<td>1460</td>
<td>2533</td>
<td>703</td>
</tr>
</tbody>
</table>

1. At least 20 years of age; 2. includes women of at least 20 years of age and those pregnant of any age; 3. pregnant women of known weight; 4. excludes Kuznetsovsk City; 5. the mean WBC of the whole county is 2,072.

*Figure 6. $^{137}$Cs temporal trends of whole body counts of women residing in Polissia.*

Women’s WBC in P and in non-P, from 2001 through 2013, exhibit large differences. In women from P and non-Pa the mean WBC are 2,352 and 523 Bq respectively. There also is a statistically significant temporal rise in Polissia (P<0.0001) shown in Figure 6 above and a statistically non-significant rise in non-Polissia (P=0.09, is not illustrated).
Incorporated Radiation and Malformations

The $^{137}$Cs burden of pregnant women during 2011-2013 was determined from WBC and body weight (kg) measurements in Polissia (N=3,865) and in non-Polissia (N=2,560). In P, the specific activity ranged from 1.4 to 629 Bq/kg with a mean value of 40.4 Bq/kg. To determine the temporal trend, a Poisson regression was used. The average caesium burden increased by 6.3 ± 1.8% per year (P=0.0006). In non-P, the specific activity ranged from 0.9 to 207 Bq/kg with a mean value of 11.3 Bq/kg and the average decreased by 15 ± 2% per year (P<0.0001). Further analyses of WBC are available upon request.

Rates of Congenital Anomalies

The number of live births and number of individuals with CA and corresponding rates are presented in Table 2. The NTD and microcephaly/microphthalmia (M/M) rates in P were 24.1 and 17.5 and 8.6 and 5.2 respectively, a statistically significant contrast (P=0.0014 and P=0.005 respectively). This difference has persisted over the years.

Table 2. Number and Rates of Congenital Anomalies in Polissia.

<table>
<thead>
<tr>
<th>Category</th>
<th>Polissia</th>
<th>Non-Polissia</th>
<th>Volodymyrets County$^{(1)}$</th>
<th>Ostroh County</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live Births (2000-2012)</td>
<td>98069</td>
<td>99429</td>
<td>21671</td>
<td>5636</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>N Rate</td>
<td>N Rate</td>
<td>N Rate</td>
<td>N Rate</td>
</tr>
<tr>
<td>NTD$^{(2)}$</td>
<td>236</td>
<td>24.1</td>
<td>174</td>
<td>17.5</td>
</tr>
<tr>
<td>M/M$^{(3)}$</td>
<td>84</td>
<td>8.6</td>
<td>52</td>
<td>5.2</td>
</tr>
<tr>
<td>Cleft lip w/o palate$^{(4)}$</td>
<td>97</td>
<td>9.9</td>
<td>108</td>
<td>10.9</td>
</tr>
<tr>
<td>Down Syndrome$^{(4)}$</td>
<td>156</td>
<td>15.9</td>
<td>142</td>
<td>14.3</td>
</tr>
</tbody>
</table>

Abbreviations: NTD, neural tube defects; M/M, microcephaly and/or microphthalmia; w/o, with or without. (1) Includes Kuznetsovsk City; (2) includes one individual with M/M from Volodymyrets County in Polissia; (3) excludes 8 individuals with holoprosencephaly and includes 6 individuals with cleft lip w/o palate from Polissia and 3 from non-Polissia, one of which is from Ostroh County; (4) includes individuals with NTD or M/M mentioned above.

For further statistical analysis, NTD and M/M cases were pooled. A logistic regression on a county level (7 counties in Polissia, 9 in non-Polissia) was conducted to test the dependency of malformation rates on WBC. Dummy coding was used to test for any systematic difference in rates between Polissia and non-Polissia. Possible excess rates in the two counties proximal to NPP, Volodymyrets in Polissia and Ostroh in non-Polissia, relative to the rates in their respective Polissia and non-Polissia regions, were also tested. A highly significant 58% excess is found in Polissia vs. non-Polissia (P=0.0004). We also note that in Ostroh County, the NTD-M/M rate is 82% higher than in the rest of non-Polissia (P=0.007); in fact it is the highest rate in Rivne province. No deviation from the expected rate in Polissia is found in Volodymyrets County. Other results of WBC patterns are available upon requests to the authors.
Table 3. Temporal Trends of Neural Tube Defects and Microcephaly/Microphthalmia in Rivne Regions.

