



An Introduction to Radiation Hormesis

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Paracelsus (more than 400 years ago):

All substances are poisons, there is none which is not a poison. The right dose differentiates a poison from a remedy.

Abstract

All living organisms evolved and exist in a sea of ionizing radiation, much of which is internal. It is a general belief that low doses of ionizing radiation produce detrimental effects proportional to the effects produced by high-level radiation. In recent decades, however, some pioneer scientists have shown that low-dose ionizing radiation is not only a harmless agent but often has a beneficial or hormetic effect. That is, low-level ionizing radiation may be an essential trace energy for life, analogous to essential trace elements. It has been suggested that about one third of all cancer deaths are preventable by increasing our low dose radiation. New theories concerning radiation hormesis and possible mechanisms are discussed.

Introduction

The expression "beneficial effects of radiation" may be very surprising not only for common people but also for many highly educated people. We have heard many things about the biological hazards of ionizing radiation but never hear anything concerning possible beneficial effects of low levels of ionizing radiation. Indeed we have learnt that when considering ionizing radiation, unalterable scientific facts show that it is a completely harmful agent.

If you conduct a simple opinion poll, it will be disclosed that many people consider ionizing radiation as one of the most important life threatening factors [[Click here to see the results of our poll](#)]. However, according to published risk estimates, the risk of malignancies from low doses of ionizing radiation (e.g. doses in diagnostic radiology) is negligible in comparison with many other common health risks such as overweight or alcohol consumption. Nowadays in many developed countries individuals are very reluctant to get X-rays even when they are told by their physician that this type of radiography is necessary for their health. Usually no one explains that the effective dose from common diagnostic X-ray procedures are typically very low. For example the effective dose from a chest X-ray is about 1 mSv and it would take ~~just~~ 10 days to accumulate the same effective dose from background radiation. So despite the safety of diagnostic X-rays, there is a kind of illogical "Radiophobia" in the minds of many highly educated people. This phobia originated from many factors but the most important of those factors are as follows:

- 1-Lack of basic radiation knowledge among general public and even highly educated people [[Click here to see the evidence](#)].
- 2-Mysterious nature of X-rays and generally ionizing radiation and also psychological problems caused by atomic bomb explosions in Japan.
- 3-Consideration of linear no-threshold model as a law and not as a theoretical model.
- 4-Vast literature indicating the biological hazards of high levels of ionizing radiation.
- 5-Exaggeration of radiation risks by press reports caused by increased use of nuclear technology.

On the other hand during the last few decades some pioneer scientists have studied numerous beneficial effects of low doses of ionizing radiation. It has been indicated by many studies that any reduction in the natural radiation causes deficiency symptoms in protozoa and bacteria [Ref. 1]. Furthermore recently many epidemiological studies have indicated that low dose irradiation may lead to beneficial effects such as increase in growth and development rates, increase in mean life span, stimulation of immune reactions and even decrease in cancer mortality [Ref. 1].

Literature Review

The word "hormesis" is derived from the Greek word "hormaein" which means "to excite". It has long been known that many popular substances such as alcohol and caffeine have mild stimulating effects in low doses but are detrimental or even lethal in high doses. In the early 1940s C. Southam and his coworker J. Erlich first found that despite the fact

that high concentrations of Oak bark extract inhibited fungi growth, low doses of this agent stimulated fungi growth. They modified Starling's word "hormone" to "hormesis" to describe stimulation induced by low doses of agents which are harmful or even lethal at high doses. They published their findings regarding the new term "hormesis" in 1943 [Ref. 5]. Generally, hormesis is a stimulatory or beneficial effect, induced by low doses of an agent, that can not be predicted by the extrapolation of detrimental or lethal effects induced by high doses of the same agent.

During the 1950's Luckey, a pioneer researcher in radiation hormesis, indicated that low dose dietary antibiotics caused a growth surge in livestock. Later he found that hormesis could be induced effectively by low doses of ionizing radiation. In 1980 the first complete report on radiation hormesis was published [Ref. 6]. In this report he reviewed numerous articles regarding radiation hormesis. Since the first reports, over 1000 reports have been published concerning radiation hormesis. The concept of radiation hormesis is usually applied to physiological benefits from low LET radiation in the range of 1-50 cGy total absorbed dose [Ref. 30]. Undoubtedly radiobiology of the next decade, as some scientists mentioned, will be focused on biomolecular and genetic implications, problems of damage and repair and connected problems such as radiation hormesis and radioadaptive response.

Hormesis and LNT Model

In the early days of X-rays and radioactivity it was generally believed that ionizing radiation has numerous beneficial effects. It was claimed that blindness might be cured by X-rays. Ladies corsets contained radium! Drinking mineral water containing radium was very popular. People went to spas to drink radioactive water or stayed for hours in caves to be irradiated by ionizing radiation. Between 1925 and 1930 over 400,000 bottles of distilled water containing radium 226 and radium 228 were sold. It was advertised that this mixture can treat over 150 diseases, especially lassitude and sexually impotence [Ref. 33]. It is estimated that the collective skeletal radiation dose of victims of such radioactive medicine may have exceeded 350 Sv by the time the user died [Ref. 34]. Gradually people found that the improper use of ionizing radiation could lead to many complications and harmful effects. Later, in 1927 Herman J. Muller, a Nobel Prize winner, found that X-rays are mutagen and there is a linear relationship between mutation rate and dose. He proposed that mutations which are induced by radiation (or other mutagens) are mostly detrimental. When it was generally accepted that excessive radiation may be harmful, the first regulations for dose limits were introduced. Despite carcinogenicity of X-rays was observed as early as 1902 [Ref. 31], the first radiation protection limits suggested in 1925 and for three decades these limits were based on the concept of a tolerance dose [Ref. 32]. Surprisingly, until the end of World War II, ionizing radiation was considered a great scientific miracle. After the war the development of nuclear weapons and later increased use of nuclear power changed this great miracle into radiophobia. At that time people became afraid of even very small doses of ionizing radiation.

