RADIATION BIOLOGY

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Are the Inhabitants of High Background Radiation Areas of Ramsar More Radioresistant?

Scope of the Problem and the Need for Future Studies

Backgroud/Objective: Ramsar in northern Iran is among the world's well-known areas with highest levels of natural radiation. Annual exposure levels in areas with elevated levels of natural radiation in Ramsar are up to 260 mGy y^{-1} and average exposure rates are about 10 mGy y^{-1} for a population of about 2000 residents. Due to the local geological features, which includes high levels of radium in rocks, soils, and groundwater, Ramsar residents are also exposed to high levels of alpha activity in the form of ingested radium and radium decay progeny as well as very high radon levels (over 1000 MBq m^{-3}) in their dwellings. In some cases, the inhabitants of these areas receive doses much higher than the current ICRP-60 dose limit of 20 mSv y^{-1} set for radiation workers. The extraordinary levels of natural radiation in Ramsar prompted us to assess the radiation susceptibility of the residents.

Material and methods: Venous blood samples were taken from 7 healthy blood donors of both sexes who lived in some areas of Ramsar with highest levels of natural radiation (dose rates were up to 155 μSv h^{-1}) and 5 healthy persons from a nearby control area. Standard condition for cell cultivation, irradiation and analysis of chromosome aberrations was used. The cells were exposed to the challenge dose of 1.5 Gy of Co-60 gamma ray 48 hours after PHA stimulation. Using mean chromosomal aberration per cell (MCAPC), the expected numbers of aberrations were calculated.

Results: Lymphocytes of Ramsar residents when subjected to 1.5 Gy of Gamma rays, showed fewer chromosome aberrations compared to residents in a nearby control area. These findings clearly show that high levels of natural radiation may induce radioadaptive response. Interestingly,

Conclusion: this radioadaptation phenomenon was found in individuals who received doses as much as a few hundred times more than the inhabitants of a nearby control area. More research is needed to precisely clarify if it is possible to relax the radiation protection guidelines for inhabitants who live in such areas.

Keywords: Background radiation, Radioadaption, Ramsar

Introduction

Humans, animals and plants have been exposed to natural radiation since the creation of life. Interestingly, life evolved in a radiation field that was much more intense than today [1]. The annual effective doses from natural and man-made sources for the world's population is currently about 2.8 mSv. Nearly 85% of this dose (2.4 mSv) comes from natural background radiation [2]. Levels of natural radiation can vary greatly. Ramsar, a northern coastal city in Iran, has some areas with one of the highest levels of natural radiation studied so far (Fig.1). The effective dose equivalents in very high background radiation areas (VHBRAs) of Ramsar in particular in Talesh Mahalleh, are few times higher than the dose limits for radiation workers.
Inhabitants who live in some houses in this area receive annual doses as high as 132 mSv from external terrestrial sources. External exposure rates from terrestrial gamma radiation in Iran and the annual background doses to the inhabitants of some areas around the world are summarized in Tables 1 and 2 respectively.

