Radiation paradigm and its shift

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By adopting the concept of scientific paradigm after L. Sagan, the history of paradigm shift in 1950 in radiation protection standard by ICRP from a threshold to a non-threshold model was critically reviewed. The motives for the shift were found later to be scientifically inappropriate. But the present paradigm of a linear, non-threshold model introduced at the 1950s' shift has been accepted in general for main radiation risk, i.e., for carcinogenesis, though there have been many controversies on risk at low dose effects. We can find some motives for another shift among these controversies now. It is the purpose of the present review to stimulate the discussion on a possible new paradigm.

INTRODUCTION

The effects of ionizing radiations on human health have been one of the most serious environmental problems for people in atomic age. Most concern is the effect of low dose irradiation which raised many debates scientific as well as decision-making-related.

As the International Conference on “Low dose irradiation and biological defense mechanism” held in Kyoto, Japan on July 12-16, 1992, Sagan\(^1\) adopted the concept of scientific paradigm originated by Thomas Kuhn, the University of Chicago philosopher of science to the specific notion of low dose irradiation effects on man. We have no clear evidence of harmful effects at low doses but radiation protection a policy in which it is assumed that even very low doses of radiations might be harmful has been adopted. Almost all laypersons and many scientists thus believe that harmful effects of low dose irradiation is quite probable. In this sense the radiation paradigm fits the pattern of a paradigm as proposed by Kuhn\(^2\). Sagan suggested that a paradigm shift at 1950s from a threshold model to a linear model. By analysing the main factors inducing the paradigm shift I will try to propose new factors which might again result in a paradigm shift in the future.
PARADIGM SHIFT IN 1950s

Sagan described the shift very clearly. The observation that exposure of ionizing radiation could produce harmful, even lethal effects, was recognized shortly after the discovery of X-ray in 1895. It was at first thought that radiation effects obey a threshold response, that is, only high doses which exceeded a threshold would produce biological effects. Following the second world war, ICRP in 1950 amended the terminology indicating the dose limit from tolerance dose to maximum permissible dose. It was not based on a non-threshold hypothesis but on the notion of a threshold with a rather large uncertainty\(^3\). In 1950s this strategy was reconsidered, partly on the basis of the genetic studies by Muller who strongly suggested that thresholds for genetic effects might not exist, and partly on the basis of leukemia induction in A-bomb survivors and the calculation of Lewis\(^4\) who suggested that radiation-induced leukemia was due to somatic mutations induced by ionizing radiations. These indicated a linear model of genetic and somatic effects of ionizing radiations\(^5\).

In addition, a linear model was also suggested for radiation-induced life-shortening in experimental animals which was supported by the data of shortened life-span of radiologists reported by Warren\(^6\), later shown to be erroneous\(^7\). Somatic mutation theory of aging was proposed by Failla\(^8\) and Henshow\(^9\) separately but at the same time in 1957. And Curtis\(^10\) devoted his scientific activity to demonstrate the correlation between somatic mutations, in his case, chromosome aberrations and aging in experimental animals.

Thus we may conclude that the paradigm introduced in the 1950s consists of a very simple assumption that genetic as well as somatic effects of low dose irradiation are based on mutation directly induced by ionizing radiation. Somatic mutation theory of carcinogenesis has been widely accepted.

The paradigm encourages the public fear that even very low doses of radiation are harmful. Specialists responsible for radiation protection have difficulty in explaining to laypersons how we can accept the low risks at low doses of radiations because of this paradigm.

PROBLEMS IN THE PRESENT PARADIGM

At low doses of radiations we have no direct data on the existence of risks. We have to use extrapolations from high doses to low doses and from animals to man resulting in large uncertainties in the estimation of risks. Many studies have been carried out to reduce the uncertainties but the paradigm remains unchanged. But some of those newer observations suggest serious problems in the present paradigm that genetic and somatic effect are induced by the same mutations induced by ionizing radiations.

First, radiation-induced life-span shortening was disproved by later studies and rejected in ICRP recommendation of the 1965\(^11\). Quite recently, noncancer mortality of A-bomb survivors was shown to be increased with radiation dose\(^12\). Statistically, a pure quadratic or a linear-threshold model [the estimated threshold dose is 1.4 Gy (0.6–2.8 Gy)] was found to fit better
than a simple linear or linear-quadratic model. Recently Bond\textsuperscript{13} made a profound analysis of the linear, non-threshold hypothesis by applying two dose concept, i.e., the absorbed dose, D, and the total collective energy, $\varepsilon$ in the epidemiological data of A-bomb survivors. In his conclusion it is emphasized the repeatedly confirmed radiobiological fact that attributable cancers and other cell-associated quantal responses will be observed at low values of D only if the irradiated mass and thus the resulting $\varepsilon$ are relatively large. He did not intend to make a paradigm-shift but proposed some revision of the present paradigm to include the above-mentioned conclusion. Kocher at the end of his recent review on the historical development of radiation standard\textsuperscript{14} expressed his impression as follows: “It appears that the practice of radiation protection for workers and the public has become increasingly distanced from any radiobiological or epidemiological basis.” This means that at low doses near background radiation level the linear non-threshold hypothesis gives too high risk compared with our daily experiences.

