March 6<sup>th</sup>, 2013.

# PERSISTING PATTERNS OF ELEVATED CONGENITAL MALFORMATIONS IN A CHORNOBYL IMPACTED REGION OF UKRAINE.

# (Extract from a Monograph on the Subject) (Please contact authors if more information is needed)

Source: OMNI-Net Ukraine – Congenital Malformations Monitoring Program.

Corresponding Author: W. Wertelecki, M.D.- werteleckiomni@gmail.com

Authors: L. Yevtushok, N. Zymak-Zakutnia, S. Lapchenko, B. Wang, Z. Sosyniuk, H. H. Hobbart,

and W. Wertelecki.

Abbreviations, key terms, short definitions and notions:

**CHORNOBYL:** (Chernobyl in Russian) is an ancient river-town on the river Prypiat. The name Chornobyl was selected to rename the V. Lenin nuclear power complex associated with the town of Prypiat some 15 km away from the Chornobyl town. Both Prypiat and Chornobyl cities stand abandoned.

**CM:** Congenital Malformations or "birth defects". In practice, these terms include abnormalities of structure and function. Examples are mental retardation and biochemical disorders.

**IR:** Ionizing Radiation, high energy waves capable of altering chemical bonds, including those of DNA. IR effects are gene mutations (genomic alterations) both of body cells (somatic cells) causing cell death or alterations that may result in neoplasia (cancers or leukemias). Impacts of IR on reproductive cells (gonadal cells or ovocytes and sperm) may give rise to heritable gene changes (mutations). IR can destroy dividing embryonal-fetal cells and cause CM. Consequently, IR is "teratogenic" (a cause of congenital malformations) in addition of being "mutagenic" (cause of gene mutations) and "carcinogenic" (cause of all types known of neoplasias). It can be said that all mutagens are potential teratogens since altered genes can cause CM. The reverse is not true, there are many teratogens that are neither mutagenic nor carcinogenic as, for example, maternal disorders such as, among other, alcoholism, rubella, and diabetes.

**MICROCEPHALY**: reduced head size/volume, a good indicator of brain size and associated (not always) intellectual deficits. In this investigation the definition is strict (3 or more standard deviations below the norm for age and sex of the occipito-frontal circumference). **MUTAGEN:** see IR.

**NTD:** Neural Tube Defects result from a failure of closure of the embryonal neural tube giving rise to a group of CM such as anencephaly, spina bifida, encephaloceles. Over 50% of NTD are preventable by supplementation of maternal nutrition with folic acid usually achieved by universal enrichment of flour products. In Ukraine, discussions to introduce such needed preventive public health measures are ongoing for over a decade. However, no interventions were implemented. Such step will reduce infant mortality. On the basis of this population-based

investigation we estimate that there are nearly 900 infants with NTD each year and most of whom perish.

**OR, P, CL**: are abbreviations denoting odds ratio, probability and confidence limits respectively. The odds ratio is the ratio of the odds of an event occurring in one group (say in Polissia) to the odds of it occurring in another group (say in non-Polissia).

**POLISHCHUKS**: native population of Polissia (a region described below), to some degree reminiscent of the Acadians who settled wetlands in Louisiana and became known as Cajuns. This ancient population has many characteristics of an isolated population. The remoteness and isolation of the wetlands they inhabit are reflected in their lifestyle, language and family name (Polishchuk is a frequent family name in Ukraine). They inhabit small settlements with predominance of characteristic family names. Our observations are consonant with those by Ukrainian scholars indicative that Polishchuks represent a large, stable, culturally distinct population living in relative proximity to Chornobyl. Evacuation of large numbers of Polishchuks living closest to the Chornobyl site prompted the Ukrainian government to establish a State Scientific Center for Protection of Cultural Heritage under the Ministry of Emergencies. Polishchuks are considered to represent an ancestral Slavic population associated with Ukrainian notions of nationhood. Research focused on Rivne-Polissia and Polishchuks offers an opportunity to learn long term health effects of an unprecedented environmental insult on the health of a large well defined and stable population within the framework of a natural experimental model. (Garruto et al. 1999) The Nijmegen (DNA) Breakage syndrome or NBS1 or 657 del5mutation may have arisen in Polissia. The NBS1 mutation increases the sensitivity of DNA to IR induced alterations.

**POLISSIA:** (Polesie, Poliesye, Polesia, Pripyat Marshes or Polesian Lowlands). The overall Polissia region in Ukraine is nearly the size of Bavaria or Louisiana, and is among the largest forested wetlands in Europe. Polissia extends between northern Ukraine and southern regions in Belarus on both sides of the floodplain of the river Prypiat. Polissia is also called "Prypiat Marshlands". Polissia starts in eastern Poland and extends eastward across the Ukrainian provinces of Volyn, Rivne, Zhytomyr, Kyiv and Chernihiv to end in western Russia. Since recorded history, Polishchuks or "forest dwellers" represent the ancestral population of Polissia.

