SESSION Ⅲ

LOW-DOSE RADIATION EFFECTS

TUESDAY, AUGUST 24

3.1 IONIZING RADIATION IN 21ST CENTURY

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Radiation protection is not only a matter of science. It is a problem of philosophy, morality and the utmost wisdom.
Lauriston S. Taylor, 1957

Trying to assess the risk of ionizing radiation from a 21st century perspective we may start by looking at what we learned from the world's greatest nuclear accident that occurred almost 20 years ago: the Chernobyl catastrophe. For myself it was a dramatic personal experience, a difficult exam, which I am not sure I passed. For many people, but not all, engaged in radiological protection, it was a watershed that changed their view on the paradigm on which the present safety regulations are based, the holy mantra of LNT – linear no-threshold assumption, according to which even the lowest, near-zero doses of radiation may cause cancer and genetic harm. For everybody it might serve as a yardstick for comparison of radiation risks from natural and man-made sources (Figure 1). It also sheds light on how easily the global community may leave the realm of rationality facing an imaginary emergency.

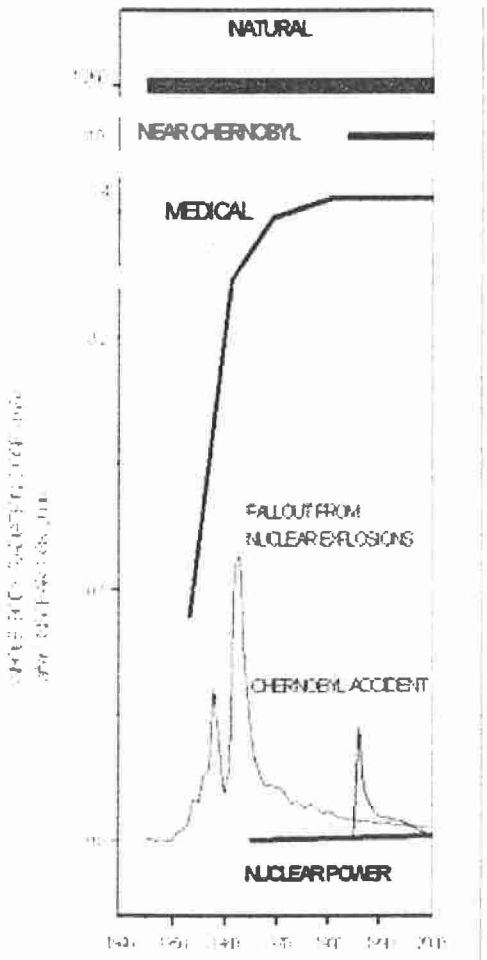

Figure 1. Average individual radiation Exposure to world population and in Chernobyl region (Based on data in years from UNSCEAR, 1988 and 2000)

The LNT assumption is in direct contradiction with a vast sea of data on the beneficial effects of low doses of radiation. When in 1980, as a chairman of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), I tried to convince its members that we should not ignore but rather peruse and assess these data, published in the scientific. The LNT assumption is in direct contradiction with a vast sea of data on the beneficial effects of low doses of radiation. When in 1980, as a chairman of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), I tried to convince its members that we should not ignore but rather peruse and assess these data, published in the scientific literature since the end of 19th century, everybody in the Committee was against it. In each of the next seven years I repeated the proposal, to no avail. Finally, the Chernobyl appeared to be an eye opener two years after the accident, in 1988, the Committee saw the light and decided to study radiation hormesis, i.e., the adaptive and beneficial effects of low levels of radiation. Six years of the Committee's work and hot discussions later, Annex B"*Adaptive Responses to radiation in cells and organisms*" appeared in the UNSCEAR 1994 Report, fourteen

years after my original proposal. The Annex started a virtual revolution in radiation protection, now in full speed.

The LNT/hormesis controversy is not limited to radiation. It poses problems for practically all noxious physical, chemical and biological agents which we meet in life [1]. Ionizing radiation was discovered rather lately, at the end of the 19th century, but, as most of these other agents, it has been with us since time immemorial.

Chernobyl accident was a radiation event unique in human history, but not in the long history of the biosphere, in which increased radiation levels occurred at much greater scales [2-4]. In terms of human losses it was a minor event as compared with many other man-made catastrophes[5]. But its political, economic, social and psychological impact was enormous. Let's have a look at what happened

Lessons of Chernobyl

About 9 a.m. on Monday 28 April 1986 at the entrance of CLOR in Warsaw I was greeted by my assistant with a statement: "*Look, at 7:00 we received a telex from Mikolajki monitoring station saying that the radioactivity of air is there 550 000 times higher than a day before. A similar increase I found in the air filter from the station in our backyard, and the pavement in front of the institute is highly radioactive*". Soon, to our relief, we found that the isotopic composition of radioactive dust was not from a nuclear explosion, but rather from a nuclear reactor. Reports inflowing successively from our 140 monitoring stations suggested that a radioactive cloud over Poland traveled westwards and that it arrived from the Soviet Union, but it was only about 6 p.m. that we learned from BBC radio that its source was in Chernobyl.

This was a terrible psychological shock. The air over the whole country was filled with the radioactive material, at levels hundreds of thousands times higher than anything we experienced in the past, even in 1963, a record year of fallout from nuclear test explosions. It is curious that all my attention was concentrated on this enormous increase in air radioactivity, although I knew that on this first day of "Chernobyl in Poland", the dose rate of external radiation penetrating our bodies reached 30 μR per hour, or 2.6 mSv per year, i.e., was only by a factor of 3 higher than a day before. This dose rate was four times lower than I would experience visiting places in Norway, where the natural external radiation (up to 11.3 mSv/year[6]) from the rocks is higher than over Central European plane. It was also some 100 times lower than in an Iranian resort Ramsar, where in a house the annual dose reaches about 250 mSv per year [7], or more than 300 times lower than at the Brazilian beaches (790 mSv per year) [8] or in South-West France (up to 870 mSv per year) [9]. No adverse health effects among the people living in those areas with high natural background radiation, were ever reported.

But in 1986 the impact of a dramatic increase in atmospheric radioactivity dominated the thinking of myself and of everybody. This state of mind led to immediate serious consequences in Poland, in the Soviet Union, throughout the Europe, and later all over the globe. First were different hectic actions, such as *ad hoc* coining of different principles and emergency countermeasures, which sense and quality was lagging far behind the excellent measuring techniques and monitoring systems. An example of this was the radionuclide concentration limits in food implemented few days after the accident by various countries and international organizations, which were varying by a factor of up to 50,000[10]. The base of

some of these limits was not scientific, but reflected the emotional state of the decision makers, and also political and mercantile factors. For example, Sweden allowed for 30 times more activity in imported vegetables than in the domestic ones, and Israel imposed lower limits for radioactivity in food imported from Eastern than from Western Europe [10]. The limit of cesium-137 concentration in meat of 6 Bq/kg was accepted in Philipines and 6000 Bq/kg in Norway [10].

The monetary costs of such restrictions were estimated in Norway. At first the cesium-137 limit for meat was accepted there as 600 Bq/kg, which from a health physics point of view is meaningless [11], as consumption of 1 kg of such a meat would correspond to a dose of 0.0078 mSv. If somebody would eat 0.25 kg of this meat each day for 1 year the internal radiation dose would reach 0.7 mSv. This limit was often surpassed in mutton, and the farmers received compensation for destroying the meat, and for special fodder they were forced to feed the sheep for months before slaughtering. Such a low limit could have destroyed the living of Lapps whose economy depends on reindeer, an animal having a special food chain based on lichens. Due to this chain the reindeer meat contained in 1986 high concentrations of cesium-137, reaching up to 40,000 Bq/kg. In November 1986 Norwegian authorities introduced a limit of 6000 Bq/kg of reindeer meat and game. Ordinary Norwegian diet includes only about 0.6 kg of reindeer meat per year [11], thus this limit was aimed to protect Norwegians against a radiation dose of 0.047 mSv/year. In 1994 the costs of this "protection" were evaluated: they reached over $51 million [12].

Sweden was not better. When the farmers near Stockholm discovered that the Chernobyl accident contaminated the milk of their cows with cesium-137 above the limit of 300 Bq per liter imposed by Swedish authorities, they wrote to them and asked if their milk could not be diluted with uncontaminated milk from other regions, until the limit were attained, for instance by mixing 1 liter of contaminated milk with 10 liters of clean milk. To the farmers' surprise the answer was no, and the milk was to be discarded. This was strange, as it always was possible to do so for other pollutants in foodstuffs, and we also dilute the fumes from fireplaces or ovens with the atmospheric air. Authorities explained that even though one could reduce the individual risk by diluting the milk, at the same time, one would increase the number of consumers, and thus the risk would remained the same, although now spread over a larger population [13]. This was a practical application of the LNT assumption, and of its offspring, the concept of the "collective dose" (i.e. reaching terrifyingly great numbers of "man-sieverts", by multiplying tiny innocuous individual radiation doses by a large number of exposed people). I believe that in an earlier paper I demonstrated the lack of sense and negative consequences both of this assumption and of the concept [14]. This practical application made that the costs of the Chernobyl accident might probably exceed in Western Europe $100 billion [15].

The most nonsensical action, however, was the evacuation of 336 000 people from the regions of the former Soviet Union, where during the years 1986 – 1995 the Chernobyl fallout increased the average natural radiation dose (of about 2.5 mGy per year) by 0.8 to 1.4 mSv per year, i.e. by about 30% to 50% [8]. The evacuation was based on radiation limits recommended by International Commission for Radiological Protection (ICRP) for "the event of major radiation accidents" [16] and on recommendations for protection of general population [17, 18], which were tens to hundreds of times lower than natural doses in many countries [19]. In the streets of the "ghost town" of Pripyat, from which about 50 000 people were relocated, and where nobody can enter without special permission, the radiation dose

rate measured by a Polish team in May 2001 was 0.9 mSv per year [20] , i.e. the same as in Warsaw, and five times lower than at the Grand Central Station in New York. The evacuation led to development of mass psychosomatic disturbances, great economical losses, and traumatic social consequences. Obviously, ICRP will never accept responsibility for the disastrous effects of practical application of its easy chair elucubrations, which make that the present system of "*radiation protection become a health hazard*"[13].

In Poland, to save the population from effects of exposure to iodine-131, the government, upon my instigation, administered during three days (starting on April 29th) a single dose of iodine to about 18.5 million people, the greatest prophylactic action in the history of medicine performed in such short a time. My medical colleagues and the Ministry of Health were rightly proud of the ingenious and innovative way they implemented this countermeasure. Recently several countries, including the USA, planned to follow in our flight [21-23]. However, now I see this action as nonsensical. We endeavored to save Polish children from developing thyroid cancers by protecting them from a radiation dose of 50 mSv to the thyroid gland [24]. At this dose ICRP recommended implementation of stable iodine prophylaxis [16]. But in studies of more than 34 000 Swedish patients whose thyroid glands received radiation doses reaching up to 40 000 mSv from iodine-131, there was no statistically significant increase in thyroid cancers in adults or children, who had not already been thought to have cancer before treatment with iodine-131. In fact, an opposite effect was observed: there was a 38% decrease in thyroid cancer incidence as compared with the non-irradiated population [25, 26]. In a smaller British study of 7417 adult hyperthyroid patients whose thyroids received average radiation doses from iodine-131 of 300 000 mSv, a 17% deficit in incidence of all studied cancers was found [27]. Without the stable iodine prophylaxis and milk restrictions the maximum thyroid dose would reach about 1000 mSv in about 5% of Polish children[24]. All what I would now expect from this dose is a zero effect.

Fourteen years after the Chernobyl accident in the highly contaminated areas of the former Soviet Union, no increase in incidence in solid cancers and leukemia was observed, except for thyroid cancers. In its 2000 Report UNSCEAR stated that the "*population need not live in fear of serious health consequences*", and "*generally positive prospects for the future health of most individuals should prevail*" [8]. No epidemics of cancers in the Northern Hemisphere, direly predicted from the LNT assumption to reach tens and hundreds of thousands, or even millions of cases, has ever occurred.

The number of 1800 new thyroid cancers registered among the children from Belarus, Russia and Ukraine should be viewed in respect to extremely high occurrence of the "occult" thyroid cancers in normal populations [28-31]. The occult cancers, not presenting adverse clinical effects, are detected at *post mortem*, or by USG examinations. Their incidence ranges from 5% in Colombia, to 9% in Poland, 13% in the USA, and 35% in Finland [29]. In Finland occult thyroid cancers appear in 2.4% of children 0 to 15 year old [28]. In Minsk, Belarus the normal incidence of occult thyroid cancers is 9.3% [32]. The greatest incidence of "Chernobyl" thyroid cancers in children under 15 years old, of 0.027%, was registered in 1994 in the Bryansk region of Russia, which was less by a factor of about 90 than the normal incidence of occult thyroid cancers among the Finish children. The "Chernobyl" thyroid cancers are of the same type and similarly invasive as the occult cancers [30]. The first increase of these cancers was registered in 1987 in the Bryansk region, Russia, one year after the accident. Since 1995 the number of registered cancers tends to decline. This is not in agreement with what we know about radiation-induced thyroid cancers, the risk of which

increases until 15 – 29 years after exposure[8]. In the United States the incidence rate of thyroid tumors detected between 1974 – 1979 during a screening program was 21 times higher than before the screening [33], an increase similar to that observed in three former Soviet countries. I believe that the increased registration of thyroid cancers in contaminated parts of these countries is a classic screening effect, i.e., a consequence of mass thyroid examinations and of the use of modern diagnostic equipment, in the countries where before 1986 such examinations were rather scarce.

Besides the 28 fatalities caused by very high doses of radiation among rescue workers and the employees of the power station, and 3 deaths in this group due to other reasons, the only real adverse health consequence of the Chernobyl catastrophe among about five million people living in the contaminated regions is the epidemics of psychosomatic diseases [8]. These diseases were not due to irradiation with Chernobyl fallout, but were caused by radiophobia, induced by years of propaganda before and after the accident, and aggravated by improper administrative decisions. These decisions caused that several million people in three countries "*has been labeled as, and perceive themselves as, actual or potential victims of Chernobyl*"[34]. This was the main factor behind the economic losses caused by the Chernobyl catastrophe, estimated for Ukraine to reach $148 billion until 2000, and $235 billion until 2016 for Belarus [34].

In 1986 most of my professional colleagues and myself, the authorities, and the public in Poland and elsewhere were pre-conditioned for irrational reactions. Victims of the LNT dogma, we all wished to protect people even against the lowest, near-zero doses of ionizing radiation. The dogma influenced behavior of everybody, leading to a mass psychosis, in fact to the greatest psychological catastrophe in history[5], into which the accident in Chernobyl, with the efficient help of media [10], and national and international authorities, quickly evolved. It seems that professionals, international and national institutions, and the system of radiological protection did not meet the challenge of the Chernobyl catastrophe.

The following main lessons can be deduced from this accident.

(1) Ionizing radiation killed only a few occupationally exposed people. The Chernobyl fallout did not expose the general population to harmful radiation doses. The area covered by the dangerous radioactive fallout, where the radiation dose rate reached 1 Gy per hour, was limited to about 0.5 km^2 in an uninhabited location, reaching a distance of 1.8 km from the burning nuclear reactor. Several hundred meters outside the 1 Gy isoline the dose rate dropped by two orders of magnitude, to a safe level of 0.01 to 0.001 Gy per hour (Figure 2). This is a situation completely different from a surface explosion of a 10 Mt nuclear bomb, when the 1 Gy per hour isoline can reach a distance of 440 km [35], and the lethal fallout can cover tens of thousands km^2, and endanger the life of millions of people.

(2) Radionuclides were injected high into the stratosphere, at least up to 15 km altitude [36], what made possible its long distance migration in the whole Northern Hemisphere, and a penetration over the Equator down to the South Pole [37]. With a unique, extremely sophisticated radiation monitoring systems, implemented in all developed countries, even the most tiny debris from the Chernobyl reactor was easily detected all over the world. No such system exists for any other potentially harmful environmental agent. Ironically, this excellence of radiological protection ignited the mass anxiety, with its disastrous consequences in the former Soviet Union, and strangulation of nuclear energy development elsewhere.

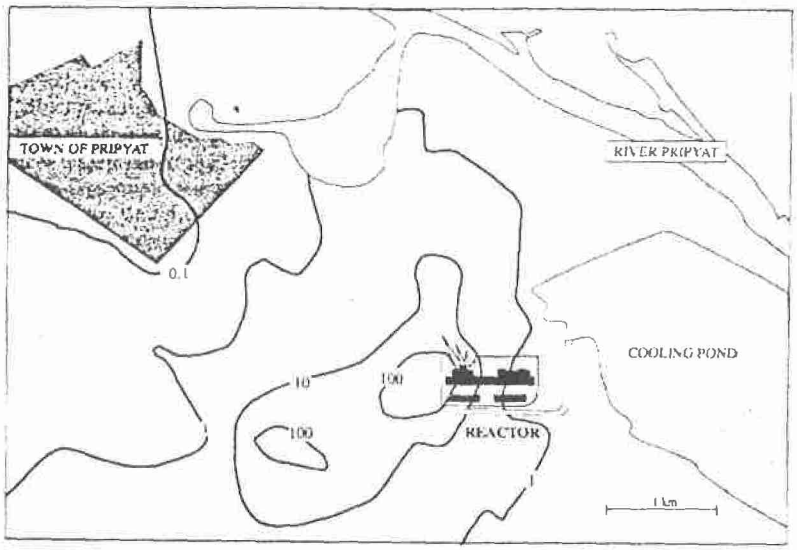

Figure 2. Measured radiation exposure rates in air on 26 April 1986 in the local area of the Chernobyl reactor. Units of isolines are Gy per hour. (After UNSCEAR, 2000).

(3) Psychosomatic disorders and the screening effects were the only detectable health consequences among the general population. Fighting the panic and mass hysteria could be regarded the most important countermeasure to protect the public against the effects of a similar accident should it occur again.

(4) This was the worst possible catastrophe of a badly constructed nuclear reactor, in which two tasks were mixed: production of electric power with production of military grade plutonium. The accident caused a complete meltdown of the reactor core, followed by the ten days long completely free emission of radionuclides into the atmosphere. Nothing worse could happen. It resulted in a comparatively minute occupational death toll, amounting to about half of that of each weekend's traffic in Poland, and tens or hundreds times lower than that of many other industrial catastrophes, and no fatalities among the public. In the centuries to come, the Chernobyl catastrophe will be seen as a proof that nuclear power is a safe means of energy production.

Beneficial radiation and regulations

After ionizing radiation and radioactivity were discovered at the end of the 19th century, their social perception has alternated between enthusiastic acceptance and rejection. This stemmed from recognition of their three basic aspects:

1) usefulness for medical applications and for technical and scientific aims;
2) beneficial effects of their low levels; and
3) harmful effects of high levels.

In the first part of the 20th century acceptance prevailed, in the second - rejection. The change of the public mood which had occurred rather abruptly after the World War II was not due to discovery of some new danger of radiation, but was caused by political and social reasons, unrelated to the actual effects of radiation[14].

The possibilities that ionizing radiation offered for medical diagnostics were first demonstrated by W. K. Roentgen, one month after his discovery, by publishing in *Nature* in January 1896 an x-ray photograph of the hand of his wife. The first therapeutic application of high doses of x-rays for pain release, rheumatic diseases and chronic bronchitis was announced in 1897 [38]. In 1902 Pierre Curie, together with two physicians: C. Balthazard and V. Bonchard, discovered that radium rays are useful in cancer therapy.

The beneficial or hormetic effects of low doses of ionizing radiation were found two years after Roentgen announced the discovery of ionizing radiation. First observed effect was an increased growth rate of blue green algae exposed to x-rays [39]. During the next decades, this observation was followed by thousands of publications on hormetic effects at all biological levels (see e.g. [40-43]), including human epidemiology (Table 1).

That ionizing radiation can be hazardous for man was first announced in 1896 in the German Medical Weekly [44]. The early students and users of radiation voluntarily or unknowingly exposed themselves to high radiation doses. Among the pioneers of radiation and radioactivity from 23 countries, scientists, physicists, medical doctors, nurses, and x-ray technicians, about 100 persons died by 1922, and 406 died until 1992, with afflictions that could be related to radiation. The names of all these victims are recorded in the "Book of Honour of Roentgenologists of All Nations" [45]. This experience sounded an alarm, and the need for protection against high doses of radiation was realised quite early.