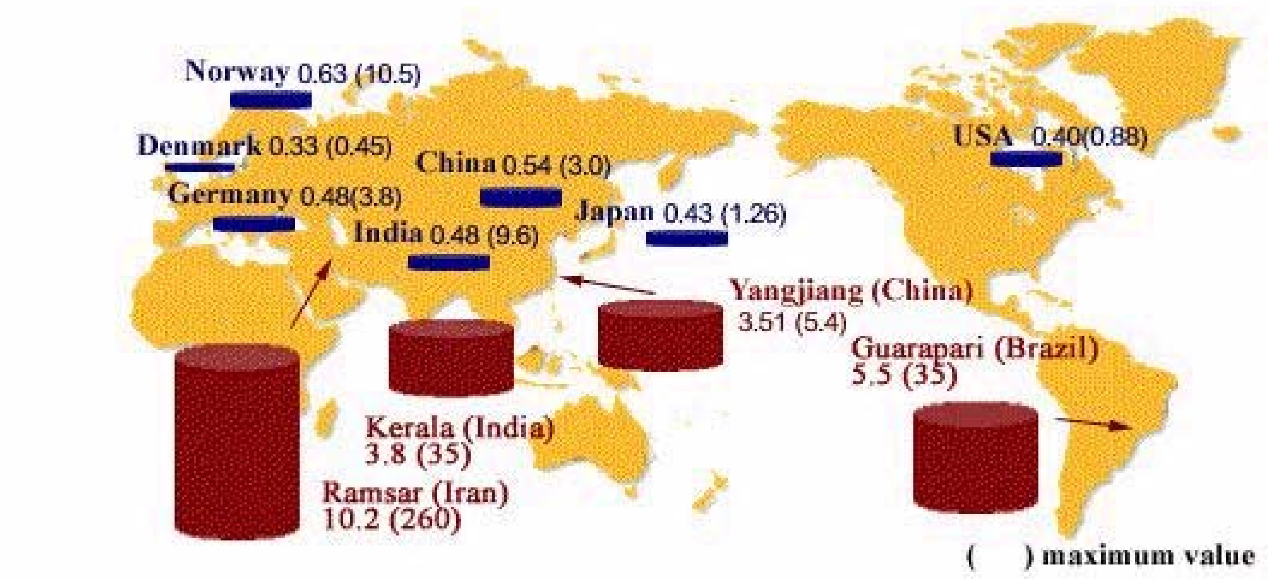

Figure1. Average and Maximum annual background absorbed doses (mGy/yr) to the inhabitants of some countries (blue) and for areas with high levels of natural radiation (red). *(Used with permission of Radiation Research Foundation, Kyoto, Japan).*

Radioactivity of the high background radiation areas (HBRAs) of Ramsar is due to ^{226}Ra and its decay products, which have been brought up to earth surface by the water of warm springs. There are more than 9 hot springs with different concentrations of radium in this city. The visitors as well as residents usually use these springs as spas. According to the results of the surveys performed by the Atomic Energy Organization of Iran (AEOI), the radioactivity seems to be first due to the mineral water and second due to some travertine deposits having thorium content higher than that of uranium [3]. Due to extraordinary levels of natural radiation in these areas that in some cases is 55-200 times higher than normal background areas, some experts suggested that dwellings having such high levels of natural radiation need urgent remedial actions [4]. However, the inhabitants still live in their unaltered paternal dwellings.

We have entered a new millennium but there are still many scientists who believe even the lowest doses are harmful. Recently, however, several phenomena have been found in cellular responses to low doses of radiation, throwing doubts in this paradigm. It is a well known that when organisms as diverse as bacteria, animals and plants are exposed to a variety of DNA damaging stresses such as UV, alkylating or oxidizing agents and heat, adaptive responses may be induced which render them resistant to the killing and mutagenic impacts. [5,6] The results of many studies indicated that when cells exposed to low doses of these agents, they often become less sensitive to the harmful effects of a subsequent higher dose.[7] The induction of radioadaptive response in human lymphocytes was first reported by Olivieri et.al.[8] There are also some reports indicating lack of radioadaptive response in cultured human lymphocytes. [9-14] Furthermore, it has been reported that in some cases a synergistic effect induced. [15-16]

Iran's Important Radiological Data	
Population in 1996 (10^6)	69.98
Average absorbed dose rate in air (nGy h^{-1}): Outdoors	71
Average absorbed dose rate in air (nGy h^{-1}): Indoors	115
Indoors/outdoors ratio	1.6

Table 1. External exposure rates from terrestrial gamma radiation in Iran.
Source: Survey of natural radiation exposure, UNSCEAR 2000

Country	Area	Approximate population	Absorbed Dose rate in air[a] (nGy h^{-1})
Brazil	Guarapari	73 000	90-170 (street) 90-90 000 (beaches)
Iran	Ramsar[b]	2 000	70-17 000
India	Kerala	100 000	200-4 000
China	Yangjiang	80 000	370 (average)

Table 2. Mean and maximum annual natural terrestrial radiation doses to the inhabitants of some well-known high background radiation areas (HBRAs) around the world.
a: includes cosmic and terrestrial radiation.
b: it should be noted that the monazite sand beaches at Guarapari in Brazil have a higher dose rate, but these areas are uninhabited. Therefore it can be claimed that Ramsar has the highest level of natural radioactivity studied so far.
Source: UNSCEAR 2000.