<table>
<thead>
<tr>
<th>Category</th>
<th>Polissia</th>
<th>Non-Polissia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NTD</td>
<td>M/M</td>
</tr>
<tr>
<td>2000-4</td>
<td>29.1</td>
<td>7.1</td>
</tr>
<tr>
<td>2000-6</td>
<td>27.2</td>
<td>6.7</td>
</tr>
<tr>
<td>2000-9</td>
<td>26.1</td>
<td>8.6</td>
</tr>
<tr>
<td>2000-11</td>
<td>24.6</td>
<td>8.5</td>
</tr>
</tbody>
</table>

Rate per 10,000 live births.

Abbreviations: M/M, microcephaly and/or microphthalmos; NTD, neural tube defects.

Table 4 shows male-female proportions in individuals with blastopathies. As further observations of these relatively rare CA accumulate, statistical analyses will become possible.

Table 4. Female Prevalence among Blastopathies in Rivne (2000-2009).

<table>
<thead>
<tr>
<th>Categories</th>
<th>N</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>M</td>
</tr>
<tr>
<td>Live Births</td>
<td>145437</td>
<td>75292</td>
</tr>
<tr>
<td>Neural Tube Defects (NTD)</td>
<td>309</td>
<td>114</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>68</td>
<td>32</td>
</tr>
<tr>
<td>Isolated</td>
<td>22</td>
<td>6</td>
</tr>
<tr>
<td>Microphthalmos</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>Conjoined Twins</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Teratomas</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Sacro-coccygeal</td>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>

A survey of at-birth head circumference showed statistically significant reductions in males and females, born in Zarichne County in Polissia in comparison to neonates born in Rivne City in non-Polissia. A follow-up investigation found a similar contrast among male and female infants born in Volodymyrets County in Polissia compared to those born in the remaining counties in non-Polissia (Figure 7) (Wang & Wertelecki 2013; Wertelecki et al. 2014).
Incorporated Radiation and Malformations

Figure 7. Comparison of 2000-2009 at-birth occipito-frontal head circumferences of infants in Zarichne County in Polissia with those in Rivne City in non-Polissia and of infants from Volodymyrets County in Polissia with infants gestated in nine non-Polissia counties (Polissia vs. non-Polissia P<0.01, unpublished data)

Discussion

Hiroshima–Nagasaki and Chornobyl
Before Chornobyl, the largest human populations impacted by IR were those living in the cities of Hiroshima and Nagasaki in Japan. As mentioned earlier, the exposures in Hiroshima-Nagasaki were external, intense, and brief, and the residual radioactivity was considered to be negligible. In contrast, those in Rivne are internal, chronic, and characterized by official agencies as of low intensity. However, uptake of incorporated nuclides by particular embryonic tissues may become concentrated in particular embryonic tissues, as is the case with high concentration of radioactive iodine or $^{90}$Sr in thyroid or skeletal embryonal tissues respectively. The severe consequences expressed as childhood thyroid carcinoma and leukemias are well known examples. As elaborated upon later, experts and officials of the IAEA-WHO are dismissive of the notion that Chornobyl IR could possibly be a cause of elevated CA because exposures compared to those in Hiroshima-Nagasaki are too low.