The radiological protection developed since the 1920s, and reached high standards after the World War II. Due to this development, the total number of persons exposed worldwide between 1945 and 2001 to significant radiation doses was only 2044. Among them 134 persons died; probably 70% of these fatalities occurred in medical applications of radiation [46]. This record includes the Chernobyl victims, and is unusually low as compared with other human activities. This testifies two facts: (1) excellency of radiological protection (but see below the criticism of exaggerated standards); and (2) a low noxiousness of ionizing radiation.

In the 1920s the concept of "tolerance dose" was introduced, defined as a fraction of the dose that caused skin reddening. This fraction corresponded originally to an annual dose (in modern units) of 700 mSv. In 1936 it was reduced to 350 mSv, and in 1941 to 70 mSv. The concept of tolerance dose, which was effectively a statement of threshold, served as the basis for radiation protection standards for three decades [47] until 1959, when the International Commission on Radiological Protection based its recommendations on the linear no-threshold assumption (LNT) [48]. Introducing LNT to radiological protection was stimulated by undue concern in the 1950s with the allegedly disastrous genetic effects on the human population of ionizing radiation produced by man. In the literature on ionizing radiation at that time, one could often see the following statements of geneticists: "*...we have reached a stage where human mistakes can have a more disastrous effect than ever before in our history - because such mistakes may drastically change the course of man's biological evolution*" [49]. In the years that followed, even in the progeny of survivors of nuclear attacks on Hiroshima and Nagasaki no radiation-induced genetic disorders were detected[50]. Also from other genetic studies it became clear that this concern was an overreaction, in tune with strong emotions, evoked by the menace of nuclear war. However, emotions are not a good basis for regulations. Professor W.V. Mayneord, the late chairman of the ICRP Committee IV, a highly respected scholar and humanist, made the following comment on using LNT as a regulatory basis: " *I have always felt that the argument that because at higher values of dose an observed effect is*

proportional to dose, then at very low doses there is necessarily some 'effect' of dose, however small, is nonsense" [51]. Mayneord's concern about the values applied in ICRP recommendations was in "*the weakness of the biological and medical foundations coupled with a most impressive numerical façade*". This numerical façade, however, is now regarded as epistemologically unacceptable to interpret a biological reality[52]. An outsider of the radiation protection community, the late professor E.T. Jaynes, presented as a classical example for a common scientific error judging the effects of radiation by assuming a linear response without threshold (LNT). He stated that "*to analyse one's data in terms of a model which does not allow even the possibility of a threshold effect is to prejudge the issue in a way that can lead to false conclusions, however good the data....The false premise built into a model which is never questioned cannot be removed by any amount of new data.... False conclusions of just this kind are now not only causing major economic waste, but also creating unnecessary dangers to public health and safety. Society has only finite resources to deal with such problems, so any effort expended on imaginary dangers means that the real dangers are going unattended.* "[53].

For the past few decades the main support of LNT assumption in radiology was the interpretation of epidemiological data from Japanese A-bomb survivor Life Span Study. This population was exposed to extremely high dose rates, as the duration of radiation pulse during nuclear explosion was about 10^{-8} second. This dose rate was larger by 2×10^{15} than the Chernobyl dose rate in the US (0.0046 mSv over 50 years). Using LNT assumption based on such an enormous difference of the dose rates to calculate exactly 53 400 cancer death toll, is not only unacceptable scientifically[14]. Indeed, Lauriston Taylor, the former president of the US National Council on Radiological Protection and Measurements, deemed such extrapolations to be "*deeply immoral use of our scientific heritage*." Recently, a meticulous revision of the cancer and leukemia incidence data from Hiroshima demonstrated that they are consistent with the threshold-like dose response model [54].

During the past several decades there was a tendency to decrease the levels of dose applied in standards of radiation protection to lower and lower values. In the 1980s and the 1990s these became 20 mSv per year for occupationally exposed people, and 1 mSv per year for the general population. For an individual who receives no direct benefit from a source of radiation, a maximum dose of 0.3 mSv in a year has been recently proposed [55], and for some instances - an exemption level of 0.01 mSv per year [56]. Justification for such low levels is difficult to conceive, as no one has ever been identifiably injured by radiation while standards set by the ICRP in the 1920s and the 1930s were in force, involving dose levels hundreds or thousands of times higher [57, 58]. The life expectancy of the survivors of nuclear attacks on Hiroshima and Nagasaki was found to be higher than that in the control groups [59], no adverse genetic effects were found in the progeny of survivors [50]. There is also ample evidence of beneficial effects of low doses of radiation in people occupationally, medically or naturally exposed to doses much higher than the current radiation protection standards (see e.g. [60], and Table 1).

To adhere to regulations based on standards involving such low dose limits, the society is paying hundreds of billions of dollars, with no detectable benefit. Each human life hypothetically saved by implementing the present regulations costs about $2.5 billion [70]. Such spending is morally questionable, as: (1) the limited resources of the society are spent on prevention of an imaginary harm, instead of achieving real progress in health care, and (2) because low radiation doses are beneficial for the individual. For these two reasons, such expenditures may have actually an adverse effect on the population.

Table 1. Deficit of mortality in large human populations exposed to low radiation doses (up to 500 mSv), in comparison with unexposed populations.

Population	Deficit (%) and causes		References
High background area, USA	15%	cancers*	[61]
High background area, China	15%	cancers	[62]
Nuclear industry workers, Canada	68%	leukemia	[63]
Nuclear shipyard workers, USA	24% 58%	all cancers leukemia	[64]
Nuclear workers, combined Hanford, ORNL, Rocky Flats, USA	9% 78%	cancers leukemia	[65]
British medical radiologists after 1955-1979	32% 29% 36%	all cancers cancers non-cancers	[66]
Plutonium workers, Mayak Eastern Ural, Russia	29%	leukemia	[67]
High residential radon, USA	35%	lung cancers	[68]
Accident in Eastern Ural, Russia	39%	cancers	[69]
Swedish patients diagnosed with iodine-131 **	38%	cancers	[26]

* incidence; ** thyroid doses 0 - 257,000 mGy

Natural radioactivity and nuclear wastes

When life began some three and half billion years ago, the natural level of ionizing radiation at the planet's surface was about three to five times higher than presently [71]. At that time, the long-lived potassium-40, uranium-238, and thorium-232 had not yet decayed to their current levels. Their content in the contemporary Earth's crust is still quite high, and it is responsible for the highest radiation exposure of every living being. One ton of average soil contains about 1.3×10^6 Bq of potassium-40, thorium-232 and uranium-238 and their daughters. This corresponds to 3.6×10^{15} Bq per cubic kilometer (Table 2). Decay of these natural radionuclides present in 1 kilometer thick soil layer produces 8000 calories per square meter annually [2].

We can compare the natural, extremely long-lived activity of potassium-40 ($T½ = 1.28 \times 10^9$ years), thorium-232 ($T½ = 1.4 \times 10^{10}$ years) and uranium-238 ($T½ = 4.47 \times 10^9$ years) in soil, with the activity of much shorter-lived radioactive wastes from the nuclear power cycle (Table 2). In 2002 the total annual production of electricity in nuclear reactors was 285.4 GW(e) [8, 80]. The global production of radioactive wastes from this source amounts to 3×10^{15} Bq per year, with the longest lived plutonium-244 ($T½ = 8.26 \times 10^7$ years). Such amount of average natural activity is contained in a relatively small block of soil from high activity areas 0.17 by 0.17 km wide and 2 km deep. None of the man-made component of these wastes has appreciably higher radiotoxicity (expressed as Sv/Bq) than the natural thorium-232 [81].

Table 2. Activity of natural radionuclides in the terrestrial crust and total activity of wastes from nuclear power. (After [72], corrected)

Natural radioactivity						
	K-40	Rb-87	Th-232	U-235	U-238	Total
Number of radionuclides in chain	1	1	**11**	**12**	14	
Concentration of parent in soil, Bq/g						
Median	0.40	0.08	0.030	0.0016	0.035	
Max	3.20	-	0.360	0.0160	0.900	
Concentration of series in soil, Bq/g						
Median	0.40	0.08	0.33	0.019	0.49	1.32
Max	3.20	-	3.96	0.192	12.60	19.95
Activity of series in 1 km^3 of soil (2.7E15 g), Bq						
Median	1.1E15	2.2E14	8.9E14	5.1E13	1.3E15	3.6E15
Max	8.6E15		1.1E16	5.2E14	3.4E16	5.4E16
Activity of series in terrestrial crust (17.3E24 g [b]), Bq						
Median	6.9E24	1.4E24	5.7E24	3.3E23	8.5E24	2.3E25
Wastes from nuclear power						
ILW and LLW from electricity production in 2002, Bq [c]	3.0E15 [e]					
Wastes accumulated until 2000 from the whole civilian nuclear fuel cycle after 500 years of storage for cooling, Bq [d]	5.8E18 [f]					

[a] After ref. [8], [73], and [74];
[b] After ref. [74];
[c] 285.4 GW_e, after ref. [75], and assuming 20% nuclear power station efficiency; and 10,000 GBq/GW(e) y^{-1} for conditioned solid intermediate level wastes (ILW), and 500 GBq/GW y^{-1} low level wastes (LLW) after ref. [76];
[d] 200,000 tones of "heavy metal" wastes after ref. [77]; decay rate of fission products and actinides from ORIGEN after ref. [78] and [79];
[e] Corresponds to **median** natural activity in **0.83 km^3 of soil**, i.e. in a block of 0.64 x 0.64 x 2 km; or in **0.06 km^3 of soil** with **maximum** concentration of natural radionuclides, i.e. in a block of about 0.17 x 0.17 x 2 km.
[f] Corresponds to activity in **1611 km^3 of soil** with **median** concentration of natural radionuclides, i.e. in a block of about 28.4 x 28.4 x 2 km; or in **107 km^3 of soil** with **maximum** concentration of natural radionuclides, i.e. in a block of about 7.3 x 7.3 x 2 km.

The activity of wastes accumulated until the end of 2000 from the whole global civilian nuclear fuel cycle is much greater. It amounts to 200 000 tones of "heavy metals". Disposal of high level wastes and spent fuel in geologic repositories may result in doses to population that do not begin to accumulate until well after 500 years [82]. After 500 years activity of all high level wastes will decrease to about 5.8×10^{18} Bq [83], corresponding to natural activity contained in a block of soil from high activity areas about 7.3 by 7.3 km wide and 2 km deep.

No special barriers prevent the natural radionuclides from migration from, say, a depth of 2 km to the surface of the ground. They can be transported by mechanical action, or move in solution. Thorium is not susceptible to leaching under most geological conditions and its

principal mode of occurrence is in refractory minerals. Uranium is highly mobile, and may migrate with ground water to distances of several tens of kilometres or more. Radium is mobile in sulphate-free neutral or acidic solutions. The average volcanic injections of alpha emitting ^{210}Po into the global atmosphere during non-eruptive activity amount to about 5 x 10^{15} Bq per year [84], i.e., almost twice as much as the 2002 production of radioactive wastes from nuclear power reactors (Table 2). Geochemical differences between uranium, thorium and radium may lead to drastic changes in their radioactive equilibrium [85].

In contrast, for man-made radioactive wastes many effective, sophisticated barriers are provided in deep underground depositories. At a first glance, one can see in Table 2 that it would take few billion years of such a global production of wastes from nuclear power reactors as in 2002, to double the total activity of natural radionuclides in the Earth's continental crust.

Conclusions

Man's contribution to the content and flow of radionuclides and of radiation energy in the particular compartments of the environment consist but a tiny fraction of the natural contribution. In some areas in the world the natural radiation doses to man and to other biota are many hundreds times higher than the currently accepted dose limits for the general population. No adverse health effects were found in humans, animals and plants in these areas. In the future reconstruction of the edifice of radiation protection which now stands on the abstract LNT foundations, a down-to-earth approach will be necessary, taking into account the apparently safe chronic doses in high natural radiation areas. It seems, therefore, that studies of these areas deserve special attention and support in the coming years.

The twentieth century witnessed the dawn of man-made ionizing radiation and radioactivity, the use of the highest human knowledge to kill people in Hiroshima and Nagasaki, and the greatest nuclear catastrophe in Chernobyl. This catastrophe claimed only 31 fatal occupational victims and probably none among the public, ultimately proving that nuclear energy is a comparatively save means of power production. It was also found that high semi-acute doses of radiation can cure cancers, and that small chronic doses of radiation are beneficial for health. It seems that the discovery of "new" radiation and of radioactivity which opened the gate to an unlimited energy resource, has a significance to humankind similar to that of the discovery of fire some 500 000 years ago. Fire made us the most ubiquitous species and enabled expansion of life outside the Earth's biosphere. Our ancestors had many thousands of years to mentally adapt to fire, sometimes even deifying it. It seems that one century has not been long enough to adapt mentally in the same manner to ionizing radiation and radioactivity. But everything now seems to proceed faster than before. Perhaps 21st century will suffice for this adaptation.

REFERENCES

1. Calabrese, E.J. and L.A. Baldwin, *Toxicology rethinks its central belief.* Nature, 2003. **421**(13 February): p. 691-692.
2. Draganic, I.G., Z.D. Draganic, and J.-P. Adloff, *Radiation and Radioactivity on Earth and Beyond.* 1993, Boca Raton: CRC Press.
3. Karam, P.A. and S.A. Leslie. *Changes in terrestrial natural radiation levels over the history of life.* in *Natural Radiation Environment VII.* 2002. Rhodes, Greece, May 2002.
4. Karam, P.A., *Gamma and neutrino radiation dose from gamma ray bursts and nearby supernovae.* Health Physics, 2002. **82**(4): p. 491-499.

5. Jaworowski, Z., *Chernobyl Proportions - Editorial.* Chernobyl Accident: Regional and Global Impacts. Special Issue of Environment International. Guest Editor Zbigniew Jaworowski, 1988. **14**(2): p. 69-73.
6. Baarli, J., *Natural Radiation in Norway*, private communication of 18 February, Editor. 2004: Oslo.
7. Sohrabi, M. *Recent radiological studies of high level natural radiation areas of Ramsar.* in *High Levels of Natural Radiation*. 1990. Ramsar, Iran: IAEA, Vienna.
8. UNSCEAR, *Sources and Effects of Ionizing Radiation. United Nations Scientific Committee on the Effects of Atomic Radiation UNSCEAR 2000 Report to the General Assembly, with Scientific Annexes*. 2000, United Nations: New York. p. 1220.
9. Delpoux, M., et al. *Experimental study of the genetic effects of high levels of natural radiation in South-France.* in *High Levels of Natural radiation 1996. Radiation Dose and Health Effects*. 1996. Beijing, China: Elsevier, Amsterdam.
10. Salo, A. and J. Daglish, *Response to an accident in theory and in practice.* Environment International, 1988. **14**(2): p. 185-200.
11. Henriksen, T., *Fallout and radiation doses in Norway after the Chernobyl accident.* The Science of the Total Environment, Special Isue: Chernoby Accident: Regional and Global Impacts, 1988. **14**(2): p. 157-163.
12. Idas, B. and J. Myhre, *Countermeasures in Norway are exaggerated (in Norwegian).* Aftenposten, 1994.
13. Walinder, G., *Has radiation protection become a health hazard?* 1995, Nykoping: The Swedish Nuclear Training & Safety Center. 126.
14. Jaworowski, Z., *Radiation risk and ethics.* Physics Today, 1999. **52**(9): p. 24-29.
15. Becker, K. *Ten years after Chernobyl.* in *ANS/ENS Conference*. 1996. Washington, D.C.: Nov. 10-14, 1996.
16. ICRP, *Protection of the public in the event of major radiation accidents: Principles for planning.* ICRP Publication 40. 1984, Oxford: Pergamon Press. 22.
17. Ilyin, L.A., *Chernobyl: Myth and Reality*. 1995, Moscow: Megapolis. 1-398.
18. Filyushkin, I.V., *The Chernobyl accident and the resultant long-term relocation of people.* Health Physics, 1996. **71**(1): p. 4-8.
19. Jaworowski, Z., *All Chernobyl's victims: A realistic assessment of Chernobyl's health effects.* 21st Century Science and Technology, 1998. **11**(1): p. 14-25.
20. Adamski, J., *Radiation dose rate measurements in Chernobyl and Prypyat*. 2001.
21. WHO, *Guidlenes for Iodine Prophylaxis floowing Nuclear Accidents*. 1999, World Health Organization: Geneva. p. 1-30.
22. Balter, M., *France distributes iodine near reactors.* Science, 1997. **275**(28 March): p. 1871-1872.
23. Milligan, P.A., *Assessment of the use of potassium iodide (KI) as a supplemental public pretective action during severe reactor accidents*. 2002, U.S. Nuclear Regulatory Commission. p. 1-38 and attachments.
24. Jaworowski, Z. *Chernobyl in Poland: The first few days, ten years after.* in *Zehn Jahre nach Tschernobyl, eine Bilanz*. 1996. Munich, Germany: Gustav Fisher Verlag, Stuttgard.
25. Holm, L.E., et al., *Thyroid cancer after diegnostic doses of iodine-131: A retrospective cohort study.* Journal of the National Cancer Institute, 1988. **80**(14): p. 1133-1138.
26. Hall, P., A. Mattsson, and J.D. Boice Jr., *Thyroid cancer after diagnostic administration of iodine-131.* Rad. res., 1996. **145**: p. 86-92.
27. Franklyn, J.A., et al., *Cancer incidence and mortality after radioiodine treatment for hyperthyroidism: a population-based cohort study.* The Lancet, 1999. **353**(June 19, 1999): p. 2111-2115.
28. Franssila, K.O. and H.R. Harach, *Occult papillary carcinoma of the thyroid in children and young adults - A sytematic study in Finland.* 1986. **58**: p. 715-719.
29. Harach, H.R., K.O. Franssila, and V.M. Wasenius, *Occult papillary carcinoma of the thyroid - A "normal" finding in Finland. A systematic study.* 1985. **56**: p. 531-538.
30. Moosa, M. and E.L. Mazzaferri, *Occult thyroid carcinoma.* The Cancer Journal, 1997. **10**(4 (July-August)): p. 180-188.

31. Tan, G.H. and H. Gharib, *Thyroid incidentalomas: Management approaches to nonpalpable nodules discovered incidentally on thyroid imaging.* Annals of Internal Medicine, 1997. **126**: p. 226-231.
32. Furmanchuk, A.W., N. Roussak, and C. Ruchti, *Occult thyroid carcinomas in the region of Minsk, Belarus. An autopsy Study of 215 patients.* Histopathology, 1993. **23**: p. 319-325.
33. Ron, E., J. Lubin, and A.B. Schneider, *Thyroid cancer incidence.* Nature, 1992. **360**: p. 113.
34. UNDP and UNICEF, *The Human Consequences of the Chernobyl Nuclear Accident: A strategy for Recovery*. 2002, United Nations Development Programme (UNDP) and the UN Children's Fund (UNICEF) with the support of the UN Office for Co-ordination of Humanitarian Affairs (OCHA) and WHO. p. 1-75.
35. Miller, C.F. *Local fallout hazard assessment.* in *Radiological Protection of the Public in a Nuclear Mass Disaster*. 1968. Interlaken, Switzerland.
36. Jaworowski, Z. and L. Kownacka, *Tropospheric and stratospheric distribution of radioactive iodine and cesium after the Chernobyl Accident.* Journal of Environmental Radioactivity, 1988. **6**: p. 145-150.
37. Kownacka, L. and Z. Jaworowski, *Nuclear weapon and Chernobyl debris in the troposphere and lower stratosphere.* The Science of the Total Environment, 1994. **144**: p. 201-215.
38. Caffrey, W.G. and N.E. Wilson, *Medical properties of Roentgen rays.* The Electrical World, 1897(January 9, 1897): p. 67.
39. Atkinson, G.F., *Report upon some preliminary experiments with Roentgen rays in plants.* Science, 1898. **7**: p. 7.
40. Luckey, T.D., *Radiation Hormesis*. 1991, Boca Raton, Florida: CRC.
41. Feinendegen, L.E. and M. Pollycove, *Biologic responses to low doses of ionizing radiation: Detriment versus hormesis. Part 1. Dose responses of cells and tissues.* The Journal of Nuclear medicine, 2001. **42**(7): p. 17N-27N.
42. Pollycove, M. and L.E. Feinendegen, *Biologic responses to low doses of ionizing radiation: detriment versus hormesis. Part 2. Dose responses of organisms.* The Journal of Nuclear Medicine, 2001. **42**(9): p. 26N-32N.
43. Pollycove, M. and L.E. Feinendegen, *Radiation-induced versus endogenous DNA damage: possible effect of inducible protective responses in mitigating endogenous damage.* Human & Experimental Toxicology, 2003. **22**: p. 290-306.
44. Marcuse, W., *Nachtrag zu dem Fall von Dermatitis in Alopecie nach Durchleuchtungversuchen mit Rontgenstrahlen.* Deutsche Medizinisches Wochenschrift, 1896. **21**: p. 681.
45. Molineus, W., H. Holthusen, and H. Meyer, *Ehrenbuch der Radiologen aller Nationen*. 1992, Berlin: Blackwell Wissenschaft. 292.
46. Toohey, R. *Radiation Accident History*. in *American Radiation Safety Conference and Exposition (Health Physics Society's 47th Annual Meeting)*. 2002. Tampa, Florida: Health Physics Society.
47. Kathren, R.L., *Pathway to a paradigm: the linear nonthreshold dose-response model in historical context: the American Academy of Health Physics 1995 Radiology Centennial Harman Oration.* Health Physics, 1996. **70**(5): p. 621-635.
48. ICRP, *Recommendations of the International Commission on Radiological Protection*. ICRP Publication No. 1. 1959, London: Pergamon Press.
49. Westergaard, M., *Man's responsibility to his genetic heritage.* Impact of Science on Society, 1955. **4**(2): p. 63-88.
50. Schull, W.J., *The genetic effects of radiation: consequences for unborn life.* Nuclear Europe Worldscan, 1998(3-4): p. 35-37.
51. Mayneord, W.V., *Radiation and Health*. 1964, London: The Nuffield Provincial Hospital Trust. 140.
52. Walinder, G., *Epistemological problems in assessing cancer risks at low radiation doses.* Health Physics, 1987. **52**(5): p. 675-678.
53. Jaynes, E.T., *Probability Theory: The Logic of Science*, ed. B.G. larry. 2003, Cambridge: Cambridge University Press. 720.
54. Baker, G.S. and D.G. Hoel, *Corrections in the atomic bomb data to examine low dose risk.* Health Physics, 2004. **85**(6): p. 709-720.

