DO LOW DOSES OF IONIZING RADIATION AFFECT THE HUMAN BRAIN?

K. Loganovsky

Dept of Radiation Psychoneurology, Institute for Clinical Radiology, State Institution "Research Centre for Radiation Medicine of Academy of Medical Sciences of Ukraine", 53 Melnikov Str., Kyiv, 04050, Ukraine
Email: loganovsky@windowslive.com

ABSTRACT

The aim of this paper is to analyze the current evidence on radiocerebral effects following exposure to <5 Sv. Dose-related cognitive and neurophysiological abnormalities among prenatally exposed children after the Chernobyl accident at gestation ages of +8 weeks were revealed at >20 mSv on the fetus and >300 mSv on the thyroid in utero; at 16–25 weeks, abnormalities were >10 mSv and >200 mSv, respectively. In adults, radiation-associated cerebrovascular effects were obtained at >0.15-0.25 Sv. Dose-related neuropsychiatric, neurophysiological, neuropsychological, and neuroimaging abnormalities following exposure to >0.3 Sv and neurophysiological and neuroimaging radiation markers at doses >1 Sv were revealed. Studies on radiation neuropsychiatric effects should be undertaken.

Keywords: Ionizing radiation, Low doses, Chernobyl accident, Brain, Radiosensitivity, Radiocerebral effects, Exposure *in utero*

1 INTRODUCTION

The current challenges of modern radiobiology and radiation protection, which include radiation accidents at nuclear reactors, radiological terrorist attacks using a radiation dispersal device (RDD), the so-called "dirty bomb", and radiation exposure during space flights, present two very important issues. The first is whether low doses of ionizing radiation have any harmful influence on human health at all, and the second is the acute and still open for more than a century discussion of the radiosensitivity/radioresistance of the brain. These two issues taken together, whether low doses of ionizing radiation affect the human brain, present an extremely contradictory problem. An accidental exposure is obviously associated with: 1) non-radiation factors, mainly, psychological stress, and 2) an absence of the base-line (before exposure) health data of victims. That is why distinguishing potential low doses effects on the human brain is quite a difficult scientific task.

According to the classical foundation of cancer radiotherapy by French radiobiologists Bergonie and Tribondeau (1906), "The sensitivity of cells to irradiation is in direct proportion to their reproductive activity and inversely proportional to their degree of differentiation". Consequently, the adult nervous tissue was recognized as an excellent example of a "closed static population", and, because of its fixed postmitotic state, this population was considered to be "extremely radioresistant". At the same time, the evidence is dramatically increasing in support of the radiosensitivity of the Central Nervous System CNS (Nyagu & Loganovsky, 1998; Wong & Van der Kogel, 2004; Gourmelon, Marquette, Agay, Mathieu, & Clarencon, 2005). The development and validation of biological markers of ionizing radiation is the primary goal of current radiobiology and radiation protection (Bebeshko, Bazyka, & Loganovsky, 2004).

Recently, reports about the beneficial health effects of low doses of radiation, as a "radio-adaptive response", were widely published (Chen, Luan, Shieh, Chen, Kung, Soong et al., 2006; Cuttler, 2007; Rodgers & Holmes, 2008). The most conservative threshold of radiation-induced neuroanatomic changes was assumed to be 2–4 Sv for whole body irradiation, while that for the CNS was assumed to be 50-100 Gy (Gus'kova & Shakirova, 1989; Gus'kova, 2007). The radiotherapeutic tolerant dose for the brain was assumed to be 55–65 Gy, and the tolerant fractional dose was assumed to be 2 Gy (Mettler & Upton, 1995). Moreover, a "glial-vascular union" was considered to be the cerebral basis of a postradiation brain damage, while neurons themselves seemed to be out of this pathogenesis: consequently, the brain white matter was considered to be much more radiovulnerable than the brain grey matter. However, the latest advances in understanding the mechanisms of CNS radiation damage demand a reassessment of these assumptions. It is now recognized that the CNS is a major dose-limiting organ in clinical radiotherapy (Wong & Van der Kogel, 2004), and the CNS is a radiosensitive system (Gourmelon, Marquette, Agay, Mathieu, & Clarencon, 2005). The analysis of our own studies in combination with the current evidence on CNS effects of exposure to ionizing radiation in humans in doses up 5 Sv is presented in this paper.

2 RADIOCEREBRAL EFFECTS AT DIFFERENT EXPOSURES SCENARIOS

2.1 Current views on low doses radiation brain injury pathogenesis

Radiation exposure has multiple effects on the brain, behavior, and cognitive functions. These changes depend largely on the dose received. It is well known that ionizing radiation influences CNS functions and behavior both as a result of direct effects on the nervous system and indirectly through CNS reactivity to the radiation damage of other systems (Kimeldorf & Hunt, 1965; Mickley, 1987). Alteration in CNS functioning is likely to occur after relatively low doses of radiation. There is now an increasing body of data indicating that the response of the CNS after irradiation is a continuous and interacting process. Specifically, the focus is on apoptotic cell death and cell death and injury mediated by secondary damage (Wong & Van der Kogel, 2004). Today, it is established that the CNS is a radiosensitive organ whose degree of dysfunction can be quantified by electrophysiological, biochemical, and/or behavioral parameters. Abnormalities in CNS function defined by these parameters may occur at a low dose of whole body radiation (Gourmelon, Marquette, Agay, Mathieu, & Clarencon, 2005).

A recent study illustrated that sub-chronic exposure with post-accidental (Chernobyl) doses of ^{137}Cs lead to molecular modifications of pro- and anti-inflammatory cytokines and NO-ergic pathways in the brain. This neuro-inflammatory response could contribute to the electrophysiological and biochemical alterations observed after chronic exposure to ^{137}Cs (Lestaevel, Grandcolas, Paquet, Voisin, Aigueperse, & Gourmelon, 2008).

Brain irradiation modulated the expression patterns of 1574 genes, of which 855 showed more than 1.5-fold variation. About 30% of genes showed dose-dependent variations, including genes exclusively affected by 0.1 Gy. About 60% of genes showed time-dependent variation with more genes affected at 30 minutes than at 4 hours. Early changes involved signal transduction, ion regulation, and synaptic signaling. Later changes involved metabolic functions including myelin and protein synthesis. Low-dose radiation also modulated the expression of genes involved in stress response, cell-cycle control, and DNA synthesis/repair. Doses of 0.1 Gy induced changes in gene expression that were qualitatively different from those at 2 Gy. The findings suggest that low-dose irradiation of the brain induces the expression of genes involved in protective and reparative functions while down-modulating genes involved in neural signaling activity (Yin, Nelson, Coleman, Peterson, & Wyrobek, 2003). Changes in the gene profile in the brain after irradiation are complex and are dependent on time and dose, and genes with diverse functions and pathways are modulated (Mahmoud-Ahmed, Atkinson, & Wong, 2006).

Neurogenesis in the adult hippocampus, which occurs constitutively, is vulnerable to ionizing radiation. Radiation cognitive impairments may involve injury to the neurogenic cell population that exists in the dentate subgranular zone (SGZ) of the hippocampus (Andres-Mach, Rola, & Fike, 2008). The pattern of hippocampus-dependent memory dysfunction is consistent with the change in neurogenesis after acute irradiation. It is suggested that a relatively low dose of acute radiation sickness (ARS) in adult ICR mice is sufficiently detrimental to interrupt the functioning of the hippocampus, including learning and memory, possibly through the inhibition of neurogenesis (Kim, Lee, Kim, Kang, Bae, Shin, et al., 2008). The cognitive impairments are associated with reductions in proliferating Ki-67-positive cells and Doublecortin-positive immature neurons in the SGZ of the dentate gyrus. The significant loss of proliferating SGZ cells and their progeny suggests a contributory role of reduced neurogenesis in the pathogenesis of radiation-induced cognitive impairments (Raber, Rola, LeFevour, Morhardt, Curley, Mizumatsu, et al., 2004). Thus, the radiation response of neural precursor cells from SGZ of the hippocampal dentate gyrus cell and altered neurogenesis may play a contributory if not causative role in radiation-induced cognitive impairment (Mizumatsu, Monje, Morhardt, Rola, Palmer, & Fike, 2003). Progressive learning and memory deficiencies following irradiation may be caused by the accumulating hippocampal dysfunction that results from a long-term absence of normal stem/progenitor activity (Monje & Palmer, 2003).

Analyses of transcriptome profiles of mouse brain tissue after whole-body irradiation showed that low-dose exposures (10 cGy) induced genes not affected by high-dose radiation (2 Gy) and that low-dose genes were associated with unique pathways and functions. The molecular response of the mouse brain within a few hours after low-dose irradiation involves the down-regulation of neural pathways associated with cognitive dysfunctions that are also down-regulated in normal human aging and Alzheimer's disease (Lowe, Bhattacharya, Marchetti, & Wyrobek, 2009).

Thus, there is new evidence for the radiation-induced molecular and cellular basis of CNS effects following exposure to low doses of ionizing radiation: disrupted neurogenesis in the adult hippocampus, changes in the gene expression profile, a neuroinflammatory response, neurosignaling alterations, apoptotic cell death, cell death and injury mediated by secondary damage, etc. together with the well-known role of the "glial-vascular union" in the pathogenesis of radiation brain injury.

2.2 Radioneuroembryological effects

The developing brain is extremely radiosensitive. Severe mental retardation, lowering of intelligence quotient (IQ), and worsening of school performance, or the occurrence of microcephalia and seizures, especially after exposure at 8–15 and 16–25 weeks after fertilization, were revealed in survivors of the atomic bombing of Hiroshima and Nagasaki (Otake & Shull, 1984, 1998; ICRP Publication 49, 1986; Shull, 1997; Shull & Otake, 1999; ICRP Publication 90, 2003). The latest reanalysis of the dosimetry data indicates that the dose threshold for the development of mental retardation after intrauterine irradiation at gestation ages of 8–15 weeks is 0.06–0.31 Gy. At a gestation age of 16–25 weeks, it is 0.28–0.87 Gy (Otake, Schull, & Lee, 1996). The question whether irradiation *in utero* is the risk factor for the increased lifetime prevalence of schizophrenia in survivors prenatally exposed to atomic bomb radiation is still open to discussion (Imamura, Nakane, Ohta, & Kondo, 1999).

The current thinking on prenatal radiocerebral effects is that 1 Sv of fetal exposure at 8–15 weeks of gestation reduces IQ by 30 points. Correspondingly, it is assumed that each 100 mSv of prenatal irradiation lowers IQ no more than 3 points. The excess of severe mental retardation is 0.4 per 1 Sv at 8–15 weeks and, to a lesser extent, at 16–25 weeks of gestation (European Commission. Radiation protection 100, 1998; ICRP Publication 84, 2000).

Thus, the evidence-based radioneuroembriologic effects in humans are: 1) dose-related intelligence reduction including mental retardation, 2) microcephalia, and 3) seizures. This IQ deterioration is dependent on the period of cerebrogenesis when the exposure has occurred. However, other possible radioneuroembriological effects, such as schizophrenia and epilepsy, are still at issue.

The data concerning brain damage *in utero* following the Chernobyl accident is very contradictory, as shown in Table 1. Extrapolation of Japanese findings to those from Chernobyl is limited. The Chernobyl accident caused lower fetal doses but significantly much higher doses on the fetal thyroid because of the radioiodine released by the burning reactor. Whereas after the Chernobyl accident the population was continuously exposed to radionuclides, mainly of radioiodine and ^{137}Cs, the Japanese population was acutely irradiated by γ-rays and neutrons. There was no separate radioiodine exposure of the thyroid in Japan. Because of the different radiobiological situations, it is not easy to predict the radiobiological effect of the Chernobyl accident from the results of the Japanese studies (Nyagu, Loganovsky, Pott-Born, Repin, Nechayev, Antipchuk et al., 2004).

Table 1. Summary of main reports on cerebral effects in the prenatally exposed as a result of the Chernobyl accident

Authors and studies	Cerebral effect	Radiation effect
IPHECA WHO, 1992–1995	++	?
Ukraine (Nyagu et al, 1992–2004)	+++	+
Belarus (Igumnov et al, 1994–2008)	++	—
Russia (Yermolina et al, 1994–1998)	+++	+
USA-Ukraine (Bromet et al, 1998–2008)	±	—
UNSCEAR 2000	±	—
French-German Initiative for Chernobyl, Ukraine [RCRM], 1998–2004	++	±
Israel (Bar Joseph et al, 2004)	±	—
UN Chernobyl Forum (2006)	+	?
Finland (Huizink et al, 2007, 2008)	++	—
Sweden (Almond et al, 2007)	++	+
Ukraine (Loganovsky et al, 2008)	++	+

In 1992–1995, the World Health Organization (WHO) conducted the Pilot Project on Brain Damage *in Utero* under the auspices of the International Program on the Health Effects of the Chernobyl Accident (IPHECA). Analysis of the results in Belorussia, Russian Federation, and Ukraine has shown the following: a) the prevalence

of mild mental retardation in prenatally irradiated children is higher when compared with the control group; b) an upward trend was detected in cases of behavioral disorders and in changes in the emotional problems in children exposed *in utero*; and c) the prevalence of borderline nervous and psychological disorders in the parents of prenatally irradiated children is higher than that of controls. The IPHECA study had several crucial limitations of which the most important was the impossibility of linking the results to individual doses. The definition of an exposed and unexposed child was based only on the contamination level of the soil of the district of residence, without reference to individual doses (WHO, 1996).

