

Review

# INVESTIGATIONS ON HEALTH CONDITIONS OF CHERNOBYL NUCLEAR POWER PLANT ACCIDENT RECOVERY WORKERS FROM LATVIA IN LATE PERIOD AFTER DISASTER

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*The paper summarises the main findings on Chernobyl Nuclear Power Plant (CNPP) accident recovery workers from Latvia and their health disturbances, which have been studied by the authors during the last two decades. Approximately 6000 persons from Latvia participated in CNPP clean-up works in 1986–1991. During their work period in Chernobyl they were exposed to external as well as to internal irradiation, but since their return to Latvia they were living in a relatively uncontaminated area. Regular careful medical examinations and clinical studies of CNPP clean-up workers have been conducted during the 25 years after disaster, gathering knowledge on radiation late effects. The aim of the present review is to summarise the most important information about Latvian CNPP clean-up worker health revealed by thorough follow-up and research conducted in the period of 25 years after the accident. This paper reviews data of the Latvian State Register of Persons Exposed to Radiation due to CNPP Accident and gives insight in main health effects found by the researchers from the Centre of Occupational and Radiological Medicine (Pauls Stradiņš Clinical University Hospital) and Rīga Stradiņš University in a number of epidemiological, clinical, biochemical, immunological, and physiological studies. Latvian research data on health condition of CNPP clean-up workers in the late period after disaster indicate that ionising radiation might cause premature ageing and severe polymorbidity in humans.*

**Key words:** Chernobyl accident, ionising radiation, health condition, mortality, premature ageing.

## INTRODUCTION

The accident at the Chernobyl Nuclear Power Plant (CNPP), on 26 April 1986, was the largest disaster in the nuclear industry ever seen by the entire world. Consequences of this tragedy can be felt until nowadays. The total amount of radioactive materials 200 times exceeded the radioactivity caused together by explosions in Hiroshima and Nagasaki (Anonymous, 2006b; Yablokov *et al.*, 2009). Consequently, a large area as well as agricultural products and water were polluted. Enormous amounts of radioactive substances were released into the atmosphere (Ginzburg and Reis, 1991). The main released radionuclides were:  $^{131}\text{I}$  (disintegration half-life:  $T_{1/2} = 8$  days),  $^{132}\text{Te}$  ( $T_{1/2} = 3,3$

days),  $^{89}\text{Sr}$  ( $T_{1/2} = 53$  days),  $^{90}\text{Sr}$  ( $T_{1/2} = 28$  years),  $^{134}\text{Cs}$  ( $T_{1/2} = 2$  years),  $^{137}\text{Cs}$  ( $T_{1/2} = 30$  years),  $^{133}\text{Xe}$  ( $T_{1/2} = 5,3$  days),  $^{106}\text{Ru}$  ( $T_{1/2} = 368$  days),  $^{35}\text{Kr}$  ( $T_{1/2} = 10,6$  years),  $^{144}\text{Ce}$  ( $T_{1/2} = 284$  days),  $^{241}\text{Pu}$  ( $T_{1/2} = 13$  years), and  $^{239}\text{Pu}$  ( $T_{1/2} = 24$  years) (Anonymous, 2000; Yablokov *et al.*, 2009). Therefore, people who settled in close proximity to the nuclear power plant were exposed not only to external ionising radiation, but also to internal radiation from incorporated radionuclides inhaled with air pollution and ingested with food and water (Aleksanin, 2010).

After the accident, the greatest exposure was received by the group of CNPP accident clean-up workers. More than 600 000 inhabitants from the former Soviet Union took part

in the CNPP accident clean-up works from 1986 till 1991 (Anonymous, 2006b; Yablokov *et al.*, 2009), including approximately 6000 people from Latvia. As in the territory of Latvia, unlike Ukraine, Belarus, and Russia, the background radioactivity after the CNPP accident was not increased significantly, we can analyse changes in the health condition of Chernobyl clean-up workers caused by factors related to the exposure received in Chernobyl. These were mainly external irradiation and radionuclides incorporated into the body. Amongst the non-radiation factors, the most significant were psycho-emotional stress, physical overload, and the effect of heavy metals and other chemicals (Viel *et al.*, 1997; Nikiforov, 2002; Zvagule, 2004). CNPP clean-up workers were mainly healthy men — military personnel and civilians of reproductive age. Most of these men were documented as having received ionising radiation exposure. Doses, as they were recorded in the „Military Passport”, might not be always accurate (Mironova *et al.*, 1998; Mironova-Ulmane *et al.*, 2001a; 2001b; Nikiforov, 2002). The data on received doses are thought to be falsified (much smaller), thus contributing to the uncertainty in analytical epidemiological studies, in which individual doses have to be estimated. As since more than 25 years have passed since the CNPP accident, now we can analyse the effects of radioactive exposure in the late period.