55. Clarke, R., *Control of low-level radiation exposure: time for a change?* Journal of Radiological Protection, 1999. **19**(2): p. 107-115.
56. Becker, K., *National and International Standards on Nuclear Waste.* atw, 1998. **43**(2): p. 113-115.
57. Taylor, L.S. *Some non-scientific influences on radiation protection standards and practice.* in *5th International Congress of the International Radiation Protection Association.* 1980. Jerusalem: The Israel Health Physics Society.
58. Coursaget, J. and P. Pellerin. *European Union facing radioprotection standards.* in *W.O.N.U.C International Conference.* 1999. Versailles -p St. Quentin-en-Yv. University, 16-18 June, 1999.
59. Kondo, S., *Health Effects of Low-level Radiation.* 1993, Osaka, Japan: Kinki University Press. 213.
60. Tubiana, M., *Health risks: Data and perceptions*, in *Science and Technology Awareness in Eaurope: New Insights*, M. Vitale, Editor. 1998, European Communities: Rome. p. 113-123.
61. Frigerio, N.A. and R.S. Stowe. *Carcinogenic and genetic hazard from background radiation.* in *Biological and Environmental Effects of Low-Level Radiation.* 1976. Chicago: International Atomic Energy Agency.
62. Wei, L., et al. *Epidemiological investigation in high background radiation areas of Yangjiang, China.* in *High Level of Natural Radiation.* 1990. Ramsar, Iran: International Atomic Energy Agency.
63. Gribbin, M.A., G.R. Howe, and J.L. Weeks, *A study of the mortality of AECL employees. V. The Second Analysis: mortality during the period 1950-1985.* 1992, AECL.
64. Matanoski, G.M., *Health Effects of Low-Level Radiation in Shipyard Workers, Final Report.* 1991, National Technical Information Service: Springfield, Virginia.
65. Gilbert, E.S., D.L. Cragle, and L.D. Wiggs, *Updated analyses of combined mortality data of workers at the Hanford Site, Oakridge National Laboratory, and Rocky Flats weapons plant.* Radiation research, 1993. **136**: p. 408-421.
66. Berrington, A., et al., *100 years od observation on British radiologists: mortality from cancer and other causes 1897-1997.* The British Journal of Radiology, 2001. **74**: p. 507-519.
67. Tokarskaya, Z.B., et al., *Multifactorial analysis of lung cancer dose-response relationship for workers at the Mayak Nuclear Enterprise.* Health Physics, 1997. **73**(6): p. 899-905.
68. Cohen, B.L., *Test of the linear-no threshold theory of radiation carcinogenesis for inhaled radon decay products.* Health Phys., 1995. **68**(2): p. 157-174.
69. Kostyuchenko, V.A. and L.Y. Krestinina, *Long-term irradiation effects in the population evacuated from the East-Urals radioactive trace area.* The Sci. Tot. Environ., 1994. **142**: p. 119-125.
70. Cohen, B.L., *Perspectives on the cost effectiveness of life saving*, in *Rational Readings on Environmental Concerns*, J.H. Lehr, Editor. 1992, Van Nostrand Reinhold: New York. p. 461-473.
71. Karam, P.A. and S.A. Leslie. *The evolution of Earth's background radiation field over geologic time.* in *IRPA 9th Congress.* 1996. Vienna, Austria: IAEA.
72. Jaworowski, Z., *Ionizing radiation in the 20th century and beyond.* Atmowirtschaft- Atomtechnik atw, 2002. **47**(1): p. 22-27.
73. Taylor, S.R., *Trace element abundances and the chondritic Earth model.* Geochim. Cosmochim. Acta, 1964. **28**: p. 1989-1998.
74. Magill, J., *Nuclides 2000 - An Electronic Chart of the Nuclides.* 1999, Eureopean Commission Joint Research Centre. Institute for Transuranium Elements.
75. IAEA, *Nuclear power status around the world.* IAEA Bulletin, 2002. **44**(2): p. 59.
76. UNSCEAR, *Sources, Effects and Risks of Ionizing Radiation.* 1988, United Nations Scientific Committee on the Effects of Atomic Radiation. New York: New York. p. 1-647.
77. Semenov, B. and M. Bell. *Progress towards the demonstration of safe disposal of spent fuel and high level radioactive waste: A critical issue for nuclear power.* in *Geological Disposal of Spent Fuel and High Level and Alpha Bearing Wastes.* 1993. Antwerp, Belgium: International Atomic Energy Agency, Vienna, Austria.
78. Bell, M., *ORIGEN - the ORNL isotope generation and depletion code.* 1973.
79. Croff, G., *ORIGEN 2 - A versatile computer code for calculating the nuclide composition and characteristics of nuclear materials.* Nuclear Technology, 1983. **62**(September): p. 335.

80. UNSCEAR, *Exposures from man-made sources of radiation*. 2000, United Nations Scientific Committee on the Effect of Atomic Radiation. p. 1-155.
81. IAEA, *International Basic Safety Standards for Protection agains Ionizing Radiation and for Safety of Radiation Sources*. Safwety Series No. 115. 1996, Vienna: International Atomic Energy Agency. 353.
82. OECD, *Radiological Impacts of Spent Nuclear Fuel Management Options - A Comparative Study*. 2000, Organisation for Economic Co-operation and Development, Nuclear Energy Agency: Paris. p. 1-124.
83. Chwaszczewski, S., *The management of the spent fuel from power reactors - technologies, economy and environment.* Polityka Energetyczna, 1999. **2**(1-2): p. 65-80.
84. Jaworowski, Z., *Natural and man-made radionuclides in the global atmosphere.* IAEA Bulletin, 1982. **24**(2): p. 35-39.
85. Jaworowski, Z., *Sources and the global cycle of radium*, in *The environmental behaviour of radium*. 1990, IAEA: Vienna. p. 129-142.

3.2 RADIOPHOBIA: A SERIOUS BUT CURABLE MENTAL DISORDER

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Symptoms, some consequences and treatments of radiophobia

The radiophobia syndrome is the excessive acute or chronical fear of small radiation doses in the range of natural background fluctuations below about 50 mSv/y. It may be considered and treated as a mental disorder. It is caused primarily by anti-nuclear activists and "green" political parties, as well as by fear-mongering sensation-oriented media, and is endemic in several industrialized countries.

The consequences are serious. Best known is the lack of public acceptance for clean, safe, and economical nuclear power. In extreme forms, e.g. in Germany, it can lead to quasi-terrorist actions against transports of nuclear materials, purely politically motivated blocking of an almost completed high-level waste repository in the Gorleben salt stock, and the premature phasing-out of some of the world's safest and most reliable nuclear power plants. At high costs for industry, electricity consumers and tax-payers, they are intended to be replaced by many vastly more expensive and controversial wind-mill parks, or even more uneconomic photovoltaic facilities in order to fullfil the German CO_2-reduction commitments according to the Kyoto Protocol. Less obvious are other side-effects, such as excessive costs of decommissioning and waste disposal, - unnecessary but very expensive radon remediation programs in former uranium mining areas, private residences, etc., reluctance of patients to accept vital radiodiagnostic or radiotherapeutic measures, administrative obstacles curbing the use of radioactive sources in industry and research, and complications for some industries involving increased natural radiation levels.

Among the relatively new aspects is that of terrorist threat with "dirty bombs" based on the distribution of radioactive materials from stolen or orphan sources. Although such devices would create only minor real radiological damage, such Weapons of Mass Disruption could, if cleverly placed, easily create tremendous costs and chaos among uninformed populations and authorities.

The therapeutic approach for treating radiophobia must include at least two measures:

(1) Changes in the regulations should abolish the LNT hypothesis and the collective dose concept. The dose limits should be increased to the lower level for observable detrimental health effects, or to the fluctuations of natural levels including the high-level areas in the world. New radiobiological and epidemiological data can accelerate this process.

(2) Closely connected are improvements in information and education regarding low-level radiation effects and the risk-benefit situation, for example by pointing out beneficial radiation effects, e.g. in the wide-spread and successful radon therapy for arthritic/rheumatic diseases and Morbus Bechterew. Such efforts should initially be

focussed on public opinion makers and multiplicators, namely the media (journalists) and politicians, progressing to teachers on all levels, physicians, clerics, community organizations, etc. Both approaches are difficult and time-consuming, but recent developments show that encouraging progress has already been made.

In a historical view, until 1940-50s low-dose radiation was generally associated with beneficial health effects. Since the Japanese A-bombs disaster and global test fallout in 1940-50s increasing worries arose about genetic disorders. After the 1950s, the antinuclear Green/alternative movements increased in some countries. Since 1986, vast exaggerations of Chernobyl effects stimulated intense anti-nuclear, mostly ideologically motivated media and political campaigns in several rich nations. After 1990, the divergence between accumulating scientific evidence and overcautious regulations increased, causing rapidly increasing costs for waste management, decommissioning, etc., and negative effects on society (inexpensive clean energy, reluctance of medical radiation uses, etc.)

The Current Situation

Discrepancies between large fluctuations of natural exposures and the restrictive limits for "artificial" population doses became increasingly problematic for the credibility of radiation protection. In Germany, for instance, there are currently release limits for radioactive materials corresponding to 0.01mSv/y population exposure (<0.5 % of average annual natural dose), and requirements for the safe final storage of radioactive waste for one million years -- perhaps exceeding the survival expectancy of homosapiens (and the U.S. requirements by a factor of 100).

The risk/benefit assessment of such measures becomes particularly serious when economic problems are not any more restricted to less developed countries, but also interfere with social structures (employment, social services, education, etc.), and become a serious burden for the taxpayer in formerly affluent countries. Radiation protection in not a luxury which only a few rich countries can afford.

For example. currently in Germany for dose reduction down to individual doses of 0.5% of average natural exposure (0.01 mSv p.a.), 100,000 ECU/Sv (about US$ 135,000) are being spent. This results in direct expenses, e.g., in Germany, of about 1,500 mill. ECU in the remediation of former U mining areas, about 5,000 mill. ECU on radiation protection measures in decommissioning and waste programs, and about 200 mill. ECU for destruction of agricultural products after Chernobyl, etc. It is important to note that indirect economic and social costs amount to a much larger amount of at least 1,000 mill. ECU annually.

Some Expert opinions

According to the study of U.S. Congress/General Accounting Office, a question has been presented as to the scientific basis of the present radiation standard as follows

(released July 14, 2000):

"A disagreement between federal agencies over what level of radiation exposure is safe was not based on scientific evidence and could cost the taxpayer billions in unnecessary spending. Current standards assume there is no safe level for radiation exposure, but many scientists say that radiation exposure is harmless below a certain threshold. Current standards of acceptable radiation exposure are based on extrapolations from studies on much higher exposure. The question is, is it justified to spend money if you are not sure that there is some benefit derived from spending that money?"

There are many relevant statements of experts, e.g. at 5th Internat. Conference on High Levels of Radiation and Radon Areas, Dose and Health Effects, IAEA/WHO/EU/BMU/BIS/UNSCEAR, Munich Sept. 4-7, 2000):

-- "We are swimming in a sea of uncertainties and contradictions. We cannot live with a consistent system for natural and artificial radiation. The cleanup industry makes a lot of money and tries to maximize profits." (Gonzalez, IAEA, Director, Radiation and Waste Safely Div.)

-- "There are no conclusive data from epidemiological studies. The risk from radiation is much less than currently estimated. The costs for decommissioning and remediation are not acceptable." (A. C. S. Amaral, Director, Inst. Radiat. Protect., Brazil)

-- "Radiation protection should avoid splendid isolation in a self-inflected ghetto. Why worry, at a cost of 100,000 EURO for one Sievert avoided down to a level of 0.01mSv/y, and look away from people living at 10mSv/y?" (W. Burkart, IAEA Dep. Direct. Gen.)

-- "We should not extrapolate from high to low levels, because the biological effects are basically different."(L. Wei, Ministry of Health, China)

Natural and "artificial" dose limits

There are no detrimental health effects up to at least 10mSv/y in high natural radiation areas, e.g. in Kerala/India, China, or, Germany. However, if current limits for "artificial" radiation (1 mSv/y) are applied also to natural radiation, large parts of many countries would have to be evacuated, and many industries (minerals, phosphate, coal, oil) have to be closed down. The extreme expenses could seriously affect whole national economies.

Possible solutions could be:

1. To apply very different standards for natural and artificial radiation, or
2. to adjust regulatory limits for artificial radiation to a much higher level

(by a factor 10-100), which would also correspond with the approx. 1:10 fluctuations in natural exposure. Unfortunately, this obvious solution seems to be not politically acceptable at present.

High natural radon concentration measured in Germany:

- Residential radon: Some basements of older houses in Saxony with more than 100,000 Bq/m^3
- Air in overground industrial facilities: In the Hof/Bavaria Public Water Works ca. 750,000 Bq/m^3,
- Air in radon spa sources: Up to 180,000 Bq/m^3
- Air in U mines around Schneeberg/Saxony (ca.1946-1950): more than 2,000,000 Bq/m^3.

The Schneeberg area of Saxony/Germany, 12% of all homes are above 15000 Bq/m^3 (maximum around 115000 Bq/m^3). Since 1990, about 3.000 mill. US $ have been spent on overground radon assessment and remediation programs, however, in 1998 there has been the official reopening of new radon therapy facilities in the same area.

Radon Therapy as an Example of Beneficial Radiation Effects

Radon therapy has a long history dating back to the ancient Romans. After the1903/04 discovery of Th/Ra (called emanation) in the U.K. and Germany, first spa studies were made in Gastein/Austria. Systematic investigations of Rn sources followed in Austria, Bohemia, Germany, and first scientific studies in Germany. There was a widespread use of Ra/Rn "emanators", and rapidly developing radon spas, e.g. Joachimstal (43 patients in 1906, 373 in 1920, 2476 in 1913, with the Radium Palace Hotel opening in 1912). In Russia, since ca.1910 there was increasing radon therapy with up to one million annual patient treatments, and in 1993 the first clinical proof of radon effects in randomized double-blind studies started Germany. A total of more than 1,000 publications appeared in scientific/medical journals on Rn therapy since 1904.

As for radon spas, there are currently >30 in Russia, 7 in Germany, 3 in Austria, and others in the Czech Republic, in Bulgaria, in Italy, Japan, Poland, and USA. Patients are treated mostly for rheumatic arthritis and spondilytis ankylosans (M. Bechterew), e.g. 75,000 p.a. in Germany and Austria. Several explanations for the effectiveness of radon treatments have been investigated, e.g. stimulation of the immune system, improved cellular repair capacity, or promotion of hormone and radical scavenger production.

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However, ICRP insists that even low and very low radiation doses are dangerous. The proposed limits remain largely unchanged with 1 mSv/y for the population dose, and 0.01 mSv/y release constrains. For radon, it is up to 600 Bq/m^3 in residences, 1,000

Bq/m^3 at the working place (national regulations are in many cases much lower, e.g. 150-250 Bq/m^3 for residential radon, and a recently proposed limit of 100 Bq/m^3 in Germany, which would cause costs of about 1.000 ECU). The weighting factor(RBE) for alphas remains at 20, and LNT the basic principle. The inconsistent consideration of natural (NORM, etc.), medical, and artificial" exposure also remains unchanged.

Among the new topics are cloudy "stakeholder" and ethical-philosophical considerations. and an increasing concern about the radiation protection of non-human species. There are slight indications of improvements in collective dose and lung risk assessment, but without any action. Remarkable is the increasing influence of non-scientific political and public-opinion factors in the formulation of ICRP recommendation.

Conclusions

The current consensus of (almost) all radiation protection and radiation biology experts may be summarized as follows:

1. For economical (cost/benefit), ethical and political (e.g. nuclear energy acceptance) reasons, low dose effects are of utmost interest.
2. Radiobiological and epidemiological evidence demonstrates that the LNT hypothesis and collective dose concept are invalid for low and very low doses, but perhaps still of limited administrative value. In particular the "collective dose" concept frequently produces, by multiplication of very small doses with large populations, obviously absurd results.
3. The RBE of high-LET (alpha, neutron) radiation should be reduced from 20 to a more realistic value around 5-10.
4. Current population limits of 1 mSv/y (individuals) and ~0.01 mSv/y (large groups) are, considering research results, e.g. effects of natural background fluctuations, much too low and should be revised.

Remark: These are notes for a lecture, and not a carefully polished scientific paper. References and additional information may be requested from the author.

3.3 Evidence for beneficial low level radiation effects and radiation hormesis

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Abstract

Low doses in the mGy range cause a dual effect on cellular DNA. One effect concerns a relatively low probability of DNA damage per energy deposition event and it increases proportional with dose, with possible bystander effects operating. This damage at background radiation exposure is orders of magnitudes lower than that from endogenous sources, such as ROS. The other effect at comparable doses brings an easily observable adaptive protection against DNA damage from any, mainly endogenous sources, depending on cell type, species, and metabolism. Protective responses express adaptive responses to metabolic perturbations and also mimic oxygen stress responses. Adaptive protection operates in terms of DNA damage prevention and repair, and of immune stimulation. It develops with a delay of hours, may last for days to months, and increasingly disappears at doses beyond about 100 to 200 mGy. Radiation-induced apoptosis and terminal cell differentiation occurs also at higher doses and adds to protection by reducing genomic instability and the number of mutated cells in tissues. At low doses, damage reduction by adaptive protection against damage from endogenous sources predictably outweighs radiogenic damage induction. The analysis of the consequences of the particular low-dose scenario shows that the linear-no-threshold (LNT) hypothesis for cancer risk is scientifically unfounded and appears to be invalid in favor of a threshold or hormesis. This is consistent with data both from animal studies and human epidemiological observations on low-dose induced cancer. The LNT hypothesis should be abandoned and be replaced by a hypothesis that is scientifically justified. The appropriate model should include terms for both linear and non-linear response probabilities. Maintaining the LNT-hypothesis as basis for radiation protection causes unreasonable fear and expenses.

Ionizing radiation and endogenous toxins at low doses

All agree that cellular responses to low values of absorbed doses of ionizing radiation are not readily predictable by extrapolation of responses observed at high doses. One reason for this unpredictability is in the physics of energy distribution in low-dose exposed tissues. In case of penetrating radiation, particle tracks arise stochastically throughout the exposed tissue with the relatively low density at low doses **[1]**. These tracks generate on the one hand unevenly distributed ionizations and excitations of constituent molecules along the track path, as well as bursts of reactive oxygen species (ROS) **[2]**. In case of exposure to internal emitters, the distribution of particle tracks is determined by the distribution of the emitter in tissue **[3]**.