Nyagu and colleagues (1992-2004) have paid great attention to the problem of brain damage *in utero* following the Chernobyl accident. In their first reports, an overestimation of mental development delay rate (up to 77%) was done, and the exposure of the thyroid *in utero* to doses more than 0.3 Sv was concluded to be the risk factor for neuropsychiatric effects (Nyagu, Cheban, Salamatov, Limanskaja, Yashchenko, Zvonariova, et al., 1993; Nyagu, Cheban, Bugayev, Korol, & Treskunova, 1997). Further, using international psychometric methodology, we found an increase of mild mental retardation and borderline and low range IQ, as well as emotional and behavioral disorders and a decrease in high IQ, in children irradiated *in utero*. One important biological mechanism in the genesis of mental disorders in prenatally exposed children could be the radiation-induced malfunction of the thyroid-pituitary system with the effect threshold of 0.3 Sv of thyroid exposure dose. The data obtained reveal mental disorders in prenatally irradiated children and obviously reflect developmental abnormalities of brain structure and function as a result of the interaction of prenatal and post-natal factors, where it is possible to assume radiation effects on the developing brain (Nyagu, Loganovsky, Loganovskaja, & Antipchuk, 1996; Nyagu, Loganovsky, Cheban, Podkorytov, Plachinda, Yuriev, et al., 1996; Nyagu, Loganovsky, & Loganovskaja, 1998). The following were observed in the prenatally exposed group: IQ performance/verbal discrepancies with verbal decrements; a higher frequency of low-voltage and epileptiformal EEG-patterns and left hemisphere lateralized dysfunction; and an increase of δ- and β-power and a decrease of α- and θ-power; an increased frequency of paroxysmal and organic mental disorders, somatoform autonomic dysfunction, disorders of psychological development, and behavioral and emotional disorders. Cerebral dysfunction was recognized to be etiologically heterogeneous (Nyagu, Loganovsky, Loganovskaja, Repin, & Nechaev, 2002)

Igumnov (1996) showed that mental disorders among children irradiated *in utero* resulted from predominantly sociodemographic and socio-cultural factors. An increased prevalence of specific developmental speech-language and emotional disorders as well as a lower mean full scale IQ and more cases of borderline IQ in prenatally exposed children in Belarus were attributed to social and psychological factors. They did not find any association between prenatal irradiation and IQ and deterioration in children's mental health (Igumnov, 1999; Kolominsky, Igumnov, & Drozdovitch, 1999). This point of view has been supported in the Annex J. Exposures and effects of the Chernobyl accident of the UNSCEAR 2000 Report to the General Assembly (2000). It was concluded that probably a significant role in the genesis of borderline intellectual functioning and emotional disorders in children exposed *in utero* in Belarus was played by unfavorable social-psychological and social-cultural factors (Igumnov & Drozdovitch, 2004).

There are data on intelligence reduction from thyroid doses of above 0.5 Gy for children exposed *in utero* and at the age of 0–1.5 years (Bazyltchik, Drozd, Reiners, & Gavrilin, 2001). Average IQ for the subgroup of highly exposed children (thyroid doses *in utero* >1 Gy) was lower in comparison with average IQ for the whole exposed group (Igumnov & Drozdovitch, 2000). Prenatally irradiated children, especially those exposed at 8–15 weeks, had more functional and organic disorders of the CNS and exhibited borderline IQ and abnormal EEG linked to both radiation and psychosocial factors (Gayduk, Igumnov, & Shalckevich, 1994). Children irradiated *in utero* had the highest indices of mental morbidity and were more likely to display borderline intelligence and mental retardation that were linked to prenatal irradiation (Ermolina, Sukhotina, Sosyukalo, Kashnikova, & Tatarova, 1996).

Recent studies using standard batteries of neuropsychological tests failed to find systematic differences in children exposed *in utero* (Litcher, Bromet, Carlson, Squires, Goldgaber, Panina, et al., 2000; Bar Joseph, Reisfeld, Tirosh, Silman, & Rennert, 2004). Interestingly, in the Litcher and colleagues (2000) study, mothers of evacuee children were 4 times more likely to report that their children had memory problems compared to controls even though there were no differences in actual neuropsychological test performance or school grades. This underscores the important contribution of perceived threat to reports about health and mental health status. However, no dosimetric data were available, and there were no normative data in Ukraine for the measures used in the study (Bromet, Goldgaber, Carlson, Panina, Golovakha, Gluzman, et al., 2000; Litcher, Bromet, Carlson, Squires, Goldgaber, Panina, et al., 2000). Moreover, the IQ tests were applied selectively: Litcher and colleagues (2000) assessed children's cognitive functions using spatial intelligence (Symbolic

Relations subtest of the Detroit Test), attention, and memory only and excluded verbal intelligence. Full scale IQ, verbal IQ, and performance IQs are not available.

It was assumed that western-based investigations indicated that no adverse neuropsychiatric effects occurred in persons exposed *in utero*, but local studies reported increased cognitive impairments in exposed compared with non-exposed children. At the same time, the experts of the UN Chernobyl Forum (WHO, 2006) stressed that the effects on the developing brain should be the focus of attention after the Chernobyl accident. Taormina and colleagues (2008) conducted an 8-year follow-up of the evacuees and classmate controls assessed in Kiev in 1997. This study re-examined the children's performance and academic achievement at age 19 years. The authors came to the conclusion that Chernobyl did not influence the cognitive functioning of exposed infants (including those irradiated *in utero*) although more evacuee mothers still believed that their offspring had memory problems. According to the authors' opinion, these lingering worries reflect a wider picture of persistent health concerns as a consequence of the accident (Taormina, Rozenblatt, Guey, Gluzman, Carlson, Havenaar, et al., 2008). However, this study has also no assessment of the doses *in utero.*

Since possible dose correlations were not investigated and contradictory results of the mental health assessment of the *in utero* exposed children and the etiology of the observed neuropsychiatric disorders were found, a thorough study in the framework of Project 3 "Health Effects on the Chernobyl Accident" of the Franco-German Initiative for Chernobyl on potential effects of prenatal irradiation on the brain as a result of the Chernobyl accident has been performed. A cohort of 154 children born between April 26th, 1986, and February 26th, 1987, to mothers who had been evacuated from Pripyat to Kiev and 143 classmates from Kiev were examined with the Wechsler Intelligence Scale for Children (WISC) and the Achenbach and Rutter A(2) tests. Mothers were tested for their verbal abilities (WAIS), depression, anxiety, and somatization (SDS, PTSD, GHQ 28). Reconstruction of the individual doses received by the children was carried out considering internal and external exposure. ICRP Publication-88 (2001) was applied for calculation of effective fetal, brain, and thyroid internal doses for children of both groups. There were 52 children from Pripyat (33.8%) who had been exposed *in utero* to equivalent thyroid doses >1 Sv; 20 of these children (13.2%) had been exposed *in utero* to fetal doses >100 mSv. The prenatally exposed children had no excess of severe mental retardation and microcephaly; however, they exhibited significantly more psychological developmental disorders, emotional and behavioral disorders, organic mental disorders, and paroxysmal disorders. Exposed children exhibited lower full-scale IQs due to lower verbal IQs and therefore an increased frequency of performance/verbal intelligence discrepancies. When IQ discrepancies of the prenatally irradiated children exceeded 25 points, there appeared to be a correlation with the fetal dose. The exposed and control mothers did not show differences in verbal abilities, but the exposed mothers had experienced many more stressful events and had more depression, PTSD, somatoform disorders, anxiety/insomnia, and social dysfunctions than the control mothers from Kiev (Nyagu, Loganovsky, Pott-Born, Repin, Nechayev, Antipchuk, et al., 2004).

Consistent with our studies, Chernobyl exposure during gestation had a significant effect on behavior in adolescent offspring in Finland. Adolescents who were exposed from the second trimester in pregnancy onwards had a 2.32-fold risk (95 % CI: 1.13 – 4.72) of having lifetime depression symptoms, an increased risk of fulfilling DSM-III-R criteria of a Major Depressive Disorder (OR = 2.48, 95 % CI: 1.06 – 5.7), and a 2.01-fold risk (95 % CI: 1.14 – 3.52) of having attention deficit hyperactivity disorder (ADHD) symptoms. No associations with anxiety conduct disorder or oppositional defiant disorder symptoms were found. The authors concluded that perturbations in fetal brain development may have resulted in increased prevalence of depressive and AHDH symptoms after prenatal stress exposure from second trimester onwards (Huizink, Dick, Sihvola, Rose, & Kaprio, 2007). In a relevant study they examined the potential effect of prenatal stress associated with the Chernobyl disaster in an ongoing genetic epidemiological study in Finland. Cortisol levels in both sexes and testosterone levels among females were significantly elevated after prenatal exposure to maternal stress from the second trimester onwards, compared to reference groups of nonexposed adolescents. Exposure explains 3% of variance in cortisol levels and 18% of variance in testosterone levels. No significant differences were found for exposure from either first or third trimester onwards. The results suggest that prenatal exposure to maternal stress in the second trimester of pregnancy may have resulted in prenatal programming of physiological systems relating to cortisol and testosterone levels (Huizink, Bartels, Rose, Pulkkinen, Eriksson, & Kaprio, 2008).

In accordance with the above mention data, a study was conducted on cognitive functions on subjects in Sweden prenatally exposed to radioactive contamination following the Chernobyl accident. In a comprehensive data set of 562,637 Swedes born during 1983–1988, the cohort *in utero* during the Chernobyl accident was found to have had worse school outcomes than adjacent birth cohorts, and this deterioration was largest for those exposed approximately 8–25 weeks post conception. Moreover, larger damage was found among students born in regions that received more fallout: students from the eight most affected municipalities were 3.6 percentage

points less likely to qualify for high school as a result of the fallout. These findings suggest that fetal exposure to ionizing radiation damages cognitive ability at radiation levels previously considered safe (Almond, Edlund, & Palme, 2007).

A radioneuroembriological effect — intelligence disharmony due to verbal IQ deterioration — caused by the accident at Chernobyl has been revealed at 8 and later weeks of gestation with a fetal dose >20 mSv and thyroid doses in utero >300 mSv and at 16–25 weeks of gestation with a fetal dose >10 mSv and thyroid dose *in utero* >200 mSv. Spectral θ-power decrease (particularly, in the left fronto-temporal area), β-activity increase together with its lateralization towards the dominant hemisphere, and disorders of normal interhemispheric asymmetry of visual evoked potentials and the vertex-potential can be considered as the neurophysiological markers of prenatal exposure. The most critical periods of cerebrogenesis resulting from the release of radioactive iodine into the environment are the later terms of gestation (16–25 weeks) rather than the earlier 8–15 weeks (Loganovskaja & Nechayev 2004; Loganovskaja, 2004, 2005). The frequency of mental disorders and personality disorders due to brain injure or dysfunction; disorders of psychological development; paroxysmal states (headache syndromes, migraine, and epileptiform syndromes); somatoform autonomous dysfunction; and behavioral and emotional disorders of childhood increased among these children (Napreyenko & Loganovskaja, 2004; Loganovskaja, 2005).

We reported earlier that there was prominent impairment of the left, dominant, cerebral hemisphere functions, especially its cortico-limbic structures, in children irradiated *in utero* as a result of Chernobyl (Loganovskaja & Loganovsky, 1999). Finally, we came to the conclusion that development of the dominant (left) hemisphere was disrupted following prenatal exposure as a result of the Chernobyl accident. The exposed children were found to have more neuropsychiatric disorders, left-brain neurological signs, lower full-scale and verbal IQs, IQ discrepancies with verbal decrement, disorganized EEG patterns, an excess of lateralized-to-left front temporal region delta and beta power with depression of theta and alpha power, and interhemispheric inversion visual information processing. Their mothers' mental health, stress, and prenatal irradiation contributed to these effects, along with several confounding factors. These findings could reasonably be considered to be the basis for the neurodevelopmental hypothesis of schizophrenia (Loganovsky, Loganovskaja, Nechayev, Antipchuk, & Bomko, 2008). Recently, important experimental radioneuroembryological research on nonhuman models of schizophrenia has also supported the hypothesis that prenatal exposure of brain tissue to ionizing (X-ray) radiation may be associated with an increased risk of schizophrenia later in life, making schizophrenia a neurodegenerative and, probably, a neurodevelopmental disease (Korr, Thorsten Rohde, Benders, Dafotakis, Grolms, & Schmitz, 2001; Gelowitz, Rakic, Goldman-Rakic, & Selemon, 2002; Schindler, Wang, Selemon, Goldman-Rakic, Rakic, & Csernansky, 2002; Schmitz, Born, Dolezel, Rutten, de Saint-Georges, Hof, & Korr, 2005; Selemon, Wang, Nebel, Csernansky, Goldman-Rakic, & Rakic, 2005) .

Thus, recent reports reveal that sub-clinical damage to human fetuses can result in cognitive deficits and other neuropsychiatric disorders. These previously unrecognized, long-term effects are apparently produced by a relatively short amount of exposure to radioactive fallout at levels that were previously thought not to be deleterious (Nowakowski & Hayes, 2008).

Obviously, a life span study should be done for the cohort of persons prenatally irradiated as a result of the Chernobyl accident, as well as those exposed at the age of 0–1 years. These survivors are under increased risk of a variety of neuropsychiatric disorders, including schizophrenia. The onset of these disorders can occur at any time in a person's life.

2.3 Long-term cerebral effects of low-doses radiotherapy in childhood

CNS radiotherapy in infancy and childhood may have serious long-term neuropsychiatric effects. As the treatment of childhood cancer has improved, long-term survival has become more common, and, consequently, the delayed cerebral effects are now recognized (Anderson, 2003). However, it was, and still it is, assumed that the lowest dose to the brain that could be associated with late deterministic effects of childhood irradiation is 18 Gy, associated with disorders of cognitive functions, histopathological changes, and neuroendocrine effects (UNSCEAR 1993).

