The Therapeutic Application of Radiation Hormesis

(from the data on the radiation hormesis research)
Sadao Hattori, Senior Advisor
Central Research Institute of Electric Power Industry (CRIEPI)

In the review article entitled "Physiological Benefits from Low Levels of Ionizing Radiation," published in *Health Physics*, December of 1982, Professor T.D. Luckey, of the University of Missouri, asserted "radiation hormesis" with 200 references.

CRIEPI organized a Hormesis Research Steering Committee composed of leading specialists in the field concerned, and began research in cooperation with a number of Universities, as well as the National Cancer Research Institute, and the National Institute of Radiological Science.

We carried out experimental activities on the effects of low-dose radiation on mammals. After years of research activities, we are recognizing Luckey's claim of radiation hormesis. Some surveys including Sakamoto's success of low dose whole body application on cancer therapy and many results of animal experiments have brought us various ideas on the beneficial utilization of the radiation hormesis.

The results we obtained can be categorized in five groups:

- 1. Cancer therapy by the enhancement of immune systems and tumor suppression genes such as p53.
- 2. Radio-adaptive response on the enhancement of genes of the enzyme synthesis for the prevention of DNA damage, DNA repair, and of the cell apoptosis (death).
- 3. Rejuvenation of cells such as the decrease of lipid peroxide and the increase of cell membrane permeability, and general enhancement of DNA repair.
- 4. Enhancement of the damage control system of cells to prevent oxidative attack of free radicals by increasing protective enzymes such as Superoxide Dismutase (SOD) and Glutathione.
- 5. Radiation effect on neuro-transmitting and thinking system through increase of key enzymes, and hormones.

Formation of great numbers of ions, free electrons, and free radicals by ionizing radiation enhances and creates many comprehensive bio-chemical reactions, followed by significant biological responses.

Living materials exist on the homeostatic potentiality which directs all of our physical activities to obtain the survival keeping health condition against all kinds of degradation occurring by the environment. This is adaptive response itself.

Categories of the therapeutic applications of radiation hormesis:

Pain relief, stress relief: The first step needed for the patients of obstinate case is obviously the relief from the incurable pain. The clear increases of the hormones effective to forget the pains were shown by animal tests, in the response data of Endorphin and Enkephalin. The dramatic increase of Adrenaline also helps to lead a positive thinking to forget about the pain. Some behaviors of stress relief were observed by animal tests following low dose exposures. The patients of following diseases are considered to be cured for the first step (pain relief): chronic rheumatic pain including arthritis, neuralgia, spondylitis, lumbago, bursitis, amyotrophia, tenosynovitis, osteoporosis, asthma.

Prevention or suppression of the disease progress: Most of the obstinate diseases are caused by local cell deaths in the organs under the attack of free radicals (e.g. diabetes, rheumatoid arthritis, amyotrophia, asthma, hepatitis, osteoporosis, Parkinson's, Alzheimer's, and allergic or atopic eczema). Responses of those enzymes such as SOD and GPx that are fundamental to suppress the oxidative attack of reactive oxygen species can help the protective activities to the oxidation. The enzymes to protect the oxidation or damage of our cells, SOD and GPx, clearly increased by low doses of ionizing radiation.

Rejuvenation or recovery of the cells: The cells are rejuvenated by low dose radiation. Reactive oxygen species attack cells continuously and cells gradually lose the fundamental function. The dominant effect of those is the loss of membrane permeability. Na, K-ATPase is one of key enzymes to keep the vital activity of the cell membrane, and lipid peroxide is one of the key materials made by reactive oxygen species attack. The membrane permeability of cells is now measurable by means of electron spin resonance.

Whole body low dose of x-ray tests by mice and rats showed clear increase of the membrane permeability with the decrease of lipid peroxide. Na,K-ATPase also showed clear increase of the activity by low dose of 25-50 cGy.

We hypothesize the low dose radiation would be effective for the patient of hypertension and generally effective for the recoveries of those cells partially damaged by reactive oxygen species in various tissues of those patients such as diabetes, rheumatoid arthritis, amyotrophia, asthma, hepatitis, osteoporosis, Parkinson's, Alzheimer's, all kinds of collagenosis and allergic or atopic eczema.