After the atomic bomb explosions in Hiroshima and Nagasaki, studies concerning life span of atomic bomb survivors showed a linear relationship between cancer mortality and high doses of radiation [Ref. 7]. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), then proposed the linear no-threshold (LNT) theory in 1958 [Ref. 8]. According to LNT theory:

1-The effects of low doses of ionizing radiation can be estimated by linear extrapolation from effects observed by linear extrapolation from effects observed by high doses.

2-There is not any safe dose because even very low doses of ionizing radiation produce some biological effect.

In 1959 the international commission on radiation protection (ICRP) adopted the LNT theory [Ref. 9].

The results of many investigations do not support the LNT theory [Ref. 10,11,12,13,14,15]. Furthermore several studies including Cohen's studies of the relationship between environmental radon concentrations and lung cancer even contradict this theory and clearly suggest a hormetic effect. This contradictory evidence is discussed in the following section.

Extensive Evidence Suggesting Hormesis

1. Experimental Evidence

1.1. Cancer Prevention

Bhattacharjee in 1996 showed that when the mice preirradiated with just adapting doses of 1 cGy/day for 5 days (without a challenge dose), thymic lymphoma was induced in 16% of the animals [Ref. 35]. Interestingly, when preirradiated mice were exposed to a 2 Gy challenge dose, thymic lymphoma was induced again in 16% of the animals. However, the challenge dose alone, induced thymic lymphoma in 46% of the mice. From these results, it can be concluded that the low dose preirradiation possibly cancel the induction of thymic lymphoma by the 2 Gy challenge dose. In 1996, Azzam and his colleagues showed that a single exposure of C3H 10T1/2 cells to doses as low as 0.1 cGy reduces the risk of neoplastic transformations. They suggested that a single low-dose at background or occupational exposure levels, may reduce cancer risk [Ref. 2]. Recently, Redpath and his co-workers have confirmed the findings of Azzam [Ref. 36]. To test the generality of the observations of Azzam and his colleagues, they used the Hela x skin fibroblast human hybrid cell. Using a similar experimental protocol, they demonstrated a significantly reduced transformation frequency for adapted to unirradiated cells (pooled data from four separate experiments). In addition, recently Mitchel and his co-workers in Canada have indicated that a low dose preirradiation (10 cGy, 0.5 Gy/h) modifies latency for radiation induced myeloid leukemia in CBA/H mice after exposure to a 1 Gy chronic radiation exposure [Ref. 37]. They showed that the latent period for development of acute myeloid leukemia (AML) was significantly increased by the prior low radiation dose. Interestingly, according to T.D. Luckey one third of all cancer deaths are premature and preventable by low-level ionizing radiation [Ref. 3,4]

1.2. Survival Rate

In 1996, Yonezawa and his colleagues indicated that when 21-ICR mice were exposed to

a 8 Gy of X-rays, about 30% of the animals survived 30 days after the irradiation. However, when mice preirradiated with 5 cGy of X-rays, the survival rate increased to about 70% [Ref. 38].

2. Epidemiological Evidence

Although radiation hormesis data are still incomplete, extensive epidemiological studies have indicated that radiation hormesis really exists. A brief review on this irrefutable evidence is as follows:

2.1. Japanese studies

- 1-According to UNSCEAR report (1994) [Ref. 1], among A-bomb survivors from Hiroshima and Nagasaki who received doses lower than 200 mSv, there was no increase in the number of total cancer deaths. Mortality caused by leukemia was even lower in this population at doses below 100 mSv than age-matched control cohorts.
- 2-Mifune (1992) [Ref. 16] and his co-workers indicated that in a spa area (Misasa), with an average indoor radon level of 35 Bq/m³, the lung cancer incidence was about 50% of that in a low-level radon region. Their results also showed that in the above mentioned high background radiation area, the mortality rate caused by all types of cancer was 37% lower.
- 3-According to Mine et al (1981) [Ref. 17], among A-bomb survivors from Nagasaki, in some age categories, the observed annual rate of death is less than what is statistically expected.
- 4-Kumatori and his colleagues (1980) [Ref. 18] reported that according to their 25 year follow up study of Japanese fishermen who were heavily contaminated by plutonium (hydrogen bomb test at Bikini), no one died from cancer.

2.2. Background Radiation Studies

- 1-In an Indian study, it was observed that in areas with a high-background radiation level, the incidence of cancer and also the mortality rate due to cancer was significantly lesser than similar areas with a low background radiation level [Ref. 19]. KERALA, INDIA
- 2-In a very large scale study in U.S.A, it was found that the mortality rate due to all malignancies was lower in states with higher annual radiation dose [Ref. 20].
- 3- In a large scale Chinese study, it was shown that the mortality rate due to cancer was lower in an area with a relatively high background radiation (74,000 people), while the control group (78,000 people) who lived in an area with low background radiation had a higher rate of mortality [Ref. 21].
- 4-In the U.S.A., it was indicated that significantly, the total cancer mortality is inversely correlated with background radiation dose [Ref. 22].

2.3. Nuclear Power Plant studies

- 1-In a Canadian survey the mortality caused by cancer at nuclear power plants was 58% lower than the national average [Ref. 23].