At the same time, evidence of delayed radiation brain damage (lower examination scores on scholastic aptitude, IQ, and psychological tests, completed fewer school grades, increased risk for mental hospital admissions, slightly higher frequency of mental retardation, and EEG abnormalities) was revealed 20 years after childhood scalp irradiation in average doses to the brain of only 1.3 Gy in a cohort of nearly 20,000 Israel children exposed to X-ray irradiation of the head for ringworm (tinea capitis) management (Yaar, Ron, Modan, Perets, & Modan,

1980; Yaar, Ron, Modan, Rinott, Yaar, & Modan, 1982; Ron, Modan, Flora, Harkedar, & Gurewitz, 1982). Among these persons 40 years after radiotherapy (the mean estimated radiation dose to the brain was 1.5 Gy), excessive relative risks per 1 Gy were observed for benign meningiomas and malignant brain tumors (Sadetzki, Chetrit, Freedman, Stovall, Modan, & Novikov, 2005). The follow up study showed that exposure of the brain to X-ray radiation for the treatment of scalp ringworm infections early in childhood (before 5 years of age) is associated with an increased risk of schizophrenia later in life. Preliminary findings suggested that those exposed early had more than a two-fold, statistically significant increase in schizophrenia risk when compared with unexposed siblings. Increased schizophrenia risk also correlated with a higher X-ray dose exposure (Gross, 2004). An increased risk of schizophrenia and related disorders was clearly seen among survivors who had been treated with radiotherapy of brain tumors in childhood or adolescence, as illustrated in a nationwide, population-based, retrospective cohort study in Denmark (Ross, Johansen, Dalton, Mellemkjaer, Thomassen, Mortensen, & Olsen, 2003).

Recently, the effect of low doses of ionizing radiation (>100 mGy) in infancy (radiotherapy of cutaneous haemangioma) on cognitive function in adulthood has been proven on the basis of a Swedish population based cohort study. This is very striking, as the head dose in childhood following X-ray CT was 120 mGy and was higher than the cognitive deficit threshold (100 mGy). Obviously, the risk-benefits of CT for mild brain injury among children should be reassessed (Hall, Adami, Trichopoulos, Pedersen, Lagiou, Ekbom, et al., 2004). In this study, a negative dose-response relationship was evident for verbal IQ but not for performance IQ, testifying to impairment of the dominating (left) hemisphere. These data closely correspond to the deteriorating level of verbal IQ associated with open air nuclear testing (Graeub, 1994).

Thus, radiation exposure in childhood is obviously associated with dose-related cognitive decline in adulthood and neuropsychiatric disorders, including schizophrenia, later in life. The possible dose thresholds of delayed radiation brain damage are as low as 0.1–1.3 Gy to the brain in childhood. However, the lowest fraction and total doses on the brain causing neurocognitive effects are assumed to be 2 Gy and 18 Gy, correspondingly. Evidently, further studies have to be done for reassessment of the risk-benefit of long-term consequences of cranial radiotherapy and CT of the head in childhood.

2.4 Postaccidental neuropsychiatric radiation-related effects in adulthood

2.4.1 Background

It is accepted in medical radiology that morphological radiation injuries of the CNS could arise following local brain irradiation by doses greater than 10–50 Gy. Radiation brain necrosis was observed at local brain exposure of 70 Gy and more, where the development of radiogenic dementia was considered to be a possibility. The tolerated dose on the brain was assumed to be 55–65 Gy and the tolerated fractional dose to be 2 Gy (Gus'kova & Shakirova, 1989; Gutin, Leibel, & Sheline, 1991; Mettler & Upton, 1995). Primary CNS damage following total body irradiation were assumed to be at an exposure >100 Gy (the cerebral form of Acute Radiation Sickness [ARS]) and secondary radiation CNS damage at an exposure of 50–100 Gy (the toxemic form of ARS) (Gus'kova & Bisogolov, 1971). The threshold for radiation-induced neuroanatomic changes was assumed to be at the level of 2–4 Gy of whole body irradiation (Gus'kova & Shakirova, 1989, Gus'kova, 2007).

However, in experimental studies morphological changes of neurons were revealed for as low as 0.25–1 Gy of total irradiation (Alexandrovskaja, 1959; Shabadash, 1964), and a dose of 0.5 Gy has been recognized to be the threshold of radiation injury to the CNS with primary neuronal damages (Lebedinsky & Nakhilnitzkaja, 1960). Persistent changes in brain bioelectrical activity occur at thresholds of 0.3 to 1 Gy and increase with the dose absorbed (Trocherie, Court, Gourmelon, Mestries, Fatome, Pasquier, et al., 1984). These data suggest that alteration in CNS functioning is likely to occur after relatively low doses of radiation (Mickley, 1987). It was shown that exposure to ionizing radiation significantly modifies neurotransmission (Kimeldorf & Hunt, 1965) resulting in multiple effects on the brain and behavior that depend largely on the dose received (Hunt, 1987). Slowly progressive CNS radiation sickness has been identified following a single exposure to total irradiation of 1–6 Gy (Moscalev, 1991). In the UNSCEAR Report (1982), it was noted that after exposure to 1–6 Gy, slowly progressive degeneration of brain cortex develops (Vasculescu, Pasculescu, Papilian, Serban, & Rusu, 1973). Thus, views on radiocerebral effects in adults are at issue.

2.4.2 Epidemiological data

In the Adult Health Study in Hiroshima, the atomic bomb radiation dose did not show any significant association with detection of vascular dementia or Alzheimer's disease 25 to 30 years later. Risk factors for

dementia were age, higher systolic blood pressure, history of stroke, history of hypertension, history of head trauma, lower milk intake, and lower education (Yamada, Sasaki, Mimori, Kasagi, Sudoh, Ikeda, et al., 1999; Yamada, Kasagi, Sasaki, Masunari, Mimori, & Suzuki, 2003). However, taking into account that increased blood pressure was the main contributor to vascular dementia (Yamada, Sasaki, Mimori, Kasagi, Sudoh, Ikeda, et al., 1999), it is important to note that in the same Adult Health Study a statistically significant effect of ionizing radiation on the longitudinal trends of both systolic and diastolic blood pressure was recently found. This phenomenon is compatible with the degenerative effect of ionizing radiation on blood vessels (Sasaki, Wong, Yamada, & Kodama, 2002). These recent analyses strengthen earlier findings of a statistically significant increase in non-cancer disease death rates with atomic bomb radiation dose. In particular, increasing trends are observed for diseases of the circulatory system (Shimizu, Pierce, Preston, & Mabuchi, 1999). There is direct evidence of radiation effects for doses of more than 0.5 Sv on heart disease, stroke, digestive diseases, and respiratory diseases (Preston, Shimizu, Pierce, Suyama, & Mabuchi, 2003).

Epidemiological studies of atomic bomb survivors have suggested dose-related increases in mortality from diseases other than cancer. Cardiovascular disease is one such non-cancer disease for which increases in both mortality and incidence have been found to be associated with radiation dose (Kusunoki, Kyoizumi, Yamaoka, Kasagi, & Kodama, 1999). The recognition in atomic-bomb survivors of non-cancer effects at doses on the order of 0.5 Sv (half the dose level considered a threshold in earlier studies) should stimulate interest in deterministic effects (Shimizu, Pierce, Preston, & Mabuchi, 1999; Fry, 2001; Preston, Shimizu, Pierce, Suyama, & Mabuchi, 2003) and non-cancer morbidity and mortality following the Chernobyl accident. However, the systematic review did not provide clear evidence of a risk of circulatory diseases at doses of ionizing radiation in the range 0–4 Sv, as suggested by the atomic bomb survivors. Further evidence is needed to characterize the possible risk (McGale & Darby, 2005).

The rate of schizophrenia in A-bomb survivors in Nagasaki was very high — 6% [60 per 1,000] (Nakane & Ohta, 1986), while the estimates of lifetime occurrence of schizophrenia vary from 0.9–6.4, and an estimate of the mean prevalence is 1.4–4.6 per 1,000 (Jablensky, 2000). Since 1990, there has been a significant increase in incidences of schizophrenia in the Chernobyl exclusion zone personnel (clean-up workers) compared to the general population (5.4 per 10,000 in the Chernobyl exclusion zone versus 1.1 per 10,000 in Ukraine, 1990) (Loganovsky & Loganovskaja, 2000).

Prior to the Chernobyl accident, consistent with the “healthy worker effect”, the clean-up workers (liquidators) had significantly lower rates of anxiety and alcohol disorders. However, the liquidators had significantly higher post-Chernobyl rates of depression (18.0% vs 13.1% in the Ukrainian population) and suicide ideation (9.2% vs 4.1%) after the accident but not alcoholism or intermittent explosive disorder. In the year preceding the interviews, rates of depression (14.9% vs 7.1%), posttraumatic stress disorder, PTSD (4.1% vs 1.0%), and headaches (69.2% vs 12.4%) were elevated. Liquidators affected with depression and PTSD lost more work days than affected controls. Exposure level was associated with current somatic and PTSD symptom severity. Thus, long-term consequences of the Chernobyl accident on the mental health of liquidators were observed. Further study is needed to collect more objective measures of exposure and physical health, consider possible cognitive impairment and psychotic symptoms, and conduct more rigorous psychiatric evaluations (Loganovsky, Havenaar, Tintle, Guey, Kotov, & Bromet, 2008). In the past, Inhabitants of radioactively contaminated zones have had increased risk of mental health symptoms and poor subjective health ratings. Thus, the long-term consequences of Chernobyl were observed in an unbiased sample of the general population of Ukraine (Havenaar, Bromet, Tinlte, & Gluzman, 2007).

Radiation risks on non-cancer effects has been revealed in the liquidators (Biryukov, Gorsky, Ivanov, S., Ivanov, V., Maksioutov, Meskikh, et al., 2001; Buzunov, Strapko, Pirogova, Krasnikova, Kartushin, Voychulene, & Domashevskaya, 2001). For some classes of non-cancer diseases among liquidators, statistically significant estimates of radiation risk were derived for the first time. For mental disorders, excess relative risk (ERR) per 1 Gy was found to be 0.4 at a 95% confidence interval (0.17; 0.64); neurologic and sensory disorders were found to be 0.35 (0.19; 0.52); and endocrine disorders to be 0.58 (0.3; 0.87) (Biryukov, Gorsky, Ivanov, S., Ivanov, Maksioutov, Meskikh, et al., 2001). The highest ERR per 1 Gy was found for cerebrovascular diseases to be 1.17 (0.45; 1.88) (Ivanov, Maksioutov, Chekin, Kruglova, Petrov, & Tsyb, 2000).

Among Russian liquidators, statistically significant radiation risks were obtained for mortality from malignant neoplasms and cardiovascular diseases, while the risk of death from all non-cancer causes is close to zero and not statistically significant (Ivanov, Gorski, Maksioutov, Tsyb, & Souchkevitch, 2001). Recently, the statistically significant dose risk of ischemic heart disease (ERR per 1 Gy ERR Gy — 0.41 (0.05; 0.78)), essential hypertension (0.36 (0.005; 0.71)), and cerebrovascular diseases (0.45 (0.11; 0.80)) was published. The

at-risk group with respect to cerebrovascular diseases are those who received external radiation doses greater than 150 mGy in less than 6 weeks (RR —1.18 (1.00; 1.40)). However, radiation risks were not adjusted for recognized risk factors such as excessive weight, hypercholesterolemia, smoking, alcohol consumption, and others (Ivanov, Maksioutov, Chekin, Petrov, Biryukov, Kruglova, et al., 2006).

According to the data of the State Register of Ukraine and Clinical and Epidemiological Registry (Scientific Centre for Radiation Medicine, Kiev) there is an increased level of cerebrovascular disorders in liquidators and evacuees. Exposure to small doses of ionizing radiation is a significant risk factor of accelerating aging. Thyroid exposure by 300 mGy and more is a significant risk factor for vascular and cerebrovascular disorders. Thyroid exposure by 2 Gy and more is a significant risk factor for mental disorders, vascular and cerebrovascular diseases, and peripheral nervous system disorders. Exposure to doses of 250 mGy and more is a significant risk factor for neuropsychiatric disorders and vascular disorders. There is a dose–effect relationship for cerebrovascular disorders in liquidators. Non-radiation risk factors for neuropsychiatric pathology (cerebrovascular) include: industrial hazards, stress, smoking, heredity, and life style (Buzunov, Strapko, Pirogova, Krasnikova, Kartushin, Voychulene, & Domashevskaya, 2001; Buzunov, Pirogova, Repin, Strapko, Krasnikova, Prikashchikova, et al., 2001; National Report of Ukraine, 2006; Krasnikova & Buzunov, 2007). Therefore, it is clear that radiation from the Chernobyl accident has long-term neuropsychiatric effects. It is very evident that follow-up neuropsychiatric epidemiological studies with dosimetric support are necessary.

2.4.3 Neuropsychiatric consequences of Acute Radiation Sickness as a result of the Chernobyl accident

Immediately after the Chernobyl accident, autonomic [vegetative] vascular dystonia (VVD) and neurotic disorders were observed: at 0.8–2.1 Gy - mild ARS [or ARS of the 1st severity degree]; at 2–4 Gy - moderate ARS [or ARS of the 2nd severity degree] causing VVD; at 4.2–6.3 Gy - severe ARS [or ARS of the 3rd severity degree] causing acute radiation and radiation-toxic encephalopathy, acute psychosis with visual and acoustical hallucinations, and brain edema; at 6–16 Gy - very severe to lethal ARS [or ARS of the 4th severity degree] causing acute radiation and radiation-toxic encephalopathy, subarachnoidal-parenchimatous hemorrhage, acute brain edema, and swelling (Torubarov, Blagoveshchenskaia, Chesalin, & Nikolaev, 1989).

No clear signs of organic brain damage were registered during the first 3 years after irradiation in ARS-survivors; however, mental working capacity deterioration and asthenisation were in proportion to the severity of ARS. Further, progressive structural-functional brain damage — postradiation encephalopathy or postradiation organic brain syndrome — was revealed, and its diagnostic criteria were elaborated in the remote period of ARS according to neuropsychiatric follow-up studies (Nyagu, Loganovsky, Chuprovskaja, Vaschenko, Kostyuchenko, Zazimko, et al., 1997; Nyagu, Loganovsky, Yuryev, & Zdorenko, 1999; Nyagu, Loganovsky, & Yuryev, 2002; Nyagu, Loganovsky, Chuprovskaya, Kostychenko, Vaschenko, Yuryev, et al., 2003). The psychoorganic nature of mental disorders in the remote period of ARS was also supported by other studies; however, no dose–effects relationships were found (Revenok, 1998).

