Biological indicators of occupational radiation exposure

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Abstract. The report presents results on finding appropriate biomarkers applicable in molecular epidemiological surveys of occupationally exposed individuals and/or population to study low dose effects. Blood samples were collected from the “strict regimen” area personnel (exposed) and the administrative staff (controls) of NPP-Kozlodui. Two levels of evaluation were used: 1) molecular - spontaneous and induced DNA repair by UDS, protein synthesis evaluated radio-metrically, DNA damage by SCGE – all of them in white blood cells, concentration of malondialdehyde in blood serum; and 2) cellular – the Ly-subsets by flow cytometry, using a FacScan analyzer and immunofluorescent stained mouse monoclonal antibodies. A significant decrease of potentially lethal damage was found in persons with “mean annual dose” lower or equal to 5 mSv/a. The highest repair capacity and protein synthesis after a challenging dose of 2,0 Gy gamma rays as well as a significant decrease in the level of oxidative stress were evaluated for persons from the same group. At doses below 200 mSv statistically different decrease of the index of $CD3^+4^+, CD4^+25^+, CD4^+62L^+$ lymphocyte populations and $CD4/CD8$ cell ratio was established, and increased levels of $NK$ cells, $CD57^+8^+, CD8^+28^+$ and $CD8^+38^-$ were recorded. The present investigation showed that annual doses lower than twice the natural radiation background exert positive effects on DNA damage and repair, increase cellular resistance and decrease oxidative stress. It is possible that the positive correlation between the dose and the cells with phenotype $CD4^+25^+ and CD57^+8^+, as well as the negative one with $CD4^+62L^+, CD8^+28^+ and CD8^+38^+$, could reflect adaptive processes and compensatory activated immune system due to low dose irradiation. Further investigations allowing analysis of the molecular endpoints, increase the sensitivity of studies and help to search effects of low radiation exposures, are needed.

KEYWORDS: low dose effects, NPP workers, molecular-epidemiological study

1. Introduction

The biological effects at doses below 200 mSv that differ from those at high-level radiation are stimulatory effects on cellular metabolisms and defence systems, called hormesis, and protective effects on subsequent high-level radiation-induced injury - the adaptive response. It is clear that newly recognized effects of low doses are not readily predictable by extrapolation of responses observed at high doses. There is no simple relationship with exposure and the outcome is not obviously dependent on dose or number of cells hit by radiation. The problem is that adaptive responses and protective mechanisms that are manifested at one level of an organism are not necessarily protective or beneficial at another level. This is one of the main reasons that until now ICRP hasn’t accepted the results of the numerous epidemiological researches for hormetic effect availability. Therefore, the research we have been dedicated to for the last 15 years were aimed at finding suitable biomarkers, both at molecular and cellular levels, for the molecular-epidemiological research of occupationally exposed people. The results could be evidence confirming or declining the validity of the basic hypothesis of low dose effects.

2. Material and methods

2.1 Study Design and Subjects

Blood samples of more than 500 exposed workers in the ‘strict regimen’ area and non-exposed NPP administration staff from the NPP Kozlodui in Bulgaria were studied between 1992-2007. The recruited subjects gave informed consent to participate in the study and were assured of complete anonymity. Retrospective information about demographic characteristics, health status and occupational exposure (including age at initial exposure, age at sampling, radiation doses, etc.) was collected. Predominantly a gamma-ray exposure (at a dose level ranging from 1 to 12 mSv/a for 94% of the studied subjects) and no reported medical irradiation over the last three years were inclusion criteria.

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2.2 Blood Sampling, Ly Isolation and Irradiation

Blood samples were collected, transferred and stored at 4°C and the processing of probes was accomplished within 48 hours. Lymphocytes were isolated by centrifugation of blood suspension with Ficoll gradient for 40 min at 1800 rpm and re-suspended in phosphate buffer pH 7.4, followed by three times washing with the same buffer and centrifugation at 1100 rpm, transferred in 0.5 ml RPMI 1640 and counted at light microscope. The cell suspension was diluted with PRMI to a concentration of 5.10^6 cells/ml. Blood samples were irradiated at room temperature with 2 Gy from ^137^Cs gamma-source at a dose rate of 92 cGy/min.