**TERATOGEN**: many environmental factors can cause prenatal and postnatal alterations of growth and development. Congenital malformations or "birth defects" as well as mental retardation and other anomalies can be the result of impacts of a large variety of environmental factors. Among the known teratogens are maternal disorders such as diabetes and rubella. Deficiencies of folates and iodine which can cause spina bifida and mental retardation are salient examples of the negative impacts of micro-nutrient deficiencies on the embryo-fetus and child development. Alcohol and ionizing radiation (IR) are well known universal teratogens that can cause severe or modest reductions of head circumferences (an index of brain size). Severe microcephaly is virtually always associated with mental retardation while minimal head size reductions may or may not be associated with reduced intellectual capacity. Other impacts of IR include reduction of pre- and post-natal growth, longevity, anomalous eye development, cataracts that may be late appearing, sterility, abortions, stillbirths, structural malformations and any number of types of cancer and leukemia.

# Introduction

The 1986 explosion of a nuclear reactor in Chornobyl polluted vast regions of Europe with ionizing radiation (IR). The disaster was followed by a plethora of investigations mostly to determine IR acute impacts on humans, in particular cancer risks. The impacts of chronic exposures to low levels of Chornobyl IR on pregnant women, the embryo-fetus, and mental development remain largely to be investigated. It is known that IR is a carcinogen, a mutagen (a cause of heritable alterations of the genome), and a teratogen (a cause of congenital malformations or CM). The need for further population-based investigations of IR impacts on the embryo-fetus is particularly compelling in the context of the vast global impacts of the Chornobyl and Fukushima disasters.



# Schematic map of Ukraine and spread of the Chernobyl radioactive plume across Ukraine. Polissia - Polishchuks are the Prypiat river forested woodlands and its native inhabitants.

Two categories of international circumstances led to a limited attention to the impacts of the Chornobyl disaster on pregnancy outcomes and CM risks. First, there were those related to the disintegration of the USSR and formation of a newly independent Ukraine. The associated

tensions and chaos rendered population-based data collection virtually impossible. The second category of circumstances stems from the disastrous acute impacts of the Chornobyl explosion on Ukraine and vicinity requiring a focus on IR doses and related acute health impacts and carcinogenic risks. The largest studies of IR human impacts were conducted after the Hiroshima-Nagasaki bomb explosions of 1945. Studies of children conceived after the explosions and born during 1948-1954 period were extensively investigated by teams led by Dr. J. Neel, a pioneer of Human Genetics. Prenatally these children were virtually not exposed to residual IR. These investigations sponsored by the Atomic Bomb Casualty Commission (ABCC) stand to this day as a "gold standard" concerning the IR impacts on the gonads of the exposed parents. The results are masterfully summarized in a book "Children of the Atomic Bomb Survivors". (Neel & Schull 1991). The aim of the investigations was to determine if acute external exposures to a short blast of enormous levels of IR would result in CM in subsequently-conceived children. The investigations showed no increase of CM rates. The impact of these investigations permeates current policies recommended by the IAEA and other agencies.

However, it is obvious that the circumstances of the "Children of Chornobyl" are clearly different. Today, in Polissia, many parents and those whom they conceive are exposed to an incessant low-dose IR emanating from continuous ingestion and inhalation of radionuclides like <sup>137</sup>Cs, <sup>90</sup>Sr and others. The IAEA, World Health Organization (WHO), and other international agencies persistently assert that the IR pollution in Ukraine is insufficient to cause detectable increases of unfavorable pregnancy outcomes (including CM). (WHO 2005 report, IAEA 2006 report). Such agencies do not recommend that these assertions be verified. Nonetheless, there is willingness in Ukraine to see those claims tested.

A continuing investigation was implemented by the OMNI-Net Ukrainian Charitable Fund, a notfor-profit international organization registered in Kyiv, Ukraine. The organization established CM monitoring programs in several provinces. The results reported here reflect events solely in the Rivne province of Ukraine. OMNI-Net secured international research partners and gained full membership in EUROCAT (European network of CM monitoring systems funded by the EU) and of ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research). These memberships signify adherence to international standards of population-based monitoring, data collection, coding, analysis, reporting, and ethics. This investigation is epidemiologic and descriptive in nature. It is designed to determine rates and associations of CM with potential risk factors. This initial step provides a focus for cause-effect prospective investigations by current and especially future additional partners.