Vegeto-vasclular and vegeto-visceral stages of neuropsychiatric pathology (3–5 years after irradiation) have changed with cerebral organic, cererbrovascular, and somatogenous neuropsychiatric disorders (5–10 and more years after irradiation). In 62% of patients who had confirmed ARS, there was postradiation organic brain syndrome. The apathetic type of organic personality disorder (microfocal neurological signs, personality changes, negative psychopathological symptoms, depression, and cognitive deficit) is characteristic of the neuropsychiatric consequences of ARS. This disorder has a progressive clinical course, its rate in proportion to the severity of ARS and, consequently, the radiation dose (Loganovsky, 2002; Nyagu, Loganovsky, & Yuryev, 2002; Loganovsky, Antipchuk, Bomko, Chuprovskaja, Kovalenko, Napreyenko, et al., 2007). Postradiation organic brain damage in the remote period of ARS has been verified by clinical neuropsychiatric, neurophysiolocial, neuropsychological, and neuroimaging methods (Loganovsky, Kovalenko, Yuryev, Bomko, Antipchuk, Denisyuk, et al., 2003).

Three to five years after irradiation, irritated electroencephalographic (EEG) changes with paroxysmal activity shifted to the left frontotemporal region (cortical-limbic overactivation), transformed by irradiation toward a low-voltage EEG pattern with excess of fast (β) and slow (δ) activity together with depression of α- and θ-activity (organic brain damage with inhibition of the cortical-limbic system), were found to exist (Loganovsky & Yuryev, 2001). Among verified ARS-patients with qEEG, the neurophysiological markers of ionizing radiation (1–5 Gy) have been revealed: left fronto-temporal dominant frequency reduction; absolute δ-power lateralization to the left (dominant) hemisphere; relative δ-power increase in the fronto-temporal areas; absolute θ-power decrease in the left temporal region; and absolute and relative α-power diffusive decrease. This may

reflect cortico-limbic dysfunction lateralized to the left, dominant hemisphere, with fronto-temporal cortical and hippocampal damage (Loganovsky & Yuryev, 2004).

qEEG and evoked potentials data in the remote period of ARS testify to injury of the cortico-limbic system, mainly in the dominant (left) hemisphere, and central afferentation dysfunction of all sensoric modalities when sensoric information is processed by non-specific afferent systems while specific systems are inhibited (Loganovsky, 2000, 2002). A dose–effect relationship on mental working capacity deterioration was revealed for ARS patients (>1 Gy) (Zdorenko & Loganovsky, 2002).

Neuropsychological studies support the pathology of the frontal and temporal cortex of the dominant hemisphere and middle structures with their cortical-subcortical connections in the remote period of ARS. The inhibition of the left (dominant) hemisphere, together with compensative overactivation of the right hemisphere, was revealed. Neuropsychological dose-effects relationships were found for associative brain areas responding to movement control and regulation, mnestic (verbal), and sophisticated intellectual activity (Antipchuk, 2003, 2004, 2005).

Neuroimaging studies in the remote period of ARS have verified the cerebral organic nature of mental disorders and revealed the cortical atrophy of cerebral hemispheres, ventricular enlargement, and lacunar abnormalities. By morfometric analysis of MRI scans, neuroimaging markers of ionizing radiation (1–5 Gy) were obtained: decreasing of the contrast index of the left internal capsule and the contrast index of white matter of the left parietal and temporal lobes. Cortical atrophy of cerebral hemispheres and damage of neuronal pathways in the dominant hemisphere are the characteristic morphometric neuroimaging features of organic brain damage in the remote period of exposure to ionizing radiation as a result of the Chernobyl accident (Bomko, 2004, 2005).

Ultrasound dopplerographic studies of cerebral hemodynamics in the remote period of ARS have revealed the decrease of vessels' involution, hemodynamic reactivity, and blood circulation in extracranial cerebral blood vessels. Characteristic changes in cerebral vessels are as follows: vasospasm, tortuosity, stenosis, and asymmetry in internal carotid arteria with the decrement of systolic circulation in the left internal carotid arteria. The latter was recognized as the marker of radiation injury to cerebral vessels, and this arteria was identified as the target for ionizing radiation (Denisyuk, 2006).

The characteristic and/or dose-related neuropsychiatric, neurophysiologcial, neuropsychological, and neuroimaging effects after ARS are lateralized in the dominant (left) hemisphere. This may testify to the radiovulnerability of this part of the brain to exposure of ionizing radiation (Loganovsky, Antipchuk, Bomko, Denisyuk, Loganovskaja, Chuprovskaja, et al., 2006). Postradiation brain damage is predominantly localized in the frontal areas of the left hemisphere and involves both white and gray matter of the brain. The functional and structural biomarkers of ionizing radiation have been established: cortical abnormalities (atrophic changes of frontal and temporal lobes) and damage to subcortical structures and neuronal pathways of the dominant hemisphere together with the cortical-limbic system, mainly in the dominant (left) hemisphere (Loganovsky & Bomko, 2004, 2007). Thus, the organic brain damage following ARS is ethyologically heterogenous as a result of both radiation and non-radiation risk factors. However, at exposure to 1 Sv and more, evidence of the crucial role of radiation has been revealed (Loganovsky, 2008).

2.4.4 Potential radiation-related neuropsychiatric effects following exposure to less than one Sv as a result of the Chernobyl accident

After the Chernobyl accident, peer reviewed publications relating neuropsychiatric consequences in exposed populations were dramatically increased; however, their main methodological limitation was an absence or lack of dosimetrical assessment. At the same time, it is necessary to pay attention to the most important original studies published in different countries that empirically discovered the peculiarities of effects on the brain from exposure to low-dose radiation.

EEG-patterns and topographical distribution of spontaneous and evoked brain bioelectrical activity in overexposed liquidators, especially long-term workers in the Chernobyl zone, were significantly different in control and comparison groups (Niagu, Noshchenko, & Loganovskii, 1992; Noshchenko & Loganovskii, 1994). There are many consistent reports about characteristic **neurophysiological** (Danilov & Pozdeev, 1994; Zhavoronkova, Kholodova, Zubovskii, Smirnov, Koptelov, & Ryzhov, 1995; Zhavoronkova, Kholodova, Zubovsky, Gogitidze, & Koptelov, 1995; Novikov, Tsygan, Borisova, & Rybina, 1997; Vyatleva, Katargina, Puchinskaya, & Yurkin, 1997; Zhavoronkova, Kholodova, Belostocky, & Koulikov, 2008), **neuropsychological**

(Khomskaja, 1995; Zhavoronkova, Gogitidze, & Kholodova, 1996, 2000; Polyukhov, Kobsar, Grebelnik, & Voitenko, 2000; Turuspekova, 2002; Gamache, Levinson, Reeves, Bidyuk, & Brantley, 2005; Zhavoronkova, Lavrova, Belostotskii, Kholodova, Skoriatina, & Voronov, 2006), **neuroimaging** (Kharchenko, Zubovskii, & Kholodova, 1995; Kholodova, Kuznetzova, Zubovsky, Kazakova, & Buklina, 1996; Voloshina, 1997), and **neuroimmune** (Lysyanyj, 1998; Nikolenko, Bondarenko, Bazyka, Golovchenko, Nikolenko, & Dubiaga, 2002) abnormalities in liquidators, supporting the clinical data about organic brain damage (Chuprikov, Pasechnik, Kryzhanovskaja, & Kazakova, 1992; Krasnov, Yurkin, Vojtsekh, Skavysh, Gorobets, Zubovsky, et al., 1993; Romodanov et al., 1993; Romodanov & Vynnyts'kyj, 1993; Napreyenko & Loganovsky, 1995, 1997, 1999, 2001; Nyagu & Loganovsky, 1998; Revenok, 1998, 1999; Zozulya et al., 1998; Morozov & Kryzhanovskaja, 1998; Rumyantseva, Chinkina, & Levina, 2002; Soldatkin, 2002). In summary, these reports testify to the organic brain damage and accelerating CNS aging in clean-up workers following exposure to more than 0.25–0.5 Sv. At the same time, the discussion is continuing: whether this is a primary neuronal postradiation low doses effect or a secondary effect due to cerebrovascular and/or autoimmune processes ("vascular-glial union"), dysmetabolic, etc.

The progressive character of neuropsychiatric disorders and somatic pathology is observed in liquidators of 1986-1987, especially in those who worked for 3-5 years at the Chernobyl exclusion zone. The rate of neuropsychiatric disorders among personnel working since 1986-1987 and irradiated in doses above 250 mSv was 80.5% while for the same contingency, but irradiated in doses below 250 mSv the rate of these disorders was 21.4% only (Nyagu, Loganovsky, Chuprovskaya, Kostychenko, Vaschenko, Yuryev, et al., 2003). Personnel in the Chernobyl exclusion zone who have been working since 1986 have the highest risk of neuropsychiatric disorders, where organic, including symptomatic, mental disorders dominate (Loganovsky, 1999).

While conventional EEG failed to reveal the dose-effect relationship, quantitative EEG allowed the discovery of radiation related peculiarities from a 0.3 Sv threshold as the increase of spectral power of δ- and β- activity shifted to the left fronto-temporal area together with a decrease in θ- and α-activity. Dose-related neuropsychiatric (mainly, negative psychopathology) and neurophysiological (Nyagu, Loganovsky, Yuryev, & Zdorenko, 1999; Loganovsky, 2000, 2002), neuropsychological or cognitive (Antipchuk, 2004, 2005), neuroimaging (Bomko, 2004, 2005), and cerebral hemodynamic (Denisyuk, 2006) abnormalities following exposure to >0.3 Sv were found. Those irradiated by moderate to high doses (more than 0.3 Sv) had significantly more left frontotemporal limbic dysfunction and schizophreniform syndrome (Loganovsky, 2000, 2002; Loganovsky & Loganovskaja, 2000).

Cytotoxic effects and humoral mechanisms (neuropeptides, brain antibodies, neurotropic lymphokines, and immune hormones) form a new view of the pathogenesis of neuropsychiatric effects following radiation exposure (Bazyka, Golyarnik, & Belyayeva, 2007). In clean-up workers exposed to 0.3-1 Sv, with organic brain damage considered to be a cerebrovascular pathology, the activation of HLA-DR+ lymphocytes under protein S-100 stimulation is revealed in comparison with those irradiated in doses lower 0.3 Sv. This probably testifies to an alteration of the glial structures in the CNS and a blood-brain barrier increasing in proportion to radiation dose (Khomenko, 2008).

A hypothesis about the development of Chronic Fatigue Syndrome (CFS) under the impact of low and very low doses combined with psychological stress has been suggested. CFS can be considered to be an environmentally induced predisposition and vestige of forthcoming neurodegeneration, cognitive impairment, and neuropsychiatric disorders (Loganovsky 2000, 2003; Volovik, Loganovsky, & Bazyka, 2005; Volovik, Loganovsky, Bazyka, Bebeshko, Cohen, Chao, et al., 2006). Moreover, CFS and metabolic syndrome X are considered to be both radiation-associated syndromes and stages of other neuropsychiatric and physical pathology developments, and CFS can be transformed into metabolic syndrome X. Radiation-induced damage of mitochondrial DNA in post-mitotic tissues with low proliferation activity may be a basis for the effects of low doses in an increase of non-cancer morbidity and mortality in the Chernobyl accident survivors (Kovalenko & Loganovsky, 2001). Currently, post-radiation syndrome is proposed to be CFS or a chronic fatigue syndrome-like illness, initiated by exposure to ionizing radiation. The symptoms and signs of post-radiation syndrome and its chronicity are similar or identical to those of CFS and can be explained as being a consequence of nitric oxide/peroxynitrite cycle etiology (Pall, 2008).

Accelerated aging and neurodegeneration are among potential low-dose radiation-induced phenomena (Bazyka, Volovik, Manton, Loganovsky, & Kovalenko, 2004; Bebeshko, Bazyka, Loganovsky, Volovik, Kovalenko, Korkushko, & Manton, 2006). Premature aging of clean-up workers was supported on the basis of comprehensive examinations. Data from an experimental study of primates irradiated with a dose of 1 Gy

revealed formation of brain atrophy in the remote period after low dose radiation exposure (Kholodova, Zhavoronkova, Ryzhov, & Kuznetsova, 2007).

Another effect that could also be attributed to exposure to ionizing radiation is schizophrenia spectrum disorders (Loganovsky & Loganovskaja, 2000; Loganovsky, Volovik, Manton, Bazyka, & Flor-Henry, 2005). There are three hypotheses concerning ionizing radiation as a risk factor for schizophrenia: 1) genetic (in off-spring of exposed); 2) prenatal exposure (neurodevelopmental hypothesis), and 3) diathesis-stressor hypothesis (Loganovsky et al., 2005), while irradiation in adulthood is considered to be a new model of schizophrenia (Iwata, Suzuki, Wakuda, Seki, Thanseem, Matsuzaki, et al., 2008).

Obviously, these findings should be confirmed by mutual international studies, and the biological basis of low dose neuropsychiatric effects must be revealed.

2.5 Occupational exposure and neurotoxicity of Uranium and transuranium elements: implementation at the Shelter Object of the Chernobyl NPP

In the 1960s, it was commonly accepted that the nervous system reacts to exposure to low doses of ionizing radiation with vegetative (autonomous) vascular dystonia, asthenia, and, in proportion to radiation dose, organic CNS damage. However, after further assessment, the conclusion was reached that the threshold of radiation injury to the nervous system is 2–4 Sv of total irradiation. All other effects at exposure to lower doses are considered to be "functional" only (Gus'kova & Shakirova, 1989; Gus'kova, 2007). The author finds this conclusion to be incorrect: there are not only "functional" disorders without a cerebral basis, but there are also technological limitations to their detection. Our position had been argued in detail above.