2.3 Single Cell Gel Electrophoresis (Comet Assay)

The pH of unwinding dictates the type of DNA damage detected by the Comet assay. Under neutral conditions mainly double strand breaks can be detected whereas at alkaline pH, both single and double strand breaks are recorded. The method consists of several stages including embedding of cells into low melting agarose to reach a concentration of 5.10^4/slide, dipping in lysis solution (154 mM NaCl; 10mM Tris pH 7.5; 30mM EDTA pH7.5), washing of slides, dipping into TBE, pH 10 for 5 min, staining with EtBr and visualizing under fluorescence microscope. For interpretation of the obtained results we chose parameters known as Tail Moment (TM); Olive Moment (OM) and %DNA in Tail (%DNA). The DNA damage in the very low dose range (<20 mSv) was evaluated by analysis of 250 cells/examined person. Cells were separated in 5 types: from I (without tail) to V (almost all DNA is in the tail). The Comet Index (CI) was calculated by the following formula: 

\[ CI = n_1 + 2n_2 + 3n_3 + 4n_4 + 5n_5, \]

where \( n \) was the relative part of cells pertaining to a definite type, and the coefficients from 1 to 5 reflected the level of damage. CI gave information about the level of DNA damage.

2.4 Determination of spontaneous and γ-induced DNA repair synthesis

Spontaneous (RSsp) and induced (RSind) after additional in vitro irradiation with 2 Gy. DNA repair was estimated by unscheduled DNA synthesis (UDS) in peripheral blood leukocytes. Both syntheses were defined in a short-term culture of whole blood. Hydroxyurea (HU, 10 mM) was used to suppress the normal DNA synthesis. The cells were then incubated for 2 hours at 37 °C with 3H-thymidine, before or after in vitro gamma-irradiation with 2 Gy. The leukocyte population was separated and the activity of the incorporated marker was measured radiometrically. This strategy concerns the physiology of cells and allows maintenance of both the original ratios of the cellular subpopulations and intercellular relations. In addition, the blood possesses larger capacity in demonstrating radiation effects at low dose levels as compared to separated lymphocyte cells. Measurement of normal DNA synthesis was performed in parallel for each individual on samples untreated with HU. The parameters were calculated as a ratio between 3H-thymine incorporations, measured as number of disintegrations per minute or irradiation in relative units (Rel.U.).

2.5. Induced protein synthesis (PS).

The radiometrical method for evaluation of PS in peripheral blood leukocytes, after additional gamma-irradiation with 2 Gy was used. The activity of the ^14^C-amino acid marker, incorporated in leukocyte population, was measured radio-metrically on LSC as disintegration per minutes (dpm).

2.6. Lipid peroxidation in blood plasma

Quantification of lipid peroxidation level was performed by malon dialdehyde concentration, measured spectrophotometrically. Under heating and acid conditions lipid peroxidation products, mainly endoperoxides, undergo decomposition producing malondialdehyde (MDA), which reacts with thiobarbituric acid to form a colored complex. MDA concentration (in nmol/ml plasma) was estimated by the following regression equation: 

\[ C = 0.21 + 26.5 D, \]

where C was the concentration of TBA active products (in nM MDA per ml plasma); and D = D_{535} - D_{580} of the sample (in units “optical density”).
2.7. Ly-subset analyses

The cellular immunity is measured by flow cytometry of peripheral blood mononuclear with flowcytometer FACS Calibur and monoclonal antibodies from Becton Dickinson USA. The phenotypic analyses of total T and B-lymphocytes, helper-inducer and suppressor-cytotoxic T lymphocytes, NK (Natural Killer) and NKT cells and the subpopulations CD4+62L -, CD4+62L+, CD57+8-, CD57+8+, CD8+28+ and CD8+38+ are performed. The percent and absolute value of lymphocytes populations are determined, as the first parameter expresses more adequately the functional changes in the lymphocytes subsets and is independent of the number of leucocytes and lymphocytes.

2.8. Statistical analysis

The version SPSS for Windows 11.0.1 is applied for obtained data processing. Correlation analysis (parametric and nonparametric) and variation analysis are used. Significance: at p<0.05* or p<0.01**.