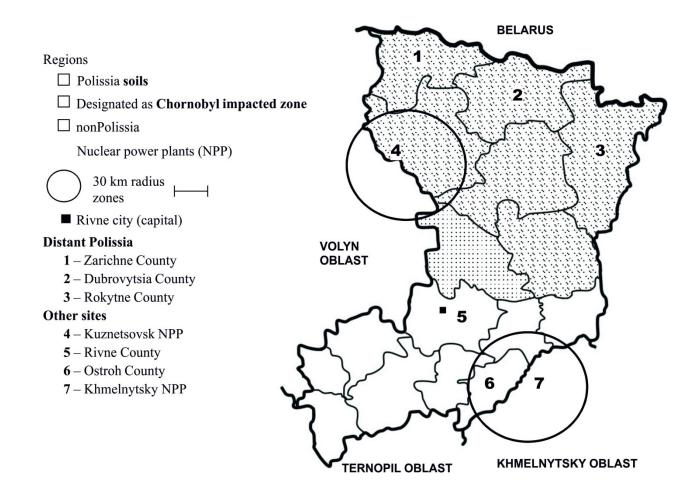
#### The study

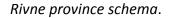
Population-based CM monitoring was established in the Ukrainian provinces (oblasts) of Volyn, Rivne, and Khmelnytsky (see Figure below). The goal is to determine overall CM rates regardless of cause. Following two years of population-based data collection, the rates of all subcategories of neural tube defects (NTD) were found to be elevated. The results of a larger follow-up investigation reported in 2010 confirmed the persistence of high NTD rates and, in addition, detected elevated rates of microcephaly (reduced head size by three or more standard deviations below the norm for age and sex). The analyses also suggested that the rates were even higher in Polissia than in the study region as a whole. (Yuskiv et al. 2004, Dancause et al. 2010, Wertelecki 2010).



Omni-Net in Ukraine. Congenital malformations are monitored in the Volyn, Rivne and Khmelnytsky provinces. The red dots and squares indicate locations of OMNI-Net teams and professional advisors respectively.

Polissia is among the most Chornobyl-IR polluted regions in Ukraine. (Likhtarev et al. 1996, and 2000, Zamostian 2002). The unique Polissia ecology, per force, is reflected in the life-style and socio-economic circumstances of the native population known as Polishchuks, among whom, characteristics of a population isolate include higher than usual rates of endogamy. Regarding IR, in Polissia, the <sup>137</sup>Cs soil-to-food transfer index is among the highest in Ukraine. These facts combined with a survival imperative to consume local IR polluted water, milk products, potato, fish, and forest products, in particular wood for heating and cooking, are reflected in high levels of incorporated whole body IR counts. In essence, Polishchuks represent a large sedentary isolated population exposed to continuous low-doses of IR conducive to considerable levels of incorporated IR. Our survey shows that by ingestion alone, disregarding inhalation, the diet consumed by pregnant women in Polissia results in radiation doses higher than considered safe by the authorities. (Dancause et al. 2010).





The current analysis includes 145,437 births in Rivne province during 2000-2009 among whom 72,379 and 73,058 were born in Polissia and non-Polissia, respectively. The array of observed CM categories is extensive and their full description is beyond the scope of this summary. Instead, the focus is on three types of CM: NTD (309 individuals); microcephaly (68 individuals); and cleft lip and/or palate (155 individuals). These CM are visually obvious at birth. Cleft lip/palate is included as a sentinel anomaly (its frequency among many populations is among the best established). Rates of conjoined twins are also included in some tables because NTD may be associated with the twinning process. (Opitz et al. 2002, Schinnzel et al. 1979). In the interest of brevity and clarity, the discussion and following tables do not allude to other observed CM. This omission does not imply that these observations are irrelevant but simply that they are dealt with elsewhere. Likewise, the causes of CM are numerous and in this summary we focus on two teratogens (causes of malformations), alcohol and IR. As indicated earlier and presented in the two tables below, the current analysis confirms prior observations and demonstrates that the rates of NTD and microcephaly are statistically significantly higher in Polissia than in the remainder of Rivne province.

	Polissia	Non-Polissia	Polis	on-Polissia	
	2000-2009	2000-2009	OR P-valu		CL
All Live Births	(72379)	(73058)			
Neural Tube Defects (NTD)	26.1	16.4	1.59	***	1.26, 2.02
Cephalad <sup>(2)</sup>	9.8	6.2	1.59	**	1.08, 2.37
Anencephaly	5.1	4.0	-	n/s	-
Spina Bifida combined	14.1	8.2	1.71	***	1.24, 2.40
Encephalocele	2.2	2.1	-	n/s	-
Microcephaly <sup>(5)</sup>	6.1	3.3	1.85	**	1.10, 3.18
Isolated	1.9	1.1	-	n/s	-
Other malf non-syndromic	2.1	n/c	7.57	***	1.76, 68.2
Syndromic	2.1	1.9	-	n/s	-
Microphthalmos <sup>(6)</sup>	2.5	0.8	3.03	*	1.15, 9.32
Other Malformations	1.0	n/c	7.07	*	0.91, 318
All	41.0	29.0	1.42	***	1.18, 1.70
Isolated	30.3	23.0	1.32	**	1.07, 1.62
Syndromes	3.3	2.2	-	n/s	-
Other Malformations	7.5	3.8	1.95	**	1.21, 3.19

Prevalence of Congenital Malformations (abridged), per 10,000 live births in Rivne Province of Ukraine. (Unduplicated individuals).