The available data on neuropsychiatric effects of occupational exposure are quite limited and contradictory. The most comprehensive related study was conducted by Azizova (1999) in atomic industry workers exposed to chronic occupational ionizing radiation, mainly external γ-irradiation. Vegetative-vascular dystonia, predominantly hypothensive, asthenic syndrome, and demyelinizating encephalomyelosis syndrome were the main neurological clinical patterns. Their rate was in proportion to the radiation dose. Together with hematological abnormalities (thrombocytopenia and leukocytopenia), these were considered to be the neurological features of Chronic Radiation Sickness. Demyelinizating encephalomyelosis was observed only at doses of 2–4 Sv and more. Cerebrovascular pathology was the most common in the remote period after irradiation. Radiation risk for cerebral atherosclerosis has been revealed; however, no connection between the dose and stroke rate has been found. Moreover, there was also no radiation-induced mortality excess from cardiovascular diseases in the workers of the "Mayak" radiochemical plant (Bolotnikova, 1994). It should be pointed out again that this systematic review does not provide clear evidence of a risk of circulatory diseases at doses of ionizing radiation in the range 0–5 Sv, as suggested by atomic bomb survivors. Further evidence is needed to characterize the possible risk (McGale & Darby, 2005).

At the same time, the increasing role of Uranium and transuranium elements (mainly Plutonium and Americium) has been shown in connection to the Chernobyl accident and the Shelter Object transformation to an ecologically safe system (National Report of Ukraine, 2006). In accordance with recent data on the neurotoxicity of Uranium (Lestaevel, Houpert, Bussy, Dhieux, Gourmelon, & Paquet, 2005), the same toxicity for transuranium elements can be reasonably supposed. It was shown that oxidative stress plays a key role in the mechanism of Uranium neurotoxicity, as well as in the double toxicity, chemical and radiological, of Uranium (Lestaevel, Romero, Dhieux, Ben Soussan, Berradi, Dublineau, et al., 2009). Neurophysiological examinations of Shelter Object personnel have revealed disorders of cerebral bioelectrical activity to be the basis for neuropsychiatric pathology development. Exposure to low and very low doses of ionizing radiation, neurotoxicity of Uranium and transuranium elements, stress, as well as other non-radiation industrial hazards were assumed to be possible risk factors (Loganovsky, Nechayev, & Perchuk, 2008).

The study of the biological effects of Uranium and transuranium elements is crucial for radiobiology, radiation hygiene, and psychophysiology. It is necessary to conduct large-scale studies in this field. The Shelter Object transformation to an ecologically safe system gives the unique possibility to study the radiotoxical effects of Uranium and transuranium elements on the human body.

3 CONCLUSION

The importance of constantly improving our knowledge and understanding of radiocerebral effects at low dose exposure is brought about by the current challenges of modern society and scientific and technological progress. We cannot and should not stop the evolution of man's scientific inquiries: these obviously involve the development of nuclear energy and nuclear technologies, medical radiological procedures, as well as space flights. Unfortunately, this evolution is also associated with social risks, such as nuclear war or local military conflicts using depleted Uranium, radiation accidents, occupational and other overexposure, and radiological terrorist attacks. We have to be prepared for these eventualities by being armed with evidence-based scientific data to protect people and to distinguish between a radiation cerebral effect and panic. That is why it is now extremely necessary to integrate international efforts for further comprehensive studies of the health effects and the biological basis of exposure to ionizing radiation of humans, in general, and on the CNS, in particular.

The current data of possible dose thresholds for radiocerebral effects are summarized in Table 2.

Table 2. Dose thresholds for radiocerebral effects

ADULTHOOD	
50−100 Gy	Radiation brain damage (o–rthodoxally)
>2−4 Sv	Radiation neurological signs (Gus'kova et al.)
>1 Sv	Neurophysiological, neuroimaging markers and postradiation cognitive deficit (postradiation encephalopathy) *[RCRM data]*
>0.3 Sv	Neuropsychiatric, neurophysiological, neuroimmune, neuropsychological, and neuroimaging dose-related effects *[RCRM data]*
>0.15−0.5 Sv	Epidemiological data on radiation risks for cerebrovascular pathology (Ivanov et al, 2006; *RCRM data*; Shimizu et al., 1999; Preston et al., 2003)
CHILDHOOD	
>1.3−1.5 Gy	Delayed cerebral effects (Ron et al., 1982; Yaar et al., 1982) – *head irradiation*
>1.3−1.5 Gy	Cerebral tumors (Sadetzki et al., 2005) – *head irradiation*
>1.3−1.5 Gy	Schizophrenia (Gross, 2004) – *head irradiation*
>0.1 Gy	Cognitive deficit (Hall et al., 2004) – *head irradiation*
IN UTERO	
0.06–0.31 Gy	at 8–15 gestation weeks – mental retardation (Otake et al., 1996)
0.28–0.87 Gy	at 16–25 gestation week – mental retardation (Otake et al., 1996)
Fetal dose >20 mSv and thyroid dose *in utero* >300 mSv	at $+8^{th}$ gestational weeks – neurophysiological and cognitive dose-related effects *[RCRM data]*
Fetal dose >10 mSv and thyroid dose *in utero* >200 mSv	at 16−25 gestational weeks – neurophysiological and cognitive dose-related effects *[RCRM data]*

Thus, it is very necessary to arrange international studies on neuropsychiatric effects of low doses and their biological basis together with the development of molecular, neuroimmunological, neurophysiological, and cognitive biomarkers of ionizing radiation.

5 REFERENCES

Alexandrovskaja, M.M. (1959) Effects of different doses of ionizing radiation on the brain morphology in animals at total irradiation. *Medical Radiology 4* (8) 79–81 [in Russian].

Almond, D., Edlund, L. & Palme, M. (2007) *Chernobyl's subclinical legacy: prenatal exposure to radioactive fallout and school outcomes in Sweden*, Discussion Paper No.: 0607-19; Department of Economics, Columbia University, New York, NY 10027.

Anderson, N.E. (2003) Late complications in childhood central nervous system tumour survivors. *Curr Opin Neurol 16* (6) 677–683.

Andres-Mach, M., Rola, R. & Fike, J.R. (2008) Radiation effects on neural precursor cells in the dentate gyrus. *Cell Tissue Res 331* (1), 251–262.

Annex J. Exposures and effects of the Chernobyl accident (2000) *UNSCEAR 2000 report to the General Assembly, with scientific annexes. Sources and effects of ionizing radiation*. United Nations Scientific Committee on the Effects of Atomic Radiation. New York, United Nations

Antipchuk, K.Yu. (2003) Memory disorders in persons who had Acute Radiation Sickness as a result of the Chernobyl accident in remote period. *Ukrainian Radiological Journal 11* 68–72 [in Ukrainian].

Antypchuk, K.Yu. (2004) Neuropsychologic method in diagnostic of radiation brain disorders. *Ukrainian Medical Journal, 3* (41) 121–128 [in Ukrainian].

Antipchuk, K.Yu. (2005) *Clinical-neuropsychological characteristic of organic mental disorders in remote period of exposure to ionizing radiation as a result of the Chernobyl accident*. (PhD thesis) The dissertation for the academic degree of a Candidate of Medical Sciences in radiobiology. Research Centre for Radiation Medicine of Academy of Medical Sciences of Ukraine. Kyiv [in Ukrainian].

Azizova, T.V. (1999) *Nervous system state in persons exposed to chronic occupational ionizing radiation.* (PhD thesis) The dissertation for the academic degree of a Candidate of Medical Sciences in internal diseases and neurology. State Scientific Centre Institute of Biophysics, Russian Federation, Moscow.

Bar Joseph, N., Reisfeld, D., Tirosh, E., Silman, Z. & Rennert, G. (2004) Neurobehavioral and cognitive performance in children exposed to low-dose radiation in the Chernobyl accident: The Israeli Chernobyl Health Effects Study. *Am J Epidemio, 160* 453–459.

Bazyka, D.A., Golyarnik, N.A. & Belyayeva N.V. (2007) Neuroimmune mechanisms of the development of early and delayed radiation effects (pp. 271-286). In Vozianov, A.F., Bebeshko, V.G. & Bazyka, D.A. (Eds.) *Health Effects of the Chernobyl Accident*, Kyiv, DIA [in Ukrainian]

Bazyka, D.A., Volovik, S.V., Manton, K.G., Loganovsky, K.N. & Kovalenko, A.N. (2004) Ionizing radiation accelerating aging and neurodegeneration. *International Journal of Psychophysioloy, 54* (1–2) 118–119.

Bazyltchik, S., Drozd, V.M., Reiners, Chr. & Gavrilin, Yu. (2001) Intellectual development of children exposed to radioactive iodine after the Chernobyl accident in utero and at the age under 1.5 years. *International Journal of Radiation Medicine, Special Issue 3* (1–2) 15.

Bebeshko, V., Bazyka, D., Loganovsky, Volovik, S., Kovalenko, A., Korkushko, O. & Manton K. (2006) Does ionizing radiation accelerate aging phenomena (pp. 13–19). In: Contributed papers to The International Conference "*Twenty years after Chornobyl accident future outlook*", April 24–26, Kyiv, Ukraine. Kyiv, HOLTEH.

Bebeshko, V.G., Bazyka, D.A. & Loganovsky, K.N. (2004) Biological markers of ionizing radiation. *Ukrainian Medical Journal 1* (39), 85–104 [In Russian].

Biryukov, A., Gorsky, A., Ivanov, S., Ivanov, V., Maksioutov, M., Meskikh, N., Pitkevitch, V., Rastopchin, E., Souchkevitch, G. & Tsyb, A. (2001) Souchkevitch, G.N. & Repacholi, M.N. (Eds.) *Low Doses of Ionizing Radiation: Health Effects and Assessment of Radiation Risks for Emergency Workers of the Chernobyl Accident*. Geneva, World Health Organization.

Bolotnikova, M.G., Koshurnikova, N.A., Komleva, N.S., Budushchev, B. & Okatenko, P.V. (1994) Mortality from cardiovascular diseases among male workers at the radiochemical plant of the "Mayak" complex. Sci Total Environ 142 29–31.

Bomko, M.O. (2004) Morphometric neurovisual characteristic of organic brain damage in remote period of exposure to ionizing radiation as a result of the Chernobyl accident. *Ukrainian Medical Journal 2* (40) 96–101 [in Ukrainian].

Bomko, M.O. (2005) *Structural-functional characteristic of organic mental disorders in clean-up workers of the consequences of the Chernobyl accident in remote period of exposure to ionizing radiation*. (PhD thesis) The

dissertation for the academic degree of a Candidate of Medical Sciences in radiobiology. Research Centre for Radiation Medicine of Academy of Medical Sciences of Ukraine. Kyiv [in Ukrainian].

Bromet, E. & Havenaar, J. (2007) Psychological and perceived health effects of the Chernobyl disaster: a 20-year review. *Health Phys 93* (5) 516–521.

Bromet, E.J., Goldgaber, D., Carlson, G., Panina, N., Golovakha, E., Gluzman, S.F., Gilbert, T., Gluzman, D., Lyubsky, S. & Schwartz, J.E. (2000) Children's well-being 11 years after the Chornobyl catastrophe. *Arch Gen Psychiatry, 57* (6) 563–571.

Buzunov, V.A., Pirogova, Ye.A., Repin, V.S., Strapko, N.P., Krasnikova, L.I., Prikashchikova, Ye.Ye., Rubel N.F., Nechaev, S.Yu., Fedirko, P.A., Kartushin, G.I., Turchina, I.A., Chukhrai, R.N. & Domashevskaya, T.Ye. (2001) Epidemiologic studies of non-cancer incidence of adult population evacuated from Pripyat and 30-km zone surround the Chernobyl NPP. *International Journal of Radiation Medicine 3* (3–4) 26–45.

Buzunov, V.A., Strapko, N.P., Pirogova, Ye.A., Krasnikova, L.I., Kartushin, G.I., Voychulene, Yu.S. & Domashevskaya, T.Ye. (2001) Epidemiology of non-cancer diseases among Chernobyl accident recovery operation workers. *International Journal of Radiation Medicine 3* (3–4) 9–25.

Chen, W.L., Luan, Y.C., Shieh, M.C., Chen, S.T., Kung, H.T., Soong, K.L., Yeh, Y.C., Chou, T.S., Mong, S.H., Wu, J.T., Sun, C.P., Deng, W.P., Wu, M.F. & Shen, M.L. (2006) Effects of cobalt-60 exposure on health of Taiwan residents suggest new approach needed in radiation protection. *Dose Response 5* (1), 63–75.

Chuprikov, A.P., Pasechnik, L.I., Kryzhanovskaja, L.A. & Kazakova, S.Ye. (1992) *Mental Disorders at Radiation Brain Damage*. Kiev Research Institute for General and Forensic Psychiatry [in Russian].

Cuttler, J.M. (2007) Health effects of low level radiation: when will we acknowledge the reality? *Dose Response 5* (4), 292–298.

Danilov, V.M. & Pozdeev, V.K. (1994) The epileptiform reactions of the human brain to prolonged exposure to low-dose ionizing radiation. *Fiziol Zh Im I M Sechenova 80* (6) 88–98 [in Russian].

Denisyuk, N.V. (2006) Chronical cerebrovascular insufficiency in clean-up workers of the Chernobyl accident at the remote period of the irradiation. *Ukrainian Medical Journal 3* (53) 54–64 [in Ukrainian].

Ermolina, L.A., Sukhotina, N.K., Sosyukalo, O.D., Kashnikova, A.A. & Tatarova, I.N. (1996) The effects of low radiation doses on children's mental health (radiation-ontogenetic aspect). Report 2. *Social and Clinical Psychiatry 6* (3) 5–13 [in Russian].

European Commission. Radiation protection 100 (1998) *Guidance for protection of unborn children and infants irradiated due to parental medical exposures.* Directorate-General Environment, Nuclear Safety, and Civil Protection. Luxembourg: Office for Official Publications of the European Communities; 1999 Retrieved June 5, 2004 from the World Wide Web: http://www.europa.eu.int/comm/environment/radprot

Fry, R.J. (2001) Deterministic effects. *Health Phys 80* (4) 338–343.