3. Results

3.1. The single cell gel electrophoresis assay ‘or Comet assay’ is a simple and sensitive technique for analysing and quantifying DNA damage caused by different genotoxic agents, including ionizing radiation. The comet assay is ideally suited for human investigations because it requires no pre labeling with radioactivity or other harmful procedures and can be applied to easily obtainable cells. Normally, white blood cells are used, as they are obtained in a relatively non invasive way, do not require tissue disaggregation, and behave well in the comet assay. The levels of DNA-damage for control and for exposed people are shown on Fugure 1 [1].

Figure 1: The DNA-damage level in control (left columns) and exposed (right columns) after alkaline Comet assay.

The three assessment parameters do not show any changes that confirm an absence of statistically significant differences between DNA-damage levels for control and exposed people within the annual dose limit. The results for DNA damage of exposed people in relation to their dose level are shown on Table 1 which relates to cumulative doses and in Table 2 - to annual doses.

Table 1: Non-parametric* correlation to the cumulative dose [mSv]

<table>
<thead>
<tr>
<th>Neutral SCGE (dsb)</th>
<th>Tail Moment</th>
<th>Olive Moment</th>
<th>%DNA in Tail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation Coefficient</td>
<td>-.433(**)</td>
<td>-.403(**)</td>
<td>-.369(**)</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.000</td>
<td>.000</td>
<td>.001</td>
</tr>
</tbody>
</table>

* Spearman's rho
Table 2: Non-parametric correlation to the annual dose [mSv/a]

<table>
<thead>
<tr>
<th>Neutral SCGE (dsb)</th>
<th>Tail Moment</th>
<th>Olive Moment</th>
<th>%DNA in Tail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation Coefficient</td>
<td>-0.423(**)</td>
<td>-0.392(**)</td>
<td>-0.377(**)</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>0.000</td>
<td>0.000</td>
<td>0.001</td>
</tr>
</tbody>
</table>

A significant negative correlation between dsb level and both annual and cumulative dose level was registered. In order to discriminate low and high dose effects, two groups of exposed subjects were analyzed. We found that the level of DNA damage is similar for the two groups but the contribution of single strand breaks increases with the dose (Figure 2).

Figure 2: Change in the level and nature of DNA damage depending on the cumulative dose

Different reasons such as genomic instability in the lower dose group or manifestation of adaptive response for the second group (>200 mSv) could be responsible for this result. The cumulative dose doesn’t render the accumulation time. Therefore, the annual dose dependence has been studied. The analysis showed dsb effect homogeneity up to 10 mSv/a in the condition of a continuous grow up of ssb (Figure 3).

Figure 3. Differences in the level of DNA-damages in dependence of annual dose

3.2 DNA-repair [2]

We used spontaneous DNA-repair synthesis (RSsp) as a measure of Potential Lethal Damage (PLD) level. After a low-dose exposure, a certain amount of un-repaired lesions remains and becomes apparent after application of inhibitors of the replicative DNA synthesis (HU and ara-C). Higher levels of spontaneous DNA repair were found in the exposed than in the control group (Table 3).

Table 3: Differences between control and exposed group macromolecular synthesis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Exposed Mean (SD)</th>
<th>Control Mean (SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative dose [mSv]</td>
<td>171.12 (156,35)</td>
<td>0,00</td>
<td></td>
</tr>
<tr>
<td>RSsp [RelU]</td>
<td>1.03 (0.54)</td>
<td>0.69 (0.30)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RSind [RelU]</td>
<td>0.99 (0.58)</td>
<td>0.68 (0.28)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>PS [RelU]</td>
<td>1.05 (0.50)</td>
<td>0.91 (0.33)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>
The analysis indicated that the professional exposure to ionising radiation has provoked a significant increase in the levels of the spontaneous repair DNA synthesis.

On Figure 4 a low, but significant positive correlation \((p < 0.05)\) between the cumulative dose and spontaneous DNA repair patterns is shown. At low cumulative dose \((< 20 \text{ mSv})\) this connection disappears and only positive associations between the age at initial exposure and spontaneous DNA repair have been found to be significant \((p < 0.05)\) (Figure 5).

**Figure 4**: Linear relationship between the cumulative dose and spontaneous DNA repair \((r = 0.144, p < 0.05)\).

**Figure 5**: Dependence of spontaneous DNA repair upon the age at initial exposure \((r = 0.410, p < 0.05)\).

![Graph of spontaneous DNA repair vs. cumulative dose](image1)

![Graph of spontaneous DNA repair vs. age at initial exposure](image2)

Legend: \(R^2\), R-squared (coefficient of determination); all presented values are log-transformed original values (the base is natural logarithm).