The lower the radiation fluence or number of particle emitters in a given tissue mass, the less crowded are the particles in the exposed mass and with them the more heterogeneous is the distribution of ionized molecules and of ROS bursts.
The other reason is the presence of compounds that may aggravate or reduce radiation effects; there is especially the abundant and constant metabolic generation of ROS and of other endogenous toxins, on top of which low-dose radiation acts **[2, 4].** The quotient between the rates of endogenous and radiogenic ROS production at background radiation exposure strongly favors the former. In fact, the average production rate of endogenous DNA double strand breaks (DSB) per cell per day in the body is about 10^3 times higher than that of radiogenic DSB from background irradiation assumed overwhelmingly to be low-LET type. However, at low-LET irradiation the probability of radiation induced DSB per primary DNA alteration of any type is about 10^5 times higher than that caused endogenously **[5].** This data set attests not only that endogenous DNA damage far outweighs radiation induced DNA damage at background level exposure, but also that irradiation is far more effective in causing DSB than are endogenous ROS.

Ratio of DNA damage and cancer probabilities

Radiation induced DNA damage increases with absorbed dose **[6].** Such cellular effects come through direct energy deposition events from traversing particle tracks by which DNA damage rises proportional with dose. Dependent of the amount of energy deposited per cell, bystander effects in non-irradiated neighboring cells may add to this damage in tissue at low doses **[7, 8].** By measuring damage in multicellular systems, values of damage per exposed cell or defined micromass are calculated averages. This implies that any bystander phenomenon that may have occurred is coregistered and expressed in the oberved values from which these calculations were made **[9].** A dose of 1 mGy of low-LET radiation, such as 100 kVp x-rays, causes on average the following effects per potentially oncogenic stem cell with an average mass of 1 nanogram: 1 particle track; about 150 ROS; 2 DNA alterations of any kind; 10^{-2} DSB; 10^{-4} chromosomal aberrations; and the probability of an oncogenic transformation of the hit cell with lethal outcome is about 10^{-13} to 10^{-14} **[10, 11, 12].** In other words, the ratio of the probabilities for radation induced lethal cancer and the corresponding DSB is about 10^{-11} to 10^{-12} . This means that the statement of even one DSB to pose a risk of causing a lethal cancer to develop from the affected cell is unreal and, in fact, scientifically unfounded.

Adaptive Responses, Protection

A sudden suprabasal yet non-lethal rise of toxin concentration in a biological target tends to elicit stress responses and to stimulate adaptation usually in terms of protective mechanisms in the sense of hormesis **[13].** Increasing evidence in the literature over the past 25 years indicates that adaptive protection responses occur in mammalian cells *in vivo* and *in vitro* after single as well as protracted exposures to X- or γ-radiation at low doses. Not only the occurrence of adaptive protection but also the nature of some biochemical mechanisms involved have been reported **[4, 11, 12, 14, 15, 16, 17].** There appear to be two principal types of adaptive protection, one is to prevent and repair DNA damage and in doing so to keep cells alive and functioning properly. The other is to remove damaged cells from tissue by inducing apoptosis, terminal differentiation, and immune responses and thus to reduce genomic instability in the tissue system and eliminate mutated cells.

Contrary to the immediate begin of repair after DNA damage has occurred, adaptive protection develops as adaptive response relatively slowly within a few hours, may last for several weeks to months, and resemble physiological stress responses that protect against accumulation of DNA damage in tissue. This damage may be from any source such as from metabolically generated or environmental toxins or renewed irradiation **[18].** Such protective responses occur in various ways. They appear to depend on mammalian species, individual genomes, cell types, cell cycle, and cell metabolism. Adaptive protection categories after single low-dose, low-LET irradiation, are as follows:

Damage prevention

Stimulation of the radical detoxification system that appears to reach a maximum at about 4 hours after irradiation and lasts for several hours to even weeks, depending on tissue and cell type. In mouse bone marrow *in vivo*, there was a delayed and temporary reduction of the incorporation of DNA precursors and of thymidine kinase activity to some 70 % of control with a concomitant rise of free glutathione; the effect slowly declined over a period of about 6 hours. **[10, 19, 20, 21].** In other low-dose irradiated rodent tissues, increased levels of superoxide dismutase (SOD) occurred in parallel with decreased lipid peroxidation lasting for weeks **[22, 23]** and an elevated level of glutathione up by a factor of close to five in spleen cells was involved in an increase in natural killer cell activity **[24].** ROS detoxification was also linked to gene activation. Thus, mRNAs for glutathione synthesis-related proteins in the

mouse liver became elevated after low-dose gamma irradiation **[25].** The increase in intracellular glutathione caused by low-dose in RAW 264.7 cells had its maximum between 3 and 6 hours after exposure; this effect was mediated by transcriptional regulation of the gamma-glutamylcysteine synthetase gene, predominantly through the AP-1 binding site in its promoter **[26].**

Damage repair

Protection against high-dose induced chromosomal aberrations in human lymphocytes increased to a maximum about 4 hours after a conditioning low-dose low-LET irradiation; the protection also operated against other DNA damaging agents **[27, 28].** This protection covered up to about 30 % of the damage seen in non-conditioned controls and varied between individuals and cells types; it was absent in some individuals and is probably determined genetically **[29, 30].** Where it operates, it appears to last up to about 3 days, as reported for various human cells *in vivo* as well as in culture **[15].** This adaptive response probably involves a several-fold enhancement of the DNA repair rate **[31, 32]** with the slow component of DSB repair being much faster at 0.5 Gy x-rays than that seen at 2 Gy **[33].** Another adaptive response of this type appeared regarding micronuclei formation in human fibroblasts **[34].** In these cells, conditioning doses from 1 to 500 mGy were equally effective; this also indicated that at the lowest dose, when approximately 40 % of the cells did not experience an energy deposition event, a bystander effect was involved in causing the adaptive protection **[35].** A similar set of data in fibroblasts showed constancy of the adaptive protection over a dose from 1 to 100 mGy gamma-rays using the micronucleus assay **[36].** The degree of inhibition of DNA synthesis and cell growth in rat glial cells in culture by a high dose of x-rays was reduced by about one fourth to one third at several hours following a conditioning low-dose exposure, when the cells were obtained from young rats. The adaptive response decreased with age of the donor rats. This adaptive response involved protein-kinase C (PCK), DNA-dependent protein-kinase (DNA-PK), and phosphatidylinositol 3-kinase (PI3K), as well as the activity of the ataxia-telangiectasia gene (ATM) **[37].**

*Damage removal by apoptosis*Damaged cells may be induced into apoptosis by intra- and intercellular cellular signaling. Apoptosis also may occur within hours after high-dose irradiation. Low-dose induced apoptosis of pre-damaged cells with replacement by healthy cells may be a major route of *in vivo* removal of oncogenically transformed cells **[38, 39, 40, 41, 42, 43, 44].** Low-dose induced apoptosis is assumed to operate also through intercellular

signaling from normal cells, which may also be activated by transformed cells in culture **[45, 46].** Non-growing human fibroblasts in culture with DSBs from low-dose low-LET irradiation readily lost this damage to the level of DSBs in non-irradiated control cells after induction of proliferation; this damage removal was mainly due to apoptosis **[47].** Low-dose induced enhancement of DNA repair may be responsible for the observation in rat thymocytes, where the incidence of radiation-induced apoptosis first declined at low doses and only rose with higher doses **[48].** The induction of apoptosis apparently requires a certain level of DNA damage.

Stimulation of immune response

Removal of damaged cells occurred *in vivo* by way of a low-dose induced immune competence **[49, 50].** This was, in another study, associated with a reduction in the incidence of cancer metastases to less than one third of control concomitantly with an increased number of circulating cytotoxic lymphocytes **[51].** Such response had its maximum *in vivo* at about 0.2 Gy **[52].** Low-dose induced immune competence may last for several weeks **[53].**

Protection and cell cycle

Damaged cells also may exit the system by premature differentiation and maturation to senescence **[54].** This was observed to occur also via bystander effect in microbeam experiments directed to single cells in complex tissue **[55].** The various mechanisms of protection may be directly or indirectly linked to transient changes in the activity of the G_1 cell cycle checkpoint **[56].** Another mechanism in this category of damage removal is known to occur in a number of tissue culture cell types by way of hypersensitivity to low-dose radiation that disappears at higher doses **[57, 58].** This hypersensitivity in some cells was linked to the cell cycle **[59, 60]** and it disappeared in a number of culture cells within about 4 hours, but not immediately, after a single low-dose, low-LET irradiation **[61].** Radiation-induced predisposition to genetic instability in culture cells also declined following low-dose irradiation **[62].** These data indicate prevention of damage removal by way of low-dose induced DNA repair.

Reduction of carcinogenesis

The coordinated action of these protective responses, in one form or another may be responsible for the observation of a reduction of spontaneously occurring cancers. In fact, single low doses of low-LET radiation in tissue culture cells initiated with a delay of 1 day,

but not immediately, a significant reduction of spontaneous clonogenic transformation to about one third of control **[63, 64, 65].** There is indication that this low-dose suppression of oncogenic transformation is not in response to cellular glutathione **[66].** It can involve bystander phenomena likely through extra-cellular signaling exchange **[67].** In mice heterozygous for the Trp-53 gene, a single low dose of low-LET radiation given at the age of about 2 months significantly delayed the appearance of "spontaneous" lymphoma and spinal osteosarcoma later in life **[68].** A review on tumor development following low-dose, low-LET irradiation in rodents showed the existence of a threshold dose **[69].** This is supported by a recently published study of induction of lymphomas, solid tumors, and ovarian tumors in BC3F1 female mice that at the age of 1 month or 3 months received single whole body doses up to 32 cGy of low-LET radiation; the threshold dose was 4 cGy **[70].** Several human epidemiological studies also indicate either a threshold or a reduced cancer incidence below control following a single low-dose irradiation **[5, 15, 16, 40].**

Low-dose induced changes in gene expression

The above listed categories of adaptive protection involve changes in gene expression **[4, 25, 26, 37, 71].** An example for DNA repair gene activation refers to the telangiectasia gene **[37].** Human fibroblasts in culture showed DNA repair in the course of adaptive protection against micronucleus formation following acute high-dose irradiation; the repair was more effective in the gene poor chromosome than in the gene rich chromosome of the cells **[72].** Another data set showed that exposure of human skin fibroblasts in culture to a single dose of 20 mGy γ-radiation caused more than 100 genes to change their expression within 2 hours. This gene group included stress response genes and was different from the group of genes in parallel cultures that concomitantly responded to 500 mGy **[73].** A similar pattern of expression amongst a total of 1574 genes developed in the γ-irradiated mouse brain more at 30 min. than at 4 hours, with 30 % of the genes exclusively affected by 0.1 Gy **[74].**

A common pattern

Despite the disparity of the examined systems and responses, there appears to be a common pattern in the data. In fact, adaptive protection following low doses of low-LET radiation appears to be the consequence of changed cellular signaling and to be ubiquitous.

Adaptive protection is a physiological expression of cellular capabilities to maintain integrity of tissue structure and function in the face of various exposures to potentially toxic agents including ROS, be they from endogenous sources or from ionizing radiation **[5, 75, 76].** One

might speculate that DNA damage accumulation from any source eventually conditions a cell to become susceptible to apoptosis induced by low doses including that from background radiation exposure **[2].** In this sense, background radiation exposure comes into focus as a possible trigger for maintaining tissue homeostasis.

Regarding their dependence on absorbed dose, the above listed categories of adaptive protection are schematically summarized in Figure 1. Except for apoptosis and terminal cell differentiation, all the above protective responses to single exposures tend to be expressed maximally after less than 0.1 and not after more than 0.5 Gy X- or γ- radiation **[10, 77, 78]** and to increasingly fail with higher doses depending on type of adaptive protection in a given cell system, as summarized previously **[5, 10, 11, 12];** in most mammalian cells so far examined, the expression of adaptive protection had a maximum above 5 mGy and below about 200 mGy.

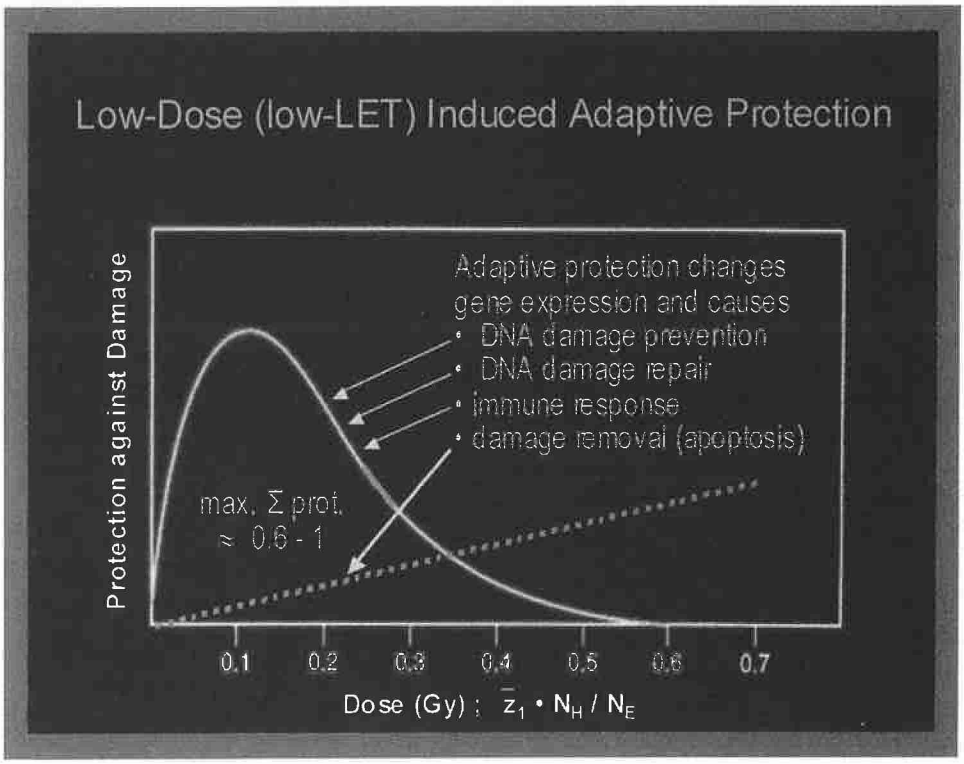

Fig. 1:
Single low-dose induced adaptive responses have a protecting function through various mechanisms. Note that mechanisms of DNA damage prevention and repair and the immune stimulation decrease after a maximum at doses between 0.1 – 0.2 Gy, in contrast to apoptosis incidence that increases with dose. Absorbed dose is in Gy and also in terms of microdosimetry, in that the mean energy deposition per particle traversal per defined micomass (specific energy $\bar{z}_1$) (ICRU 1983) is multiplied by the number of such events (N_H) in the number of exposed micomasses (N_E).

Regarding the duration of their effectiveness, Figure 2 gives a schematic summary of available published data. The time scales of duration of adaptive protection of various kinds are crucially important for the assessment of dose rate effects **[79].** Depending on radiation type and dose rate, energy deposition events per defined miocromass such as a cell happen at certain average time intervals. The time interval between repetitive energy deposition events in a defined biological target at a given dose rate may determine to what degree damage or adaptive protection prevails.

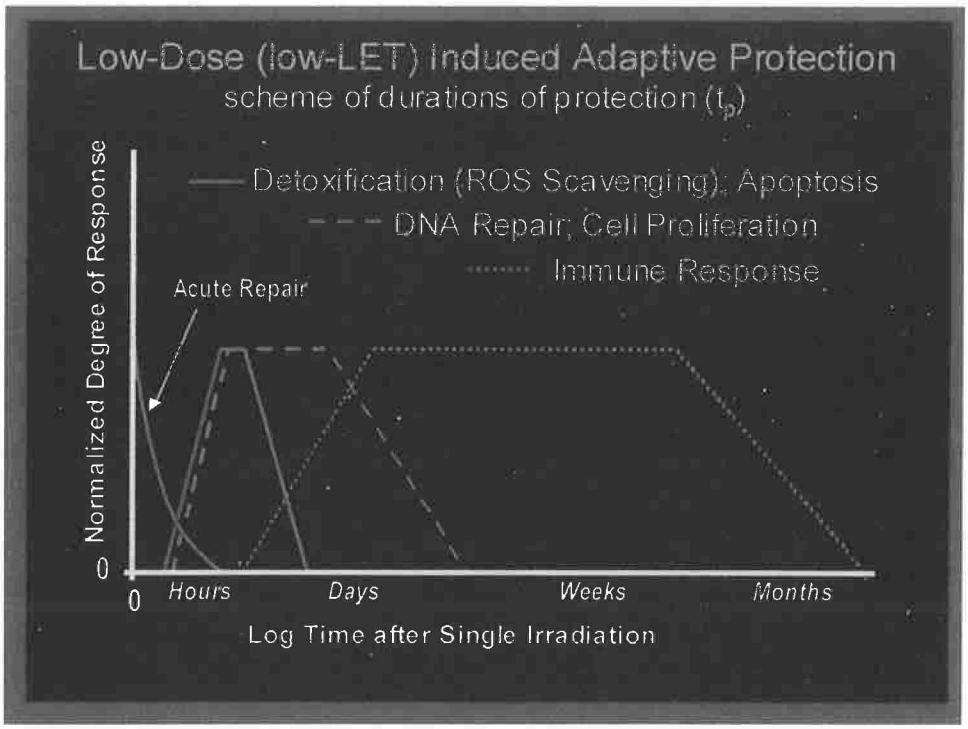

Fig. 2:
Single low-dose induced adaptive responses have different times of duration depending on protective mechanisms, that begin with a delay of several hours and may last for up to months regarding immune response. Note that repair in response to radiation damage begins immediately after damage has occurred.

Since DNA damage and cancer in mammals arise mainly from non-radiogenic sources, it is justified to relate the low-dose induced various adaptive protection mechanism mainly to non-radiogenic, i.e., "spontaneous" DNA damage and cancer in addition to their potential effect against radiogeneic damage and cancer, as presented in more detail in a model elsewhere **[5, 11, 12, 17].** A summarizing graphical display applying the model of risk evaluation after single low-dose irradiation is shown in Figure 3. It illustrates in principle that low-doses induce adaptive protection against DNA damage and its accumulation in tissue, mainly from endogenous, i.e., "spontaneous" sources and thus counterbalances effects from radiation

exposure. The net risk of cancer, then, becomes lower than predicted by the LNT-hypothesis, or even negative with more benefit than damage to the low-dose exposed system.

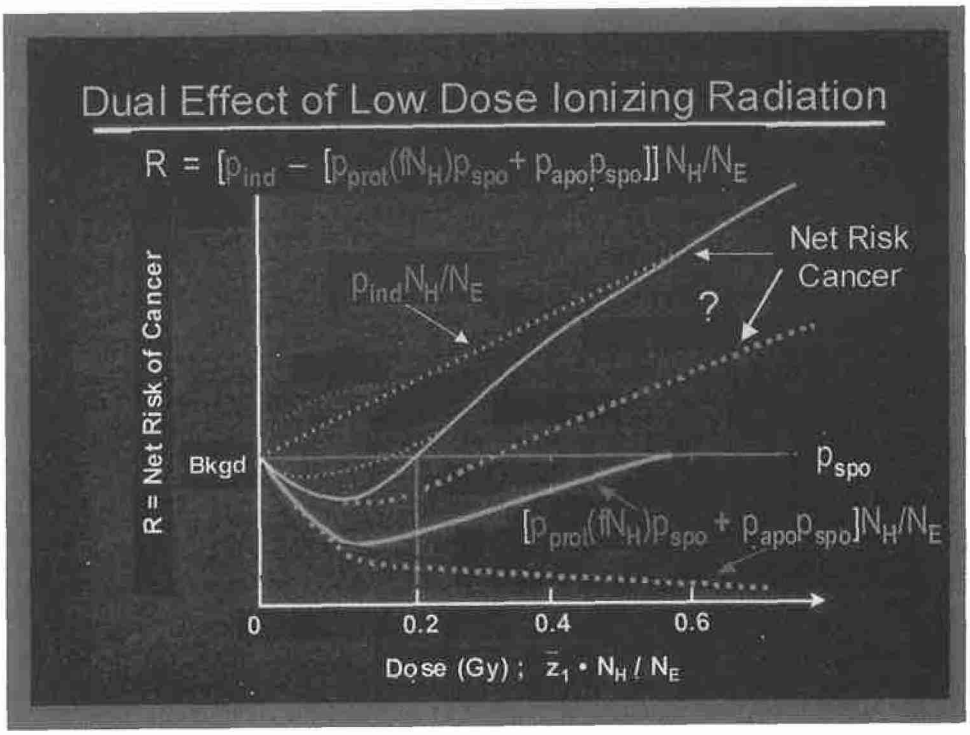

Fig. 3:
The dual effect of single low-dose irradiation is schematically analyzed according to a simplified model (see also text). This encompasses as a function of dose D, i.e. of N_H/N_E for a given radiation quality, the following probabilities: a) of DNA damage induction per energy deposition event $\bar{z}_1$ (see Fig. 1), p_{ind}, with a potential contribution from bystander effect, in red; this function appears linear with dose beyond the contribution from bystander effect; b) of the net protection provided by dose dependent mechanisms, $p_{prot}(fN_H)$, plus of apoptosis p_{apo}, - both against spontaneous cancer with the probability p_{spo} per affected cell, in green. The net cancer risk derives from the difference between cancer induction and prevention at the various dose levels; the solid curve of net cancer risk is without protection from apoptosis, and the dotted curve of net cancer risk is with protection from apoptosis.