Gamache, G.L., Levinson, D.M., Reeves, D.L., Bidyuk, P.I. & Brantley, K.K. (2005) Longitudinal neurocognitive assessments of Ukrainians exposed to ionizing radiation after the Chernobyl nuclear accident *Arch Clin Neuropsychol 20* (1) 81–93.

Gayduk, F.M., Igumnov, S.A. & Shalckevich, V.B. (1994) The complex estimation of neuro-psychic development of children undergone to radiation exposure in prenatal period as a result of Chernobyl disaster. *Social and Clinical Psychiatry 4* (1) 44–49 [in Russian]

Gelowitz, D.L., Rakic, P., Goldman-Rakic, P.S. & Selemon, L.D. (2002) Craniofacial dysmorphogenesis in fetally irradiated nonhuman primates: implications for the neurodevelopmental hypothesis of schizophrenia. *Biol Psychiatry 52* (7) 716–720.

Gourmelon, P., Marquette, C., Agay, D., Mathieu, J. & Clarencon, D. (2005) Involvement of the central nervous system in radiation-induced multi-organ dysfunction and/or failure. *BJR Suppl. 27*, 62–68.

Graeub, R. (1994) *The Petkau Effect: The Devastating Effect of Nuclear Radiation on Human Health and the Environment*. New York, Four Walls Eight Windows.

Gross, R. (2004) Head X-rays during childhood associated with higher risk of later schizophrenia Retrieved Sep 8, 2008 from the World Wide Web: http://www.schizophrenia.com/prevention/xray4.htm

Gus'kova, A.K. & Bisogolov, G.D. (1971) *Radiation Sickness of Human*. Moscow, «Meditzina» Publishing House [in

Gus'kova, A.K. & Shakirova, I.N. (1989) Reaction of the nervous system on alterative ionizing irradiation. *Zh Nevrol Psikhiatr Im S S Korsakova 89* (2), 138–142 [in Russian].

Gus'kova, A.K. (2007) Establishment of the radiation etiopathogenesis of neurological syndromes and

symptoms: summary and sources of mistakes. *Zh Nevropatol Psikhiatr Im S S Korsakova 107* (12), 66–70 [in Russian].

Gutin, P.H., Leibel, S.A. & Sheline, G.E. (Eds.) (1991) *Radiation Injury to the Nervous System*. New York, Raven Press.

Hall, P., Adami, H.O., Trichopoulos, D., Pedersen, N.L., Lagiou, P., Ekbom, A., Ingvar, M., Lundell, M. & Granath, F. (2004) Effect of low doses of ionising radiation in infancy on cognitive function in adulthood: Swedish population based cohort study. *BMJ 328* (7430) 19–24.

Havenaar, J., Bromet, E., Tinlte, N. & Gluzman, S. (2007) The lingering mental health consequences of Chornobyl: an unbiased appraisal. *Australian and New Zealand Journal of Psychiatry 41* (suppl. 2) A266.

Huizink, A.C., Bartels, M., Rose, R.J., Pulkkinen, L., Eriksson, C.J.P. & Kaprio, J. (2008) Chernobyl exposure as stressor during pregnancy and hormone levels in adolescent offspring. *J Epidemiol Community Health*; 62:e5 Retrieved Sep 8, 2008 from the World Wide Web: http://jech.bmj.com/cgi/content/full/62/4/e5. doi:10.1136/jech.2007.060350.

Huizink, A.C., Dick, D.M., Sihvola, E., Rose, R.J. & Kaprio, J. (2007) Chernobyl exposure as stressor during pregnancy in adolescent offspring. *Acta Psychiatr Scand 116* (6) 438–446.

Hunt, W.A. (1987) Effects of ionizing radiation on behavior (pp. 321–330). In Conklin, J.J. & Walker, R.I. (Eds.). *Military Radiobiology*. San Diego, Academic Press, Inc.

ICRP Publication 49 (1986) Developmental Effects of Irradiation on the Brain of the Embryo and Fetus. A report of a Task Group of Committee 1 of the International Commission on Radiological Protection, 1986. In Thorne, M.C. (Ed.). *Annals of the ICRP 16* (4). Oxford: Pergamon Press.

ICRP Publication 88 (2001) Doses to the Embryo and Fetus from Intake Radionuclides by the Mother. *Ann ICRP 31* 19–515.

ICRP Publication 90 (2003) Biological Effects after Prenatal Irradiation (Embryo and Fetus). In Valentin J. (Ed.) *Annals of the ICRP*. Amsterdam: Elsevier.

Igumnov, S. & Drozdovitch, V. (2000). The intellectual development, mental and behavioral disorders in children from Belarus exposed in utero following the Chernobyl accident. *Eur Psychiatry15* 244–253.

Igumnov, S.A. & Drozdovitch, V.V. (2004) Antenatal exposure following the Chernobyl accident: neuropsychiatric aspects. *International Journal of Radiation Medicine 6* (1–4) 108–115.

Igumnov, S.A. (1996) Psychological development of children exposed to radiation in prenatal period as a result of Chernobyl disaster. *The Acta Medica Nagasakiensia 41* (3-4) 20–25.

Imamura, Y., Nakane, Y., Ohta, Y. & Kondo, H. (1999) Lifetime prevalence of schizophrenia among individuals prenatally exposed to atomic bomb radiation in Nagasaki City. *Acta Psychiatrica Scandinavia 100* (5), 344–349.

Ivanov, V.K., Gorski, A.I., Maksioutov, M.A., Tsyb, A.F. & Souchkevitch, G.N. (2001) Mortality among the Chernobyl emergency workers: estimation of radiation risks (preliminary analysis). *Health Phys 81* (5) 514–521.

Ivanov, V.K., Maksioutov, M.A., Chekin, S.Y., Petrov, A.V., Biryukov, A.P., Kruglova, Z.G., Matyash, V.A., Tsyb, A.F., Manton, K.G. & Kravchenko, J.S. (2006) The risk of radiation-induced cerebrovascular disease in Chernobyl emergency workers. *Health Phys 90* (3) 199–207.

Ivanov, V.K., Maksioutov, M.A., Chekin, S.Yu., Kruglova, Z.G., Petrov, A.V. & Tsyb, A.F. (2000) Radiation-epidemiological analysis of incidence of non-cancer diseases among the Chernobyl liquidators. *Health Physics 78* (5) 495–501.

Iwata, Y., Suzuki, K., Wakuda, T., Seki, N., Thanseem, I., Matsuzaki, H., Mamiya, T., Ueki, T., Mikawa, S., Sasaki, T., Suda, S., Yamamoto, S., Tsuchiya, K.J., Sugihara, G., Nakamura, K., Sato, K., Takei, N., Hashimoto, K. & Mori, N. (2008) Irradiation in adulthood as a new model of schizophrenia. *PLoS ONE 3* (5) e2283.

Jablensky, A. (2000) Epidemiology of schizophrenia: the global burden of disease and disability. *Eur Arch Psychiatry Clin Neurosci 250* (6) 274–285.

Kharchenko, V.P., Zubovskii, G.A. & Kholodova, N.B. (1995) Changes in the brain of persons who participated in the cleaning-up of the Chernobyl AES accident based on the data of radiodiagnosis (single-photon emission-computed radionuclide tomography, X-ray computed tomography and magnetic resonance tomography) *Vestn Rentgenol Radiol 1* 11–14 [in Russian].

Kholodova, N.B., Kuznetzova, G.D., Zubovsky, G.A., Kazakova, P.B. & Buklina, S.B. (1996) Remote consequences of radiation exposure upon the nervous system. *Zh Nevropatol Psikhiatr Im S S Korsakova 96* (5) 29–33.

Kholodova, N.B., Zhavoronkova, L.A., Ryzhov, B.N. & Kuznetsova, G.D. (2007) Premature aging of an organism and characteristics of its manifestation in remote period after low dose irradiation *Adv Gerontol 20* (4) 48–55 [in Russian].

Khomenko VI (2008) Study of lymphocyte activation reactions to neuro- specific antigenes in Chernobyl clean-up workers against the doses of radiation exposure Ukrainian Medical Journal, 4(66): 132–135 [in Ukrainian].

Khomskaja, E.D. (1995) Some results of neuropsychological study of Chernobyl accident consequences clean-up workers. *Social and Clinical Psychiatry 5* (4) 6–10 [in Russian].

Kim, J.S., Lee, H.J., Kim, J.C., Kang, S.S., Bae, C.S., Shin, T., Jin, J.K., Kim, S.H., Wang, H. & Moon, C. (2008) Transient impairment of hippocampus-dependent learning and memory in relatively low-dose of acute radiation syndrome is associated with inhibition of hippocampal neurogenesis. *J Radiat Res (Tokyo) 49* (5), 517–526.

Kimeldorf, D.J. & Hunt, E.L. (1965) *Ionizing Radiation: Neural Function and Behavior*. New York, Academic Press.

Kolominsky, Y., Igumnov, S. & Drozdovitch, V. (1999) The psychological development of children from Belarus exposed in the prenatal period to radiation from the Chernobyl Atomic Power Plant. *J Child Psychol Psychiatry 40* (2) 299–305.

Korr, H., Thorsten Rohde, H., Benders, J., Dafotakis, M., Grolms, N. & Schmitz, C. (2001) Neuron loss during early adulthood following prenatal low-dose X-irradiation in the mouse brain. *Int J Radiat Biol 77* (5) 567–580.

Kovalenko, A.N. & Loganovsky, K.N. (2001) Whether Chronic Fatigue Syndrome and Metabolic Syndrome X in Chernobyl accident survivors are membrane pathology? *Ukrainian Medical Journal 6* (26) 70–81 [in Russian].

Krasnikova, L.I. & Buzunov, V.A. (2007) Risks for non-tumor diseases incidence in the Chornobyl clean-up workers on the data of comprehensive clinical-and-epidemiological monitoring. *Problems of Radiation Medicine and Radiobiology 13* 199–207 [in Ukrainian].

Krasnov, V.N., Yurkin, M.M., Vojtsekh, V.F., Skavysh, V.A., Gorobets, L.N., Zubovsky, G.A., Smirnov, Yu.N., Kholodova, N.B., Puchinskaja, L.M. & Dudayeva, K.I. (1993) Mental disorders in clean-up workers of the Chernobyl accident consequences. Report I: structure and current pathogenesis. *Social and Clinical Psychiatry 3* (1) 5–10 [in Russian].

Kusunoki, Y., Kyoizumi, S., Yamaoka, M., Kasagi, F., Kodama K. & Seyama, T. (1999) Decreased proportion of CD4 T cells in the blood of atomic bomb survivors with myocardial infarction. *Radiat Res 152* (5) 539–543.

Lebedinsky, A.V. & Nakhilnitzkaja, Z.N. (1960) *Ionizing Radiation Influence on the Nervous System*. Moscow, Publishing House Atomizdat [in Russian].

Lestaevel, P., Grandcolas, L., Paquet, F., Voisin, P., Aigueperse, J. & Gourmelon, P. (2008) Neuro-inflammatory response in rats chronically exposed to (137)Cesium. *Neurotoxicology*. *29* (2), 343–348.

Lestaevel, P., Houpert, P., Bussy, C., Dhieux, B., Gourmelon, P. & Paquet F. (2005) The brain is a target organ after acute exposure to depleted uranium. *Toxicology 212* (2–3) 219–226.

Lestaevel, P., Romero, E., Dhieux, B., Ben Soussan, H., Berradi, H., Dublineau, I., Voisin, P. & Gourmelon, P. (2009) Different pattern of brain pro-/anti-oxidant activity between depleted and enriched uranium in chronically exposed rats. *Toxicology 258* (1) 1–9.

Litcher, L., Bromet, E.J., Carlson, G., Squires, N., Goldgaber, D., Panina, N., Golovakha, E. & Gluzman, S. (2000). School and neuropsychological performance of evacuated children in Kiev eleven years after the Chernobyl disaster. *J Child Psychol Psychiatry 41* 219–299.

Loganovskaja TK (2004) Psychophysiological pattern of acute prenatal exposure to lonizing radiation as a result of the Chernobyl accident. *Int J Psychophysiol 54* (1–2) 95–96.

Loganovskaja TK (2005) *Mental disorders in children exposed to prenatal irradiation as a result of the Chernobyl accident.* (PhD thesis) The dissertation for the academic degree of a Candidate of Medical Sciences in radiobiology, Research Centre for Radiation Medicine of Academy of Medical Sciences of Ukraine. Kiev.

Loganovskaja, T.K. & Loganovsky, K.N. (1999) EEG, cognitive and psychopathological abnormalities in children irradiated in utero. *Int J Psychophysiol 34* (3) 213–224.

Loganovskaja, T.K. & Nechayev, S.Yu. (2004): Psychophysiological effects in prenatally exposed children and adolescents as a result of the Chernobyl accident. *World of Medicine 4* (1) 130–137 [in Ukrainian]

Loganovsky, K.N. (1999) Clinical-Epidemiological aspects of psychiatric consequences of the Chernobyl disaster. *Social and Clinical Psychiatry 1* (9): 5–17 [in Russian].

Loganovsky, K.N. (2000) Neurological and psychopathological syndromes in the follow-up period after exposure to ionizing radiation. *Zh Nevrol Psikhiatr Im S S Korsakova 100* (4) 15–21 [in Russian].

Loganovsky, K.N. (2000) Vegetative-vascular dystonia and osteoalgetic syndrome or Chronic Fatigue Syndrome as a characteristic after-effect of radioecological disaster: the Chernobyl accident experience. *Journal of Chronic Fatigue Syndrome 7* (3) 3–16.

Loganovsky, K.N. (2002) *Mental disorders at exposure to ionising radiation as a result of the Chernobyl accident: neurophysiological mechanisms, unified clinical diagnostics, treatment*. The dissertation for the academic degree of a Doctor of Medical Sciences in radiobiology (03.00.01) and psychiatry (14.01.16). Research Centre for Radiation Medicine of Academy of Medical Sciences of Ukraine, Kiev [in Ukrainian].

