

# **Rates of Neural Tube Defects in Ukraine Highest in Chernobyl Impacted Regions**

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Based on a presentation during the

**HUMANITARIAN FORUM**

**COMMEMORATING THE 20<sup>TH</sup> ANNIVERSARY OF  
THE CHORNOBYL DISASTER**

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In commemoration of the 20<sup>th</sup> anniversary of the Chernobyl nuclear disaster, the First Lady of Ukraine, Kateryna Yushchenko, and other Ukrainian and international collaborators, organized a two-day international symposium held in Kyiv, Ukraine. This symposium, entitled “Rebirth, Renewal, and Human Development” assessed the accident’s long term impact on the health of affected populations, and brought together representatives of the United Nations, WHO, government leaders, humanitarian activists, scientific and medical experts, technological innovators and key decision-makers from fifteen nations across the globe.

Recently, the Nuclear Energy Agency noted that in Ukraine the impact of the Chernobyl disaster is profound and that “*the concern of people for their own health is only overshadowed by the concern for the health of their children and grandchildren*”. During the past twenty years, this has been the heaviest burden imposed by the disaster. The dismissive term “radiophobia”, often used by international experts, is not appropriate in regards to the profound concerns in Ukraine about the Chernobyl threat to the genome of the population.

In 1988, the U.S. Congress adopted a “Birth Defects Prevention Act” (S419), calling for collection of birth defects (BD) data to provide information and education to the public on prevention of such defects and to establish and maintain a National Information Clearinghouse on Birth Defects. This initiative culminated in the creation in 2000 of the National Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control (CDC). These developments provided an important model for emulation in Ukraine. BD are defined as any anomaly, structural or functional, of genetic or environmental nature that manifests at any age and are due to causes preceding birth. Under this definition, BD are the leading cause of infant mortality and developmental disabilities.

Following the Chernobyl disaster, it was determined that the areas most heavily contaminated by ionizing radiation lie principally in Northwest Ukraine. The distribution of the contamination is complex and contamination maps are very approximate.