The Chernobyl accident created a new problem for health professionals in Latvia, since inhabitants of Latvia participated in clean-up works in Chernobyl. Information about the CNPP accident clean-up workers' health condition and diseases in Latvia has been gathered regularly starting with 1987. Since 1994, data have been included in the Latvian State Register of Persons with Occupational Diseases and Persons Exposed to Radiation due to the CNPP Accident maintained by the specialists of the Centre of Occupational and Radiological Medicine (Pauls Stradiņš Clinical University Hospital). On the basis of information collected in the Centre four doctoral theses (Kurjane, 2001; Zvagule, 2004; Reste, 2013; Silova, 2015) and a lot of scientific studies were completed (Bruvere *et al.*, 1995; 2003; Churbakova *et al.*, 1996; 1999; Eglite *et al.*, 1997; 2009; Mironova *et al.*, 1998; Kalnina *et al.*, 2001; 2012; 2013; 2013a; Kumerova *et al.*, 2000; Kurjane and Sočņevs, 1999; Kurjane *et al.*, 1999; 2000; 2001; Mazarevica *et al.*, 2000; Mironova-Ulmane *et al.*, 2001; 2001a; Petukhov *et al.*, 2011; Reste *et al.*, 2012; 2014; Skesters *et al.*, 2005; 2006; 2006a; 2006b; 2008; 2010; 2010a; Viel *et al.*, 1997; Zvagule *et al.*, 2002; 2003). Clinical observations and epidemiological studies among Chernobyl recovery workers showed that these persons suffer from a broad spectrum of different kinds of diseases more seriously than in the non-exposed general Latvian population. This creates a need for further research to determine the reasons and mechanisms of progressing health disturbances.

Complex assessment of Chernobyl NPP accident biological consequences in humans exposed to radiation becomes a topical problem nowadays due to the high number of nuclear power plants in the world and increasing probability of

radioactive accidents. The relevance of the medical effects of Chernobyl NPP accident is also shown by many international seminars, symposiums, and congresses that take place each year on these issues. The current paper represents an overview of the main radiation-related health effects in Chernobyl accident clean-up workers from Latvia revealed by a number of studies conducted in the Centre of Occupational and Radiological Medicine during the last 25 years.

## AGEING AND MORTALITY OF CHERNOBYL NUCLEAR POWER PLANT CLEAN-UP WORKERS

Research in the Centre of Occupational and Radiological Medicine of Pauls Stradiņš Clinical University Hospital is presently focused on the exploration of early senescence signs of CNPP clean-up workers and assessment of late effects of ionising radiation low-dose chronic exposure. Studies were conducted on incidence of different groups of diseases in CNPP clean-up workers from Latvia, in comparison with incidence in the general Latvian male population (Zvagule, 2004; Reste *et al.*, 2012; Reste, 2013; 2014). Many immunological and biochemical observations and studies have been conducted in the Centre.

The Chernobyl Nuclear Power Plant clean-up workers from Latvia received certain amounts of radionuclides that were absorbed in their body due to breathing contaminated air, drinking water and eating local food (Yablokov *et al.*, 2009; Nikiforov, 2002). Many of these radionuclides have long disintegration half-life (for example,  $^{137}\text{Cs}$  — 30 years). The pathology process created by the incorporated radionuclides, involves all organs and systems of the body, but not to the same extent. It depends on the organotropism of chemical elements, for example,  $^{131-135}\text{I}$  accumulates in thyroid,  $^{90}\text{Sr}$ ,  $^{140}\text{Ba}$ ,  $^{226}\text{Ra}$ ,  $^{47}\text{Ca}$  and  $^{239}\text{Pu}$  — in bones,  $^{144}\text{Ce}$  and  $^{60}\text{Co}$  — in liver, and  $^{134}\text{Cs}$  and  $^{137}\text{Cs}$  evenly disperses into the organism — mainly in the lymphatic system, soft tissue, and genitalia (Anonymous, 2001). The radionuclides residing in the body also have a toxic effect on tissue (Anonymous, 2006c).