Summary

1) Ionizing radiation causes DNA damage in mammalian cells proportional with dose with additional possible bystander effects. 2) At background radiation exposure levels, DNA damage comes overwhelmingly from non-radiation sources. 3) The probability of radiation induced adaptive protection measurably outweighs that of damage from doses well below 200 mGy low-LET radiation. 4) The delayed and temporary adaptive protection at low doses involves damage prevention, damage repair, and immune responses. They appear to operate

primarily against DNA damage from non-radiation sources. Moreover, apoptosis and terminal cell differentiation also occur at higher doses and tend to remove susceptible damaged cells as does the low-dose induced stimulation of the immune system. Cell removal reduces genomic instability and mutated cells from tissue. 5) At higher absorbed doses in tissue, cell and DNA damage appear increasingly to overrule, negate, or annihilate the more subtle signaling effects seen after low doses that lead to adaptive protection, whereas apoptosis and terminal cell differentiation continue to function. 6) The linear-dose-risk function appears invalid and should be replaced by a function that includes both linear and non-linear terms. Basic research data and human epidemiological data conform to threshold or hormesis in the low-dose range.

References

1. ICRU (International Commission on Radiation Units and Measurements). . Microdosimetry, ICRU-Report 36, Bethesda, MD, USA, 1983

2. Feinendegen LE.. Reactive oxygen species in cell responses to toxic agents. Human & Exper Toxicol 2002; 21: 85 – 90

3. ICRU (International Commission on Radiation Units and Measurements). Absorbed-Dose Specification in Nuclear Medicine, ICRU-Report 67, Bethesda, MD, USA, 2002.

4. DOE/NIH, Feinendegen LE, Neumann RD. eds. Cellular Responses to Low Doses of Ionizing Radiation Workshop of the US Department of Energy (DOE), Washington, DC, and the National Institutes of Health (NIH), Bethesda, MD, USA, 2000;.DOE Report Publication SC-047.

5. Pollycove M, Feinendegen LE. Radiation-induced versus endogenous DNA damage: Possible effect of inducible protective responses in mitigating endogenous damage. Human & Exper Toxicol 2003; 22: 290-306

6. Hall EJ. Radiobiology for the Radiologist, 5th Edition, Lippincott Williams & Wilkins, Philadelphia, Baltimore, New York, USA, 2000

7. Nagasawa H, Little JB. Induction of sister chromatid exchanges by extremely low doses of alpha-particles. Cancer Res 1992; 52: 6394-6396

8. Little JB. Radiation sensitive tissue: cell volume, bystander effects and genomic instability. In: Chronic Irradiation: Tolerance and Failure in Complex Biological Systems, eds. Fliedner TM, Feinendegen LE, Hopewell JW; Brit. J Radiol Suppl. 2002; 26, 15-18

9. Feinendegen LE, Pollycove M. Biologic responses to low doses of ionizing radiation: Adaptive Response versus bystander effect: Reply. J Nucl Med 2003; .44: 125-126.

10. Feinendegen LE, Loken MK, Booz J, Muehlensiepen H., Sondhaus CA, Bond VP. Cellular mechanisms of protection and repair induced by radiation exposure and their consequences for cell system responses. Stem Cells 1995; 13 (suppl 1): 7-20

11. Feinendegen LE, Bond VP, Sondhaus CA. The dual response to low-dose irradiation: Induction vs. prevention of DNA damage. In: Biological Effects of Low Dose Radiation, eds. Yamada T, Mothersill C, Michael BD, Potten C; Excerpta Medica. International Congress Serie 1211, Elsevier, Amsterdam, London, New York, USA, 2000; 3 –17

12. Feinendegen LE. Relative implications of protective responses versus damage induction at low-dose and low-dose rate exposures, using the microdose approach. Radiat Prot Dosim 2003; 104: 337-346

13. Calabrese EJ, Baldwin LA. Toxicology rethinks its central belief. Nature 2003; 421: 691-692

14. Sugahara T, Sagan LA, Aoyama T. eds. Low-Dose Irradiation and Biological Defense Mechanisms. Excerpta Medica, Amsterdam, The Netherlands, 1992

15. UNSCEAR. Sources and Effects of Ionizing Radiation, Annex B, Adaptive Responses to Radiation in Cells and Organisms. United Nations, New York, USA, 1994.

16. Académie des Sciences, Institut de France. Problems associated with the effects of low doses of ionizing radiations. Rapport de l'Académie des Sciences, No.38; Lavoisier, TecDoc, Paris, France, 1995

17. Feinendegen L.E., Pollycove M., Sondhaus C.A. Responses to low doses of ionizing radiation in biological systems. Nonlinearity in Biol Toxicol Med (in press)

18. Wolff S. The adaptive response in radiobiology: evolving insights and implications. Environ Health Perspect 1998;.106: 277-283

19. Zamboglou N, Porschen W, Muehlensiepen H, Booz J, Feinendegen LE. Low dose effect of ionizing radiation on incorporation of iodo-deoxyuridine into bone marrow cells. Intern J Radiat Biol 1981; 39: 83-93

20. Feinendegen LE, Muehlensiepen H, Lindberg C, Marx J, Porschen W, Booz J. Acute and temporary inhibition of thymidine kinase in mouse bone marrow cells after low-dose exposure. Intern J Radiat Biol 1984; 45: 205-215

21. Feinendegen LE, Muehlensiepen H, Bond VP, Sondhaus CA. Intracellular stimulation of biochemical control mechanisms by low-dose low-LET irradiation. Health Phys 1987; 52: 663-669

22. Yamaoka K. Increased SOD activities and decreased lipid peroxide in rat organs induced by low X-irradiation. Free Radical Biol Med 1991; 11: 3-7

23. Yamaoka K, Edamatsu R, Mori A. Effects of low dose x-ray irradiation on old rats – SOD activity, lipid peroxide level, and membrane fluidity. In: Sugahara T, Sagan LA,

Aoyama T. eds. Low-Dose Irradiation and Biological Defense Mechanisms. pp 419-422. Excerpta Medica, Amsterdam, The Netherlands, 1992

24. Kojima S, Ishida H, Takahashi M, Yamaoka K. Elevation of glutathione induced by low-dose gamma rays and its involvement in increased natural killer activity. Radiat Res 2002; 157: 275-280

25. Kojima S, Matsuki 0, Nomura T, Kubodera A, Honda Y, Honda S, Tanooka H, Wakasugi H, Yamaoka K. Induction of mRNAs for glutathione synthesis-related proteins in the mouse liver by low doses of g-rays. Biochim Biophys Acta 1998; 1381: 312-318

26. Kawakita Y, Ikekita M, Kurozumi R, Kojima S. Increase of intracellular glutathione by low-dose gamma-ray irradiation is mediated by transcription factor AP-1 in RAW 264.7 cells. Biol Pharm Bull 2003; 26: 19-23

27. Olivieri G, Bodycote J, Wolff S. Adaptive response of human lymphocytes to low concentration of radioactive thymidine. Science 1984; 223: 594-597

28. Wolff S, Afzal V, Wienke JK, Olivieri G, Michaeli A. Human lymphocytes exposed to low doses of ionizing radiations become refractory to high doses of radiation as well as to chemical mutagens that induce double-strand breaks in DNA. Inern J Radiat Biol 1988; .53: 39-49

29. Wojcik A, Bonk K, Muller WU, Streffer C, Weissenborn U, Obe G. Absence of adaptive response to low doses of X-rays in preimplantation embryos and spleen lymphocytes of an inbred mouse strain as compared to human peripheral lymphocytes: a cytoiogenetic study. Intern J Radiat Biol 1992; 62: 177-186

30. Raaphorst GP, Boyden S. Adaptive response and its variation in human and tumour cells. Intern J Radiat Biol 1999; 75: 865-873

31. Ikushima T, Aritomi H, Morisita J. Radioadaptive response: Efficient repair of radiation-induced DNA damage in adapted cells. Mutation Res 1996; 358: 193-198

32. Le XC, Xing JZ, Lee J, Leadon SA, Weinfeld M. .Inducible repair of thymine glycol detected by an ultrasensitive assay for DNA damage. Science 1998; 280: 1066-1069.

33. Okada M, Saito S, Okayasu R. Facilitated detection of chromosome break and repair at low levels of ionizing radiation by addition of wortmannin to G(1)-type PCC fusion incubation. Mutation Res 2004; 562: 11-17

34. Azzam EI, de Toledo SM, Raaphorst GP, Mitchel REJ. Résponse adaptive au rayonnement ionisant des fibroblastes des peau humain. Augmentation de la vitesse de reparation de l'ADN et variation de l'expression des génes. J de Chimie Physique 1994 ; 91: 931-936

35. Broome EJ, Brown DL, Mitchel REJ. Dose response for adaptation to low doses of ^{60}Co-gamma rays and ^{3}H beta particles in normal human fibroblasts. Radiat Res 2002; 158: 181-186

36. Ulsh BA, Miller SM, Mallory FF, Mitchel RE Morrison DP, Boreham DR. Cytogenetic dose-response and adaptive response in cells of ungulate species exposed to ionizing radiation. J Environ Radioact 2004; 74: 73-81

37. Miura Y, Abe K, Urano S, Furuse T, Noda Y, Tatsumi K, Suzuki S. Adaptive response and influence of aging: effects of low-dose irradiation on cell growth of cultured glial cells. Intern J Radiat Biol 2002; 78: 931-921

38. Potten CS. Extreme sensitivity of some intestinal crypt cells to X and γ irradiation. Nature 1977: 269: 518-521

39. Kondo S. Altruistic cell suicide in relation to radiation hormesis. Intern J Radiat Biol 1988; .53: 95-102

40. Kondo S. Health Effects of Low Level Radiation. Kinki Univ. Press, Osaka, Japan; Medical Physics Publishing, Madison, WI., USA, 1993

41. Kondo S. Evidence that there are threshold effects in risk of radiation. J Nucl Sci Technol 1999; 36: 1-9

42. Norimura T, Nomoto S, Katsuki M, Gondo Y, Kondo S. p53-dependent apoptosis suppresses radiation-induced teratogenesis. Nature Med 1996; 2: 577-580

43. Yamada T, Hashimoto Y. eds. Apoptosis, its roles and mechanisms. Business Center for Academic Societies Japan, Tokyo, Japan, 1998

44. Ohyama H, Yamada T. Radiation-induced apoptosis: a review. In: Apoptosis, its Roles and Mechanisms. eds. Yamada T, Hashimoto Y. pp 141-186. Business Center for Academic Societies Japan, Tokyo, Japan, 1998

45. Bauer G. Reactive oxygen and nitrogen species: efficient, selective, and interactive signals during intercellular induction of apoptosis. Anticancer Res 2000; 20: 4115-4139

46. Scott BR, Walker DM, Walker VE. Lowe dose radiation and genotoxic chemicals can protect against stochastic effects. Nonlinearity in Biol Toxicol Med 2003;. (in press)

47. Rothkamm K, Löbrich M. Evidence for a lack of DNA double-strand break repair in human cells exposed to very low x-ray doses. Proc Natl Acad Sci US 2003; 100: 5057-5062

48. Liu S-Z, Yin-Chun Z, Ying M, Xu S, Jian-Xiang L. Thymocyte apoptosis in response to low-dose radiation. Mutation Res 1996; 358:185-191

49. James SJ, Makinodan T. T-cell potentiation by low dose ionizing radiation: possible mechanisms. Health Physics 1990; 59: 29-34

50. Anderson RE Effects of low-dose radiation on the immune response. In: Biological Effects of Low Level Exposures to Chemicals and Radiation. Ed. E.J. Calabrese. Lewis Pub. Inc., Chelsea, Michigan, USA, 1992; 95-112

51. Hashimoto S, Shirato H, Hosokawa M, Nishioka T, Kuramitsu Y, Matushita K, Kobayashi M, Miyasaka K. The suppression of metastases and the change in host immune response after low-dose total-body irradiation in tumor-bearing rats. Radiat Res 1999; 151: 717-724

52. Sakamoto K, Myojin M, Hosoi Y, Ogawa Y, Nemoto K, Takai Y, Kakuto Y, Yamada S, Watabe N. Fundamental and clinical studies on cancer control with total or upper half body irradiation. J Jpn Soc Ther Radiol Oncol 1997; 9: 161-175

53. Makinodan T. Cellular and subcellular alteration in immune cells induced by chronic, intermittent exposure *in vivo* to very low dose of ionizing radiation (ldr) and its ameliorating effects on progression of autoimmune disease and mammary tumor growth. In: Low-Dose Irradiation and Biological Defense Mechanisms. eds. Sugahara T, Sagan LA, Aoyama T. Exerpta Medica; Amsterdam, London, New York, Tokyo, Japan, 1992; 233-237.

54. Trott KR, Rosemann M. Molecular mechanisms of radiation carcinogenesis and the linear, non-threshold dose response model of radiation risk estimation. Radiat Environ Biophys 2000; 39: 79-87

55. Belyakov OV, Folkard M, Mothersill C, Prise KM, Michael BD. Bystander-induced apoptosis and premature differentiation in primary urothelial explants after charged particle microbeam irradiation. Radiat Prot Dosimetry 2002; 99: 249-251

56. Boothman DA, Meyers M, Odegaard E, Wang M. Altered G_1 checkpoint control determines adaptive survival responses to ionizing radiation. Mutation Res 1996, 358: 143-153

57. Joiner MC, Lambin P, Malaise EP, Robson T, Arrand JE, Skov KA, Marples B. Hypersensitivity to very low single radiation doses: Its relationship to the adaptive response and induced radioresistance. Mutation Res 1996; 358: 171-183

58. Joiner MC, Lambin P, Marples B. Adaptive response and induced resistance. Compt Rend Acad Sci Paris, Life Sciences 1999; 322: 167-75

59. Short SC, Woodcock M, Marples B, Joiner MC. Effects of cell cycle phase on low-dose hyper-radiosensitivity. Intern J Radiat Biol 2003; 79: 99-105

60.. Marples B, Wouters BG, Collis SJ, Chalmers AJ, Joiner MC. Low-dose hyper-radiosensitivity: A consequence of ineffective cell cycled arrest of radiation-damaged G_2-phasyed cells. Radiat Res 2004; 161: 247-255

61. Joiner MC. 2002. personal communication

62. Suzuki K, Kodama S, Watanabe M. Suppressive effect of low-dose preirradiation on genetic instability induced by X rays in normal human embryonic cells. Radiat Res 1998; 150: 656-662

63. Azzam EI, de Toledo SM, Raaphorst GP, Mitchel REJ. Low-dose ionizing radiation decreases the frequency of neoplastic transformation to a level below the spontaneous rate in C3H 10T1/2 cells. Radiat Res 1996; 146: 369-373

64. Redpath JL, Antoniono RJ. Introduction of an adaptive response against spontaneous neoplastic transformation *in vitro* by low-dose gamma radiation. Radiat Res 1998; 14: 517-520

65. Redpath JL, Liang D, Taylor TH, Christie C, Elmore, E. The shape of the dose response curve for radiation-induced neoplastic transformation *in vitro*: evidence for an adaptive response against neoplastic transformation at low doses of low-LET radiation. Radiat Res 2001; 156: 700-707

66. Pant MC, Liao XY, Lu Q, Molloi S, Elmore E, Redpath JL . Mechanisms of suppression of neoplastic transformation in vitro by low doses of low LET radiation. Carcinogenesis 2003; 24: 1961-1965

67. Mitchell SA, Marino SA, Brenner DJ, Hall EJ. Bystander effect and adaptive response in C3H 10T½ cells. Intern J Radiat Biol 2004; 80: 465-472

68. Mitchel REJ, Jackson JS, Morrison DP, Carlisle SM. Low doses of radiation increase the latency of spontaneous lymphomas and spinal osteosarcomas in cancer prone, radiation sensitive Trp53 heterozygous mice. Radiat Res 2003; 159: 320-327

69. Tanooka H. Threshold dose-response in radiation carcinogenesis: An approach from chronic β-irradiation experiments and a review of non-tumor doses. Intern J Radiat Biol 2001; 77: 541-551

70. Di Majo V, Rebessi S., Pazzaglia S,. Saran A, Covelli V. Carcinogenesis in laboratory mice after low doses of ionizing radiation. Radiat Res 2003; 159: 102-108

71. Amundson SA, Do KT, Fornace AJ. Induction of stress genes by low doses of gamma rays. Radiat Res 1999; 152: 225- 231

72. Broome EJ, Brown DL., Mitchel REJ. Adaptation of human fibroblasts to radiation alters biases in DNA repair at the chromosomal level. Intern J Radiat Biol 1999; 75: 681-690

73. Golder-Novoselsky E, Ding L-H, Chen F, Chen DJ. Radiation response in normal HSF (human skin fibroblasts): cDNA microarray analysis. Abstract, DOE Low Dose Radiation Research Program Workshop III, March. Office of Biological and Environmental Reserarch, US. Department of Energy, Washington, DC, USA, 2002.

74. Yin E, Nelson DO, Coleman MA, Peterson LE, Wyborek AJ. Gene expression in mouse brain after exposure to low-dose ionizing radiation. Intern J Radiat Biol 2003; 79 759-775

75. Feinendegen LE, Muehlensiepen H, Lindberg C, Marx J, Porschen W, Booz J. Acute effect of very low dose in mouse bone marrow cells: a physiological response to background radiation? in: Biological Effects of Low Level Radiation. International Atomic Energy Agency, Vienna, Austria, 1983; 459-471

76. Feinendegen LE, Muehlensiepen H, Bond VP, Sondhaus CA. Intracellular stimulation of biochemical control mechanisms by low-dose low-LET irradiation. Health Phys 1987; 52: 663-669

77. Shadley JD, Wiencke JK. Induction of the adaptive response by X-rays is dependent on radiation intensity. Intern J Radiat Biol 1989; 56: 107-118

78. Feinendegen LE, Bond VP, Sondhaus CA, Muehlensiepen H. Radiation effects induced by low doses in complex tissue and their relation to cellular adaptive responses. Mutation Res. 1996; 358: 199 – 205

79. Feinendegen LE, Graessle DH. Energy deposition in tissue during chronic irradiation and the biological consequences. In: Chronic Irradiation: Tolerance and Failure in Complex Biological Systems, eds. Fliedner TM, Feinendegen LE, Hopewell JW; Brit J Radiol Suppl 26 2002; 6-14

3.4 Health Effects of Low Dose Radiation

低線量放射線の健康影響

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Abstract

Studies of 30,000 children born to atomic bomb survivors exposed to an average of 400 mSv revealed no statistically significant increase in the genetic indicators when compared with 40,000 control children. Nevertheless, UNSCEAR reports in 2001 gave estimates of hereditary effects of radiation using experimental data on mice. Four cases (people living at a high background radiation area in China, British radiologists, European airline pilots and children in Belarus exposed to high level of radioactive fallout from the Chernobyl accident) of epidemiologic data are presented to show that cancer incidences after chronic exposure to radiation at the level of a few mSv to 100 mSv are not higher than those after exposure to the normal level of natural radiation. Radiation, when given at a low dose, is safe.