Following the Hiroshima-Nagasaki atomic blasts, the United States established the Atomic Bomb Casualty Commission (ABCC) to sponsor and coordinate investigations of IR health impacts on exposed survivors and their children. We are aware of a single investigation of in-utero exposed children - the results were inconclusive largely due to the limited number of subjects and the difficult circumstances that followed the atomic bomb detonations (Plummer 1952). A larger investigation was focused on unexposed in-utero children aptly summarized in a detailed report “The Children of Atomic Bomb Survivors – a Genetic Study”. Among 14,768 and 12,324 infants in Hiroshima and Nagasaki, 165 and 154 had CA, compared to 49,645 births observed in the Tokyo Red Cross Maternity Hospital between 1922 and 1940 among whom 456
had CA (tables 8.2 and 8.3 on pages 101 and 103 respectively) (Neel & Schull 1991). Due to the diverse nature of the two cohorts of children, no conclusions can be drawn regarding CA rates nor patterns. The main conclusion was that “... the frequency of malformed ... reveals no significant, consistent effect of parental exposure” (page 117). This conclusion is often extrapolated to sustain IAEA-WHO assertions that implicitly equate external with internal IR radiation and distinctions of teratogenic from mutagenic impacts.

The ABCC sponsored investigations did show a clear association of IR external exposures with microcephaly and reduced mental capacity (Neel 1958, 1994; Otake & Schull 1984; Schull & Otake 1999; Wood et al. 1967a, 1967b, 1967c; Miller & Blot 1972).

In Rivne, IR impacts on human health emanate from incorporated radionuclides by individuals and mother-embryo pairs. Earlier studies concerned with Chornobyl IR, including our own, rely solely on measurements of $^{137}$Cs. Measurements of other nuclides are technically and financially more burdensome. As indicated earlier, the chemical nature of nuclides determines their impact on embryonic sites where the sensitivity and regeneration-repair of IR damage differ as the embryo develops. Compared with adults, the human fetus and children remain highly sensitive to IR impacts, in particular during periods of rapidly developing tissues. Perhaps early impacts on blastogenesis could disrupt body-axis formation expressed as conjoined twins, an anomaly quite frequent in P, a subject elaborated upon later.

After Hiroshima and Nagasaki

An official study of congenital malformations in Bavaria, the German region most affected by the Chernobyl fallout, reported no increase of malformation rates after Chernobyl (Schoetzau et al. 1994). But an analysis of the prevalence of malformations at birth (1984-1991) as a function of $^{137}$Cs burden, which was approximated by the district average cesium soil contamination times the trend of the (calculated) cesium concentration in pregnant women, found a significant association when a linear-quadratic trend model was used, with a negative slope at low cesium values and a steep increase at higher values. The investigators also indicated that the results should be interpreted with caution since the analysis was conducted as an explorative observational study (Kuchenhoff et al. 2004).

In a European context, the NTD and M/M rates in P are persistently among the highest reported to EUROCAT (Wertelecki et al. 2014). After P, the next highest rates of NTD and of M/M in Europe are noted in northern regions of Great Britain known to have been more severely impacted by Chornobyl IR that the rest of the country (Figure 8). This region also includes the Sellafield nuclear complex where one investigation demonstrated elevated rates of NTD (Parker et al. 1999). Such observations may be fortuitous but it is imprudent to disregard them. Perhaps follow-up investigations by EUROCAT may clarify the relevance of these patterns of CA.
Table 5. Rates\textsuperscript{(a)} of Neural and Other Malformations in Polissia and Remaining Counties of Rivne Province in Ukraine and Other Regions of Europe