The clean-up workers have been living in radiologically non-contaminated area since their return from Chernobyl. However, in the case of Chernobyl clean-up workers in the period after exposure, the effects have not been due to small doses of external ionising radiation and stochastic effects, because in addition to the external radiation they also received internal radiation (Ginzburg, 1991; Zvagule *et al.*, 2002). Official documented doses of radiation exposure in Chernobyl are not reliable, because they do not reflect ionising radiation effects from incorporated radionuclides. A documented exposure dose exists only for about 57% of the clean-up workers (Eglite *et al.*, 2009). The mean radiation dose estimated from data in the Latvian State Register for Persons Exposed to Radiation in Chernobyl was about  $128.76 \pm 70.73$  mSv (min 0.1 mSv, max 500 mSv) (Eglite *et al.*, 2009; Reste, 2014). Higher doses were received in 1986 mainly by 20–29-year-old men ( $n = 1231$ ), smaller doses were received in 1987 and later by workers with age

older than 30 years ( $n = 1832$ ) (Eglite *et al.*, 2009; Reste, 2014). We believe that the real radiation doses may be higher than those documented ones (Mironova *et al.*, 1998; Mironova-Ulmane *et al.*, 2001; 2001a), as radiation exposure effects in tissues and organs can accumulate.

Mean age of clean-up workers from Latvia at time of participation was  $31.9 \pm 7.3$  years mostly they had age 20–39 years and were healthy. In 2011, their mean age was already  $56.6 \pm 7.3$  years (Reste, 2013; 2014). CNPP clean-up workers become older and suffered from illness more often. Polymorbidity has been typical for this group of people (Nikiforov, 2002). Existence of several disorders at the same time in one person is more frequently observed in CNPP clean-up workers than in the Latvian male population with corresponding age (Zvagule, 2004). Mean number of diseases for one person in CNPP clean-up workers in 1986–1997 gradually increased from 1.3 to 3.2 (Reste, 2013; 2014). A significant increase in the mean number of diseases for one person was observed in the period after 1998. Mean number of diseases in 2000–2007 was 9.6–11.0 (Reste, 2013; 2014), which was higher than in the general Latvian male population with corresponding age (Eglite *et al.*, 2009; Zvagule, 2004). One of the reasons for such high morbidity in CNPP clean-up workers may be regular complete health examination in the Centre of Occupational and Radiological Medicine, which would result in more diseases recorded.

Mortality rates for the time period 1999–2009 were recorded in the Latvian State Population Register (Reste, 2013; 2014). In total, 954 of 5906 CNPP clean-up workers died in the period from 1988 to 2010. Mortality of the clean-up workers gradually increased from 0.2 per 1000 in 1988 to 18.6 per 1000 in 2009. Every year since 2003, about 1.3% of the initial number of all CNPP clean-up workers died. The most frequent age at which CNPP clean-up workers died in 1999–2009 was between 46–57 years, but in total the largest number of clean-up workers died at the age of 50–59 years (Reste, 2013; 2014). In 1999, the most common cause of death was for exogenous reasons, such as traffic accidents, violent accidents, acute intoxications, suicides etc. (42.6% of all deaths in 1999), followed by cardiovascular (12.8%) and oncological (12.8%) diseases (Reste, 2013; 2014). During the last 10 years, the causes of mortality changed. Exogenous reasons of death decreased, and mortality due to cardiovascular diseases has risen dramatically. Mortality due to oncological diseases is growing progressively, but it does not exceed and is even lower than mortality in corresponding general Latvian male population of similar age (Reste, 2013; 2014). These results may be due to regular examination of CNPP clean-up workers, for which the main attention is focused on diagnosis of cancer in early stages. In 2009, in CNPP workers cardiovascular diseases was the main cause of mortality (43.0% of all deaths), followed by oncological diseases (25.3%) and exogenous reasons (12.7%) (Reste, 2013; 2014). These proportions are similar to those in the general Latvian male population. The main disorders among cardiovascular rea-

sons of death in CNPP clean-up workers are myocardial infarction, cerebral infarction, cardiomyopathy etc. (Reste, 2013; 2014). Life expectancy at birth for Latvian males in the 2007–2009 period was 65–68 years. In CNPP clean-up workers from Latvia in the time period 1999–2009, mortality was slightly higher in age group 40–54 years than in the general Latvian male population of this age, which might be explained by early ageing (Reste, 2013; 2014; Yablokov *et al.*, 2009; Nikiforov, 2002). In the age group over 55 years, mortality was lower (Reste, 2013; 2014), likely due to regular health observation and lower mean age of the CNPP clean-up workers cohort (mainly not older than 60 years) than that of the general population > 55 years of age (increase in mortality may be expected after age 60 years).