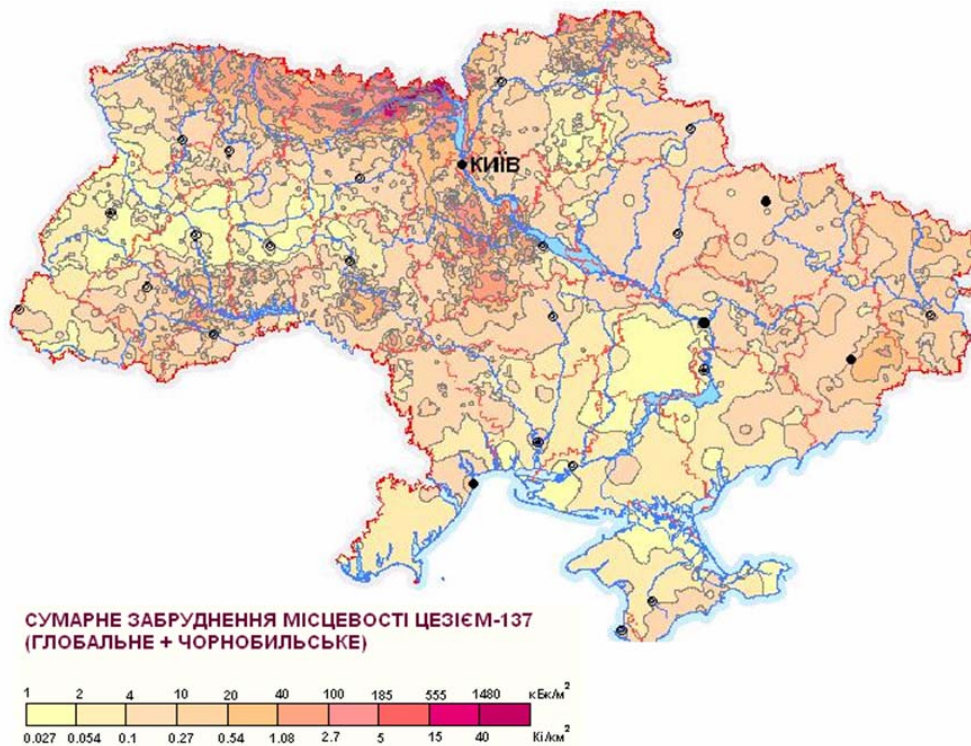


Figure 1. Irregular patterns of Caesium-137 (Cs) pollution of Ukrainian territories.<sup>(1)</sup>

In 1991, the number of scientific presentations at the International Congress of Human Genetics that were concerned with Chernobyl were few. This was surprising in view that the disaster was the most massive global threat to the stability of the human genome. During the next International Congress of Human Genetics, on August 24, 1996, coincidentally the date of the fifth anniversary of the independence of Ukraine, our team organized a conference concerned with “Chernobyl: Implications of a Decade”. The participating experts underscored that contrary to other nuclear accidents, Chernobyl represented a challenge of an unprecedented scale because of its magnitude and because ionizing radiation is one of the most widely known causes of genetic mutations resulting in BD, as well as cancer. It was also noted, that the role played by independent investigators, in contrast to experts engaged by “bureaucratized agencies”, had been quite modest and that scientific contributions by non-governmental investigators tend to increase public confidence. Others noted that “atomic agencies” have not gained public credibility. One investigator reported that direct measurements taken from Ukrainian population showed that 65 percent of internal radiation was from Caesium (Cs-137) ingested with food. It was also established that levels of ionizing radiation accrued by rural populations were significantly higher than urban populations, mostly due to weaker control of sources of food. By then, there were more childhood thyroid cancers in the countries affected by Chernobyl than all cancers induced by the atomic bombs that fell on Japan. In a paper submitted by Dr. J. Neel, a world renown geneticist who pioneered many studies of the Hiroshima/Nagasaki bomb survivors and their children, he stated “if we had to do such studies over again, the most obvious change in the research design

would be to include studies at the DNA level from the outset”. He also recommended that the frequency of congenital malformations, stillbirths, death rates of live born children, and growth and development of surviving children should be investigated.<sup>(2)</sup>

In 1994, the March of Dimes Birth Defects Foundation sponsored a meeting following which the “World Alliance for the Prevention of Birth Defects” was organized, and the author of this report was chosen as its secretary.<sup>(3,4)</sup> The World Alliance was to promote BD prevention and in 1995 the President and the Secretary of the World Alliance visited Ukraine.

In 1998, by invitation of the Ukrainian Minister of Health, Dr. A. M. Serdiuk, the President of the March of Dimes Birth Defects Foundation, the President of the World Alliance for the Prevention of Birth Defects and other experts, visited Kiev. The goal was to establish international links with Ukrainian professionals and to gather information about the effects of radiation from the Chernobyl disaster and its impact on BD in Ukraine. It was noted that there was a great interest in the subject of BD, and that some very basic BD data was maintained by the Ministry of Health. Ukrainian physicians and scientists, however, emphasized the need for an improved BD data collection system. At the time, there was a proposal pending to the United States Agency for International Development (USAID) for pilot birth defects (BD) surveillance programs to be established in the regions of Rivne and Volyn, which were quite impacted by the Chernobyl disaster.

In 1999, through a cooperative agreement with the USAID, Dr. W. Wertelecki, through the Department of Medical Genetics, University of South Alabama, with assistance from Drs. I. Baryliak, L. Yevtushok, and other Ukrainian specialists (Reference 5 – Acknowledgements) initiated the slow and complicated process of establishing BD surveillance systems in Ukraine. After the USAID component ended in 2005, BD surveillance continues by the OMNI-Net, an international not-for-profit Ukrainian organization.<sup>(5)</sup> The OMNI-Net BD surveillance system began formal data collection in 2000 in the Northwest region of Ukraine (Rivne and Volyn oblasts). Nine raions (counties) of the Northwest region have been designated as impacted by Chernobyl, six are in Rivne and three are in the Volyn oblast.