<table>
<thead>
<tr>
<th>Categories\textsuperscript{(b)}</th>
<th>Births</th>
<th>NTD (Average)</th>
<th>MIC</th>
<th>mOPH</th>
<th>CL/P</th>
<th>DS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Polissia (2000-2011)</strong></td>
<td>89680</td>
<td>24.42 (49)\textsuperscript{(d)}</td>
<td>6.24</td>
<td>3.35</td>
<td>10.04</td>
<td>15.05</td>
</tr>
<tr>
<td><strong>Non-Polissia (2000-2011)</strong></td>
<td>90879</td>
<td>16.95 (68)</td>
<td>4.40</td>
<td>1.10</td>
<td>10.89</td>
<td>14.19</td>
</tr>
<tr>
<td><strong>EUROCAT Registries (2005-2011)\textsuperscript{(c)}</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>UNITED KINGDOM (UK)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northern England</td>
<td>233134</td>
<td><strong>14.41 (79)</strong></td>
<td>1.46</td>
<td>0.73</td>
<td>10.90</td>
<td>22.86</td>
</tr>
<tr>
<td>Wales</td>
<td>243992</td>
<td>14.02 (82)</td>
<td><strong>4.75</strong></td>
<td><strong>1.52</strong></td>
<td>10.94</td>
<td>22.91</td>
</tr>
<tr>
<td>East Midlands &amp; South Yorkshire</td>
<td>510172</td>
<td>11.92 (76)</td>
<td>0.92</td>
<td>0.33</td>
<td>8.96</td>
<td>19.25</td>
</tr>
<tr>
<td>Thames Valley</td>
<td>209508</td>
<td>11.41 (83)</td>
<td>1.00</td>
<td>0.76</td>
<td>9.07</td>
<td>27.45</td>
</tr>
<tr>
<td>Wessex</td>
<td>206120</td>
<td>11.30 (90)</td>
<td>1.31</td>
<td>0.63</td>
<td>10.96</td>
<td>27.70</td>
</tr>
<tr>
<td>South West England</td>
<td>343636</td>
<td>11.09 (83)</td>
<td>4.51</td>
<td>1.08</td>
<td>8.79</td>
<td>27.97</td>
</tr>
<tr>
<td><strong>CONTINENTAL EUROPE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paris (France)</td>
<td>187658</td>
<td>12.26 (87)</td>
<td>2.61</td>
<td>1.07</td>
<td>7.99</td>
<td><strong>43.06</strong></td>
</tr>
<tr>
<td>Basque Country (Spain)</td>
<td>145543</td>
<td>10.72 (87)</td>
<td>3.78</td>
<td>1.37</td>
<td>5.57</td>
<td>34.08</td>
</tr>
<tr>
<td>Norway</td>
<td>425676</td>
<td>9.44 (74)</td>
<td>0.52</td>
<td>0.70</td>
<td>12.4</td>
<td>19.52</td>
</tr>
</tbody>
</table>

Figure 8. The path of a Chornobyl radioactive cloud across Europe from April 27 to early May 1986 (Yablokov & Nesterenko 2009).
Incorporated Radiation and Malformations

| Nine others – highest rates\(^{(a)}\) | 9.16 (56) | 4.11 | 1.28 | **13.18** | 24.04 |

\(^{(a)}\) **In bold**, highest rates per 10,000 births – for further information see Wertelecki et al. 2014; 
\(^{(b)}\) Abbreviations: CL/P, cleft lip with/without cleft palate; DS, Down syndrome; EUROCAT, European Surveillance of Congenital Anomalies; MIC, microcephaly; mOPH, microphthalmia; NTD, neural tube defects; (c) EUROCAT occasionally introduces data updates, the data analyzed was last accessed on December 25, 2013; (d) Percent of pregnancy terminations.

Two investigations in proximities to the cluster of NPPs in Hanford, Washington State, U.S.A. were sponsored by the CDC (Centers for Disease Control) to determine CA rates and patterns. The results of both investigations found increased rates of NTD. However, although the investigators judged both studies as scientifically sound they dismissed their significance because the results contradicted those reported to the ABCC and disseminated by the IAEA/WHO (Sever et al 1988a, 1988b). Interestingly, recent reports of clusters of NTD in proximities to the Hanford site have triggered another investigation by the CDC (Centers for Disease Control and Prevention 2013).

Two independent investigations in central regions of Norway and Sweden of children found that those exposed in-utero to Chornobyl fallout had reduced mental capacities as teenagers. These observations are concordant with ABCC sponsored investigations that demonstrated an association of IR exposures with intellectual deficits. ABCC sponsored studies also showed an association of IR with microcephaly which is consonant with our observations in P (Almond et al. 2009; Heiervang et al. 2010; Schull & Otake 1999).
In addition to microcephaly, we also noted modest reduction of at-birth occipito-frontal head circumferences among infants gestated in two counties in P. These observations must be confirmed by further investigations.

Regarding Europe, high concurrent rates of similar blastopathies to those noted in P in areas of the British Isles, call attention. It remains to be investigated if such patterns are associated with higher exposures to IR or other teratogens.