Loganovsky, K.N. (2003) Psychophysiological features of somatosensory disorders in victims of the Chernobyl accident. *Fiziol Cheloveka 29* (1) 122–130.

Loganovsky, K.N. (2008) Neuropsychiatric aftermath of the Chernobyl disaster: current state of evidences. *Ukrainian Medical Journal 6* (68) 44–51 [in Ukrainian].

Loganovsky, K.N. & Bomko, M.O. (2004) Structural-functional pattern of radiation brain damage in Chernobyl accident clean-up workers. *Ukrainian Medical Journal 5* (43) 67–74 [in Ukrainian].

Loganovsky, K.N. & Bomko, M.A. (2007) Structural cerebral basis of functional disorders of the brain in Chernobyl accident clean-up workers (pp. 262–271). In Vozianov, A.F. & Bebeshko, V.G., Bazyka, D.A. (Eds.) *Health Effects of the Chernobyl Accident*, Kyiv, DIA, [in Ukrainian]

Loganovsky, K., Havenaar, J.M., Tintle, N.L., Guey, L.T., Kotov, R. & Bromet, E.J. (2008) The mental health of clean-up workers 18 years after the Chernobyl accident. *Psychol Med 38* 481–488.

Loganovsky, K.N. & Loganovskaja, T.K. (2000) Schizophrenia spectrum disorders in persons exposed to ionizing radiation as a result of the Chernobyl accident. *Schizophr Bull 26* (4) 751–773.

Loganovsky, K.N. & Yuryev, K.L. (2001) EEG patterns in persons exposed to ionizing radiation as a result of the Chernobyl accident: part 1: conventional EEG analysis. *J Neuropsychiatry Clin Neurosci 13* (4) 441–458.

Loganovsky, K.N. & Yuryev, K.L. (2004) EEG patterns in persons exposed to ionizing radiation as a result of the Chernobyl accident. Part 2: quantitative EEG analysis in patients who had acute radiation sickness. *J Neuropsychiatry Clin Neurosci 16* (1) 70–82.

Loganovsky, K.N., Antipchuk, Ye.Yu., Bomko, M.A., Denisyuk, N.V., Loganovskaja, T.K., Chuprovskaja, N.Yu., Yuryev, K.L. & Zdorenko, L.L. (2006) Interhemispheric asymmetry as a cerebral basis of psychopathology in remote period after radiation exposure due to the Chernobyl accident. *Ukrainian Medical Journal 5* (55) 54–64 [in Ukrainian].

Loganovsky, K.N., Antipchuk, Ye.Yu., Bomko, M.A., Chuprovskaja, N.Yu., Kovalenko, A.N., Napreyenko, A.K., Loganovskaja, T.K., Zdorenko, L.L., Denisyuk, N.V., Kolosinskaja, E.A., Perchuk, I.V., Chumak, S.A. & Kreinis, G.Y. (2007) Neuropsychiatric consequences of Acute Radiation Sickness (pp. 177-186). In Vozianov, A.F., Bebeshko, V.G. & Bazyka, D.A. (Eds.) *Health Effects of the Chernobyl Accident*, Kyiv, DIA [in Ukrainian]

Loganovsky, K.N., Kovalenko, A.N., Yuryev, K.L., Bomko, M.A., Antipchuk, Ye.Yu., Denisyuk, N.V., Zdorenko, L.L. Rossokha, A.P., Chorny, A.B.& Dubrovina, G.V. (2003) Verification of organic brain damage in remote period of Acute Radiation Sickness. *Ukrainian Medical Journal 6* (38) 70–78 [in Ukrainian].

Loganovsky, K.N., Loganovskaja, T.K., Nechayev, S.Y., Antipchuk, Y.Y. & Bomko, M.A. (2008) Disrupted development of the dominant hemisphere following prenatal irradiation. *J Neuropsychiatry Clin Neurosc 20* (3) 274–291.

Loganovsky, K.N., Nechayev, S.Yu. & Perchuk I.V. (2008) Neurotoxicity of Uranium and transuranium elements. *Ukrainian Medical Journal 2* (64) 135–143 [in Russian].

Loganovsky, K.N., Volovik, S.V., Manton, K.G., Bazyka, D.A. & Flor-Henry, P. (2005) Whether ionizing radiation is a risk factor for schizophrenia spectrum disorders? *World Journal of Biological Psychiatry 6* (4) 212–230.

Lowe, X.R., Bhattacharya, S., Marchetti, F. & Wyrobek, A.J. (2009) Early brain response to low-dose radiation exposure involves molecular networks and pathways associated with cognitive functions, advanced aging and Alzheimer's disease. *Radiat Res 171* (1) 53–65.

Lysyanyj, M.I. (1998) Current view on radiation effects on the nervous system. *Bulletin of Ukrainian Association of Neurosurgeons 7* 113–118 [in Ukrainian].

Mahmoud-Ahmed, A.S., Atkinson, S. & Wong, C.S. (2006) Early gene expression profile in mouse brain after exposure to ionizing radiation. *Radiat Res 165* (2), 142–154.

McGale, P. & Darby, S.C. (2005) Low doses of ionizing radiation and circulatory diseases: a systematic review of the published epidemiological evidence. *Radiat Res 163* (3) 247–257.

Mettler, F.A. & Upton, A.C. (Eds.) (1995) *Medical Effects of Ionizing Radiation*. 2nd ed. Philadelphia: Saunders W. B. Company

Mickley, G.A. (1987) Psychological effects of nuclear warfare (pp 303–319). In Conklin, J.J. & Walker, R.I. (Eds.). *Military Radiobiology*. San Diego, Academic Press, Inc.

Mizumatsu, S., Monje, M.L., Morhardt, D.R., Rola, R., Palmer, T.D. & Fike, J.R. (2003) Extreme sensitivity of adult neurogenesis to low doses of X-irradiation. *Cancer Res 63* (14), 4021–4027.

Monje, M.L. & Palmer, T. (2003) Radiation injury and neurogenesis. *Curr Opin Neurol 16* (2), 129–134.

Morozov, A.M. & Kryzhanovskaja, L.A. (1998) *Clinic, Dynamic and Treatment of Borderline Mental Disorders in Liquidators of Chernobyl Accident*. Kiev, Publishing House Chernobylinterinform [in Russian].

Moscalev Yu.I. (1991) *Delayed Consequences of Ionizing Radiation.* Moscow, «Meditzina» Publishing House [in Russian].

Nakane, Y. & Ohta, Y. (1986) An example from the Japanese Register: some long-term consequences of the A-bomb for its survivors in Nagasaki (pp. 26–27). In Ten Horn, GHMM., Giel, R., Gulbinat, W.H., & Henderson, J.H. (Eds.) *Psychiatric Case Registers in Public Health*. Amsterdam, Elsevier Science Publishers B.V.

Napreyenko, A.K. & Loganovskaja, T.K. (2004) Mental disorders in prenatally irradiated children and adolescents as a result of the Chernobyl accident: diagnostic system, treatment and rehabilitation. *World of Medicine 4* (1) 120–129 [in Ukrainian].

Napreyenko, A.K. & Loganovsky, K.N. (1995) The systematics of mental disorders related to the sequelae of the accident at the Chernobyl Atomic Electric Power Station. *Lik Sprava 5–6* 25–29 [in Russian].

Napreyenko, A.K. & Loganovsky, K.N. (1997) *Ecological psychiatry*, Kiev Polygraphkniga Publishing House [in Russian].

Napreyenko, A.K. & Loganovsky, K.N. (1999) Current problems of emergency psychiatry at the radioecological disaster pp 199–202. In De Clercq, M., Andreoli, A., Lamarre, S. & Forster, P. (Eds.) *Emergency Psychiatry in a Changing World.* Amsterdam, Elsevier Science B.V.

Napreyenko, A. & Loganovsky, K. (2001) Psychiatric management of radioecological disaster victims and local wars veterans. *New Trends in Experimental and Clinical Psychiatry XVII* (1–4) 43–48.

Napreyenko, A.K. & Loganovsky, K.N. (2001) Ecological psychiatry (pp. 417–461). In Napreyenko, A.K. (Ed.) *Psychiatry.* Kyiv, Zdorovja Publishing House [in Ukrainian].

National Report of Ukraine (2006) *20 Years of the Chornobyl Catastrophe: Future Outlook*. Kyiv, Atika [in Ukrainian].

Niagu, A.I., Noshchenko, A.G. & Loganovskii, K.N. (1992) Late effects of psychogenic and radiation factors of the accident at the Chernobyl nuclear power plant on the functional state of human brain. *Zh Nevropatol Psikhiatr Im S S Korsakova 92* (4) 72–77 [in Russian].

Nikolenko, V.Iu., Bondarenko, G.A., Bazyka, D.A., Golovchenko, Iu.I., Nikolenko, Iu.I. & Dubiaga, V.V. (2002) Features of immune disorders in miners who took part in cleaning up after the accident at Chernobyl Atomic Energy Station *Lik Sprava 3-4* 33–35 [in Russian].

Noshchenko, A.G. & Loganovskii, K.N. (1994) The functional brain characteristics of people working within the 30-kilometer area of the Chernobyl Atomic Electric Power Station from the viewpoint of age-related changes. *Lik Sprava*, *2* 16–19 [in Russian].

Novikov, V.S., Tsygan, V.N., Borisova, E.D., Rybina, L.A. (1997) Cerebral bioelectrical activity changes among Chernobyl Nuclear Station accident recover workers. *Human Physiology 23* (5) 34-39 [in Russian]

Nowakowski, R.S. & Hayes, N.L. (2008) Radiation, retardation and the developing brain: time is the crucial variable. *Acta Pædiatrica 97* 527–531.

Nyagu, A., Loganovsky, K., Loganovskaja, T. & Antipchuk, Ye. (1996) The WHO Project on «Brain Damage in Utero»: mental health and psychophysiological status of the Ukrainian prenatally irradiated children as a result of the Chernobyl accident. *Bambino: Progetto Salute* (pp. 34–58). Ancona, Italy, June 12–13, 1996.

Nyagu, A.I. & Loganovsky, K.N. (1998) *Neuropsychiatric Effects of Ionizing Radiation*. Kiev: Publishing House Chernobylinterinform [in Russian].

Nyagu, A.I., Cheban, A.K., Bugayev, V.M., Korol, N.O. & Treskunova, T.V. (1997) Health of children subjected to intrauterine irradiation. In Baryakhtar, V.G. (Ed). *Chornobyl Catastrophe* (pp. 454–458). Kyiv, Ukraine: Editorial House of Annual Issue "Export of Ukraine"

Nyagu, A.I., Cheban, A.K., Salamatov, V.A., Limanskaja, G.F., Yashchenko, A.G., Zvonariova, G.N., Yakimenko G.D., Melina, K.V., Plachinda, Yu.I., Chumak, A.A., Bazyka, D.A., Gul'ko, G.M., Chumak, V.V. & Volodina, I.A. (1993) Psychosomatic health of children irradiated *in utero* as a result of the Chernobyl accident. *Social, Psychological, and Psychoneurological Aspects of Chernobyl NPP Accident Consequences* (pp. 265–270). Kiev, Ukraine, September 28–30, 1992 [in Russian]

Nyagu, A.I., Loganovsky, K.N, Loganovskaja, T.K., Repin, V.S. & Nechaev, S.Yu. (2002) Intelligence and brain damage in children acutely irradiated in utero as a result of the Chernobyl accident. In Imanaka, T. (Ed.) *KURRI-KR-79. Recent Research Activities about the Chernobyl NPP Accident in Belarus, Ukraine and Russia* (pp. 202–230). Kyoto, Japan: Research Reactor Institute, Kyoto University.

Nyagu, A.I., Loganovsky, K.N. & Loganovskaja, T.K. (1998). Psychophysiologic aftereffects of prenatal irradiation. *Int J Psychophysiol, 30* (3), 303–311

Nyagu, A.I., Loganovsky, K.N. & Yuryev, K.L. (2002) Psychological consequences of nuclear and radiological accidents: delayed neuropsychiatric effects of the acute radiation sickness following Chernobyl (pp. 27–47). In *Follow-up of delayed health consequences of acute accidental radiation exposure. Lessons to be learned from their medical management*. IAEA-TECDOC-1300, IAEA, WHO. Vienna, IAEA

Nyagu, A.I., Loganovsky, K.N., Cheban, A.K., Podkorytov, V.S., Plachinda, Yu.I., Yuriev, K.L., Antipchuk, Ye.Yu., & Loganovskaja, T.K. (1996) Mental health of prenatally irradiated children: a psychophysiologycal study. *Social and Clinical Psychiatry 6* (1) 23–36 [in Russian].

Nyagu, A.I., Loganovsky, K.N., Chuprovskaja, N.Yu., Vaschenko, E.A., Kostyuchenko, V.G., Zazimko, R.N., Plachinda, Yu.I., Yuriev, K.L., Loganovskaja & Zdorenko, L.L. (1997) Postradiation encephalopathy in the remote period of Acute Radiation Sickness. *Ukrainian Medical Journal 2* (2) 33–44 [in Russian].

Nyagu, A.I., Loganovsky, K.N., Chuprovskaya, N.Yu., Kostychenko, V.G., Vaschenko, E.A., Yuryev, K.L., Zazymko, R.N., Loganovskaya, T.K. & Myschanchuk, N.S. (2003) Nervous system (pp. 143–176). In Vozianov, A., Bebeshko, V. & Bazyka, D. (Eds.) *Health Effects of Chornobyl Accident*. Kyiv, DIA.

Nyagu, A.I., Loganovsky, K.N., Pott-Born, R., Repin, V.S., Nechayev, S.Yu., Antipchuk, Ye.Yu., Bomko, M.A., Yuryev, K.L. & Petrova, I.V. (2004) Effects of prenatal brain irradiation as a result of the Chernobyl accident. *International Journal of Radiation Medicine 6* (1–4) 91–107.