## FUNCTIONAL CONDITION OF CHERNOBYL NPP CLEAN-UP WORKERS

The study on functional status of CNPP clean-up workers (unpublished data) was conducted in the Centre of Occupational and Radiological Medicine as one of the research directions. The study was conducted in 2010–2011, i.e. 24 years after Chernobyl accident. The study group consisted of 53 CNPP clean-up workers and as control group 47 persons of appropriate age, who were not chronically exposed to ionising radiation. Mean age was  $55.5 \pm 7.3$  in the CNPP clean-up worker group and  $57.4 \pm 9.4$  years in the control group. The World Health Organisation recommended a questionnaire on disability assessment for health services research (WHO Disability Assessment Schedule II for Health Services Research, 12-Item Self-Administered Version, 2001) which was used for the estimation of functional status. The questionnaire included questions about non-physical, mental, psychosocial behaviour, and ability. For each person the sum of all answers was calculated (functional ability index — FAI). Participation in the study was on the optional basis. The study was approved by the Regional Committee for Medical Research Ethics.

Mean value of FAI in CNPP clean-up workers was  $54.9 \pm 8.4$ , compared to  $60.7 \pm 9.1$  in the control group, and this difference was statistically significant ( $p < 0.01$ ). This indicated a lower functional status in CNPP clean-up workers comparing with control group. A slight negative correlation between FAI and age was observed in the CNPP workers group, while there was no significant correlation observed in control group (unpublished data). This indicated a declining functional status in older CNPP workers, which was not apparent in the control group.

The study revealed major disability in CNPP workers performing tasks such as standing for long time or at least 30 minutes (73.6% vs 32.6% in control group), walking at least 1 km or equivalent load (49.1% vs 19.6% in control group), taking care of household responsibilities (60.4% vs 41.3%), learning a new task (56.6% vs 34.8%), and concentrating on doing something for ten minutes (43.4% vs 34.8%). Health problems emotionally affected 88.7% of CNPP clean-up



workers, while only 71.7% of respondents in the control group (unpublished data).

The observed differences between observed groups might be explained by polymorbidity and higher morbidity in CNPP clean-up workers, comparing with the general Latvian population. One of the explanations for poor functional condition of CNPP clean-up workers may be also their premature ageing.

## DISABILITY OF CHERNOBYL NPP CLEAN-UP WORKERS

During the time period of 25 years after the Chernobyl disaster, approximately 85.7% of the total number of CNPP clean-up workers became disabled (4352 persons) (data of the State Medical Commission for the Assessment of Health Condition and Working Ability; unpublished). The largest part of the disabled CNPP workers lost 25–59% of working capacity. Most of them are about 40–59 years old. Information from the State Medical Commission for the Assessment of Health Condition and Working Ability indicates that the main reasons of disability of CNPP clean-up workers are:

- 1) disorders of the nervous system (for example, encephalopathy of mixed origin with psychoorganic syndrome);
- 2) cardiovascular diseases (complications of arterial hypertension, atherosclerosis, coronary heart disease, cerebrovascular disorders);
- 3) musculoskeletal and connective tissue disorders.

During the last years, the disability degree progressively worsened due to accompanying ageing related diseases.

## HEALTH DISTURBANCES IN CHERNOBYL CLEAN-UP WORKERS

Clinical observations and examinations of CNPP accident clean-up workers, as well as epidemiological and clinical studies, revealed simultaneous pathologies of many organs characteristic for this group of people (Zvagule, 2004; Eglite *et al.*, 2009; Reste, 2013; 2014). The pathogenesis of these pathologies is very complicated and up to now is not completely clear (Nyagu and Loganovsky, 1996). Our attention was particularly attracted by high and progressively increasing number of the CNPP clean-up workers with diseases of the nervous system as well as the lasting low levels of functional indicators of the immune system. The analysis of morbidity showed changes in the structure of diseases. In 2007, the most frequent diseases affected the nervous system, sense organs of sense and included mental disorders. Morbidity with diseases of the cardiovascular and endocrine systems increased after period 1996–2001, but morbidity with respiratory diseases and disorders of digestive system decreased (Reste, 2013; 2014). The prevalence of non-oncological illnesses analysed in 2010 revealed the follow-