In order to deeper analyse the relationships of RSsp with the cumulative dose, the exposed group has been arbitrarily divided into 3 sub-groups: low (below 20 mSv, annual dose below 1 mSv), moderate (from 20 to 200 mSv, annual dose about 9.3 mSv) and high (above 200 mSv) doses (Table 4).

**Table 4**: Demographic and biological characteristics of the exposed group by dose*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sub-groups</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 20 mSv</td>
<td>21-200 mSv</td>
</tr>
<tr>
<td>Cumulative dose [mSv]</td>
<td>7.27 (5.77)</td>
<td>92.81 (54.07)</td>
</tr>
<tr>
<td>RSsp [RelU]</td>
<td>0.86 (0.45)</td>
<td>1.02 (0.54)</td>
</tr>
<tr>
<td>RSind [RelU]</td>
<td>1.07 (0.59)</td>
<td>0.94 (0.59)</td>
</tr>
<tr>
<td>PS [RelU]</td>
<td>0.82 (0.41)</td>
<td>1.08 (0.47)</td>
</tr>
</tbody>
</table>

*Data are mean (SD); **The number of subjects for spontaneous DNA repair is 32, 96 and 63, for the induced DNA repair is 39, 95 and 81, for PS – 38, 78 and 64 respectively; $\text{Rel.U.}$., relative units.

The multiple comparisons have shown statistically significant differences in spontaneous DNA repair. Since there is a trend for differences between the strata, the \(p\)-values of the median \(\chi^2\) test and, of the Kruskal-Wallis test for spontaneous DNA repair, might be considered marginal and, therefore, significant at \(p < 0.05\) (Table 5). However, this trend is due mainly to the difference between the group of cumulative doses above 200 mSv (mean 340 mSv) and the other two strata. The probability distributions of study parameter in the other two strata are similar \((p > 0.05\), results not shown). Therefore, it could be concluded that, at cumulative doses below 200 mSv, the level of spontaneous repair DNA synthesis is homogeneous.
Table 5: Multiple comparisons of parameters between the three strata by dose (p-value)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-parametric tests*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kruskal-Wallis</td>
<td>Median $\chi^2$</td>
<td>Jonckheere-Terpstra</td>
<td></td>
</tr>
<tr>
<td>RSsp [RelU]</td>
<td>0.083</td>
<td>0.107</td>
<td>0.029*</td>
<td></td>
</tr>
<tr>
<td>RSind [RelU]</td>
<td>0.266</td>
<td>0.444</td>
<td>0.366</td>
<td></td>
</tr>
<tr>
<td>PS [RelU]</td>
<td>0.004*</td>
<td>0.004*</td>
<td>0.006*</td>
<td></td>
</tr>
</tbody>
</table>

*The difference is considered significant when $p < 0.05$ where the H-test of Kruskal-Wallis compares mean ranks (equivalent to one-way ANOVA), the next test compares medians and the Jonckheere-Terpstra test directly compares probability distributions. SRel.U., relative units.

Induced DNA repair synthesis (RSind). In an attempt to understand and ascertain the stimulatory effect of low dose ionising radiation (adaptive response), we compare the changes in the gamma-induced repair capacity (after 2Gy additional irradiation). The occupational exposure was considered a priming dose. A significant increase in the rate of induced repair synthesis in lymphocytes pre-exposed to low doses of ionizing radiation (Table 3) as well as a lack of differences in RSind level between three subgroups (Table 4 and 5) were observed.

3.4. Induced protein synthesis (PS) [3]

Data on dose-dependent changes in rats (in vivo and in vitro) and in human blood (in vitro) showed a steep slope, indicative of a high radio-sensitivity of protein synthesizing systems (Figure 6). In addition, a lack of post-irradiation increase was established after blocking of the repair systems with caffeine (Figure 7).