はじめに

20 世紀の科学文明発展の基礎を支えた物理学の分野におけるノーベル賞は、40%が放射線関連分野の研究に与えられている。放射線は科学的に最もよく研究された対象である。しかしながら、広島・長崎の原爆災害が余りにも甚大であったので、原爆災害の主因は、よくしられている爆風や熱線であった[4]にもかかわらず、放射線という魔物の作用であったと信じている人が多い。さらに、人工放射線の一般人への被ばくは 1mSv 以下に限るように法的に厳しく規制されている。このため、一般には、放射線は 1mSv でも浴びると危険だと誤解されている。人類は数百万年前に地上に誕生して以来、昼も夜も自然放射線を浴びながら毎日暮らしてきた。そうして、現在では平均寿命 70 年の長寿を享受している。自然放射線の年間の量は 1 mSv を少し上回る。数百万年も浴び続けたこの程度の放射線が人体に危険であるはずはない。なぜなら、人類はこの自然放射線による人体影響に対しては、数百万年間の進化の過程で、防衛機能を獲得しているに違いないからである[4]。しかし、数 mSv の放射線の被ばくが健康に危険か否は、科学的課題であるから、低線量放射線

の健康影響に関する疫学的調査に基づいて詳細に検討しなければならない。以下、このような調査結果の実例を引用して、この問題を総括的に検討する。

1. 原爆放射線の遺伝的影響[4,6]

原爆被ばく者の二世の人たちに対するアンケート調査によれば、４人に１人が差別を受けてきたということである。被ばく二世の多くが、親の原爆被ばくの遺伝的悪影響が自分たちに異常として現れるかも知れないと心配して暮らしているということである。

原爆放射線の遺伝的影響の調査は、広島の Atomic Bomb Casualty Commission (ABCC) で 1948 年最重要項目として取り上げられ、1975 年に、ABCC が RERF (Radiation Effects Research Foundation: 放射線影響研究所) と組織替えされてからも、継続され、約 40 年にわたり追跡調査がなされ、人類遺伝学史上で最大規模の調査である[4,6]。

原爆放射線の遺伝的影響の調査は、被ばく者の子、「被ばく二世」すなわち、Exposed F_1 (F_1= first filial generation) と被ばくしていない対照者の子「対照二世」(Control F_1) との間で、適当な遺伝的指標 (genetic indicator) に関する異常頻度の比較でなされた。Table1 に調査結果を総括して示す[4,6]。

Table1 Genetic effects of atomic bomb radiation[a]; comparison of abnormality frequencies between children (F_1) of control parents and F_1 of exposed parents [b]
原爆放射線[a]の遺伝的影響；対照二世と被ばく二世の間の異常頻度の比較[b]

Genetic indicators 遺伝的指標	Translocations of chromosomes 転座；染色体異常	Sex chromosome abnormalities 性染色体数の異常	Mutations in blood proteins 血液蛋白質の変異
Control F_1 対照二世	0.31% (25/7976)	0.30% (24/7976)	0.00064% (3/(4.7x10^5))
Exposed F_1 被ばく二世	0.22% (18/8322)	0.23% (19/8322)	0.00045% (3/(6.7x10^5))

Genetic Indicators 遺伝的指標	Childhood leukemia 小児白血病	Congenital defects and stillbirths 発生異常と死産	Childhood deaths 小児期の死亡
Control F_1 対照　二世	0.05% (21/41,069)	4.99% (2,257/45,234)	7.38% (2,451/33,361)
Exposed F_1 被ばく二世	0.05% (16/31,159)	5% (503/10,069)	7.08% (989/13,969)

a) Average value of parental exposure doses was 0.4 Sv
b) Awa et al (1989), Neel et al (1988), Yoshimoto et al (1991), Otake et al (1990), Yoshimoto et al (1991)

染色体の異常が遺伝的異常の指標としては一番分りやすい。Table 1 に示すように、常染色体の転座の頻度では被ばく二世の値 0.22%は対照二世の値 0.31%より小さく、性染色体の数の異常頻度では、被ばく二世の値 0.23%は対照二世の値 0.30%より小さい[1]。血液細胞で生産される蛋白質を生産する遺伝子に被ばく二世または対照二世で突然変異が発生すると、蛋白質の特性が異常として現れる場合が少なくない。このような異常特性を検出するため、被ばく二世と対照二世の各人について、血球細胞の蛋白質３０種類の特性が生化学的に調査された[6]。被ばく二世では、調査された遺伝子の述べ総数 67 万個当たり３個に変異蛋白質が検出されたので、1 個の遺伝子当たりの変異頻度は 0.00045％であり、対照二世の血液蛋白質生産遺伝子の変異頻度の 0.00064%より小さい（Table 1 参照）。親の放射線被ばくのため、その子でがん頻度が増えている可能性がある。２０歳までに発生した白血病頻度では、被ばく二世も対照二世も 0.05%で両者間に差がなかった[10]（Table 1）。親の被ばくが原因で、子供に「発生異常・死産」[7] または「小児期の死亡」[10] が増加する可能性がある。いずれの調査でも被ばく二世と対照二世とで頻度に有意の差はなかった。.

２．自然放射線の高い地区と対照地区のがん死亡率の比較[4, 9]

中国広東省陽江県には自然放射線が普通地区(Control Area)より約３倍高い地区（HBRA: High Background Radiation Area）がある。両地区の年間がん死亡率の比較を Table 2 に示す。この地区の調査は 1970 年に開始され、現在も調査は継続されている。統計的に有意差はないが、自然放射線線量率が３倍高くてもがんリスクは高くない。

Table 2 Comparison of cancer death rates in control and high background radiation areas in China [a]
中国の自然放射線の高い地区（HBRA）と対照地区のがん死亡率の比較

	Radiation dose [b] rates 自然放射線線量率	Cancer death rates がん死亡率	Relative cancer death rates がん死亡率相対比
Control Area 対照地区	0.7mSv/year	6.8×10^{-4}/year	1
HBRA	2.2mSv/year	5.7×10^{-4}/year	0.96 (0.8~1.2)

[a] Wei, L.X. and Sugahara, T. : J. Radiat. Suppl. Vol. 41 (2000)
[b] External natural radiation dose only ; 外部自然放射線線量のみ

3．英国放射線科医と一般臨床医の死亡率の比較 [2)]

英国の放射線科医として1955年～1979年の間に初めて登録した医師の1955~1997年間の死亡数Oと放射線を臨床現場で使用しない一般臨床医の期待死亡数Eの比O/EをSMR (standardized mortality ratio 標準化死亡比)という。期待死亡数は次式によって求める：

$$E = n_1P_1 + n_2P_2 + \cdots + n_kP_k \qquad (1)$$

ここに、n_iは放射線科医集団のi番目の年齢階級の人数、P_iは一般臨床医のi番目の年齢階級の死亡率、kは調査集団で採用した年齢階級数である。

Table 3に放射線科医の観察死亡数、一般臨床医の期待死亡数、標準化死亡比を示す。

Table 3 Observed (O) deaths in British radiologists and expected deaths (E) in medical practitioners and SMR(standardized mortality ration) stratified by cause of death [a)]
英国における放射線科医と一般臨床医の死亡率の標準化した相対比SMR

Cause of death 死因	O 観察死数、 E 期待死数	SMR 標準化死亡比
All cancers 全がん	32	45.03	0.71
All non-cancer diseases がん以外の病気	77	120.66	0.64***

***p<0.001

[a)] Berrington, A. et al. Br J Radiol 74: 507-519 (2001)
The death rates given in this table are for radiologists, who entered the profession during 1955 and 1979, and have been annually exposed to an estimated dose of 5 mSv.
この表は、1955~1979年に放射線医になり、年間5mSvを浴び続けた放射線医のデータ。

Table 3によれば、放射線科医のがん死率は一般臨床医のがん死亡率にくらべ0.71で、29%低いが統計的に有意の低下ではない。他方、がん以外の病気死亡率のでは、放射線医の値は一般臨床医の値に比べ0.64と低く、この値は統計的に有意の低下である。放射線科医は毎年約5mSvのX線など人工放射線を被ばくしたと推定されている。

4．欧州の定期航空便パイロットの宇宙線被ばく量と死亡数の標準化死亡比との関係 [5)]

定期航空便のパイロットは毎年数mSvの宇宙線を高度飛行のために浴びている。この宇宙線被ばく量が地上の一般人の宇宙線被ばく量より増加しているため、がん死が地上の一般人より高い可能性が重要な関心事になっている。欧州7ヶ国の飛行機パイロットの調査結果をTable 4に示す。

Table 4 Standardized mortality ratios (SMR) stratified by cumulative dose of cosmic radiation in European airline pilots [a)]
欧州の定期航空便パイロットの標準化死亡相対比 SMR と累積宇宙線被ばく量の関係

Cumulative dose (mSv) 累積線量 (mSv)	0~4.9	5~14.9	15~24.9	25.0+
SMR for all cause deaths 全原因死に対する SMR	0.97 (0.89~1.06)	0.66 (0.58~0.74)	0.64 (0.57~0.72)	0.46 (0.39~0.53)
SMR for all cancer deaths がん死に対する SMR	0.91 (0.72~1.09)	0.67 (0.53~0.87)	0.71 (0.58~0.91)	0.6 (0.45~0.77)

a) Langner, I. et al.: Radiat Environ Biophys 42:247-256 (2004)
Pilots were exposed to annual cosmic radiation doses of 2~5 mSv..
パイロットは年間 2~5 mSv の宇宙線を浴びた。

Table 4 は、欧州の定期航空便パイロットを、宇宙線被ばく累積線量の大きさにしたがって 4 群に分割して、各亜群ごとに、全原因死亡またはがん死亡に対する SMR 値を、地上の一般国民の死亡率と比較して示したものである。例えばがん死亡に対するＳＭＲ値は、宇宙線被ばく量が 4.9mSv 以下の亜群では 0.91 であり、地上の一般国民の死亡率と統計的に有意差はない.。他方、宇宙線被ばく量が 25 mSv 以上の亜群では、がん死亡のＳＭＲ値は 0.6 と大きく低下し、この値は統計的に有意の低下である。すなわち、放射線は２５ｍＳｖを越す程度になると、放射線を浴びた方が、がん死亡率を低下させる有益効果があることが示唆されている。

５． 原爆放射線被ばく量と小児白血病頻度の関係 [8)]

原爆放射線被ばくによるがんでは、小児の白血病が被ばく後一番早く発病し、しかも誘発頻度も高い。原爆ひばく時に１５歳以下であって、被ばく後６～１０年間に急性リンパ性白血病（ALL: acute lymphoblastic leukemia）を発病した人に対する線量とＡＬＬ発病率の関係を Table 5 に示す。

Table 5 は、被ばく量が 0.03 ~ 0.3 Sv の低線量域では、急性リンパ性白血病の年間発病率は、非被ばく群の発病率 0.3×10^{-5}/年にくらべ、1 ~1.3×10^{-5}/年と微増したことを示す。被ばく量が 1Gy 以上になるとは血病の発病率は桁違いに激増する（Table 5)。小児の白血病の頻度は線量 0.03 Sv 付近では増加しないで、しきい値がることが示唆されるが、Table 5 のデータでは、数値を額面通りとれば、しきい値が 30 mSv 付近にあることは断定でき

ない。放射線誘発小児白血病にしきい値があるか否かは、もっと多数の小児の低線量被ばくのデータを調査しなければ結論をだすことはできない。

Table 5 Incidence rates of acute lymphoblastic leukemia (ALL) in children 0-15 years old at the time of atomic bombings stratified by dose of atomic bomb radiation [a)]

原爆放射線被ばく量と小児の急性リンパ性白血病発生率の関係

Atomic bomb radiation dose (Sv) 原爆放射線被ばく線量 (Sv)	0	0.03	0.3	1	≥1.5
Incidence rates (10^{-5}/year) 白血病の発病率 (10^{-5}/年)	0.3	1	1.3	23	149

a) Tomonaga, M et al : RERF TR-9-91, RERF, Hiroshima (1993)
Leukemia incidence rates given are average rates during 6 ~10 years after the atomic bombings.
白血病発生率は原爆被ばく後6~10年間の平均値。

6．チェルノブイリ事故による放射性降下物高濃度汚染地域の小児白血病の発病率 [3)]

ベラルーシ国では、1982年以降１５歳未満の小児の白血病発病は登録が義務になっている。この国には、チェルノブイリ事故による放射性降下物が高濃度で汚染した地域がある。例えばＧｏｍｅｌ付近は、放射性Ｃｓ137の高濃度汚染地であり、平均値が370kBq/m^{2}であった。この地区の15歳未満の男の子１６万人における白血病の年間発生率は、1982年～1994年の間ではTable 6のような変動をした。

Table 6によれば、チェルノブイリ事故が発生した1986年の前と後の年間白血病発病率の平均値は$(3.98 \pm 1.94) \times 10^{-5}$と$(4.45 \pm 2.09) \times 10^{-5}$であり、両者の間に有意の差はない。従って、チェルノブイリ事故で放出された放射性Ｃｓ１３７による汚染による線量率約４mSv/年の放射線を被ばくした男の子（女の子の場合も、白血病発病率は１９８６年の前と後で統計的有意の差なし）には白血病の有意の上昇は起こらなかった。すなわち、放射線による小児白血病の誘発は線量率約４mSv/年では起こらない証拠がえられた。

Table 6 Annual childhood leukemia incidence rates for boys aged <15 years in Gomel, Belarus plotted against calendar years [a)]

ベラルーシ国ゴメルのおける男の子（15 歳未満）の白血病の年間発病率の経年変化 [a)]

Calendar year 白血病を調査した年	1982	83	84	85	86	87	88	89	90	91	92	93	94
Incidence (10^{-5}/year) 発病率（10^{-5}/年）	4.5	5	5	1.4	6.8	6	3.4	3	6.4	3.5	7.3	1	5

a) Ivanov, EP et al: Radiat Environ Biophys 35: 75-80 (1996)
b) The average of leukemia incidence rates for the period before and after the year of Chernobyl accident (1986) is $(3.98 \pm 1.94) \times 10^{-5}$ and $(4.45 \pm 2.09) \times 10^{-5}$, respectively. Gomel was polluted with radioactive Cs-137 at ca. 370 kBq/m² (= 4 mSv/year)
ゴメル地区の放射性 Cs-137　汚染濃度≒37 万 Bq/m² (= 4 mSv/年)

むすび

原爆放射線を平均約 400 mSv 被ばくした人たちの子供さん達には、遺伝的異常頻度の統計的に有意な上昇は見られなかった。この結果は、３万人の被ばく二世と４万人の対照二世を４０年間追跡調査した大規模の研究によってえられたものである。この調査結果は、一般にはあまりしられていなくて、知識人にもこの調査結果の意義はほとんど理解されていない。

放射線は、年間数 mSv 程度の被ばくであるなら、安全で発がんの危険はなくて、しばしば健康に有益である。この結論は、英国の放射線科医、欧州の定期航空便パイロット、チェルノブイリ事故で放出された大量の死の灰からの放射線を浴びた Belarus 国の小児について、がん死または白血病発病の疫学的調査を行った結果からえられたものである。

放射線は少しなら害がない証拠が、上述の例のように多数存在するのに、国際放射線防護委員会や文部科学省の当局は、このような実例を無視し、微量放射線の管理を強めている。この結果、教育の現場では、放射線はどんなに微量でも危険だという考えが普及し、放射線を正しく怖がる科学的な教育は無視されている。

References 参考文献

1) Awa, A.A. et al. (1989): Cytogenetic Study of the Offspring of Atomic Bomb urvivors, Hiroshima and Nagasaki. RERF TR 21-88, Radiation Effects Research Foundation,Hiroshima, pp. 1-20.
2) Berrington, A. et al (2001) 100 years of observation on British radiologists: mortality from cancer and other causes 1897-1997. Br. J. Radiol. 74:507-519.
3) Ivanov, E.P. et al. (1996) Childhood leukemia in Belarus before and after the Chernobyl accident. Radiat. Environ. Biophys. 35:75-80.
4) 近藤宗平（１９９８）「人は放射線になぜ弱いか」ブルーバックス、講談社、東京
5) Langner, I. et al (2004) Cosmic radiation and cancer mortality among airline pilots: results from European cohort study (EECAPE). Radiat. Environ. Biophys. 42:247-256.
6) Neel, J.V. et al. (1988) Search for mutations altering protein charge and/or function in children of atomic bomb survivors: final report. Am. J. Hum. Genet. 42:663-676.
7) Otake, M. et al (1990) Congenital malformations, stillbirths and early mortality Among the children of atomic bomb survivors: reanalysis. Radiat. Res. 122:1-11.
8) Tomonaga, M. et al. (1993) Differential Effects of Atomic Bomb Irradiation in Inducing Major Leukemia Types: Analysis of Open-City Cases Including the Life Span Study Cohort Based upon Updated Diagnostic Systems and the Dosimetry System 1986 (DS86), RERF TR9-91. Radiation Effects Research Foundation, Hiroshima
9) Wei, L.X. and Sugahara, T. (Eds) (2000) High Background Radiation Area. J. Radiat. Res. Suppl. Vol. 41, pp. 1-76.
10) Yoshimoto, Y. et al. (1991) Mortality among the Offspring (F1) of Atomic Bomb Survivors, 1946-85 (RERF TR 1-91) Radiation Effects Research Foundation, Hiroshima, pp. 1-27.

3.5 Recent Advances in Research on Radiation Adaptive Responses

放射線適応応答に関する最近の研究から

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The radiation adaptive responses have been typically demonstrated as an acquired resistance induced by a low dose of radiation to a large (challenge) dose administered after some interval. The responses have been demonstrated in various types of cultured cells; the endpoints include micronucleus formation, sister chromatid exchange, mutation induction, *in vitro* transformation, and cell death. The adaptive response has been also demonstrated in the whole body system; mice irradiated with a small dose developed a resistance against a lethal irradiation. The response was also demonstrated in terms of radiation and carcinogen induced tumors.

The adaptive responses seem to work in a protective way against radiation damage and contradicts what is assumed in the current radiation protection system: radiation is harmful, no matter how low the dose is.

1. はじめに

放射線はどんなに微量であっても有害であると言われる。一般の人々はこれが放射線防護のための仮定であることを認識せず、あたかも事実のように受け止めている場合が多い。これが放射線に対する恐怖感の一因ともなり、中学校、高校の教科書や一般向けの書籍の中には放射線を危険なものの代表として取り扱い、恐怖感をあおるような記述すら見られる。[1)]

高線量の放射線が有害であることは様々な事例が示す通りであるが、高線量での障害のイメージもこのような誤解の原因のひとつと考えられる。高線量の場合の影響に目が奪われていたためか、低線量域の放射線の生物作用に関する研究の歴史はまだ浅い。しかし、低線量放射線の生物作用が詳細に調べられるようになるにつれ、その様相が高線量の場合とは大きく異なることが明らかとなりつつある。その代表的な例が放射線適応応答[2)]である。

2. 放射線適応応答とは

放射線適応応答とは、予め低線量の放射線を照射しておくと、その後の高線量照射に対して抵抗性を示す現象のことを指す。代表的な解析の手順は図1に示すとおりである。まず、わずかな線量を照射し、時間をおいた後で予め照射する低い線量を priming dose、adapting dose、あるいは conditioning dose などとよぶ。これに対し、その後に照射する高い線量は challenge dose とよばれる。

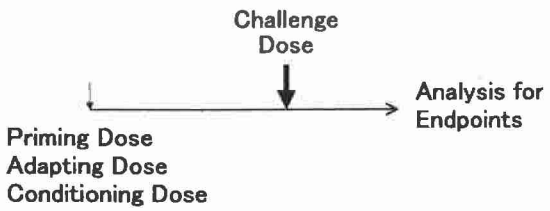

図 1：放射線適応応答の解析法

Fig.1 : Typical protocol to demonstrate radiation adaptive responses

(1)細胞レベルで見られる適応応答

放射線によって DNA に切断が生じこれが修復されずに残ってしまうと、本来の細胞核のほかに、DNA の断片を含む小さな核と類似の構造体が残る。このような構造を「小核」あるいは「微小核」とよび、修復されずに残ってしまったDNA切断の指標とされている(図2)。さて、V79という培養細胞に3GyのX線を照射したところ、20%余りの細胞に小核が生じた。これに対して3Gy の照射の 4 時間前に 0.1Gy の照射をしておくと、小核を持つ細胞の割合は約 17%に、0.2Gy の照射をしておいた場合には約15%に低下した。0.1Gy のみあるいは 0.2Gy のみの場合は、照射しなかった場合(0Gy)とほとんど差がなかった(図3)。ここでは 4 時間という間隔が重要で、0.1Gy あるいは 0.2Gy の照射の直後に3Gy を照射しても小核形成の低下は見られない。

このことから、0.1Gy あるいは 0.2Gy の事前照射が細胞内で 4 時間の間に DNA 切断が後に残らないような仕組み、おそらくはDNAの損傷を修復する機能の増強を引き起こしたものと考えられる。

(2)マウスの急性死を指標とした適応応答

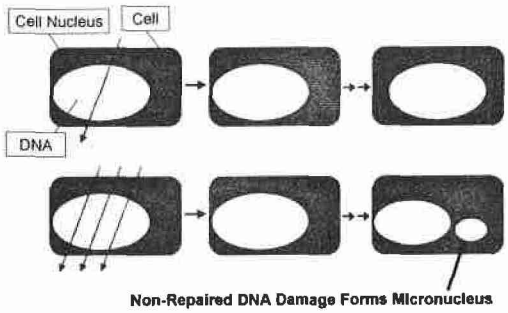

図 2 : 小核とは
Fig2 : What is a micronucleus ?