Case No.	Age (years)	Sex	Whole body dose (mSv)
1 (NBRA) [a]	69	F	11.65
2 (NBRA) [a]	29	M	17.78
3 (NBRA) [a]	33	M	15.41
4 (NBRA) [a]	44	F	17.34
5 (NBRA) [a]	26	M	15.41
1 (HBRA) [b]	23	M	362.6
2 (HBRA) [b]	47	F	394.2
3 (HBRA) [b]	70	F	362.7
4 (HBRA) [b]	57	F	6850
5 (HBRA) [b]	63	M	8460
6 (HBRA) [b]	75	F	953.0
7 (HBRA) [b]	14	M	1065

Table 3. Mean accumulated effective doses from exposure to external Gamma rays in 12 blood donors.
a: Normal background radiation area.
b: High background radiation area

Materials and Methods

Cell Culture

Venous blood samples were taken from 7 healthy blood donors of both sexes who lived in some areas of Ramsar with highest levels of natural radiation (dose rates were up to 155 µSv h^{-1}) and 5 healthy persons from a nearby control area (dose rates ranged from 0.07 to 0.11 µSv h^{-1}). Blood donors were non-smokers and had no alcohol or drug consumption, history of medical irradiation or viral infection. Standard condition for cell cultivation, irradiation and analysis of chromosome aberrations was used (Ikushima and Mortazavi 2000). Separate cultures were set up from each blood sample, using 0.3 ml blood in 4.7 ml Ham's F10 medium (Gibco), supplement with 20% fetal calf serum (FCS Gibco) 100 U/ml penicillin 100 µg/ml streptomycin, 1.0% L-glutamine and 1.0% phytohemagglutinin (PHA, Gibco) for mitogenic stimulation. The lymphocytes were cultured in dark at 37°C in an incubator.

Irradiation

The cells were exposed to the challenge dose of 1.5 Gy of Co-60 gamma ray 48 hours after PHA stimulation. Dose rate was 114 mGy/sec for the challenge dose. Dose rates were measured by expert physicists at Gamma Irradiation Center, Atomic Energy Organization of Iran. After the challenge dose the culture flasks were returned to the incubator for a further incubation of 6 hours.

Harvesting

Colcemid was added 2 hours before harvesting (52 h after stimulation) at a final concentration of 0.25 µg/ml to arrest the dividing lymphocytes in mitosis.

After harvesting, the cells were exposed to 0.075 M KCl for 10 min at 37°C and fixed with methanol-acetic acid (3:1 *v/v*). The fixed cells were dropped onto wet slides, air dried and stained with Giemsa. For each data point, 200 well-spread metaphases were examined for chromosomal aberrations. The number of

chromatid-type aberrations was determined. Gaps (achromatic lesions smaller than the width of a chromatid) were not included in the statistical analysis.

Data Analysis

Using mean chromosomal aberration per cell (MCAPC), the expected numbers of aberrations were calculated as follows:

Expected MCAPC = [(MCAPC of Adapting Dose Alone + MCAPC of Challenge Dose Alone) - MCAPC of Controls]

In this formula, MCAPC of Adapting Dose is the mean frequency of aberrations in non- irradiated cells of each blood donor who lived in HBRAs. MCAPC of Challenge Dose is the mean frequency of chromosome aberrations in cultured cells of NBRA residents that exposed to 1.5 Gy of gamma rays and MCAPC of Controls is the mean frequency of chromosome aberrations in non-irradiated cells of blood donors who lived in a nearby NBRA.

Case No.	Age (years)	Sex	MCAPC [c] in non-irradiated cells	MCAPC [c] in cells exposed to 1.5 Gy Gamma rays	Induction of radioadaptive response (RAR)
1 (NBRA) [a]	69	F	0.02 ± 0.01	0.17 ± 0.03	ND [d]
2 (NBRA)	29	M	0.01 ± 0.01	0.14 ± 0.03	ND
3 (NBRA)	33	M	0.02 ± 0.01	ND	ND
4 (NBRA)	44	F	0.01 ± 0.01	0.16 ± 0.03	ND
5 (NBRA)	26	M	0.02 ± 0.01	0.23 ± 0.04	ND
1 (HBRA) [b]	23	M	0.01 ± 0.01	0.12 ± 0.02	Positive (P<0.05)
2 (HBRA)	47	F	0.01 ± 0.01	0.13 ± 0.03	Positive (P<0.05)
3 (HBRA)	70	F	0 ± 0	0.09 ± 0.03	Positive (P<0.01)
4 (HBRA)	57	F	0.02 ± 0.01	ND	ND
5 (HBRA)	63	M	0.01 ± 0.01	ND	ND
6 (HBRA)	75	F	0.03 ± 0.02	0.05 ± 0.02	Positive (P<0.001)
7 (HBRA)	14	M	0.01 ± 0.01	ND	ND