We suggest that low-doses of ionizing radiation unlock specific genes that give rise to gene products, which might have a compensatory protective reaction in the cells. The performed gel electrophoresis research showed a clearly observed spectral line of newly synthesized proteins, which do not exist in the non-irradiated samples, in samples treated with UV-irradiation or with thermal shock. Differences in protein synthesis for control and exposed persons (Table 3), as well as between subgroups of exposed NPP personal (Table 4 and 5) were observed.

We propose that reported low dose positive effects on DNA damage and PLD repair are result of the cell defense systems activation that makes it more resistant to next higher dose irradiation. To clarify this probability we studied simultaneously protein synthesis and induced DNA repair synthesis as well as DNA damages and plasma lipid per oxidation for every exposed person after additional in vitro γ-irradiation with 2 Gy. The obtained results unambiguously substantiated this speculation (Figure 8 and 9).
The induced DNA repair synthesis decreased with increasing the dose (Figure 8a). The highest repair capacity was evaluated for persons with “mean annual dose” lower or equal to 5 mSv/a. It could be related to repair and antioxidant enzyme synthesis and supports the hypothesis for similar molecular mechanisms of low dose effects (Figure 8b, see also Figure 9a).

3.4. Lipid peroxidation in blood plasma [4]

Overproduction of free radicals and their toxicity is one of the problems that cells encounter upon irradiation with ionizing radiation. They induce late health effects and lead to accumulation of various quantitative and qualitative changes in the cells, commonly described as oxidative stress. The significant decrease in the level of oxidative stress determined in the blood plasma could be interpreted as favorable low dose effect (Figure 9a). The straight line represents the mean value of the control group. The MDA values are below the mean control values at doses below 5 mSv/a. The significant decrease in the level of oxidative stress determined in the blood plasma could be interpreted as favorable low dose effect.

A significant decrease of dsb DNA damage in persons with “mean annual dose” lower or equal to 5 mSv/a, was found compared to the control group (Figure 9b). At the same doses ssb were similar to that of the control level (Figure 9c). A significant decrease of potentially lethal damage in persons with “mean annual dose” lower or equal to 5 mSv/a, was found, compared to the controls (not shown here).
Figure 10. Neutral comet assay. Distribution of comet types

The results of neutral comet assay are presented on Figure 10. Cells pertaining to a definite comet type were summed up for all 10 neutral samples for each examined group. In the group with annual doses lower than 5 mSv/a a higher number of normal cells were recorded compared to the control. In all studied groups normal cells were predominating over damaged cells. Increase of damaged cells was observed at annual doses above15 mSv/a.

3.5. Ly-subset analysis [1]

The results for the main lymphocytes populations are presented on Figure 11a concerning the cumulative dose, and figure 11b –the average annual dose. The slight tendency of decreasing in the count of CD3+ T cells with the dose is confirmed by weak inverse correlations ($r=-0.120$ and $r=-0.130$). The proportion of helper-inducers (CD3+CD4+) T lymphocytes is significantly lower for doses up to 1 mSv/a or 20 mSv compared to the controls. A significant weak inverse correlation with cumulative dose ($r=-0.123$) is also observed.

Figure 11: Values for the leucocytes and the lymphocytes count

Examination of CD3+4+T lymphocyte subpopulations CD4+62L- and CD4+62L+. There isn’t any difference between the control and the groups of occupationally exposed persons for the CD4+62L-cells, but the CD4+62L+ lymphocytes show a significant decrease in their percent values for exposed individuals (<20mSv) and average annual dose (<1mSv/a).

CD8+38+ activated subpopulation of suppressor-cytotoxic T cell. The similar tendency is observed in CD8+38– increased % and absolute values, significant only according to D <20mSv, which decrease, but is still higher compared to the control level in the next two groups. The role of this subpopulation in the antiviral immunity pose the issue whether these results reflect the more effective reaction of the activated immune system to some exogenous factors due to adaptation set in.
Cytotoxic subpopulation CD8+28+ of the suppressor–cytotoxic CD3+8+ T Ly. A significant higher percent and absolute average values in the group with cumulative dose <20 mSv or annual dose <1 mSv/a were observed, which decrease and reach the level of the control at higher doses. Probably, this tendency reflects the adaptation of occupationally exposed persons to radiation effect. Shu-Zeng Lui et al. [5], has found that the low dose radiation causes increase of CD28+ expression and enhancement of the immunity, while the high dose–to higher expression of CTLA-4 and suppression of the immunity.