NOTE: Shown are rates of Neural Tube Defects (NTD) and microcephaly (MIC). The footnotes shown are not relevant to this abbreviated presentation, nor are subcategories of NTD and MIC or other CM observed. The abbreviations OR and CL mean odds ratio and confidence limits, respectively. The \*, \*\*, \*\*\* represent p-value of <0.05, <0.01, and <0.001 respectively and n/c or n/s indicate not computed or not significant, respectively. For an additional comment regarding OR, please see the preceding abbreviations list.

Alcohol is a major teratogen worldwide, including in Ukraine. In addition, in Ukraine and more recently in Japan, IR is another widely distributed teratogen. In Ukraine, many unborn are exposed to either or both of these teratogens. Experimentally, IR is a cause of NTD and microcephaly. In humans, both, alcohol and IR are causes of microcephaly. It is not known if concurrent exposure to both teratogens is synergistic augmenting their potency to damage a developing embryo-fetus-child. Of those exposed prenatally to alcohol, only a minority reveal at birth the physical and functional signs sufficient to establish a medical diagnosis of FAS (fetal alcohol syndrome) or FASD (fetal alcohol spectrum disorders). It is well established that many infants without evidence of FAS or FASD may have varying degrees of reduction of head size, some sufficiently severe to be included among the microcephaly individuals reported here. However, many others with lesser head size reduction may therefore not be included in the microcephaly category. The same considerations apply to exposures to IR. The most characteristic CM associated with IR are microcephaly, microphthalmia, prenatal and postnatal growth restriction, cataracts that may be late appearing and a shortened lifespan. In view that reductions of head size may be minimal, we investigated this possibility and the results are shown below. The impact on cognitive capacity of mild degrees of head size reductions may be sub-clinical and become apparent in below-par performances during high school or adulthood as noted in Scandinavia presented later.

Returning to FAS/FASD, there is an international effort to investigate modes of early diagnosis, preferably prenatally. Such achievement will facilitate early treatment and prevention of teratogenic impacts of alcohol. To this end, the National Institute on Alcohol Abuse and Alcoholism sponsors an international collaborative investigation implemented in various countries. In Rivne, the initiative is coordinated by teratologists from the University of California-San Diego (Drs. C. Chambers and K. Jones) and is implemented in partnership with investigators from the Universities of California-Davis, Emory University and Indiana University. One result of this partnership is a greater recognition and documentation of rates of FASD, the highest in Europe. However, these results also indicate, that alcohol is an unlikely primary teratogen that caused the higher rates of microcephaly in Polissia (see tables below). While in Polissia, the rates of microcephaly are statistically significantly less. Furthermore, the frequency of FASD individuals is not greater in Polissia and it is more frequent among males, in contrast to non-syndromic microcephaly which is more frequent among females.



National Institute on Alcohol Abuse and Alcoholism

# Alcohol Exposed (AE) Pregnant Women (%)

Area of Residence	Women	AE <sup>(1)</sup>	OR	P-value	CL
Polissia	852	13 (1.53)	-	-	-
non-Polissia	1417	67 (4.73)	0.31	<0.001	0.16, 0.58
Rivne City	566	36 (6.36)	0.23	<0.001	0.11, 0.45
Khmelnytsky City	1062	47 (4.43)	0.33	<0.001	0.17, 0.63

P-values refer to Polissia vs. non-Polissia, Rivne city, and Khmelnytsky city respectively

Category	Polissia	non-Polissia	Combined
FASD <sup>(a)</sup>	37 <sup>(a)</sup>	42	79 <sup>(b)</sup>
and Microcephaly <sup>(c)</sup>	9	11	20
Males	7 <sup>(e)</sup>	6 <sup>(g)</sup>	13
Females	2 <sup>(f)</sup>	5 <sup>(h)</sup>	7
No microcephaly	27	31	58
Males	12	19	31
Females	15	12	27
Gestational age (weeks) <sup>(d)</sup>			
<35	8	10	18
35-37	9	14	23
≥38	9	6	15
Birth weight (grams)			
<2500	21	25	46
≥2500	6	6	12

# Individuals with Fetal Alcohol Spectrum Disorders (FASD)

(a) Number of individuals observed (not applicable to calculation of population-based rates). Other comments are found in the full report available upon request.

NOTE: The consumption of alcohol by pregnant women in Polissia is statistically significantly less than among those from Rivne or Khmelnytsky, the capital cities of their respective provinces. Please also note that the birth weight of infants exposed to alcohol is diminished, even in the lack of other clinical signs.