Genetic dose for population introduced in 1958 in ICRP recommendation was removed from its 1977 recommendation\textsuperscript{15} and more emphasis was placed on somatic carcinogenetic effects than on genetic effects. In 1990 ICRP published its new recommendations based on new risk estimate from A-bomb survivors. As a biological framework ICRP still presumes that even small radiation doses may produce some deleterious health effects since some of DNA changes induced by ionizing radiation may result in mutation. A history of radiation paradigm before 1950 to 1990 as reviewed above is summarized in Fig. 1. In general, mutations including chromosome aberrations induced by ionizing radiation are random events because of the nature of ionizing radiations. Genetic effects may be based on these random mutations. But how about carcinogenesis? Recent advances in the studies on the mechanisms of carcinogenesis clearly indicate that carcinogenesis is a multiple stage process\textsuperscript{16}. The mutations in the process are mutations on specific genes. The processes are apt to be modified by various endogenous and exogenous factors. Thus we cannot say now that genetic effects and carcinogenic effects are induced by the same type of mutation processes randomly induced by ionizing radiations. Such complicated carcinogenic processes may not be linear to radiation dose but rather may be curvilinear with a threshold\textsuperscript{17} as usual biological responses in general. In support of the discrepancy between somatic mutation frequency and carcinogenesis, we have a few reports on

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<thead>
<tr>
<th>Year</th>
<th>Biological hypotheses</th>
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<td>Before 1950</td>
<td>With a threshold</td>
<td>General features of biological response</td>
</tr>
<tr>
<td>1958</td>
<td>Leukemia, life-shortening, and genetic effects follow a linear non-threshold model with cumulative dose effect</td>
<td>Somatic mutation for leukemogenesis and aging</td>
</tr>
<tr>
<td>1977</td>
<td>Induction of malignant tumors as a major risk with a linear non-threshold model.</td>
<td>Somatic mutation for carcinogenesis</td>
</tr>
<tr>
<td>1990</td>
<td>Even small radiation doses may produce some deleterious health effects.</td>
<td>DNA change → Mutation → Cancer</td>
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populations exposed to low doses at high background radiation areas with no increased incidence of cancer\textsuperscript{18,19,20}) but increased incidence of chromosome aberrations in peripheral blood cells\textsuperscript{20,21}). Now it is generally accepted that somatic mutations in peripheral blood are useful as a biological dosimeter but not as a health indicator.

Recently there have been published papers on adaptive response to low doses\textsuperscript{22}) but the relation of these response to carcinogenesis is not clear. Thus they are not powerful enough to induce a paradigm shift. If low dose irradiations and biological responses induced by them are indispensable for the growth of living cells as Plane\textsuperscript{23}) reported, we will have another problem to consider. But we need further study on this possibility before moving further.

**MOTIVES FOR POSSIBLE SHIFT**

Cancer induction has been the most important hazard of low dose radiation as shown in the recent ICRP recommendation. Studies on the mechanisms of radiation-induced carcinogenesis should be at the key point on which we should shift the present paradigm to new one. Too simple models of somatic mutation as the primary mechanism of radiation-induced carcinogenesis should be abandoned. We still do not have any theory on the precise mechanisms of radiation-induced carcinogenesis but recent progress promises to clarify the role of ionizing radiation in cancer-induction which will give us a model for a new paradigm for radiation protection.

I would like to propose two models as shown in Fig. 2. In the first one, the fates of chromosome aberrations and/or mutations in somatic cells are under the control of host factors which are still unclear. Cancer incidence may be largely dependent on the host factors to be investigated. In the second one radiations may induce some gene expressions as shown in adaptive response which results in mitotic stimulation and instability of genes and/or chromosome. Various oncogenic changes may be induced during these processes which finally result in cancer.

![Fig. 2. Two possible models for radiation carcinogenesis](image)

These are only my suggestions. There may be many alternative processes to that proposed by the present paradigm supported by ICRP. Proposals of new ideas would be very much appreciated.
REFERENCES

13. Bond, V. P. (1992) When is a dose not a dose. Lecture No. 15, NCRP.