General recovery of cells and tissues: It is obvious from the various data we obtained by animal tests that many kinds of genes for bio-positive activities - such as recovery of tissues or organs - respond and enhance the activities. We can expect ordinary recovery activities of the tissues or organs and enhancement of these by low dose radiation.

On the recovery of the tissues, it is obvious that DNA repairs are also to be adequately done, and cell apoptosis to eliminate abnormal cells. The essential gene for these activities, p53, is also enhanced by low dose of radiation.

Creation of the better condition: Immune systems enhancement - increase of the helper T cells through the decrease of the suppressor cells which are essentially weak to the radiation brings stronger immune system; tumor suppression gene, p53, is activated.

Hormones, response and optimization - the hormones such as enkephalin, endorphin, insulin, histamine, and adrenaline which are fundamental to make you healthy and positive to your daily life are increased and optimized by low dose of radiation.

Enzymes increase - it is essential to live longer that protections against reactive oxygen species have to be adequately established. After middle age, many causes bring the reduction of the essential enzymes as SOD, GPx, and Catalase.

On this consideration, we expect the relief of pain, stopping or suppressing the progress of the disease and recovery from the diseases by low dose application of ionizing radiation - especially for the case of the patients of obstinate diseases. Certain optimum dose rates for various bio-positive effects shall be found in the future through really comprehensive animal tests in all kinds of responses categorized above for actual therapeutic application of low level radiation to obtain healthful condition of the human being. Not only dose rate optimization but also various optimum combination with other factors such as food and circumstantial temperature for the therapeutic application of radiation hormesis shall be the most economical research subject to obtain really increased quality of lives of human beings in the next century.

Acknowledgements:

We appreciate the sincere advice and direction for our research activities given by Dr. T.D. Luckey, Dr. S. Kondo, Dr. A. Mori, Dr. T. Sugawara, Dr. K. Sakamoto, Dr. T. Yamada and Dr. H. Tanooka.

References:

- ICLB (1992). Proceedings of the International Conference of Low-Dose Irradiation and Biological Defense Mechanisms, Kyoto, Japan, 12-16 July, 1992 (T. Sugahara, L.A. Sagan, and T. Aoyama, eds.). Elsevier Science Publishers B.V., Amsterdam.
- 2. IKUSHIMA T. (1989). "Radio-adaptive: Characterization of cytogenetic repair induced by low-level ionizing radiation in cultured Chinese hamster cells". Res. 227:241-246.
- 3. ISHII K., MUTO N., and YAMAMOTO I. (1990). "Augmentation in mitogen-induced proliferation of rat splenocytes by low-dose whole-body x-irradiation." Nippon Acta Radiological 50:1262-1267. [In Japanese]
- 4. ISHII K., HOSOI Y., and SAKAMOTO K. (1993). Stimulation of Anti-Tumor Effect by Low-Dose Irradiation-Inhibition of Spontaneous Metastasis. Central Research Institute of Electric Power Industry Report T92030. [In Japanese]
- 5. KONDO S. (1998). "Radiation Hormesis". Radiat. Biol. Res. Comm. 23(4):1197-198. [In Japanese]
- 6. KONDO S. (1993). Health Effects of Low-Level Radiation. Kinki University Press, Osaka, Japan and Medical Physics Publishing, Madison, Wisconsin.
- 7. LIU S.-Z., LI X.Y., XIA F.Q., YU H.Y., QI J., WANG F.L., and WANG S.K. (1985). "A restudy of immune functions of the inhabitants in a high-background area in Guangdong." Chin. J. Radiol. Med. Prot. 5:124-127.
- 8. LORENZ E. (1954). Biological Effects of External Gamma Radiation, Part I (R.E. Zirkle, ed.). McGraw-Hill, New York, p.24.
- 9. LUCKEY T.D. (1980). Hormesis with Ionizing Radiation, CRC Press. Boca Raton, Florida.
- 10. LUCKEY T.D. (1982). "Physiological benefits from low levels of ionizing radiation." Health Phys. 43:771-789.
- 11. LUCKEY T.D. (1991). Radiation Hormesis, CRC Press. Boca Raton, Florida, p239.
- 12. MIFUNE M., SOBUE T., ARIMOTO H., KOMOTO Y., KONDO S., and TANOOKA H. (1992). "Cancer mortality survey in a spa area (Misasa, Japan) with a high radon background." Jpn. J. Cancer Res. 83:1-5.
- 13. MINE M., NAKAMURA T., MORI H., KONDA H., and OKAJIMA S. (1981). "The current mortality rates of A-bomb survivors in Nagasaki City." Jpn. J. Publ. Health 28:337-342.
- 14. MIYACHI Y., KASAI H., OHYAMA H., and YAMADA T. (1992). "Depression of mouse aggressive behavior by very low-dose x-irradiation and its unusual dose-effect relationship." In: Low-Dose Irradiation and Biological Defense Mechanisms, Kyoto, Japan, 12-16 July, 1992 (T. Sugahara, L.A. Sagan, and T. Aoyama, eds.). Elsevier Science Publishers B.V., Amsterdam. pp.171-174.
- 15. MORI T., KUMATORI T., HATAKEYAMA S., IRIE H., MORI W., BABA K., MARUYAMA T., UEDA A., and AKITA Y. (1989). "Current status of the Japanese follow-up study of the Thorotrast patients and its relationships to the statistical and analysis of the autopsy series." In: BIR Report 21, Risks from Radium and Thorotrast. British Institute of Radiology, London. pp.119-124.
- 16. MORI T. (1990). "Japanese Thorotrast Study." In: Current Encyclopedia of Pathology. Vol.10, Nakayamashoten, Tokyo, pp.135-184. [In Japanese].
- 17. OHNISHI T., MATSUMOTO H., OMATSU T., and NOGAMI M. (1993). "Increase of wpt53 pool size in specific organs of mice by low doses of X rays." J. Radiat. Res. 34:364.
- 18. STEWART A.M. (1982). "Delayed effects of A-bomb radiation: A review of recent mortality rates and risk estimates for 5-year survivors." J. Epidem. Commun. Health 36:80-86.
- 19. WATANABE M., SUZUKI M., SUZUKI K., NAKANO K., and WATANABE K. (1992). "Effect of multiple irradiation with low dose of γ rays on morphological transformation and growth ability of human embryo cells in vitro." Intl. J. Radiat. Biol. 62(6):711-718.
- 20. YAMAOKA K., EDAMATSU R., MORI A. (1991). "Increased SOD activities and decreased lipid peroxide level in rat organs induced by low-dose x-irradiation." Free Rad. Biol. Med. 11(3):299-306.

- 21. YONEZAWA M., TAKEDA A., and MISONOH J. (1990). "Acquired radioresistance after low-dose x-irradiation in mice." J. Radiat. Res. 31:256-262.
- 22. YONEZAWA M., MISONOH J., and HOSOKAWA Y. (1993). "Radioresistance acquired after low doses of X rays in mice." In: Proceedings of the International Symposium on the Biological Effects of Low-Level Exposures of Radiation and Related Agents (ISBELLES '93). Changchun, China. p48.
- 23. HATTORI S., State of Research and Perspective on Radiation Hormesis in Japan International Journal of Occupational Medicine and Toxicology. Vol. 3, No. 2, 1994.
- 24. FEINENDEGEN L.E. etal. Radiation Effects Induced by Low Doses in Complex Tissue and Their Relation to Cellular Responses personal communication, March, 1996.
- 25. ISHI K., WATANABE M., Participation of gap junctional cell communication on the adaptive response in human cells induced by low dose of X-rays, Int. J. Radiat. Biol. Vol. 69, No. 3, 291-299, 1996.
- 26. BILLEN DANIEL, Spontaneous DNA Damage and its Significance for the Negligible Dose "Controversy in Radiation Protection", Radiation Research 124, 242-245, 1990.
- 27. COHEN A.F. and COHEN B.L. Tests of the Linearity Assumption in Dose-Response Relationship for Radiation Induced Cancer. Health Phys. 38:53, 1980.
- 28. CALABRESE E.J., McCARTHY M.E., and KENYON E. "The Occurrence of Chemically Induced Hormesis," Health Phys. 52:531-542 (1987).

NOTE: This information is distributed at no cost to interested individuals by the:

Free Enterprise Radon Health Mine P.O. Box 67 Boulder MT 59632-0067 USA 406 225-3383 http://www.radonmine.com info@radonmine.com

Printed: March 2001