*Table 4***.** Mean frequency of chromatid aberrations in non-irradiated and 1.5 Gy irradiated cells of NBRA and HBRA residents.
a: *Normal background radiation area,* ***b***: *High background radiation area,* ***c***: *Mean chromosome aberrations per cell,* ***d:*** *Not determined*

Case No.	MCAPC of Adapting Dose	MCAPC of Challenge Dose	MCAPC of Controls	Expected MCAPC	Observed MCAPC	k-Value
1 (HBRA) [a]	0.01 ± 0.01	0.18 ± 0.02	0.02 ± 0.004	0.166 ± 0.019	0.12 ± 0.02	0.72 ± 0.14
2 (HBRA)	0.01 ± 0.01	0.18 ± 0.02	0.02 ± 0.004	0.166 ± 0.019	0.13 ± 0.03	0.78 ± 0.20
3 (HBRA)	0 ± 0	0.18 ± 0.02	0.02 ± 0.004	0.156 ± 0.016	0.09 ± 0.03	0.58 ± 0.20
4 (HBRA)	0.02 ± 0.01	0.18 ± 0.02	0.02 ± 0.004	0.176 ± 0.016	ND	ND
5 (HBRA)	0.01 ± 0.01	0.18 ± 0.02	0.02 ± 0.004	0.166 ± 0.016	ND	ND
6 (HBRA)	0.03 ± 0.02	0.18 ± 0.02	0.02 ± 0.004	0.186 ± 0.026	0.05 ± 0.02	0.27 ± 0.11
7 (HBRA) [b]	0.01 ± 0.01	0.18 ± 0.02	0.02 ± 0.004	0.166 ± 0.019	ND	ND

Table 5: Induction of radioadaptive response in the residents of HBRAs of Ramsar.
a *High background radiation area,* ***b*** *Mean chromosome aberrations per cell,* ***d*** *Not determined*

SE Expected MCAPC = [(SE MCAPC of Adapting Dose Alone)2 + (SE MCAPC of Challenge Dose Alone) 2+ (SE MCAPC of Challenge Dose Alone) 2] 1/2
as follows:

k = Observed MCAPC/ Expected MCAPC

Standard error of the k was calculated according the formula:

$(SE_k / k)^2 = (SE_{Observed\ MCAPC} / Observed\ MCAPC)^2 + (SE_{Expected\ MCAPC} / Expected\ MCAPC)^2$

In this formula, SE_k is standard error of the k, $SE_{Observed\ MCAPC}$ and $SE_{Expected\ MCAPC}$ are standard errors of observed and expected MCAPC respectively. Obviously, when the k value is less than one, it indicates that a radioadaptive response occurred. If k=1, it means that there is a simple additivity effect. Finally, when there is a k which is significantly greater than 1, it means that a

Study group	Sample size	Whole body dose (mSv)	MCAPC[a] in non-irradiated cells	MCAPC[a] in cells exposed to 1.5 Gy
HBRA[b]	7	2635	0.01 ± 0.003	0.10 ± 0.012
NBRA[c]	5	15.52	0.02 ± 0.004	0.18 ± 0.016
P-value[d]			Not significant	< 0.001

Table 6. Frequency of chromosomal aberrations in non-irradiated and irradiated cells of the residents of high background radiation areas and the residents of the control area.
a *Mean chromosome aberrations per cell,* ***b*** *High background radiation area,* ***c*** *Normal background radiation area,*
d Student's t-test

synergistic effect is induced. The statistical significance of increased or decreased frequencies of chromosome aberrations was evaluated using Student's t-test.