ing distribution of disorders: diseases of nervous system took the first place — 941 diseases per 1000 CNPP clean-up workers (e.g., encephalopathy — 880 per 1000, non-inflammatory polyneuropathy — 595 per 1000), followed by musculoskeletal disorders with 933 cases per 1000 workers (with frequent diffuse pain in bones, specially highlighting cases of osteoporosis among relatively young males — 78 cases per 1000) and mental disorders with 922 cases per 1000 CNPP recovery workers (e.g., cognitive impairment — 454 per 1000, depression — 35 per 1000). Other diseases included disorders of sense organs (853 per 1000; the most frequent were retinal angiopathy and peripheral retinopathy), disorders of digestive organs (852 per 1000), and cardiovascular diseases (720 per 1000) (Reste, 2013; 2014). The frequency of the diseases of the nervous system for clean-up workers was constantly high. The modern methods of examinations using electroencephalography (EEG) and nuclear magnetic resonance (MR) confirmed brain pathologies (Nikiforov, 2002; Zvagule *et al.*, 2003; Zvagule, 2004). The functional disturbances without changes practically decreased, but the organic pathology increased (Aleksanin, 2010; Holodova *et al.*, 2012).

The clean-up workers with seizures and unconsciousness episodes more often suffer from diseases of nervous systems and sense organs, digestive and circulatory systems, skeleton, muscular and connective tissue systems, as well as with mental disturbances (Zvagule, 2004). It can be stated that these men were more exposed to environmental and occupational factors and should be considered to be more at risk. The stress, overload, psychological, and social problems are more related to those people who were in Chernobyl in 1986 (Viel *et al.*, 1997). It must be pointed out that the energy of radiation had effect on the nervous system elements in stressful conditions (accident itself), and therefore the mental status of clean-up workers during clean-up works was of major importance. As the radiation has an indisputable role in the pathogenesis of some diseases of nervous system and organs of sense (Anonymous, 2006c) the patients from the mentioned group provoke special interest.

In earlier studies it was shown that lead (Pb) levels in blood until 1993–1994 were elevated ( $> 40 \mu\text{g/dl}$ ) for 60–72% of the clean-up workers (Churbakova *et al.*, 1996; 1999; Kumerova *et al.*, 2000; Zvagule, 2004). In subsequent years the incidence of elevated Pb level decreased by  $6.927\% \pm 0.329$  per year. The Pb level in blood decreased (correlation coefficient  $R = 0.922$ ; determination coefficient  $R^2 = 0.984$ ) and in 1998 it did not exceed  $40 \mu\text{g/dl}$  (Zvagule, 2004).

Individual susceptibility to radiation can be very different and certainly is important. Also, the effect of radiation on any biological system can be hidden and can become expressed in the presence of other provoking factors. In the case of clean-up workers, the combined effect of chemical factors (heavy metals etc.) and incorporated radionuclides can be provoked by physical exertion (Nikiforov, 2002).

Small doses of ionizing radiation cause disturbances in microcirculation (Anonymous 2006b; 2006c; Vlasova-Rozanskaya, 2009). Due to disturbed microcirculation all the organ systems suffer, including the peripheral nervous system. This leads to failure of adaptive capability of the central nervous system (Holodova *et al.*, 2012), leading to mental disorders with cognitive disturbances, depression, and vegetative paroxysms. Biologically active substances caused by exposure to ionising radiation do not primarily cause health effects through the circulatory system, but rather through effects on the vegetative nervous system at the site of their origin (sympathetic and parasympathetic ganglions) (Anonymous, 2006b; 2006c).

## ONCOLOGICAL DISEASES IN CHERNOBYL CLEAN-UP WORKERS

The oncological morbidity of CNPP accident clean-up workers from Latvia has progressively increased (Kurjane *et al.*, 2000; Eglite *et al.*, 2009; Reste *et al.*, 2012). During 1998–2004, there was a notable increase in occurrence of oncological diseases of thyroid gland, prostate and stomach. In 2005–2007, the most important increase in occurrence of oncological diseases of prostate, stomach and lungs was observed in CNPP accident clean-up workers, and it was higher than that among age- and sex-matched groups of the Latvian population (Eglite *et al.*, 2009; Reste *et al.*, 2012; Reste, 2013; 2014). In recent years an increase in number of malignant tumours of urogenital system organs was observed (mainly cancer of prostate and urinary bladder) (Reste *et al.*, 2012; Reste, 2013; 2014), that might be explained by excretion of incorporated radionuclides through kidneys and excessive irradiation of urogenital organs (Anonymous, 2001).