The coincidence of substantial radioactive pollution in Polissia with elevated rates of microcephaly cannot be ignored. At least, monitoring of rates of microcephaly in Polissia must continue. Stark contrasts emerge from an analysis of whole body counts (WBC) of IR. The WBC solely reflect incorporated levels of <sup>137</sup>Cs (Cesium 137) and do not detect incorporated levels of <sup>90</sup>Sr (Strontium 90). The analysis included 25,059 ambulatory patients who agreed to the procedure. As shown in the table below, individuals living in the three northern counties in Polissia, incorporate much higher levels of IR than those who live in non-Polissia. The analysis of WBC of 6026 pregnant women shows that in 48% of those residing in the three counties of northern Polissia, the concentration of <sup>137</sup>Cs exceeded the upper limits established by the government in consultation with international agencies. These limits identify individuals who need assistance from public health agents to reduce exposures by inhalation or ingestion of <sup>137</sup>Cs and <sup>90</sup>Sr. A small survey of these radionuclides in locally grown potato plants shows that the ratio of <sup>137</sup>Cs to <sup>90</sup>Sr is approximately 2:1. Locally grown potatoes and dairy products are prominent in Polissia diets as established by our prior survey. (Dancause et al. 2010).

	Distant Polissia <sup>(a)</sup>	Non-Distant Polissia <sup>(b)</sup>	Non-Polissia <sup>(c)</sup>
Pregnant Women <sup>(d)</sup>	1156	2534	2336
Above Bq norm <sup>(e)</sup> (%)	557 (48.2)	155 (6.1)	3 (0.1)
Children <sup>(f)</sup>	1338	3671	1697
Above Bq norm (%)	162 (12.1)	50 (1.4)	1 (0.1)
Adult Males <sup>(f)</sup>	2117	5885	4325
Above Bq norm (%)	136 (6.4)	22 (0.4)	-

# Whole Body 137Cs Counts (Bq) Rivne Diagnostic Center's Ambulatory Outpatients

(a) Includes Zarichne, Dubrovytsia, and Rokytne counties. (b) Includes Volodymyrets, Sarny, Berezne, and Kostopil counties. (c) Includes remaining Rivne counties not mentioned in (a) or (b). (d) Pregnant women seeking prenatal ultrasound examinations at the Rivne Regional Diagnostic Center (2008-2011) who volunteered to undergo the procedure. (e) Official limits (norms) are 3700 and 14800 Bq of 137Cs for children under 15 years of age and adults respectively.(f)2000-2011 data.

> <sup>137</sup>Cs and <sup>90</sup>Sr Concentration (Ba/kg) in Dried Stems of Potato Plants from Polissia

Measurements						
<sup>90</sup> Sr (Bq/kg)		<sup>137</sup> Cs ( Bq/kg)				
First	Repeat					
43,4	46,3	88,3				
50,0	32,1	63,6				
41,3	46,4	24,0				
82,3	72,2					
88,3	84,4	46,1				
95,6	143,2					
327,2	87,5	54,8				

NOTE: virtually all IR doses that frame policies in Ukraine are based on doses solely from <sup>137</sup>Cs. The impact of <sup>90</sup>Sr, which is bound differently in the body (mimicking calcium), is particularly important in the context of a developing embryo-fetus. The differential impacts of <sup>137</sup>Cs (which mimics potassium) and <sup>90</sup>Sr (which mimics calcium) on the unborn, are generally unknown and unlikely to be similar. Calcium-rich nutrients such as milk products from Polissia are bound to contain both <sup>137</sup>Cs and <sup>90</sup>Sr. From the perspective of the rapid prenatal growth, this consideration is of particular importance.

Three investigations of NTD in the context of chronic radiation exposure are of interest. The first two were conducted by epidemiologists from the U.S. Centers for Disease Control (CDC) in two counties proximal to the Hanford Nuclear complex in Washington State, U.S. The aim was to establish rates of CM. Both investigations determined that NTD rates were statistically significantly elevated but both results were considered spurious. The investigators concluded that the IR emissions from the Hanford Nuclear Complex on the local population could not explain the findings and furthermore, pointed out that the results contradicted conclusions from earlier Hiroshima-Nagasaki investigations sponsored by the ABCC. (Sever et al. 1988a, b). A third investigation concerned fathers employed at the Sellafield Nuclear Complex in Northern England. The results showed a statistically significantly higher risk for stillbirths with congenital anomaly, highest for NTD. (Parker et al. 1999). To our knowledge, neither the investigations in Hanford nor in Sellafield in Northern England were repeated. An investigation by EUROCAT, conducted relatively soon after the Chornobyl explosion and limited to Western Europe and Scandinavia, did not detect a significant change in reported CM frequencies. (Dolk et al. 1999).