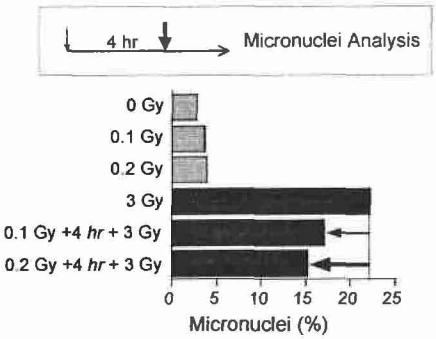

図 3 : 小核形成を指標とした適応応答
Fig3 : Adaptive response in terms of micronucleus formation.

個体レベルの適応応答としてはマウスの生存率を指標とした例が典型的である[1](図4:米澤らの結果をもとに筆者が作成)。C57BL/6N という系統のマウスに7Gy ほどの X 線を照射すると、1ヵ月後に生き残っている割合は10%であった。ところが、7Gyの照射の 2 週間前に 0.5Gy の照射をしておくと、7Gy 照射1ヵ月後の生存率は80%であった。ここでも 2 週間の間隔をあけることが重要であり、間隔をあけずに 0.5Gy に引き続いて7Gy を照射した場合には抵抗性の獲得は見られない。つまり、0.5Gy という線量がマウスの体の中で何らかの変化を引き起こし、2 週間の間に次第に抵抗性が獲得されたと考えられる。また、ここで獲得された抵抗性はいつまでも続くわけではない。このことは、0.5Gy 照射後 1 ヵ月たってから7Gy の照射をしても抵抗性の獲得が見られないことからわか

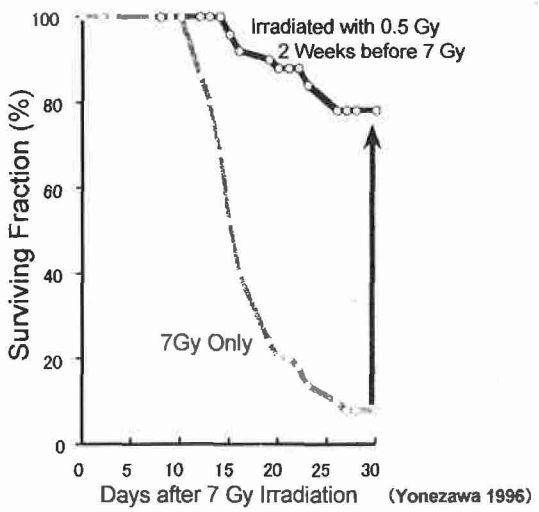

図 4 : マウスの放射線感受性を指標とした適応応答
Fig.4 : Radiation adaptive response in terms of radiosensitivity of mice

る。

(3)発がんを指標とした適応応答

マウスに放射線を週に1回の割合で4回照射すると胸腺リンパ腫と呼ばれるある種のがんが生ずることが知られている。C57BL/6Nという系統のマウスに1.8GyのX線を4回照射した場合には90%のマウスに胸腺リンパ腫が発症した。これに対して、1.8Gyの照射の6時間前に0.075Gyを照射すると胸腺リンパ腫の発症は約70%にとどまった[2]。このことは、0.075Gyの事前照射が1.8Gyの照射による胸腺リンパ腫の発生を抑えたことを示している。同様の、胸腺リンパ腫の発症の抑制は他の系統のマウスでも報告されている[5]。また、がん抑制遺伝子p53に異常を持つマウスにおいて自然に生ずるリンパ腫や骨肉腫の発症の時期が低線量照射によって遅れるという報告がある[6]。

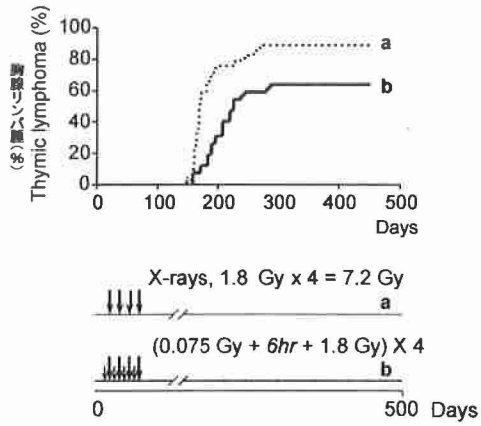

図5：胸腺リンパ腫の発生を指標とした放射線適応応答
Fig5: Adaptive response in terms of thymic lymphoma inductions

(4)低線量率長期照射による発がん抑制

以上の結果はいずれも、「事前照射」を短時間のうちに与えた場合に観察されたものであるが、同様の現象が微量の放射線を長期間にわたって照射した場合にも起こるかどうかを化学発がんの場合について調べた。

マウス(ICR系統)に3.5、1.2、あるいは0.35mGy/hrの線量率で35日間照射し、その後そけい部にメチルコラントレンと呼ばれる化学発癌剤を投与した。投与後はそれぞれの線量率で引き続き照射を行い、腫瘍が生ずるまで観察を続けた。216日後までの累積発がん率は、非照射群の場合には94%であった。0.35mGy/hr照射群ではほとんど差が見られなかったが、3.5mGy照射群では若干発がん率の低下が認められた。1.2mGy/hr照射群ではさらに低下が見られ、発がん率は74%であった[7]。

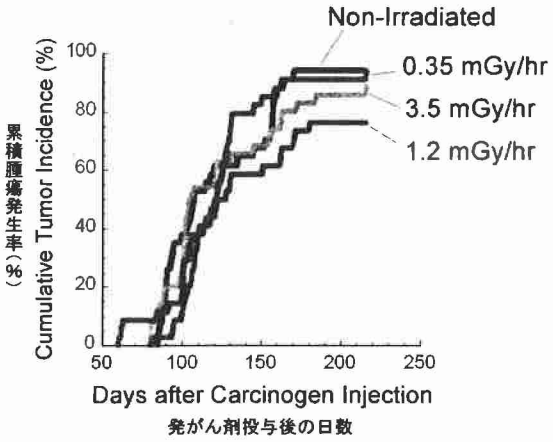

図6：低線量率照射による発がんの抑制
Fig.6: Suppression of carcinogenesis by low dose rate irradiation

5. まとめ

放射線適応応答の機構の解明は現在も進行中の研究分野である。詳細は今後の研究の進展を待たなければならないが、活性酸素を除去する機能、DNAの損傷を修復する機能、体内に生じた変異細胞を排除する仕組み(アポトーシス)、あるいは免疫機能などいわゆる「生体防御機能」の活性化が

起こっているものと考えられている。別の見方をすれば、生体には微量の放射線に対する絶妙な応答の機構が備わっていると言えよう。

放射線適応応答は生物学の題材として興味深いだけでなく、放射線の影響というものを正しく理解する上で非常に重要な現象である。今後人類と放射線との関わりがますます深まる中で、次の世代には放射線に対する生き物の応答のおもしろさと生物影響に対する正しい知識を伝えることが大事であろう。

引用文献

1. 松浦 辰男「学校・社会における放射線教育の重要性とその在り方」 *Isotope News* No.588, 60-62 (2003)

2. G. Olivieri, J. Bodycote, and S. Wolff: Adaptive response of human lymphocytes to low concentrations of radioactive thymidine. *Science* **223**, 594-597 (1984)

3. M. Yonezawa, J. Misonoh and Y. Hosokawa: Two types of X-ray-induced radioresistance in mice: presence of 4 dose ranges with distinct biological effects. *Mutat. Res.* **358**: 237-243 (1996)

4. Y. Ina, T. Yamada, H. Tanooka, and K. Sakai: Suppression of Thymic Lymphoma Induction by Life-Long Low Dose-Rate Irradiation Accompanied by Immune Activation in C57BL/6 Mice. *Radiat. Res.* (2005) In press.

5. D. Bhattacharjee: Role of radioadaptation on radiation-induced thymic lymphoma in mice. Mutat. Res. 358, 231-235 (1996)

6. R. E. J. Mithel, J. S. Jackson, D. P. Morrison, and S. M. Carlisle: Low doses of radiation increase the latency of spontaneous lymphomas and spinal osteosarcomas in cancer-prone, radiation-sensitive Trp53 heterozygous mice. Radiat Res.159: 320-327 (2003)

7. K. Sakai *et al.* Suppression of Carcinogenic Processes in Mice by Chronic Low Dose Rate Gamma-Irradiation, *Int. J. Low Radiat.* 1: 142 (2003)

3.6 Concerns on the health effects of low-dose ionizing radiations from naturally occurring radioactive materials (NORM)

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Abstract

It is a widely known fact that man evolved in a naturally radioactive environment. Even today life exists in an atmosphere of cosmic and terrestrial radiation. Radionuclides are found naturally in air, water and soil. They are even found in us, we being the products of our environment. Every day, we ingest and inhale radionuclides in our air and food and the water. Natural radioactivity is common in the rocks and soil that makes up our planet, in water and oceans, and in our building materials and homes. There is nowhere on earth that one cannot find natural radioactivity. Radioactive materials which occur naturally and expose people to radiation occur widely, and are known by the acronym 'NORM' (Naturally Occurring Radioactive Materials). Besides, around the globe there are some areas with an elevated background radiation. These areas include parts of Brazil, Iran, India and China. The sources of radiation in these areas include monazite containing beach sands and radium from hot springs. On the southwest coast of India, there are large deposits of thorium bearing monazite sands that contribute to an external radiation dose of about 5 - 6 mGy/yr, but in some parts doses up to 32.6 mGy/yr have been reported. Nevertheless, most general public associate ionising radiations only with the nuclear industry. Antinuclear activists often fail to accept the fact that coal-fired power stations and the oil and gas exploration operations may emit more radioactivity than an operating nuclear reactor. Another NORM issue relates to radon exposure in homes, particularly those built on granite grounds. The solid airborne Rn-222 progeny, particularly Po-218, Pb-214 and Bi-214 are of health importance because they can be inspired and retained in the lung causing cancer. Man-made operations like oil and gas production and processing operations result in technologically enhanced naturally occurring radioactive materials (TENORM) to accumulate at elevated concentrations in by-product waste streams. The concern arises because of the very large amounts of TENORM needing recycling or disposal from many sources. The largest TENORM waste stream is coal ash. In India and Australia mining of beach minerals is a profitable industry. The beach sands along the south Indian coast are rich sources of minerals such as ilmenite, rutile, zircon, silimanite and garnet. The tailings obtained after the extraction of the above minerals get enriched with monazite, a thorium bearing mineral that is radioactive. Recent studies show that the activities in the tailings are somewhat more than the natural background levels in some parts of south India. Studies on health effects (cancer) from doses arising from these levels of natural radiation exposure are contradictory, some reporting adverse effects, others null and a few others beneficial hormetic effects. Systematic and large-scale epidemiological studies and laboratory investigations are called for in order to resolve this issue. Concerns on biological effects of radiations from NORM are growing and efforts are on to implement radiation protection standards in TENORM industries in the same way as in the nuclear industry.

Introduction

Radiation is ubiquitous. It is naturally present in our environment and has been since the birth of this planet. In fact life has evolved in an environment which had significant levels of ionizing radiation. It comes from outer space (cosmic), the ground (terrestrial), and even from within our own bodies. It is present in the air we breathe, the food we eat, the water we drink, and in the construction materials used to build our homes. Foodstuffs like bananas and ice-creams contain significant amounts of radioactive potassium.

The major radionuclides contributing to NORM are uranium, thorium, and potassium. These radioactive elements are found in granite, sandstone, cement, limestone concrete, sandstone

concrete, dry wallboard, and gypsum by-product. Another source of radiation exposure in dwelling places is radon gas, which may be present in the soil beneath the dwelling. This gas can diffuse into a building and together with its radioactive decay products (polonium-214 and polonium-218), cause large radiation doses to the lungs of the occupants. This is especially true in closed or poorly ventilated indoor areas. Radon has been identified by the EPA as the second leading cause of lung cancer. (1) Radon in domestic water supplies can be released into the air within a home. Water obtained from wells and other groundwater sources can contain high radon concentrations. Besides, due to the presence of large deposits of thorium bearing sands, people residing in some parts of India, Brazil and China are exposed to more natural radiation than those living in other parts of the globe. Improper ventilation in homes and mines and more recently the radioactive mineral content in tailings of beach sand mining has raised concerns on elevating natural background radiation levels.

Technologically Enhanced naturally Occurring Radioactive Materials (TENORM)

Uranium-238, radium-226, and other members of the uranium decay series are present in varying amounts in nearly all rocks, soils, and water. Sometimes human activities, such as mining and milling of ores, extraction of petroleum and natural gas resources, use of groundwater for domestic purposes may alter the natural background radiation environment, either by moving NORMs from inaccessible locations to places where humans are present or by concentrating them. Situations due to anthropogenic activities causing an enhancement of NORM result in TENORM.

Mining and processing of phosphate for fertilizer is another major source of TENORM. The currently used process generates large piles of phosphogypsum, in which naturally occurring radium is concentrated. NORM is also technologically enhanced in the course of producing and processing oil and gas. Although in the early '70s there were concerns about radioactive material associated with oil and gas operations, a series of investigations resulted in a conclusion that radioactivity was not a serious health threat thus, any concern about it dissipated until the 1980s. In the early 1980s, it was discovered that large production facilities in the North Sea were generating concentrated quantities of NORM wastes that required special management techniques. In 1986, NORM was identified in tubing in a Mississippi well by Chevron during routine maintanance (2). Ra-226, an alpha emitter, is a potential internal hazard to workers from the inhalation and ingestion of the dust produced during descaling or pipe cleaning operations. The largest TENORM waste stream is coal ash, with 280 million tonnes arising globally each year, and carrying uranium-238 and all its non-gaseous decay products, as well as thorium-232 and its progeny. Most coal contains uranium and thorium, as well as potassium-40, lead-210, and radium-226.

Radon exposures from NORM also include visit to caves and spas. In a recent study, the annual exposure of cave tour guides was estimated to fall between 3 and 10 mSv, which is the range of action levels recommended by the ICRP (3).

In India and Australia mining of beach minerals is a profitable industry. The south Indian coast beach sands are rich sources of minerals such as ilmenite, rutile, zircon, silimanite and garnet. The tailing obtained after the extraction of the above minerals get enriched with monozite, a thorium bearing mineral that is radioactive. Recent studies show that the activities in the tailings are somewhat more than the natural background levels (4).

Regulations and Regulatory Issues:

Due to strict measures, radiation exposures to workers are stringently measured and kept far below the permissible limits in the nuclear industry. However, as a result of TENORM industries and certain tourism related activities a new group of radiation workers in the non-nuclear industry now emerge. These include maintenance workers in the oil and gas industry, miners, cave tour guides and spa workers. Americans living near coal-fired power plants are exposed to higher radiation doses, particularly bone doses, than those living near nuclear power plants that meet government regulations (5). The Marina 11 study revealed that as a result of the activities discharged and the higher biological effectiveness of alpha radiation, phosphate and oil production currently are the major

contributors to collective dose to the population of the European Union from industrial activities (6). Nevertheless, in many European countries double standards operate for radiation doses emitted from non-nuclear operations compared to those from nuclear industries. In these countries 0.3 to 1.0 mSv/yr individual dose constraint is applied to oil and gas recyclables, and 0.01 mSv/yr for release of materials with the same kind of radiation from the nuclear industry. Decommissioning experts are increasingly concerned about these double standards (7).

It is now being strongly felt among radiation protectionists that radionuclides must be regulated in a uniform and consistent manner on the basis of the following:

· "If a radionuclide is a hazard at a given concentration, it is a hazard regardless of the regulatory environment;
· If an atom of uranium poses a hazard at a licensed site, then the atom of uranium poses the same hazard at an alumina or rare earth production site"(8).

Following radiation measurements in TENORM industries, radiation protection agencies worldwide are now implementing similar guidelines to workers in the TENORM industries . Table 1 is an example of the type of control measures proposed to be implemented in the European Union.

Table 1. Control Bands for Radiation Protection (9)

Control Band	Level of Control	Effective Dose	
		Normal	Unlikely
1	No regulations	<1 mSv/y	< 6 mSv/y
2	Lower level regulation	1 mSv/y	6 mSv/y
3	Higher level regulation	6 mSv/y	20 mSv/y-50mSv/y
4	Process not permitted unless dose can be reduced	> 20 mSv/y	> 50 mSv/y

In India, the Atomic Energy Regulatory Board's (AERB) recommendations are based on ICRP for both occupational and public exposure categories. A stringent watch is also maintained on the beach sand mineral industry and control bands are currently being worked out.

Health effects of low-dose ionising radiations

A typical breakdown between natural background radiation and artificial sources of radiation is shown in the pie chart below. It shows natural radiation contributes about 82% of the annual dose to the population while medical procedures contribute most of the remaining 18%. Both natural and artificial radiations affect us in the same way.

Although mutations are the basis for cancer initiation, the association between radiation exposure and the development of cancer has been well established only with high dose exposures (> 0.5 Gy). Cancers associated with such high dose exposure include leukemia, breast, bladder, colon, liver, lung, esophagus, ovarian, multiple myeloma, and stomach cancers (10). Reports on the health effects of low dose ionising radiations are contradictory. The EPA has identified radon as the major cause of lung cancer among non-smokers and based on current exposure and risk estimates, radon exposure in single-family houses may be a cause of as many as 20,000 lung cancer fatalities each year (1). Besides, a dose-response relationship between chromosome aberrations and increased levels of radon has been reported among miners (11). Although the presence of chromosomal aberrations is a

biomarker of effect, the potential range of chemicals which could cause this effect is so great that it would not necessarily be considered radon-specific.

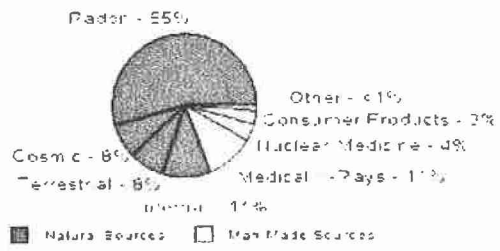

Fig.1. Sources of Radiation Exposures (NCRP 93)

For low levels of radiation exposure, the biological effects are so small they may not be detected. The body has repair mechanisms against damage induced by radiation as well as by chemical carcinogens. Consequently, injured or damaged cells can repair themselves, resulting in no residual damage, some may die, much like millions of body cells do every day, being replaced through normal biological processes. Sometimes, cells incorrectly repair themselves resulting in mutations.

Extensive studies have been undertaken on populations residing in areas with high natural background radiation and among nuclear employees. While there are a few reports that relate cancer incidence and mortality to background radiation and occupational exposures (12, 13), most surveys have frequently indicated decreased rates in cancer mortality (14,15,16,17). Others show no adverse biological effects (18,19).

Reports from our laboratory (20,21) and elsewhere (22,23,24) show that DNA repair capacities are enhanced when human lymphocytes are exposed to low doses of gamma radiations and this phenomenon popularly termed as radio adaptive response (RAR) is though to occur via error-free repair mechanism. However, compared to gamma rays, the penetrating power of alpha particles is low and if alpha emitters are inhaled, ingested or absorbed into the blood stream, sensitive living tissue can be exposed to alpha radiation. Also, due to the high linear energy transfer (LET), alpha radiation may have a adverse biological effect at low doses.

Taking into considerations these controversies, the radiation protection community conservatively assumes that any amount of radiation may pose some risk for causing cancer and hereditary effect, and that the risk is higher for higher radiation exposures. A linear, no-threshold (LNT) dose response relationship is used to describe the relationship between radiation dose and the occurrence of cancer. This dose-response model suggests that any increase in dose, no matter how small, results in an incremental increase in risk. However, contenders to the LNT hypothesis are those supporting hormesis and adaptive responses on one hand and those who support an inverse dose/rate effect claiming disproportionately higher risks at lower doses on the other (Fig 2).