Thyroid cancer occurred 10.6 times more frequently in Chernobyl accident clean-up workers than in the rest of population (period from 1990 until 2000), and also at earlier age in CNPP clean-up workers (Kurjane, 2001; Kurjane *et al.*, 1999). CNPP recovery workers developed thyroid cancer most often at age 40–50, but for the general population at age 55–65 years. This clearly indicates that radiation was a dangerous risk factor for thyroid cancer after the Chernobyl nuclear accident (Kurjane, 2001). In this study only data on thyroid cancer in men was used, since the thyroid cancer in women in Latvia is much more frequent (8:1).

The relative risk (RR) of cancer in 1996 was 33.27, and in 1997 increased to 42.64 (Kurjane, 2001). The calculated cancer relative risk clearly indicates the danger of the 1986 nuclear accident to the health of those people who took part in the clean-up works. In further years, the morbidity of the thyroid cancer exhibited a tendency to decrease (RR 18.27 in 1998, and 9.42 in 1999). The peak morbidity of thyroid cancer was observed in 1992 in the population not exposed to irradiation (age group from 25 to 65, which corresponds to age of Chernobyl accident clean-up workers). Later the morbidity tended to decrease, and, starting from 1995, the morbidity increased but with fluctuations (Kurjane, 2001).

A similar trend in increasing morbidity of the thyroid cancer was observed not only in Latvia, but also in the rest of the world (Anonymous, 2006a; Yablokov *et al.*, 2009).

Amongst the thyroid cancers of the Chernobyl accident clean-up workers from Latvia, the prevailing cancer was papillary adenocarcinoma (5/8 of clean-up workers having surgery). The characteristic morphological modifications of thyroid tissue in Chernobyl clean-up workers were follicle atrophy with epithelium sclerosis, which was more frequent than for other men of similar age having surgery during that period of time and who did not have occupational exposure to radiation (Kurjane, 2001; Kurjane *et al.*, 2001).

Benign thyroid nodules were found three times more often in Chernobyl NPP accident clean-up workers during 1999 than in other men of similar age who did not have occupational exposure to ionising radiation (the control group) (Kurjane, 2001).

## IMMUNOLOGICAL DISTURBANCES IN CHERNOBYL CLEAN-UP WORKERS

Severe disorders of the immune system were observed among Chernobyl NPP accident clean-up workers from Latvia; characteristic late symptoms included leukocytosis, lymphopenia and malfunction of interferon (IFN) system (Kurjane, 2001; Kurjane *et al.*, 2001). The ability of peripheral blood lymphocytes (PBL) to produce IFNs has been found to be significantly decreased in 65–90% of accident clean-up workers and there was an increased level of circulating IFN in 40% of patients.

Compared to the control group, the Chernobyl NPP accident clean-up workers had significantly ( $p < 0.05$ ) lower number of T-leukocytes (CD3+), T-helpers (CD4+), natural killer cells (CD16+) and B-cells (CD19+), higher IgA level and lower IgG concentration. In addition, decreased functional activity of the alternative (APH50) pathway of complement, an increased C3d concentration and depressed neutrophil phagocyte activity of neutrophil were found (Kurjane, 2001; Kurjane *et al.*, 2001).

Functional deficiency of the immune system of clean-up workers was observed during 1990–2005 (Bruvere *et al.*, 1995; 2003; Kalnina *et al.*, 2001; Kurjane, 2001; Kurjane *et al.*, 2001; Eglite *et al.*, 2009). The CNPP clean-up workers were found to have a significantly lower proliferative ability of T and B lymphocytes and had elevated plasma concentrations of interleukin-6 (IL-6). Induction of TNF- $\alpha$  in the PBMC of clean-up workers was higher than that in healthy controls and this was correlated with age. Significant increases were also observed in the functions of the complement system as well as in levels of IL-6, TNF- $\alpha$  and SP-selectin. These observations suggest that the CNPP accident clean-up workers have a systemic chronic inflammatory process with possible accompanying dysfunction of major organs in period of over two decades following the accident (Kurjane, 2001; Kurjane *et al.*, 2001).