Polissia and Radionuclides

Geographic isolation and contrasts in ecology, traditions, language, and contamination by Chornobyl IR render the native population in P distinct from other populations in Ukraine (Dancause et al. 2010).

Analyses of WBC show that levels of $^{137}$Cs incorporated by males, females and pregnant women living in P are consistent with the official categorization of P as significantly impacted by Chornobyl IR. The analyses also demonstrate higher WBC in men than women but those of pregnant women approach or may surpass those of males. Presumably, this is a reflection of increased weight during pregnancy. We also note that since 2001, the average WBC of women has steadily and significantly risen. This rise is unlikely to reflect human bio-concentration of $^{137}$Cs since an association with age and corresponding weight gain are lacking. Instead, perhaps the temporal rise of WBC reflects a growing bio-concentration of radionuclides in locally produced food which continue to be consumed by the mostly rural populations in Polissia.
Of particular interest is the city of Kuznetsovsk in Volodymyrets County in P. The city arose as a component of the local NPP. The average WBC of men, women and pregnant women from this city are significantly lower than those from individuals living in the rest of Volodymyrets County. Presumably, this difference is indicative of the largely imported food low or free from $^{137}\text{Cs}$ consumed in Kuznetsovsk City. This proposition is consistent with observations in Japan which demonstrated a rapid reduction of $^{137}\text{Cs}$ WBC when dietary intakes excluded contaminated edibles (Tsubokura et al. 2014). Furthermore, ongoing analyses of samples of milk from markets in Kuznetsovsk confirm that the $^{137}\text{Cs}$ levels are nearly four folds lower than in samples of home produced milk from rural households.

Ostroh County is also adjacent to the Khmelnysky NPP. However, in contrast to Volodymyrets County, in Ostroh County, the $^{137}\text{Cs}$ WBC recordings are among the lowest in Rivne while the rates of NTD, M/M are the highest in Rivne, even higher than those in P counties. On the other hand, the rates of both sentinel CA in Volodymyrets and Ostroh counties are similar to those in P, non-P and in Europe in general (Tables 2, 5).

The populations in Volodymyrets and Ostroh counties are not obviously distinct from those in other counties in their respective P and non-P regions with the exception that they live in proximity to NPP. The possibility of IR leaking from these NPP is suggested by studies of tritium in Prypiat river waters upstream from the Chornobyl site. Studies by Gudkov and Kuzmenko (Gudkov & Kuzmenko 1996, 1997) noted high levels of tritium and concluded that the likely source were discharges from the Kuznetsovsk and Khmelnysky NPP into tributary Prypiat rivers flowing across P (Figure 4). Within the overall context of our studies, investigations of tritium pollution of waters consumed by the populations in P and Ostroh County gain urgency.

**Radionuclides, Blastopathies and Female Prevalence**

It is generally accepted that CA reflect outcomes of “multi-factorial” interactions of teratogenic and regeneration-repair processes. It is known that IR is a cause of anencephaly, microcephaly, microphthalmia and other anomalies of the neural and other developing systems. It has also been demonstrated that IR destruction of neurons during early embryogenesis is followed by full or nearly complete recovery (D’Amato 1982). It is also known that alcohol may interfere with folate metabolism and that folate supplements reduce but do not entirely eliminate the occurrence of NTD. These examples suffice to conclude that it is of considerable interest to establish to what extent folate supplements will reduce NTD rates in P compared to non-P which may aid in defining similarities or contrast attributable to their pathogenesis or etiology.

A review of effects after prenatal irradiation on embryonic development by the ICRP (International Commission on Radiological Protection) asserts that “no human data are available for these parameters ... and that female mice have a higher radio-sensitivity (Valentin 2003, page 7). In a companion report, we also find a significant prevalence of females among the blastopathies noted in P and non-P. The same is noted by earlier investigators although such is
not stressed in some reports. Recent molecular studies led multiple investigators to propose that any factors that delay embryonal growth and maturation may result in blastopathies, including monozygotic twinning, conjoined twins, and NTD, among others. It is also noted that blastogenesis and early embryogenesis in females is slower than in males, a difference attributed to the process resulting in the inactivation of one of the two X-chromosomes (Juriloff & Harris 2012).