Figure 2. OMNI-Net BD surveillance centers were established in 2000 (in blue) and in 2002-2003 (in green). In the upper left corner are shown the raions (counties) of Rivne and Volyn oblasts, nine of which have been designated as contaminated by Chornobyl ionizing radiation, a region called Polissia (shaded in gray).

In 2002, we noted elevated rates of spina bifida, anencephaly and encephaloceles, collectively referred to as neural tube defects (NTD). In 2004, we reported a prevalence of NTD in Northwest Ukraine of 21 per 10 000 live births, nearly 4 times what it would have been were the population consuming enough folic acid. <sup>(6)</sup>

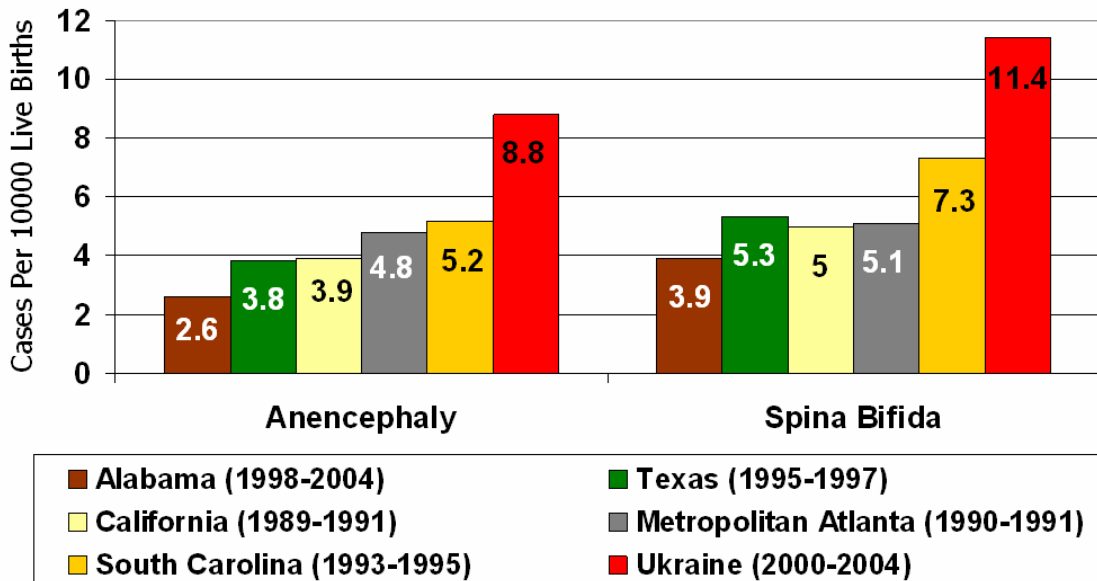


Figure 3. Prevalence rates per 10 000 live births of anencephaly and spina bifida in Northwest Ukraine, California, South Carolina, Texas and metropolitan Atlanta.

Data collected during 2002-2004 and preliminary data from 2005 confirmed ongoing epidemic rates of NTD in Ukraine. High prevalence rates persist in the Northwest and were also found in the Central and South regions of Ukraine. The lowest prevalence rate, 10.7 per 10 000 live births, was in the South region (Kherson oblast and the Autonomous Republic of Crimea). Nonetheless this rate is three times as high as in many other countries, including the U.S.<sup>(7)</sup> It must be noted that prevalence rates in Ukraine reflect prenatal ascertainment. BD surveillance systems inclusive of prenatal ascertainment report higher rates than those that do not. In the U.S., BD surveillance systems with prenatal ascertainment revealed rates for spina bifida and anencephaly of 6.4 and 4.2 before folic acid fortification of flour and 4.1 and 3.5 after flour fortification, in comparison with those without prenatal ascertainment which revealed rates of 5.1 and 2.5 before flour fortification and 3.4 and 2.1 after flour fortification.<sup>(8)</sup>