## CHANGE OF OXIDATIVE STRESS LEVEL 25 YEARS AFTER THE CHERNOBYL NPP DISASTER

During the work at the site CNPP clean-up workers were exposed not only to direct  $\gamma$ -radiation, but they inhaled toxic and radioactive isotopes, and volatile heavy metals derived from the reactor meltdown (Yablokov *et al.*, 2009). These damaging factors produce different kinds of oxidative stress: radiation, chemical, psycho-emotional, and later — inflammatory, pain and others. Radiation is known to reduce levels of antioxidants in body, thus causing greater risk for the organism (Halliwell and Gutteridge, 2007), since antioxidants are used for DNA repair, i.e. antioxidants remove free radicals that arise after exposure to radiation. It has been suggested that this reduction in different antioxidants may be responsible for increased levels of mutation (Halliwell and Gutteridge, 2007; Kumerova *et al.*, 2000).

A study was started in 1998 as a long-term investigation on the role of changes in the antioxidant defence system in development of the post-radiation (post-Chernobyl) syndrome in clean-up workers from Latvia, who were involved in the recovery works following the Chernobyl NPP accident (Skesters *et al.*, 2005; 2006a; 2006b; 2008; 2010). This was a randomised, double-blind, placebo-controlled, parallel group investigation involving 76 Chernobyl clean-up workers. The following parameters were determined: content of lipid-hydroperoxides, oxidisability and lipid peroxidation ratio in blood plasma, activity of glutathione peroxidase (GPx), catalase and concentration of Cu, Zn-Superoxide Dismutase (SOD), selenium (Se), zinc (Zn), and copper (Cu) (Skesters *et al.*, 2005; 2006a; 2006b; 2008; 2010).

First results showed 5.5 times higher content of lipid peroxides and hydroperoxides, 3.5 higher blood plasma oxidisability, lipid peroxidation ratio, and concentration of TBARS products. Accordingly, activity of glutathione peroxidase in blood plasma was significantly decreased. Data showed that the level of selenium was very low ( $46.0 \pm 7.8$   $\mu\text{g}/\text{L}$ ); the lowest Se concentration in the investigated groups was  $17.0$   $\mu\text{g}/\text{L}$ . Zn concentration in the serum of irradiated clean-up workers was higher by 50%, and Cu concentration in blood was also elevated. All these data testify that there is high level of oxidative stress (Skesters *et al.*, 2005; 2006a; 2006b; 2008; 2010).

Ten years later, the second stage results showed that concentration of Se in plasma had increased; intensity of lipid peroxidation, free radical production and content of TBARS product had decreased but remained quite high and nearly the first stage levels. Similarly, as before, concentrations of Cu and Zn remained unbalanced (Skesters *et al.*, 2005; 2006a; 2006b; 2008; 2010). These data show that there is still a high level of oxidative stress, at a time even more than 20 years after direct contact with radioactive materials.

It is well known that oxidative stress provokes many different diseases and promotes development of some pathological conditions. It is clear that practically all of the diseases observed in medical examination were more or less are af-

ected by oxidative stress. Some of these diseases are very strongly associated effect of oxidative stress (Barrow and Tanner, 1988; Halliwell and Gutteridge, 2007; Kumerova *et al.*, 2000).

As mentioned above, most of the CNPP disaster clean-up workers from Latvia had progressive multiple illnesses that exhibited a tendency to progress; their morbidity exceeded that observed in the general Latvian male population. Most of these workers had up to 11 and more different illnesses. Chernobyl clean-up workers are characterised by significantly increased biological ageing processes of the body systems — neuroendocrine, gastrointestinal, cardiovascular, *etc.* Thus, they suffer from poly-symptomatic diseases almost in all body systems.

All these progressive changes in Chernobyl accident recovery workers' health as well as disturbances in functioning of immune system and increasing morbidity with oncological diseases confirms the evidence of prolonged systemic oxidant stress injury (Eglite *et al.*, 2009; Skesters *et al.*, 2010). Oxidative stress is imposed on cells as a result of one of three factors: 1) an increase in oxidant generation, 2) a decrease in antioxidant protection, or 3) a failure to repair oxidative damage. Cell damage is induced by reactive oxygen species (ROS). The main source of ROS *in vivo* is aerobic respiration, although ROS are also produced by peroxisomal  $\beta$ -oxidation of fatty acids, microsomal cytochrome P<sub>450</sub> metabolism of xenobiotic compounds, and stimulation of phagocytosis by pathogens or lipopolysaccharides, arginine metabolism, and tissue specific enzymes. Under normal conditions, ROS are cleared from the cell by the action of SOD, catalase, or GPx. The main damage to cells results from the ROS-induced alteration of macromolecules such as polyunsaturated fatty acids in membrane lipids, essential proteins, and DNA. Additionally, oxidative stress and ROS have been implicated in diseases such as Alzheimer's disease, Parkinson's disease, cancer, and ageing (Sies, 1991; Yin and Chen, 2005; Halliwell and Gutteridge, 2007).