Results

Table 1 shows the age, sex and mean accumulated effective doses from exposure to external Gamma rays in 12 blood donors including 7 inhabitants who lived in dwellings with highest levels of natural radiation and 5 residents of a nearby control area. The average accumulated effective dose in the 7 residents of HBRAs was 2 635 mSv (2.6 Sv) while the 5 residents of the nearby control area received only 15.5 mSv. Considering the average accumulative doses received by these two groups of blood donors, it is evident that the 7 inhabitants of HBRAs were exposed to doses about 170 times higher than those received by the 5 residents of a nearby control area. In table 2, the mean frequencies of chromosomal aberrations per cell in either non-irradiated cells or cells exposed to 1.5 Gy Gamma rays are presented. The existence or lack of radioadaptive response in each inhabitant of HBRAs is also shown in this table. As seen in this table among 7 residents of HBRAs, the induction of radioadaptive response was not determined in 3 individuals. Interestingly, all of the 4 blood donors whom were assessed for induction of radioadaptive response, showed a significant radioadaptive response.

According to formula mentioned before, the expected MCAPC is the summation of the frequencies of chromosome aberrations in the cells only exposed to the adapting dose and cells only exposed to challenge dose minus the frequency of aberrations in cells neither exposed to adapting nor challenge dose. Table 5 shows the expected as well as observed MCAPC in the blood donors who lived in HBRAs. The k-values which indicate the coefficients of the induced radioadaptive response are also shown in the table. As seen in the table, all of the k values are significantly less than one, indicating the existence of a radioadaptive response.

Overall MCAPCs of 7 blood donors who lived in dwellings with highest levels of natural radiation and 5 donors who lived in a nearby control area are shown in Table 6. Interestingly, there is no significant difference between MCAPCs in non-irradiated cells of residents of HBRAs and those of the control area. On the other hand, there is a statistically significant difference between the MCAPCs in cells exposed to 1.5 Gy of Gamma rays of the residents of HBRAs and the control area ($P<0.001$).

Discussion

This study is the first study on the induction of radioadaptive response in the residents of high background radiation areas in Iran. The results obtained in this experiment clearly indicated that in Ramsar, residents of the areas with elevated levels of natural radiation show a significant radioadaptive response. Through this study, it was observed that all of the 4 persons whom were tested for the induction of radioadaptive response, were responders and showed a significant radioadaptive response. This finding is very important and should be investigated more by further studies. It should be noted that some investigators reported the radioadaptive response only in 2 of 6 volunteers [17]and even just in 1 of 8 healthy donors who lived in normal background radiation areas.[18] Interestingly, the magnitudes of the adaptive response observed in the residents whom were exposed to doses as high as 200 mGy/y were considerable. In this study the k-values that indicate the magnitude of the induced adaptive response ranged from 0.27 to 0.78 (Table 5) indicating the existence of a significant radioadaptive response. It should be noted that there was no difference between the frequencies of chromosomal aberrations in non-irradiated cells of the residents of HBRAs and that of the control area (Table 6). This finding is inconsistent with the report published by Fazeli[33] that the frequency of chromosomal aberrations in lymphocytes of HBRA residents was significantly higher than that of NBRA residents. The origin of this discrepancy is not clear at present. Based on our results obtained in this study, high levels of natural radiation may have some bio-positive effects such as enhancing radiation-resistance. More research is needed to assess if these bio-positive effects have any implication in radiation protection[19]. The risk of low-dose radiation exposure has for a variety of reasons been highly politicized. This has led to a frequently exaggerated perception of the potential health effects, and to lasting public controversies.[20] Current radiation protection recommendations are based on the predictions of an assumption on linear, no-threshold dose-effect relationship (LNT). Beneficial effects and lack of detriment after irradiation with low levels of ionizing radiation, including a prolonged exposure to high levels of natural radiation of the inhabitants of HBRAs, are inconsistent with LNT. Our preliminary results clearly showed that prolonged exposure to very high levels of natural radiation could induce the phenomena leading to induction of a considerable radioresistance in the inhabitants. The phenomenon of radioresistance in living organisms has long been a matter of interest for scientists. Experiments on Drosophila nebulosa collected in the woods of a high background radiation area in Brazil indicated that addition of some genes caused the radioresistance found in these flies compared to flies collected from adjacent control woods. [21] In human also possibly genetical alterations induce this radioresistance. More research is needed to clarify the mechanisms that make individuals radioresistant. There are many other areas with high levels of background radiation around the world, and epidemiological studies have indicated that natural radiation in these areas is not harmful for the inhabitants.[22-27]Results obtained in our study are consistent with the hypothesis that a threshold possibly separates the health effects of natural radiation from the harm of large doses. This threshold seems to be much higher than the greatest level of natural radiation (e.g. lifetime doses up to 19.6 Sv in VHBRAs of Ramsar).