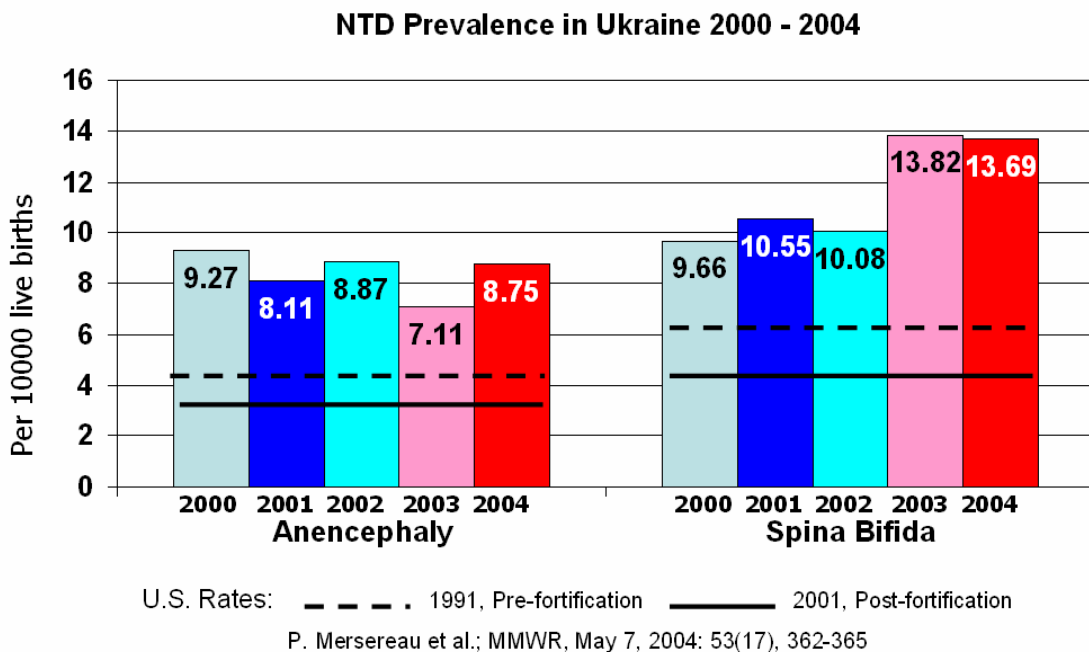
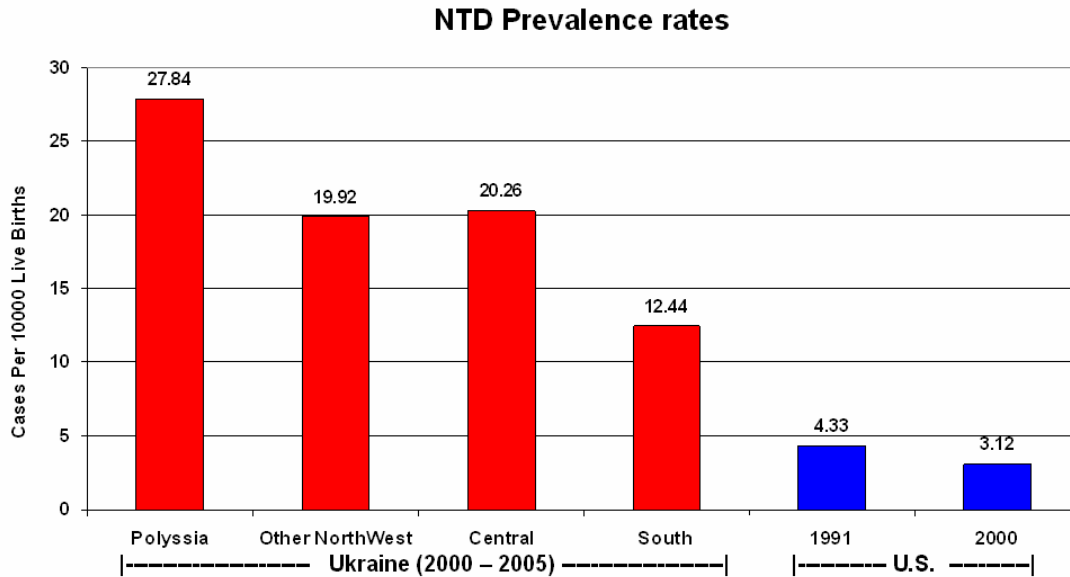