In general, regardless of observed improvement by increased antioxidative defence and decrease in some lipid peroxidation parameters, intensive long-term oxidative stress still remains as an important risk factor for CNPP clean-up workers (Skesters *et al.*, 2005; 2006a; 2006b; 2008; 2010). Therefore, it is necessary to provide treatment to improve the antioxidative condition. For this purpose, some antioxidants and, possible, non-steroid anti-inflammatory drugs should be indicated for long-term application (Skesters *et al.*, 2010).

## FUTURE DIRECTIONS AND RESEARCH NEEDS

The research on victims of the Chernobyl accident in last 25 years has covered a broad spectrum of scientific directions, including epidemiological studies, biochemical and immunological studies, neurophysiological studies and many others. Nevertheless, changing morbidity structure of CNPP



workers diseases and clinical manifestations show a need to continue studies on late effects of ionising radiation exposure. The importance of such studies is raised by other accidents in nuclear power plants with release of radioactive substances, which regularly occur in different parts of the globe. The latest accident in Japan in March 2011 in the Fukushima nuclear power plant was a clear demonstration of unsafety of nuclear power, which may have long-lasting consequences for inhabitants of the Earth.

Acute severe exposure to ionising radiation and chronic low dose exposure differ greatly. External high dose exposure was studied in great detail in victims of Hiroshima and Nagasaki bombings, as well as after other atom bomb tests. But knowledge on incorporated radionuclides biological effects in humans is insufficient. More studies are needed to reveal changes in molecular interaction inside the organism due to chronic exposure to ionising radiation. Studies are needed to identify chronic exposure to ionising radiation (e.g. incorporated radionuclides with long disintegration half-life) genetic effects not only in victims of Chernobyl accident, but also in their offspring.

The epidemiological studies on CNPP clean-up workers should be continued, as it is the main source of information on late effects in a large cohort. The epidemiological studies on progeny of CNPP clean-up workers are also necessary.

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## PĒTĪJUMI PAR ČERNOBIĻAS AVĀRIJAS SEKU LIKVIDĒTĀJU NO LATVIJAS VESELĪBAS STĀVOKLI VĒLĪNĀ PERIODĀ PĒC KATASTROFAS

Šis raksts apkopo galvenos pētījumu rezultātus par Černobiļas atomelektrostacijas (ČAES) avārijas seku likvidētāju no Latvijas veselības stāvokli, kuri iegūti pēdējo divdesmit gadu laikā. Aptuveni 6000 Latvijas iedzīvotāju piedalījās ČAES avārijas seku likvidācijas darbos 1986.–1991. gadā. Atrāšanās laikā Černobiļā viņi tika pakļauti gan ārējam, gan iekšējam apstarojumam, bet pēc atgriešanās Latvijā dzīvoja ar radioaktīvām vielām salīdzinoši nepiesārņotā vidē. Divdesmit piecu gadu laikā pēc katastrofas ČAES avārijas seku likvidētāji izgāja rūpīgas regulāras medicīniskas apskates, tika veikti klīniskie pētījumi par viņu veselību, un tas ļāva uzkrāt vērtīgu informāciju par jonizējošā starojuma ietekmes vēliniem efektiem. Šis publikācijas mērķis ir apkopot galvenos faktus par ČAES avārijas seku likvidētāju no Latvijas veselības stāvokli, kas savākti rūpīgā apsekojumā 25 gadu garumā pēc katastrofas. Šis raksts atspoguļo ČAES avārijas rezultātā radiācijas ietekmei pakļauto personu Latvijas valsts reģistra datus un dod ieskatu galvenajos veselības traucējumos, kuri tika konstatēti epidemioloģiskajos, klīniskajos, bioķīmiskajos, imunoloģiskajos un fizioloģiskajos pētījumos. Latvijas pētījumu dati vēlīnā periodā pēc avārijas liecina par to, ka jonizējošais starojums varētu izraisīt cilvēku priekšlaicīgas novecošanas un polimorbiditātes attīstību.