To place the Rivne observations in an international perspective, we compared the observed rates of NTD, microcephaly, conjoined twins, and CL/P with those reported to EUROCAT from other regions in Europe. Admittedly, even though all EUROCAT partners, including us, strive to use the same methods, other factors render direct statistical comparisons inappropriate without an additional exploration of potential confounding factors. Nonetheless, it is provocative to note persistent reports of higher rates of particular CM in adjoining regions. As illustrated below, the highest rates of NTD, microcephaly, and conjoined twins, besides Polissia, are noted in Northern England and Wales.

Categories	Births	CTW		NTD		MIC		CL/P		
		N*	Rate	Ν	Rate	Ν	Rate	Ν	Rate	
Rivne Province in Ukraine (2000-2009)										
Polissia Region	72800			189	25,96	46	6,32	78	10,71	
Non-Polissia Region	73488	8**	0,55	120	16,33	25	3,40	79	10,75	
EUROCAT	EUROCAT Registries (2005-2009) (Ukraine Excluded)									
Highest rate in bold (gray cells) report	ed by 16 re	gistrie	s with c	over 100	0,000 mc	onitored	l births			
Northern England (UK)	164501	9	0,55	238	14,47	32	1,95	179	10,88	
Wales (UK)	172085	6	0,35	234	13,60	92	5,35	199	11,56	
Norway	301408	2	0,07	302	10,02	16	0,53	390	12,94	
Second highest rate										
Wales (UK)	172085	6	0,35	234	13,60	92	5,35	199	11,56	
Wessex (UK)	143432	5	0,35	163	11,36	20	1,39	165	11,50	
South West England (UK)	240454	<5	0,17	263	10,94	121	5,03	209	8,69	
Third highest rate	Third highest rate									
East Midlands & South Yorkshire (UK)	358590	11	0,31	415	11,57	30	0,84	317	8,84	
Paris (France)	133880	2	0,15	172	12,85	32	2,39	114	8,52	
Valencia Region (Spain)	165859	4	0,24	116	6,99	75	4,52	95	5,73	
Wessex (UK)	143432	5	0,35	163	11,36	20	1,39	165	11,50	

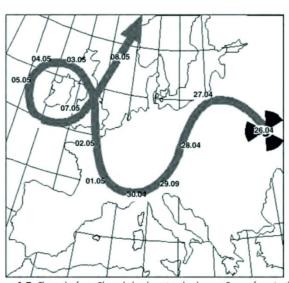
# Congenital Malformation Rates in Europe (per 10,000\*)

All 33 Full Member Registries									
Total	4123785	79	0,19	4006	9,71	1106	2,69	3724	9,03

Abbreviations: CL/P (cleft lip and/or palate), CTW (conjoined twins), MIC (microcephaly), (\*) N (number, births include live births, stillbirths and terminations of pregnancy), NTD (neural tube defects), UK (United Kingdom). (\*\*) Includes three conjoined twin sets from Polissia region. Note: EUROCAT updates the above figures on an ongoing basis evident at <u>http://www.eurocatnetwork.eu/ACCESSPREVALENCEDATA/PrevalenceTables</u>.

# Wales – Northern England ... among most heavily contaminated regions (Busby, 1995)

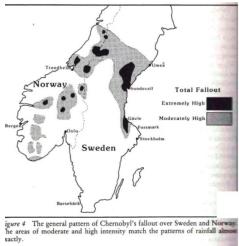
Annals of the New York Academy of Scie

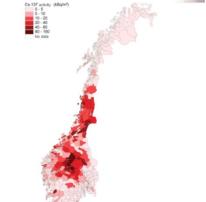


2012 - Chornobyl sheep movement restrictions finally lifted. .. but there are still 334 farms in Wales and eight in Cumbria where the restriction applies.

Figure 1.7. The path of one Chernobyl radioactive cloud across Europe from April 27 to early May 1986 (Pakumeika and Matveenka, 1996).

Of equal interest are investigations in Scandinavia where the Chornobyl fallout impacted mainly the central regions. Two independent investigations focused on cognitive functions of those exposed in-utero to radiation from the Chornobyl fallout. A large investigation in Sweden demonstrated that students who were most exposed in-utero to IR demonstrated diminished levels of performance. A similar but smaller investigation in Norway noted, less-conclusively, negative impacts on cognitive functions. (Almond et al. 2009, Heiervang et al. 2010) (see Figure below).