Figure 4. Rates of anencephaly and spina bifida in Northwest Ukraine compared with U.S. prevalence rates computed with consideration to prenatal ascertainment.<sup>(8)</sup>

In partnership with the Ukrainian Academy of Medical Sciences, the Ministry of Health of Belarus and the WHO Regional Office for Europe, conferences were held in Minsk, Belarus and Rome, Italy concerned with “Folic acid: from research to public health practice”.<sup>(9)</sup> The participating experts calculated that folic acid flour fortification at the level 0.42 mg/100g flour would reduce annual NTD pregnancies in Ukraine from 884 to 460.

In 2006, there was sufficient data to permit analysis of NTD prevalence rates in raions designated as impacted and not impacted by Chernobyl. The raions impacted by Chernobyl belong to a region called Polissia where the NTD rates were the highest we found in Ukraine (Figure 5).



T.J. Matthews et al.; MMWR, September 13, 2002: 51, pp. 9

*Figure 5. NTD prevalence rates in the Polissia region, other raions of the Northwest (Rivne and Volyn oblasts), Central (Khmelnysky) and Southern regions (Kherson and Autonomous Republic of Crimea) compared with U.S. prevalence rates.<sup>(7)</sup>*

The terrain in Polissia is unique, its soil is soddy with low humus content and there are many meadow-bog and peat-bog areas (see Figure 2). Some have estimated that a person living in Polissia would absorb 10 times as much radioactivity as a person living in Minsk. The local environment of peat-swampy soil is characterized by the highest values of soil-to-milk transfer coefficients of Cs-137.<sup>(10)</sup> The levels of Cs-137 in milk in Polissia have diminished since 1999 but nonetheless remain high. The lifestyle of the local residents, most of whom live in small villages surrounded by forests, has changed since 1987. The reliance on locally produced vegetables and milk and foraging for mushrooms, berries, cranberries, and wild game from the surrounding forests has increased. These nutrients are known to concentrate radionuclides, particularly Cs-137. The half-life of Cs-137 in berries and mushrooms is estimated at 10 and 20 years respectively.