**IAEA/WHO attitudes**

It is difficult to reconcile our observations in Rivne with untested notions disseminated by the IAEA/WHO and recently by USCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation). For nearly a decade, these agencies have asserted that the levels of IR exposures after Chornobyl are too low to cause increases of CA that can be attributed to the Chornobyl event (Chernobyl Joint News Release 2005, IAEA 2006). A relevant precedent is the regrettable dismissive attitude of these agencies of early indications of an emerging epidemic of childhood thyroid carcinomas that soon followed the Chornobyl explosion (Baverstock 2007). A recent UNSCEAR report concerning the Fukushima Daiichi disaster conveys a similarly dismissive attitude (Sources, effects and risks of ionizing radiation 2013). This report, produced by scientists engaged by a relatively small number of governments cites the same results of ABCC studies extrapolated earlier to dismiss potential Chornobyl impacts. In both instances, similar arguments are presented. The UNSCEAR report asserts that accumulated IR doses are “… unlikely to cause observable effects” and that “… effects at the population levels are unlikely to be observable”. Concerning children, the report asserts that “… no heritable effects in humans due to radiation exposure have been explicitly identified ...” and that “There is essentially no evidence of an increase in chromosomal instability, mini-satellite mutations, trans-generational genomic instability, change in sex ratio of offspring, congenital anomalies or increased cancer risk in the offspring of parents exposed to radiation”. Readers may conclude that further investigations are unwarranted. Another concurrent impact of such declarations is a chilling effect on agencies willing to fund research to independently verify such critical assertions. The UNSCEAR report is found by some independent to quite troubling. The vice president of IRPA (International Radiation Protection Association), for example, during a panel session at the World Nuclear Association's 2014 Symposium stated that the nuclear industry and governments "have not been honest in presenting the risks of radiation at low levels" (World Nuclear Association’s 2014 Symposium site). Other investigators view the UNSCEAR report as misleading because it ignores studies that are contrary to its conclusions (Mousseau & Moller 2014). Perhaps this may be the reason why our report published in the journal of the American Academy of Pediatrics is not included in what UNSCEAR presents as an unbiased comprehensive review of the scientific literature (Wertelecki 2010). The above circumstances are indicative of the need for IAEA, WHO, UNSCEAR, and other agencies to include genuinely independent scientists and to avoid relying solely on experts and staff beholden to governments.
that employ them. The potential impacts of IR on the unborn are too critical to be solely judged by those whose mission is to serve governments or to promote the nuclear industry.

Summary and Conclusions

The observations reported here stem from descriptive epidemiological studies of a population chronically impacted by IR emanating from incorporated $^{137}$Cs and to identify associations that may guide prospective investigations of cause-effects manifested as particular CA. Among the most salient observations are that pregnant women living in P incorporate nearly four times more $^{137}$Cs (40.4 Bq/kg) than those living in non-Polissia (11.3 Bq/kg). Furthermore, the levels of incorporated $^{137}$Cs have significantly risen with in P but not in non-P. The concurrent elevated levels of incorporated $^{137}$Cs by pregnant women and higher rates of female prevalent blastopathies in P do not constitute proof of cause and effect. However, our view is that disregarding these facts is imprudent. Prospective collaborative cause-effect investigations are essential and likely to expand the knowledge concerning the CA observed.

Finally, the reported observations and prospective cause-effect studies are, in our view, relevant to the circumstances arising in Japan after the Fukushima Daiichi disaster. Dual, concurrent and coordinated investigations are likely to accelerate and enhance the significance of virtually any sort of prospective studies.

Acknowledgments: We thank Drs. C. Chambers, A. Korblein, and Y. Korzhynsky for their contributions toward the categorization of congenital anomalies, statistical analyses, and coordination of clinical studies respectively.

References


Plummer G. 1952. Anomalies occurring in children exposed in utero to the atomic bomb in Hiroshima. Pediatrics 10:687–693. Available at: http://pediatrics.aappublications.org/content/10/6/687 [September 17, 2013].

22


Incorporated Radiation and Malformations


Finis
20141013a