4. Discussion:

The main problem for both medical and non-medical use of IR is the possible carcinogenic risks associated with the low doses. The rapidly growing knowledge in molecular biology and radiobiology during the last decade prompted us to examine the effects of low (<100 mSv) and very low doses (<10 mSv). The events caused by an irradiation trigger a series of signals and reactions that can profoundly alter the fate of DNA. The defense mechanisms induced in a cell depend on number and nature of the cellular damage. Modern transcriptional analysis of cellular genes using microarray technology reveals that, without modification of the genome, numerous genes are activated or inhibited following doses much lower than those for which mutagenesis is observed [6]. In this study, a well expressed directly proportional relationship between the mean annual dose and the level of potentially lethal damage (PLD) was established. A significantly lower level of PLD in comparison to that of the controls was registered at doses below 5mSv/a. The results showed that in all studied groups the undamaged cells were predominant. Their number however was reduced with increasing of the dose (Figure 10). At annual doses below 5 mSv/a undamaged cells in the exposed group were more than those in the controls.

The results obtained for the spontaneous repair synthesis and with the comet assay were in accordance with data that ssb, stimulate repair systems and could be connected with the cell radio-resistance. The stimulated cell protection led to statistically significant decrease of cells with dsb (at doses below 5 mSv/a) in comparison to the control group (Figure 9). The favorable effect of low doses established in this study was probably due to activation of cell safeguard systems increasing the radio-resistance of the cell to subsequent irradiation. To clarify this suggestion we conducted an additional in vitro irradiation with 2 Gy and analyzed the induced repair synthesis. The chronic occupational exposure of workers has been accepted as “initiating exposure” according to adaptive response classical scheme. The repair capacity decreased regularly by increasing the dose and only at doses below 5 mSv/a it is statistically higher (Figure 8a). These results were indicative of a relation between the increased repair activity and the lower number of dsb detected by the neutral comet assay. This correlated also to the recorded increase of Comet Index in the same exposure group. The tendency of a decrease in the induced DNA repair synthesis at annual doses above 20 mSv/a corresponded to decrease of induced protein synthesis as well as to the increase of PLD assessed by the spontaneous repair synthesis. Some authors have also established adaptive response in the lymphocytes of occupational exposed persons [7, 8, 9]. They proposed the repair mechanisms could be activated by doses 30-40% above the natural background, a condition that is fulfilled only for doses below 5 mSv/a (mean annual dose for the group 1.93 mSv/a).

There is a direct correlation between the oxidative and genotoxic stress. Lipid peroxidation products such as MDA have been shown to exert carcinogenic properties. DNA adducts produced by the interaction with MDA are connected with malignancy. The damage of cell membrane might be the first step to explain the relation between cancer and low radiation doses [10]. A significant increase of MDA concentrations in the blood serum of occupationally exposed NPP workers has been reported by Đurovich et al [11]. Similar results were further interpreted as a direct effect and/or insufficient functioning of anti-oxidative systems [12, 13]. The results obtained in this study also suggest that occupational exposure provokes dose dependent damage of the cell membrane. The level of damage was lower than that in the control only at annual doses below 5 mSv/a (Figure 9a) and was probably due to the radiation-induced synthesis of anti-oxidant enzymes.

The present study also demonstrates that there are not direct evidences for radiation–induced alterations in the examined parameters of cellular immunity in occupationally exposed persons. The
obtained results for immunity indices generally are within the age reference ranges. Most of the indices are not statistically significantly different. Weak correlation coefficients of some parameters and the received dose are found, which means that the influence of the radiation factor would be expressed like a tendency of variation. Differences in the immune parameters of the groups with lower dose compared to the control, demonstrate the possibility of adaptation of occupationally exposed persons to different stresses, including radiation.

5. Conclusion

Occupational irradiation can stimulate the adaptive mechanisms elevating DNA repair capacity of human Ly at subsequent high dose irradiation. Annual doses no higher than twice the natural radiation background exert positive effects on DNA damage and repair, increase cellular resistance and decrease the oxidative stress. It is possible that the positive correlation between the dose and the cells with phenotype CD8+28+ and CD8+38+, as well as the negative one with CD4+62L+, could reflect adaptive processes and compensatory activated immune system due to low dose irradiation.

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