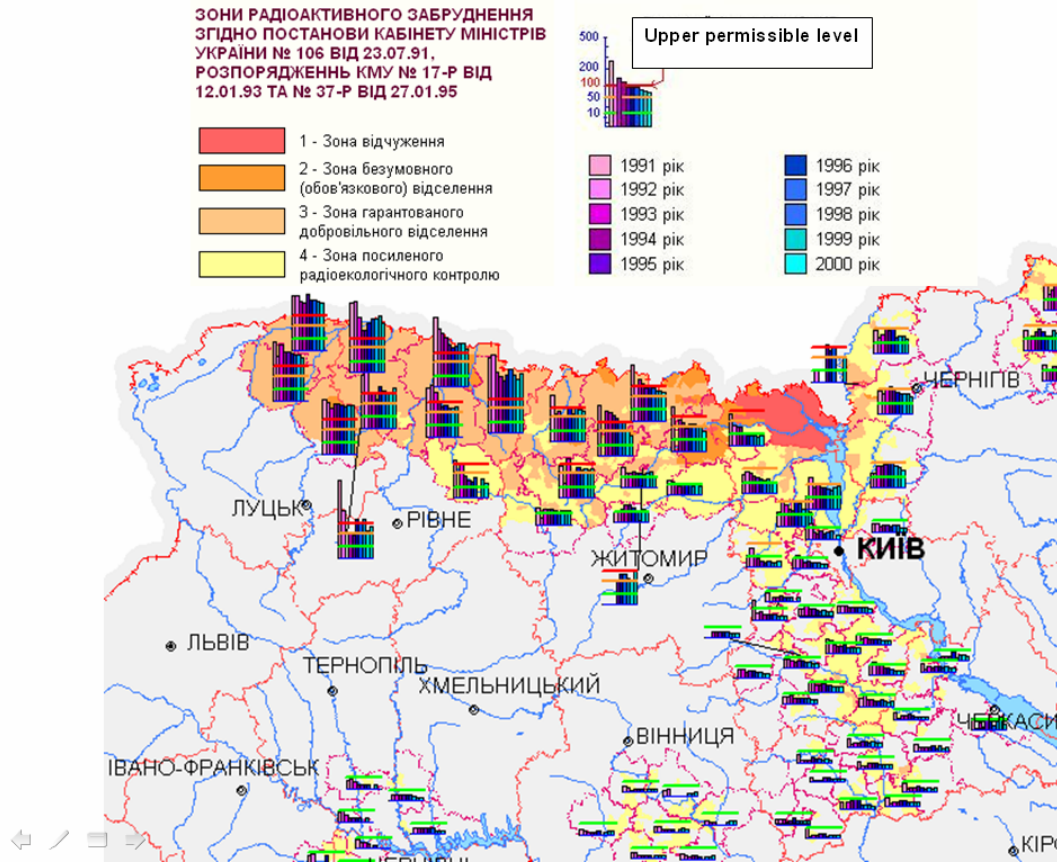


Figure 6. Map illustrating Cs-137 milk contamination in Polissia raions.

Population based BD surveillance systems, such as the OMNI-Net, are designed to promote the prevention and better care of children with malformations, mental subnormality and other developmental disabilities. In view that most BD are due to unknown causes, surveillance systems are also designed to promote research. One strategy, among others, is to monitor the occurrence of very rare malformations. In this regard, between 2000 and 2005 we noted five instances of conjoined twins in the Rivne oblast. Notably, one of the twins had spina bifida. For the period 2000-2005, there were 81 909 live births in the Rivne oblast. In an informal review of ten large BD surveillance systems, each monitoring at least one million pregnancies, none reported more than one instance of conjoined twins.



Year	Rivne <sup>(a)</sup>	Volyn	Khmel'nitskyj	Kherson <sup>(b)</sup>	Crimea
2000	2	0	-	-	-
2001	0	0	-	-	-
2002	1	0	0	-	-
2003	1 <sup>(c)</sup>	0	0	0	0
2004	1	0	0	0	0
2005	0	0	0	1	0

(a) 81 909 live births (2000-2005)

(b) 46 883 live births (2003-2005)

(c) One twin in this series had a spina bifida

Figure 7. The prevalence rate of conjoined twins, a very rare malformation, is not established.

The noted high prevalence of NTD in Polissia most likely reflects dietary folate deficiencies, perhaps magnified by significant alcohol consumption. Whether low dose chronic ionizing radiation is an additional risk factor remains speculative.