Douglas Almond Lena Edlund Mårten Palme

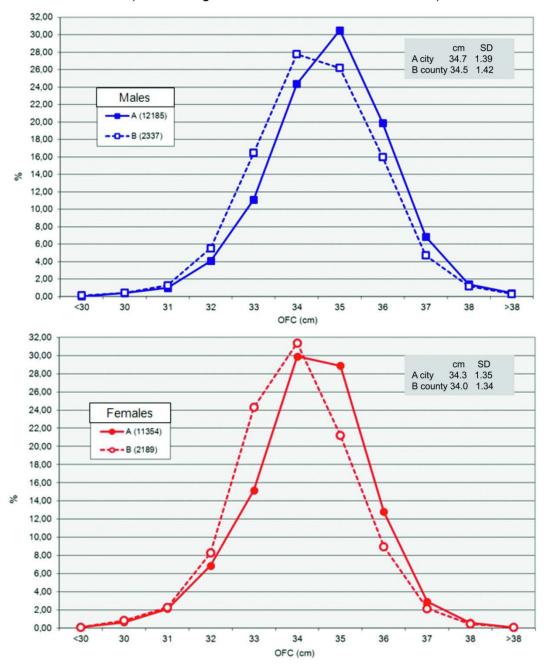
CHERNOBYL'S SUBCLINICAL LEGACY: PRENATAL EXPOSURE TO RADIOACTIVE FALLOUT AND SCHOOL OUTCOMES IN SWEDEN\*

The Quarterly Journal of Economics, November 2009

**Heiervang, K. S.,** Mednick, S., Sundet, K. & Rund, B. R. (2010). *Effect of low dose ionizing radiation exposure in utero on cognitive function in adolescence.* Scandinavian Journal of Psychology, 51, 210–215.

A comprehensive review of the impacts of Chornobyl IR, including many in Russian, shows the importance of impacts on mental health. (Yablokov 2009). From an examination of this review and other reports, we conclude that indicators of mental development and health can be added to investigations of birth defects. (Nyahu et al. 1998). For example, head circumference, age of initiation of speech and rates of suicides can be objective indicators as are visually obvious at birth CM such as an encephaly, spina bifida, cleft lip or microcephaly. In this context, we expanded our analysis and computed birth weights and at-birth occipito-frontal head circumferences of 2,398 male infants born in a county in northern Polissia, and 12,542 born in the capital city Rivne located in non-Polissia. The corresponding numbers of females are 2,240 and 11,649. Comparison of male-male and female-female were made three ways, first including all live births, second, including only those born after at least 38 weeks long gestation and third, all infancts born after at least 38 weeks long gestation and a normal physical neonatal examination. We found no contrasts in terms of birth weights. However, head circumferences of males and females were slightly but systematically statistically significantly smaller in Polissia. (Wang & Wertelecki 2012). Although these clearly are preliminary results, they are sufficiently compelling to demand further attention. The investigated neonates from Polissia were born in one of the three northern Polissia counties where the radiation exposure of

pregnant women reflected by measures of <sup>137</sup>Cs is among the highest in Rivne province. Confirmation of these observations in combination of additional factors is required.



Occipito-Frontal Circumferences (> 37 weeks gestation - normal neonatal examination)

# Conclusions

The implications of the observations in Rivne are several. First, the possibility that the observations are spurious must be considered, although this is unlikely since the third analysis confirms two previous analyses. Second, the CM rates may reflect the impact of a variety of teratogens other than radiation exposure. Such possibility must be tested before being accepted. The third possibility is, as schematized below.

# Ionizing Radiation - Chornobyl

Either

The observed elevated congenital malformations are not due to ionizing radiation.

or

The fetus is much more sensitive to radiation than officially assumed.

or

The fetus is exposed to higher doses than officially estimated.

It is generally accepted that CM such as NTD and microcephaly often are the result of multiple impacts by teratogenic risks modulated by other factors and that CM reflect an imbalance of damage/repair interactions. Although the present descriptive epidemiologic investigation is not designed to study cause-effect issues, it provides a foundation that can accelerate prospective cause-effect investigations. The access in Rivne to two distinct stable populations in terms of IR exposures and socio-economic conditions is ideal for further investigations of low doses IR impacts on embryonic development.

The conclusions emanating from this investigation cannot overshadow the principle of "prevention before epidemiology". There is immediate need to reduce IR exposures in Polissia and a concurrent need to reduce the rates of NTD. Such measures can be implemented by health authorities without delay. A continuous surveillance can detect the effectiveness of such measures. However, novel international partnerships aimed at learning from such a process would greatly enhance its feasibility and results. Much can be learned from reduction of exposures to IR combined with enhanced consumption of micronutrients on the noted rates and patterns of CM in Rivne. Furthermore, an assessment of the impacts of preventive interventions can be further enhanced by the inclusion of two other ongoing CM monitoring systems in the adjoining provinces of Volyn and Khmelnytsky.

End

(Full report is available upon request) (Power Point related presentation also available upon request)

# References

Almond D, Edlund L, Palme M. 2009. Chernobyl's subclinical legacy: prenatal exposure to radioactive fallout and school outcomes in Sweden. Quart J Economics 124:1729-1772.

Dancause KN, Yevtushok L, Lapchenko S, Shevchenko G, Wertelecki W, Garruto RM. 2010. Chronic Radiation Exposure in the Rivne-Polissia Region of Ukraine: Implications for Births Defects. Am J Hum Biol 22:657-674.