Conclusion

Preliminary results of our experiments clearly showed that chronic exposure to extraordinary high levels of natural radiation could make the individuals more radioresitant to subsequent high doses. Interestingly, this radioadaptation phenomenon found in individuals received doses as much as a few hundred times more than the inhabitants of a nearby control area. Using LNT and ALARA, public health is best served by relocating HBRAs' inhabitants. Several statistically significant epidemiological studies contradict the validity of LNT concept by showing hormetic effects in a form of risk decrements of cancer mortality and mortality from all causes in populations exposed to low-dose radiation.[28,29] Populations in areas with high levels of natural radiation show no adverse health effects when compared to low-dose populations. Furthermore, several studies of large populations indicate beneficial health effects of low doses of ionizing radiation, i.e., lower mortality and disease rates.[27,30,31] Our preliminary findings on the biological effects of prolonged exposure to high levels of natural radiation in the inhabitants of VHBRAs of Ramsar, showed no harmful health effects. Based on our results obtained to date it can be concluded that in HBRAs the LNT model may be inappropriate to use as the basis for public health measures.

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References

1. Jaworowski Z. Beneficial effects of radiation and regulatory policy. Australas Phys Eng Sci Med, 20(3):125-38, 1997.
2. UNSCEAR. Sources and effects of ionizing radiation, Report to the general assembly, New York. United Nations Scientific Committee on the Effects of Atomic Radiation, Sources and Effects of Ionizing Radiation, 2000.
3. Sohrabi M. Recent radiological studies of high background radiation areas of Ramsar. Proceeding of International Conference on High Levels of Natural Radiation (ICHLNR), Ramsar, Iran, 3-7, 1990.
4. Sohrabi M. World high level natural radiation and/or radon prone areas with special regards to dwellings. In: Proceeding of the 4th International Conference on High Levels of Natural Radiation (ICHLNR), Beijing, China, 1996 (Wei L, Suahara T and Tao Z Ed), pp. 3-7, 1997.
5. Samson L.and Carins J., A new pathway for DNA repair in Escherichia coli, Nature, 267, 281-282, 1977.
6. Samson L.and Schwartz J.L., Evidence for an adaptive DNA repair pathway in CHO and human skin fibroblast cell lines, Nature, 287, 861-863, 1980.
7. Ikushima T. Radioadaptive response: responses to the five questions. Human and Experimental Toxicology, 18: 433-435, 1999.
8. Olivieri G., Bodycote J. and Wolff S., Adaptive response of human lymphocytes to low concentrations of radioactive thymidine, Science, 223, 594-597, 1984.
9. Bosi A., and Olivieri G. Variability of the adaptive response to ionizing radiations in humans. Mutat. Res., 211, 13-17, 1989.

10. Olivieri G., and Bosi A. Possible causes of variability of the adaptive response in human lymphocytes. In Chromosomal Aberrations Basic and Applied Aspects (G. Obe and E. D. induced DNA damage in adapted cells, Mutat. Res., 358,193-8, 1990.

11. Hain J., Jaussi R., and Burkart W. Lack of adaptive response to low doses of ionizing radiation in human lymphocytes from five different donors. Mutat. Res., 283, 137-44, 1992.

12. Vijayalaxmi, B.Z.Leal, T.S.Deahl, M.L.Meltz, Variability in adaptive response to low dose radiation in human blood lymphocytes: consistent results from chromosome aberrations and micronuclei., Mutat. Res., 348, 45-50, 1995.

13. Kalina and G.Nemethova, Variability of the adaptive response to low dose radiation in peripheral blood lymphocytes of twins and unrelated donors, Folia. Biol. Praha., 43, 91-5, 1997.

14. Gadhia P.K., Possible age-dependent adaptive response to a low dose of X-rays in human lymphocytes, Mutagenesis, 13, 151-152, 1998.

15. Mortazavi, S. M. J., Ikuhima, T., Mozdarani, H., Sharafi, A. A. and Y. Ishi. Is low-level pre-irradiation of human lymphocytes an absolutely beneficial phenomenon. A report on the extra-ordinary synergism. Kowsar Medical Journal, Vol 5, No 4, 235-240, 2000.