Nyagu, A.I., Loganovsky, K.N., Yuryev, K.L. & Zdorenko, L.L. (1999) Psychophysiological aftermath of irradiation. *International Journal of Radiation Medicine 2* (2) 3–24.

Otake, M. & Schull, W.J. (1984) In utero exposure to A-bomb radiation and mental retardation: A reassessment. *British Journal of Radiology 57*, 409–414.

Otake, M. & Schull, W.J. (1998) Radiation-related brain damage and growth retardation among the prenatally exposed atomic bomb survivors. *Int J Radiat Bio, 74* (2), 159–171.

Otake, M., Schull, W.J. & Lee, S. (1996) Threshold for radiation-related severe mental retardation in prenatally exposed A-bomb survivors: a re-analysis. *Int J Radiat Biol 70* (6), 755–763.

Pall, M.L. (2008) Post-radiation syndrome as a NO/ONOO(-) cycle, chronic fatigue syndrome-like disease. *Med Hypotheses 71* (4) 537–541.

Polyukhov, A.M., Kobsar, I.V., Grebelnik, V.I. & Voitenko, V.P. (2000) The accelerated occurrence of age-related changes of organism in Chernobyl workers: A radiation-induced progeroidsyndrome? *Experimental Gerontology 35*, 105–115.

Preston, D.L., Shimizu, Y., Pierce, D.A., Suyama, A., Mabuchi, K. (2003) Studies of mortality of atomic bomb survivors. Report 13: Solid cancer and noncancer disease mortality: 1950–1997. *Radiat Res 160* (4) 381–407.

Raber, J., Rola, R., LeFevour, A., Morhardt, D., Curley, J., Mizumatsu, S., VandenBerg, S.R. & Fike, J.R. (2004) Radiation-induced cognitive impairments are associated with changes in indicators of hippocampal neurogenesis. *Radiat Res 162* (1), 39–47.

Revenok, A.A. (1998) Non-psychotic mental disorders in persons who had Acute Radiation Sickness as a result of the Chernobyl disaster (10 years after catastrophe). *Ukrainian Medical Journal 2* (4) 45–50 [in Russian].

Revenok, O.A. (1999) *Structural and dynamical characterization of organic brain damage in persons exposed to ionizing radiation as a result of the Chernobyl accident* The dissertation for the academic degree of a Doctor of Medical Sciences in psychiatry. Ukrainian Research Institute for General and Forensic Psychiatry, Kiev.

Rodgers, B.E., & Holmes, K.M. (2008) Radio-adaptive response to environmental exposures at Chernobyl. *Dose Response 6* (2), 209–221.

Romodanov, A.P. & Vynnyts'kyj, O.R. (1993) Brain lesions in mild radiation sickness. *Lik Sprava 1* 10–16 [in Ukrainian].

Romodanov, A.P. (Ed.) (1992) *Postradiation Encephalopathy. Experimental Research and Clinical Observation*. Kyiv, Ukrainian Research Institute for Neurosurgery [in Ukrainian].

Ron, E., Modan, B., Flora, S., Harkedar, I. & Gurewitz, R. (1982) Mental function following scalp irradiation during childhood. *Am J Epidemiol 116* 149–160.

Ross, L., Johansen, Chr., Dalton, S.O., Mellemkjaer, L., Thomassen, L.H., Mortensen, P.B., & Olsen, J.H. (2003) Psychiatric hospitalizations among survivors of cancer in childhood or adolescence. *The New England Journal of Medicine 359* (7) 650–657.

Rumyantseva, G.M., Chinkina, O.V. & Levina, T.M. (2002) Psychosomatic aspects of mental disorder development in Chernobyl accident clean-up workers. *Psychiatry and Psychotherapy 4* 1. Retrived March 14, 2009 from the World Wide Web: http://www.consilium-medicum.com/magazines/special/psychiatry/article/10532 [in Russian].

Sadetzki, S., Chetrit, A., Freedman, L., Stovall, M., Modan, B. & Novikov, I. (2005) Long-term follow-up for brain tumor development after childhood exposure to ionizing radiation for tinea capitis. *Radiat Res 163* (4) 424–332.

Sasaki, H., Wong, F.L., Yamada, M. & Kodama, K. (2002) The effects of aging and radiation exposure on blood pressure levels of atomic bomb survivors. *J Clin Epidemiol 55* (10), 974–981.

Schindler, M.K., Wang, L., Selemon, L.D., Goldman-Rakic, P.S., Rakic, P. & Csernansky, J.G. (2002) Abnormalities of thalamic volume and shape detected in fetally irradiated rhesus monkeys with high dimensional brain mapping. *Biol Psychiatry 51* (10): 827–837.

Schmitz, S., Born, M., Dolezel, P., Rutten, B.P., de Saint-Georges, L., Hof, P.R. & Korr, H. (2005) Prenatal protracted irradiation at very low dose rate induces severe neuronal loss in rat hippocampus and cerebellum. *Neuroscience 130* 935–948.

Selemon, L.D.,Wang, L., Nebel, M.B., Csernansky, J.G., Goldman-Rakic, P.S. & Rakic, P. (2005) Direct and indirect effects of fetal irradiation on cortical gray and white matter volume in the macaque. *Biol Psychiatry 57* 83–90.

Shabadash, A.L. (1964) Cytochemical characterization of reactivity and inhibit-protective states of the nervous cells at radiation injuries (pp. 53–60). In: *Restoration processes at radiation injuries*. Moscow, Atomizdat Publishing House, [in Russian].

Shimizu, Y., Pierce, D.A., Preston, D.L. & Mabuchi, K. (1999) Studies of the mortality of atomic bomb survivors. Report 12, part II. Noncancer mortality: 1950–1990. *Radiat Res 152* (4)374–389.

Soldatkin, V.A. (2002) *Mental disorders in the Chernobyl accident clean-up workers: clinical and pathogenetical approach.* (PhD thesis) The dissertation for the academic degree of a candidate of Medical Sciences in psychiatry. State Scientific Centre for Social and Forensic Psychiatry, Russian Federation, Moscow [in Russian].

Taormina, D.P., Rozenblatt, S., Guey, L.T., Gluzman, S.F., Carlson, G.A., Havenaar, J.M., Zakhozha, V., Kotov, R., & Bromet, E.J. (2008) The Chornobyl accident and cognitive functioning: a follow-up study of infant evacuees at age 19 years. *Psychol Med 38* (4) 489–497.

Torubarov, F.S., Blagoveshchenskaia, V.V., Chesalin, P.V. & Nikolaev, M.K. (1989) Status of the nervous system in victims of the accident at the Chernobyl atomic power plant. *Zh Nevrol Psikhiatr Im S S Korsakova 89* (2) 138–142 [in Russian].

Trocherie, S., Court, L., Gourmelon, P., Mestries, J.-C., Fatome, M., Pasquier, C., Jammet, H., Gongora, H. & Doloy, MTh. (1984) The value of EEG signal processing in the assessment of the dose of gamma or neutron-gamma radiation absorbed dose (pp. 633–644). In Court, L., Trocherie, S. & Doucet, J. (Eds.) *Le Traitment du Signal en Electrophysiologie Experimentale et Clinique du Systeme Nerveux Central,* Vol. II.

Turuspekova, S.T. (2002) Neuropsychological functions in individuals exposed to small dose ionizing radiation. *Zh Nevrol Psikhiatr Im S S Korsakova 102* (3) 16–19 [in Russian].

UNSCEAR 1982 Report to the General Assembly (1982) Vol. 2, Biological Effects. *UNSCEAR 1982 Report to the General Assembly, with Scientific Annexes.*. United Nations Scientific Committee on the Effects of Atomic Radiation. New York, United Nations

UNSCEAR 1993 Report to the General Assembly (1993) Annex I. Late deterministic effects in children. Sources and effects of ionizing radiation (pp. 899–908). *UNSCEAR 1993 Report to the General Assembly, with*

Scientific Annexes. United Nations Scientific Committee on the Effects of Atomic Radiation. New York, United Nations.

Vasculescu, T., Pasculescu, G., Papilian, V., Serban, I. & Rusu, M. (1973) The effect of low X-ray doses on the central nervous system. *Radiobiol. Radiother. (Berl.), 14* (4) 407–416.

Voloshina, N.P. (1997) *Structural and functional brain disorders in patients with dementia of different genesis*. The dissertation for the academic degree of a Doctor of Medical Sciences in neurology and psychiatry. Kharkiv Institute of Advanced Medical Studies, Kharkiv, Ukriane [in Ukrainian].

Volovik, S., Loganovsky, K. & Bazyka, D. (2005) Chronic Fatigue Syndrome: molecular neuropsychiatric projections. Abstract XIII World Congress of Psychiatry Cairo, September 10–15, 2005, p. 225.

Volovik, S., Loganovsky, K., Bazyka, D., Bebeshko, V., Cohen, H., Chao, N., Ginsburg, J.S., Siedow, J. & Goldschmidt, P. (2006) Chronic Fatigue Syndrome as Chornobyl aftermath: aetiobiomedical dimesions (pp. 114–116). In: Contributed papers to The International Conference "*Twenty years after Chornobyl accident future outlook*", April 24–26, Kyiv, Ukraine. Kyiv, HOLTEH.

Vyatleva, O.A., Katargina, T.A., Puchinskaya, L.M. & Yurkin, M.M. (1997) Electrophysiological characterization of the functional state of the brain in mental disturbances in workers involved in the clean-up following the Chernobyl atomic energy station accident. *Neurosci Behav Physiol 27* (2) 166–172.

Wong, C.H. & Van der Kogel, A.J. (2004) Mechanisms of radiation injury to the central nervous system: implications for neuroprotection. *Molecular Intervention 4* (5), 273–284.

World Health Organization (1996). *Health consequences of the Chernobyl accident. Results of the IPHECA pilot projects and related national programmes*. Geneva, World Health Organization

World Health Organization (2006) *Health effects of the Chernobyl accident and special health care programmes. Report of the UN Chernobyl Forum Expert Group «Health» (EGH).* Bennet, B., Repacholli, M., Carr, Zh. (Eds.). Geneva, World Health Organization.

Yaar, I., Ron, E., Modan, B., Rinott, Y., Yaar, M. & Modan, M. (1982) Long-lasting cerebral functional changes following moderate dose X-radiation treatment to the scalp in childhood: an electroencephalographic power spectral study. *J Neurol Neurosurg Psychiatry 45* (2) 166–169.

Yaar, I., Ron, E., Modan, M., Perets, H. & Modan, B. (1980) Long–term cerebral effects of small doses of X–irradiation in childhood as manifested in adult visual evoked responses. *Ann Neurol 8* 261–268.

Yamada, M., Kasagi, F., Sasaki, H., Masunari, N., Mimori, Y. & Suzuki G (2003) Association between dementia and midlife risk factors: the radiation effects research foundation adult health study. *J Am Geriatr Soc 51* (3) 410–414.

Yamada, M., Sasaki, H., Mimori, Y., Kasagi, F., Sudoh, S., Ikeda, J., Hosoda, Y., Nakamura, S., & Kodama, K. (1999) Prevalence and risks of dementia in the Japanese population: RERF's adult health study Hiroshima subjects. Radiation Effects Research Foundation. *J Am Geriatr Soc 47* (2) 189–195.

Yin, E., Nelson, D.O., Coleman, M.A., Peterson, L.E. & Wyrobek, A.J. (2003) Gene expression changes in mouse brain after exposure to low-dose ionizing radiation. *Int J Radiat Biol 79* (10), 759–775.

Zdorenko, L.L. & Loganovsky, K.N. (2002) Mental working capacity in liquidators with organic mental disorders in the remote period after the Chernobyl accident. *Ukrainian Medical Journal 4* (30) 120–126 [in Ukrainian].

Zhavoronkova, L.A., Gogitidze, N.V. & Kholodova, N.B. (1996) The characteristics of the late reaction of the human brain to radiation exposure: the EEG and neuropsychological study (the sequelae of the accident at the Chernobyl Atomic Electric Power Station) *Zh Vyssh Nerv Deiat Im I P Pavlova 46* (4) 699–711 [in Russian].

Zhavoronkova, L.A., Gogitidze, N.V. & Kholodova, N.B. (2000) Postradiation changes in the brain asymmetry and higher mental functions of right- and left-handed subjects (the sequelae of the accident at the Chernobyl Atomic Electric Power Station) *Zh Vyssh Nerv Deiat Im I P Pavlova 50* (1) 68–79 [in Russian].

Zhavoronkova, L.A., Kholodova, N.B., Belostocky, A.P. & Koulikov, M.A. (2008) Reduced electroencephalographic coherence asymmetry in the Chernobyl accident survivors. *Span J Psychol 11* (2) 363–373.

Zhavoronkova, L.A., Kholodova, N.B., Zubovskii, G.A., Smirnov, Yu.N., Koptelov, Yu.M. & Ryzhov, N.I. (1995) Electroencephalographic correlates of neurological disturbances at remote periods of the effect of ionizing radiation (sequelae of the Chernobyl NPP accident). *Neurosci Behav Physiol 25* (2) 142–149.

Zhavoronkova, L.A., Kholodova, N.B., Zubovsky, G.A., Gogitidze, N.V., Koptelov, Y.M. (1995) EEG power mapping, dipole source and coherence analysis in Chernobyl patients. *Brain Topogr 8* (2) 161–168.

Zhavoronkova, L.A., Lavrova, T.P., Belostotskii, A.V., Kholodova, N.B., Skoriatina, I.G. & Voronov, V.P. (2006) Impairment of space-frequency parameters of EEG coherence during cognitive performance (consequences of Chernobyl accident)] *Zh Vyssh Nerv Deiat Im I P Pavlova 56* (2) 193–201 [in Russian]

Zozulya, Yu.P. (Ed.) (1998) *Chronic Influence of Small Doses of Ionizing Radiation: Experimental Studies and Clinical Observations*. Kiev, Publishing House Chernobylinterinform [in Ukrainian].