Folates are required for cell division and cell maintenance. They are essential for the *de novo* construction or repair of DNA, re-methylation of plasma homocysteine to methionine and the “site-specific” methylation of the cytosine base in DNA, which regulates gene expression.<sup>(11)</sup> Folate deficiency is common, as in the UK 5 to 8 percent of young adults and 21 percent of older people have signs of folate deficiency.<sup>(11)</sup> It is reasonable to assume that in Ukraine, and particularly in Polissia, folate deficiency is even more common. Deficiencies of folate result in higher prevalence rates of NTD and other birth defects. Folate deficiencies are also associated with elevated plasma homocysteine, a risk factor for cardiovascular disease, and perhaps higher risks for breast cancer and colon cancer.

The impact of alcohol on a developing fetus often results in serious BD and mental subnormality. Our studies in Ukraine show that 10 percent of children in Ukrainian orphanages have BD suggestive of prenatal exposure to alcohol. Furthermore, alcohol also impairs folate absorption and chronic alcohol use decreases liver stores of folates. Folic acid was the most common vitamin deficiency in the United States, because of its association with excessive alcohol intake, which affects 5 percent of the population. After the introduction of mandatory folic acid flour fortification in the US, the frequency of folate deficiency anemia has fallen by 96 percent.<sup>(12)</sup> Pregnant women are often folate deficient since their daily requirement increases by as much as five times the normal.

The impact of ionizing radiation was most devastating to the Polissia region. To what degree the ongoing chronic low dose ionizing radiation alters the DNA of the population, is not known, nor is it known if it contributes to increased NTD rates. On the other hand,



it is known that folate deficiency results in suboptimal cellular DNA repair capacity.<sup>(13)</sup> These are issues that should be clarified by more research.

The children of Ukraine bore the brunt of Chernobyl and continue to bear a heavy daily burden of BD because the Ukrainian government has not implemented mandatory folic acid fortification, as done by some other 40 countries of the world. The cost of each day of delay is the life of an infant. Regardless of future investigations, we urge Ukrainian authorities to immediately institute an intensive folic acid supplementation program in Polissia for all women of reproductive age. The Ukrainian Ministry of Health has already published protocols for folic acid supplementation programs. After implementations in Polissia, such programs should be quickly expanded to other regions. Concurrently, a folic acid flour fortification program of large flourmills should also be urgently initiated based upon international standards, which our team has already provided to the Ukrainian Academy of Medicine and the Ministry of Health. Prompt implementation of a folic acid supplementation and flour fortification program in Ukraine will spare the lives of nearly 500 Ukrainian infants each year and prevent many others from life-long paralysis and other disabilities.

Regarding Chernobyl ionizing radiation effects, a UN Chernobyl Forum expert review group concerned with human reproduction concluded that “... *because the doses were so low, there was no evidence of any effect on the number of stillbirths, adverse pregnancy outcomes, delivery complications or overall health of children. A modest but steady increase in reported congenital malformations in both contaminated and uncontaminated areas of Belarus, appear to be related to better reporting, not radiation.*” The reactions have been mixed.<sup>(14)</sup> According to Moller and Mousseau, the UN experts may have not included in their review 30 recent studies, 25 of which showed increased mutations and cytogenetic effects of Chernobyl related radiation.<sup>(15)</sup> New molecular genetic techniques offer approaches of greater sensitivity and specificity than those available a decade ago. Further molecular, genetic, folic acid, alcohol and epidemiologic studies by an international consortium are, in our view, essential. The results are likely to elucidate new facts important to the Ukrainian public and contribute to a better understanding of the complexities of the causes of BD.

Ukraine has, perhaps more than most countries, much to gain from an established and experienced BD surveillance system upholding international standards. The OMNI-Net BD surveillance system can facilitate the immediate introduction of folic acid supplementation, rapidly show the impact of the introduction of flour fortified with folic acid and facilitate studies of low dose chronic ionizing radiation effects on human reproduction. In the final analysis, the resolution of the questions discussed, are bioethical by nature and for Ukrainian authorities to resolve. Every day folic acid enrichment programs are delayed, there is a tragic cost measured in infant lives lost.

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## Notes and References

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