16. Ikushima, T., and Mortazavi, S. M. J. Radioadaptive response: its variability in cultured human lymphocytes, In: Yamada T, Mothersil C, Michael BD, and Potten CS, eds. Elsevier, Amsterdam, pp. 81-86, 2000.

17. Pereira Luis JH and Pova VL. Individual variability of adaptive response of human lymphocytes primed with low dose gamma rays. In: Low Dose Irradiation and Biological Defence Mechanisms. Pp. 315-317, Elsevier Science Publication, Tokyo, 1992.

18. Gajendiran N, Tanaka K, Kumaravel TS, Kamada N. Neutron-induced adaptive response studied in go human lymphocytes using the comet assay. J Radiat Res (Tokyo), 42(1): 91-101, 2001.

19. Mortazavi S. M. J., Ghiassi Nejad M, and Beitollahi M.Very High Background Radiation Areas (VHBRAs) of Ramsar: Do We Need any Regulations to Protect the Inhabitants? Proceedings of the 34th midyear meeting, Radiation Safety and ALARA Considerations for the 21st Century, California, USA, 177-182, 2001.

20. Kellerer AM. Risk estimates for radiation-induced cancer--the epidemiological evidence. Radiat Environ Biophys, 39(1):17-24, 2000.

21. Kratz FL. Radioresistance in natural populations of Drosophila nebulosa from a Brazilian area of high background radiation. Mutat Res, 27(3):347-55, 1975.

22. Nair MK, Nambi KS, Amma NS, Gangadharan P, Jayalekshmi P, Jayadevan S, Cherian V, Reghuram KN. Population study in the high natural background radiation area in Kerala, India. Radiat Res;152(6 Suppl), S145-8, 1 999.

23. Jaikrishan G, Andrews VJ, Thampi MV, Koya PK, Rajan VK, Chauhan PS. Genetic monitoring of the human population from high-level natural radiation areas of Kerala on the southwest coast of India. I. Prevalence of congenital malformations in newborns. Radiat Res, 152 (6 Suppl), S149-53, 1999.

24. Sobue T, Lee VS, Ye W, Tanooka H, Mifune M, Suyama A, Koga T, Morishima H, Kondo S. Residential randon exposure and lung cancer risk in Misasa, Japan: a case-control study. J Radiat Res (Tokyo), 41(2), 81-92, 2000.

25. Zou J, Sun Q, Akiba S, Yuan Y, Zha Y, Tao Z, Wei L, Sugahara T. A case-control study of nasopharyngeal carcinoma in the high background radiation areas of Yangjiang, China. J Radiat Res (Tokyo), 41 Suppl:53-62, 2000.

26. Tao Z, Zha Y, Akiba S, Sun Q, Zou J, Li J, Liu Y, Kato H, Sugahara T, Wei L. Cancer mortality in the high background radiation areas of Yangjiang, China during the period between 1979 and 1995. J Radiat Res (Tokyo), 41 Suppl:31-41, 2000.

27. Jagger, J. Natural background radiation and cancer death in Rocky Mountain states and Gulf Coast states. Health Phys. 75:428-430, 1998.

28. Pollycove M. Nonlinearity of radiation health effects. Environ Health Perspect, 106 Suppl 1(9806):363-8 1998.

29. Mortazavi, S. M. J., Ikuhima T, Mozdarani H and Sharafi AA. Radiation Hormesis and Adaptive Responses Induced by Low Doses of Ionizing Radiation. Journal of Kerman University of Medical Sciences, Vol. 6, No. 1, 50-60, 1999.

30. Cohen B.L. Test of the linear no-threshold theory of radiation carcinogenesis for inhaled radon decay products. Health Phys, 68:157-174, 1995.

31. Wei, L. High background radiation area-an important source of exploring the health effects of low dose ionizing radiation. In: Wei, L.; Sugahara, T.; Tao, Z., ed. High Levels of Natural Radiation: Radiation Dose and Health Effects. Beijing, China; Amsterdam, The Netherlands: Elsevier: 1-66, 1997.

32. Cohen, B.L. Problems in the radon versus lung cancer test of the linear no-threshold theory and a procedure for resolving them. Health Phys, 72:623-628, 1996.

33. Fazeli T.Z. Cytogenetic studies of inhabitants of a high background radiation area of Ramsar. Proceeding of International Conference on High Levels of Natural Radiation (ICHLNR), Ramsar, Iran, 459-464, 1990.