Dolk H, Nicols R, EUROCAT Working Group. 1999. Evaluation of the impact of Chernobyl on the prevalence of congenital anomalies in 16 regions of Europe. Int J Epidemiol 28:941-948.

EUROCAT Prevalence Data (under continuous updates). <u>http://www.eurocat-</u> <u>network.eu/ACCESSPREVALENCEDATA/PrevalenceTables</u> (last accessed, 4th of March, 2013).

Garruto RM, Little MA, James GD, Brown DE. 1999. Natural experimental models: The global search for biomedical paradigms among traditional, modernizing, and modern populations. Proc. Natl. Acad. Sci. USA 96:10536-10543.

Heiervang KS, Mednick S, Sundet K, Rund BR. 2010. Effect of low dose ionizing radiation exposure in utero on cognitive function in adolescence. Scand J Psychol 51:210-215.

IAEA 2006 Report. Chornobyl's legacy: Health, environmental and socio-economic impacts and recommendations to the governments of Belarus, the Russian Federation and Ukraine. Technical Report, International Atomic Energy Agency, 2006. <u>http://www.iaea.org/Publications/Booklets/Chernobyl/chernobyl.pdf</u> (last accessed, 4<sup>th</sup>of March, 2013).

Likhtarev IA, Kovgan LN, Vavilov SE, Gluvchinsky RR, Perevoznikov ON, Litvinets LN, Anspaugh LR, Kercher JR, Bouville A. 1996. Internal exposure from the ingestion of foods contaminated by 137Cs after the Chernobyl accident. Report 1. General model: ingestion doses and countermeasure effectiveness for the adults of Rovno Oblast of Ukraine. Health Phys 70:297-317.

Likhtarev IA, Kovgan LN, Vavilov SE, Perevoznikov ON, Litvinets LN, Anspaugh LR, Jacob P, Prohl G. 2000. Internal exposure from the ingestion of foods contaminated by 137Cs after the Chernobyl accident. Report 2. Ingestion doses of the rural population of Ukraine up to 12 y after the accident (1986-1997). Health Phys 79:341-357.

Neel JV, Schull WJ. 1991. The Children of Atomic Bomb Survivors. A Genetic Study. Washington, D.C.: National Academy Press.

Nyahu, AI, Loganovsky KN, Loganovskaja TK. 1998. Psycophysiologic After effects of Prenatal Irradiation. Int. J. Pshychophysiol. 30:303-311.

Opitz JM, Zanni G, Reynolds JF Jr., Gilbert-Barness E. 2002. Defects of blastogenesis. Am J Med Genet 115: 269-286.

Parker L, Pearce MS, Dickinson HO, Aitkin M, Craft AW. 1999. Stillbirths among offspring of male radiation workers at Sellafield nuclear reprocessing plant. Lancet 354:1407-1414.

Schinzel AA, Smith DW, Miller JR. 1979. Monozygotic twinning and structural defects. J Pediatr. 95:921-930.

Sever LE, Gilbert ES, Hessol NA, McIntyre JM. 1988. A case-control study of congenital malformations and occupational exposure to low-level ionizing radiation. Am J Epidmiol 127:226-242.

Sever LE, Hessol NA, Gilbert ES, McIntyre JM. 1988. The prevalence at birth of congenital malformations in communities near the Hanford site. Am J Epidemiol 127:243-254.

Wang B, Wertelecki W. 2012. Density estimation for data with rounding errors. Comput Stat Data Anal. http://www.sciencedirect.com/science/article/pii/S0167947312000989. Accessed January 30, 2013.

Wertelecki W. 2010. Malformations in a Chornobyl-Impacted Region. Pediatrics 125:836-843.

WHO 2005 report. Chernobyl: the true scale of the accident: 20 years later, UN report provides definitive answers and ways to repair lives (press release). http://www.who.int/mediacentre/news/releases/2005/pr38/en/index.html.

Yablokov AV. 2009. Nonmalignant Diseases after the Chernobyl Catastrophe. *in* Consequences of the Catastrophe for People and the Environment. Ed. Yablokov AV, Nesterenko VB, Nesterenko AV. Ann NY Acad Sci 1181, Chapter 2:58.

Yuskiv N, Andelin CO, Polishuk S, Shevchuk O, Sosynyuk Z, Vihovska T, Yevtushok L, Oakley JP Jr, Wertelecki W. 2004. High rates of neural tube defects in Ukraine. Birth Defects Res A Clin Mol Teratol 70:400-402.

Zamostian P, Moysich KB, Mahoney MC, McCarthy P, Bondar A, Noschenko AG, Michalek AM. 2002. Influence of various factors on individual radiation exposure from the Chernobyl disaster. Environ Health 1:4.