The studies conducted so far on the Indian population residing in HNBRA for over 1000 years indicate that high level natural radiation has no discernible impact on the health of population and in fact may provide valuable input to understand the biological mechanism of response to radiation at low dose rates. Cytogenetic studies were done using cord blood samples from nearly 23,000 newborns. Rate of constitutional anomaly was around 0.5% which is comparable to the international value. Cytogenetic preparations from over 10,000 children were also screened for detection of chromosomal aberration. Frequency of aberration was 1.87/10,000 cells for dicentrics, 3.42/10,000 cells

for stable aberrations and 7.72/10,000 cells for total chromosomal type aberrations (25). These figures are comparable to those in published literature from other parts of the world.

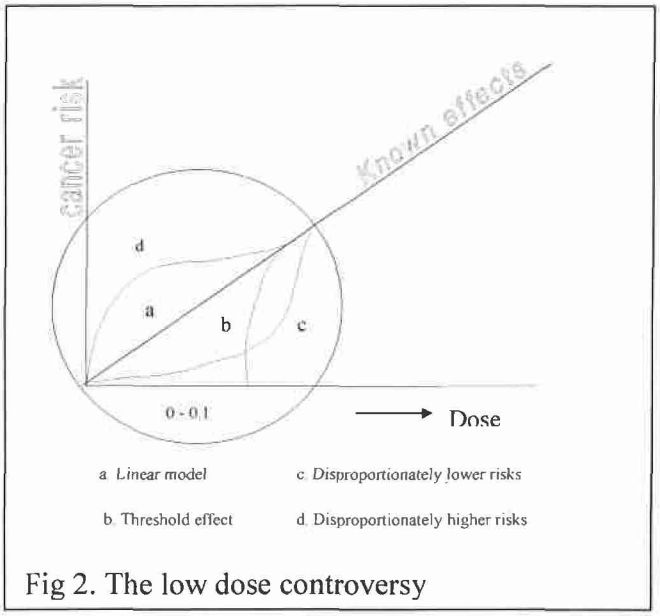

Fig 2. The low dose controversy

In summary, none of these approaches has provided unambiguous evidence of cancer induction at low dose levels, and the issue remains highly controversial. Moreover, the complexity of the biological effects induced by alpha emitting radionuclides poses a problem in estimating risks due to low dose radiation.

Long-term systematic studies on occupationally exposed personnel and epidemiological surveys of areas with high natural background radiation together with laboratory investigations are therefore required before meaningful conclusions could be drawn and influence current radiation protection standards. The existence of inter-individual differences in radiation sensitivity governed by genetic factors making some individuals more sensitive to radiation-induced damage remains a confounding factor in relaxing radiation protection norms (26). Although it may be not too early to accept the beneficial or null biological effects of low doses of ionising radiation, it is certainly so to set standards and threshold doses for purposes of cancer risk estimates and radiation protection.
If low levels of radiation turn out to have a threshold below where there really is no risk to speak of, then laws may be loosened. However, if low levels of radiation actually are proven to be carcinogenic, or have mutagenic, teratogenic, or some other detrimental effects, then current regulatory efforts may fall short of protecting the public and workers. Until then it may be prudent to follow the LNT model for purposes of radiation protection for those engaged in both nuclear and non-nuclear industries.

Regarding NORM and TENORM we are in the enviable position, given that a potential health concern is being identified ahead of any visible problem among workers. By recognizing a potential problem, it is now possible for industries with some level of risk to protect their workers using fairly simple, low-cost methods.

References:

1. Environmental Protection Agency. Technical support document for the 1992 citizen's guide to radon. EPA publication 400-R-92-011. Washington, D.C (1992).
2. Bulletin on Management of Naturally Occurring Radioactive Material (NORM) in Oil and Gas Production," *American Petroleum Inst. Bull.* E2, 1st ed., Apr. 1992
3. Papachristodoulou C.A., Ioannides K.G., Stamoulis KC., Patiris D.L., Pavlides SB. Radon activity levels and effective doses in the Perama Cave, Greece. Health Phys. (2004) 86:619-624.

4. Suresh K., Ajoy K.C., Dhanasekaran A., Bala-Sundar S., Santhanam R., Gajendiran. V., Meenakshisundaram V. Investigation of radiation levels in beach sand mineral industries – A preliminary study. Radiation Protection and Environment (2003) 26: 478 – 481.
5. McBride J. P., Moore R. E., Witherspoon J. P., Blanco R. E. Radiological impact of airborne effluents of coal and nuclear plants. Science (1978) 202:1045.
6. Pilot Study for the update of the MARINA Project on the radiological exposure of the European Community from radioactivity in North European marine waters. Final Report: December 1999, (http://www.europa.eu.int/comm/energy/nuclear/radioprotection/doc/studies/rp132/marina_en.pdf)
7. Nucleonics Week 43 (17) April 25, 2002.
8. Scott L.M. NORM in the Non-Nuclear Industries in the USA, in: Proceedings of NORM-II Second International Symposium, November 10-13, 1998, Krefeld, Germany, paper V/4, pp.163-167.
9. Simmons 2000. NORM in Europe - A Regulation Perspective. Charles Simmons. The NORM Report Fall99/Winter 00. Peter Gray, Editor. Fort Smith, AK.
10. UNSCEAR (1994). Sources and effects of ionising radiation, United nations report to the general assembly with scientific annexes.
11. Smerhovsky Z., Landa K., Rossner P., Juzova D., Brabec M., Zudova Z., Hola N., Zarska H., Nevsimalova E. Increased risk of cancer in radon-exposed miners with elevated frequency of chromosomal aberrations. Mutat Res. (2002) 514:165-176.
12. Baum J.W Population heterogeneity hypothesis on radiation induced cancer. Health Phys. (1973) 25:97-104.
13. Kneale, G. W., Stewart A., Mancuso T. F (1978). Reanalysis of Data relating to the Hanford study of the cancer risks of radiation workers. Proceedings of the international symposium on the late effects of ionising radiation. Vol 1. IAEA, Vienna, STI/PUB/489.
14. Frigerio N A., Showe R S (1976). Carcinogenic and genetic hazard from background radiation. In Biological and Environment Effects of Low Level Radiation, IAEA, 2, 385-393.
15. Liu S Z (1989). Radiation hormesis- A new concept in radiological science. Chinese Med. J. 1032: 750-755.
16. Wei L. (1990). Epidemiological investigations of radiological effects in high background radiation areas, Yangjiang, China. J. Radiat. Res: 119-136.
17. 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 (2000) 41 Suppl:53-62.
18. Savitz DA., Zuckerman DL. Childhood cancer in the Denver metropolitan area 1976-1983. Cancer (1987) 59:1539-1542.
19. Nambi, K.S.V and Soman, S. D (1987). Environmental radiation and cancer in India. Health Phys. 52: 653 - 658.
20. Mohankumar, M.N., Paul S.F.D., Venkatachalam P., Jeevanram R.K. Influence of in vitro low-level gamma-radiation on the UV-Induced DNA repair capacity of human lymphocytes-analysed by unscheduled DNA synthesis (UDS) and comet assay, Radiat. Environ. Biophysics (1998) 37: 267 – 275.
21. Mohankumar, M.N, Venkatachalam P., Prabhu B.K., Jeevanram R.K., Comparison of UV-induced unscheduled DNA synthesis in lymphocytes exposed to low doses of ionising radiation in vivo and in vitro, Mutation Res (2000) 447, 199-207.
22. Ikushima T., Aritomi H., Morisita J. Radioadaptive response: Efficient repair of radiation-induced DNA damage in adapted cells Mutation Res(1996) 358, 193-198.
23. Wolff S The adaptive response in radiobiology: Evolving insights and implications. Environ.Health.Perspectives (1998)106: 277-283 (suppl).
24. A. Wojick, C. Streffer. Adaptive response to ionising radiation in mammalian cells a review, Biologisches Zentralblatt (1994) 113: 417-434.

25. Cheriyan VD., Kurien CJ., Das B., Ramachandran EN., Karuppasamy CV., Thampi MV., George KP., Kesavan PC., Koya PK., Chauhan PS. Genetic monitoring of the human population from high-level natural radiation areas of Kerala on the southwest coast of India. II. Incidence of numerical and structural chromosomal aberrations in the lymphocytes of newborns. Radiat Res. (1999) 152(6 Suppl):S154-158.
26. Mohankumar MN, Prabhu B.K.,.Jeevanram R.K (2000) Adaptive response to ionizing radiation and its role in influencing radiation protection standards. Proceedings of the 10th International Congress of Radiation Protection (IRPA 10), Japan P-2b-74.

3.7 Ramsar Hot Springs: How Safe is to Live in an Environment with High Level of Natural Radiation

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Abstract

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 geology, 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}. As the biological effects of low doses of radiation are not fully understood, the current radiation protection recommendations are based on the predictions of an assumption on the linear, no-threshold (LNT) relationship between radiation dose and the carcinogenic effects. Considering LNT, areas having such levels of natural radiation must be evacuated or at least require immediate remedial actions. Inhabitants of the high level natural radiation areas (HLNRAs) of Ramsar are largely unaware of natural radiation, radon, or its possible health effects, and the inhabitants have not encountered any harmful effects due to living in their paternal houses. In this regard, it is often difficult to ask the inhabitants of HLNRAs of Ramsar to carry out remedial actions. Despite the fact that considering LNT and ALARA, public health in HLNRAs like Ramsar is best served by relocating the inhabitants, the residents' health seems unaffected and relocation is upsetting to the residents. Based on the findings obtained by studies on the health effect of high levels of natural radiation in Ramsar, as well as other HLNRAs, no consistent detrimental effect has been detected so far. However, more research is needed to clarify if the regulatory authorities should set limiting regulations to protect the inhabitants against elevated levels of natural radiation.

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1. Introduction

Humans, animals and plants have been exposed to cosmic radiation since the beginning of life. The level of cosmic radiation varies in different parts of the world due to differences in elevation and the geomagnetic latitude, and of terrestrial radiation due to geochemical diversity. About 4 billion years ago, when the living organisms appeared on the Earth, the level of natural radiation was about 3-5 times higher than its current level (Jaworowski 1997, Karam 1999, Karam 2001). The annual level of radiation from internal potassium-40 has decreased to 1/8 while the external radiation from geologic materials has decreased from about 1.6 mGy to 0.66 mGy since the beginning of life. Thus, the annual background radiation exposure from these two sources has decreased from about 7.0 to 1.35 mGy (Karam and Leslie 1999). The annual per caput effective dose 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 (UNSCEAR 2000). People who live in high-altitude areas such as Tibet in China, Andes in South America, or cities like Denver, Colorado, are exposed to higher levels of cosmic radiation due to a thinner atmosphere than people living in areas at sea level. Also astronauts, pilots and cabin crew are exposed to higher than normal levels of cosmic radiation. The study of these population groups may reveal information on adaptive responses (AR) induced by exposure to higher than normal levels of natural radiation.

When living organisms are exposed to a variety of DNA damaging stresses such as UV, alkylating or oxidizing agents and heat, adaptive responses (AR) are induced which cause resistance to the agent (Samson and Cairns 1977). The early investigations of Olivieri and his colleagues (1984) showed that cultured human lymphocytes, which were exposed to a low dose of ionizing radiation had fewer chromatid aberrations induced by a subsequent high dose as compared to the lymphocytes that have not been exposed to a low dose. Since 1984, many investigators have demonstrated AR in plant cells (Cortes et al. 1990), insects (Fritz-Niggli and Schaeppi-Buechi 1991), Chinese hamster V79 cells (Ikushima 1987), cultured human lymphocytes (Wiencke et al. 1986, Shadley and Wolff 1987, Wolff et al. 1988, Shadley and Wiencke 1989, Sankaranarayanan et al. 1989), human embryonic and HeLa cells (Ishii and Watanabe 1996), occupationally exposed persons (Barquinero et al. 1995, Gourabi and Mozdarani 1998), cultured animal lymphocytes (Flores et al. 1996), and *in vivo* studies on laboratory animals (Wojcik and Tuschl 1990, Cai and Liu 1990, Liu et al. 1992, Farooqi and Kesavan 1993). Mortazavi et al. (2003c) have recently reported that the inter-individual variability of adaptive response in humans is much greater than what is usually expected. Recent data on different aspects of adaptive response, obligate us to reevaluate the current conservative radiation protection regulations (Pollycove and Feinendegen 2001, Mortazavi et al. 2002, Mortazavi 2002). In this paper, studies on adaptive responses related to natural radiation levels are shortly reviewed.

2. Adaptation after Exposure to Cosmic and Terrestrial Radiation

2.1. Underground Studies

Early experiments carried out on single cell organisms shielded against background radiation showed that at the levels of natural radiation lower than normal, the proliferation of these organisms can be inhibited. Interestingly, this inhibitory effect disappeared when shielded cells were exposed to very low doses of gamma radiation

close to background levels (Planel et al. 1987). Later it was shown that yeast cells cultured in a low background environment were less protected from mutational damage induced by methyl methane sulfonate than the cells grown in a normal background radiation environment (Satta et al. 1995). The results of a recent study on mammalian cells showed an increase in both the basal *hprt* mutation frequency and sensitivity to the mutagenic effects of gamma rays in cells grown in an underground laboratory, compared to the cells grown in a laboratory with natural radiation environment (Satta et al. 2002).

2.2. High Altitude Areas

The people who live in Tibet, "the roof of the world", are exposed to high levels of cosmic radiation. At the mean elevation of about 4000 meters above the sea level, the atmosphere is less thick, and the residents are exposed to external annual radiation doses up to 2.12 mSv (Shouzhi 2000). This dose is 3.5 times higher than that at the sea level. Recently the Glycophorin A-based somatic mutation assay was carried out on the residents of high-altitude areas and on those who lived at low-altitude. The life time cumulative doses for the high-altitude and low-altitude areas were 111 mSv and 27 mSv respectively. This study showed no significant difference between the Glycophorin A-based somatic mutation frequencies in these two populations (Jensen et al. 1997). An epidemiological study on mortality due to cancer (Xin 1983) showed that the standardized mortality of cancer (56.26×10^{-5}) in the high-altitude area of Tibet was lower than those of the whole country (66.92×10^{-5}). The mean annual dose equivalent for high altitude area was 1.8 mSv that is a few times higher than that of areas at sea level. The mortality from leukemia in the high-altitude area was lower than those of the whole country either.

In an old paper, Frigerio and Stowe (1976) reported that in the United States they found a consistent and continuous inverse relationship between levels of natural background radiation and cancer mortality-rates in 50 states. Again in the Unites States a negative correlation of normal background radiation with overall cancer death was observed in a more recent study. In Rocky Mountain States, where the level of natural radiation is 3.2 times higher than that in Gulf States, the age adjusted overall cancer death was 79% of that in Gulf States (Jagger 1998).

2.3. Flights and Space Journeys

Zwingmann *et al.* (1998) recently measured the DNA damages in 23 flight engineers. Despite that oxidative DNA damage in flight engineers was higher than the control ground personnel, it was observed that DNA damage in flight engineers who had a relatively longer flight time (>7,500 hr) and a higher cumulative radiation dose (53.6 mSv) was less than that of the flight engineers with a shorter flight history (<7,500 hr) and a lower cumulative radiation dose (30.7 mSv). They also observed that frequencies of hprt mutations and micronuclei also tend to be higher in flight engineers with a shorter flight history. These findings are in keeping with the results of another study that was performed on flight crew using the chromosomal aberrations as the end point (Zwingmann *et al.* 1998). It was indicated that pilots and stewardesses with a flight history of only 1-6 years had more chromosome aberrations compared to crew with more than 20 years of intercontinental flights. The frequency of chromosome aberrations in the pilots and stewardesses who were exposed to cosmic radiation for a long-term, i.e.

more than 20 years of intercontinental flights, and those who had been flying only 1-6 years were 1.4×10^{-3} and 3.2×10^{-3}, respectively.

In a recent study on the frequency of chromosome aberrations in eighteen supersonic Concorde pilots (Heimers 2000), it was indicated that the dicentric yield in pilots who were employed over 28 years was about 50% of that observed in pilots with 16-26 years of occupation ($1.3\pm0.5 \times 10^{-3}$ and $2.9\pm0.5 \times 10^{-3}$ respectively). Also the frequency of cells with translocations in pilots with 28-34 years of flight occupation was 78% of that in pilots with 16-26 years of flight occupation ($2.8\pm0.7 \times 10^{-3}$ and $3.6\pm0.6 \times 10^{-3}$ respectively). Despite the fact that there are statistical uncertainties in these data, this kind of adaptive response has been well documented in eukaryotes such as yeast. Deorukhakar and Rao (1995) investigated the radiation induced genetic damage in yeast by culturing the cells continuously at a radiation level of 0.383 – 1.275 $\mu Sv\ h^{-1}$ by selecting appropriate concentrations of tritiated water in the growth medium. It was shown that cells which were incubated at higher radiation levels and for longer duration had a higher conversion frequency. However, when subculturing continued beyond 900h, the gene conversion frequency reverted back to normal value. Such a response could not be detected when the cells were exposed to an acute high dose. The authors concluded that chronic exposure of yeast to low dose radiation might induce an AR.

In a recent study on 6061 male cockpit personnel which yielded 105,037 person-years of observation it was shown that cockpit crew had a low overall and cancer mortality (Zeeb et al. 2002). This result is consistent with the results obtained from previous studies on Canadian (Band et al. 1996) and British Air Ways pilots (Irwin et al. 1999). That this is not a healthy worker effect, suggests mortality from all cancers, which in cabin crew who received 5-14.99 mSv cumulative radiation dose, was lower than in those who received either 0-4.99 or 15-29.99 mSv (Zeeb et al. 2002).

Results of a cytogenetic study on 22 cosmonauts who stayed on average 4-6 months in MIR station shows that the after mission percentage of chromosomal aberrations in 6 cosmonauts is less than that of the scored frequency before the mission (Fedorenko et al. 2001). Also the after mission frequency of the cells with dicentrics and centric rings in four cosmonauts was less than that of before mission. Interestingly, in one case, the after mission frequency of chromosomal aberrations was about 1/3 of the before mission value.

2.4. Very High Levels of Natural Terrestrial Radiation

People in some areas around the world live in dwellings with radiation and radon levels as much as 100 times the global average. Inhabited areas with high levels of natural radiation are found in different areas around the world including Yangjiang, China; Kerala, India; Guarapari, Brazil and Ramsar, Iran. (Figure. 1).

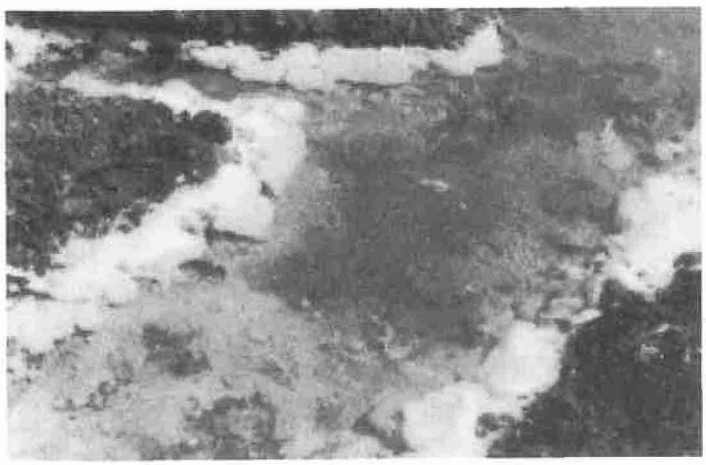

Figure 1. Ramsar hot springs. White-colored sediments at the streams' bed have high concentrations of Radium-226. In some cases, residents of these hot areas have used the residue of the hot springs as building materials to construct their houses.

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.

Biological Findings on HLNRAs of Ramsar

- **Chromosome Aberrations**. Preliminary results showed no significant difference even in the case of the inhabitants who lived in houses with extraordinarily elevated levels of natural radiation.
- **Dose-Effect Relationship**. There is a great controversy about the dose-effect relationship in published reports on the frequency of chromosome aberrations induced by chronic exposure to elevated environmental levels of radiation. This controversy exists in studies of residents in areas with elevated levels of natural radiation as well as the residents of areas contaminated by nuclear accidents. Using chromosomal aberrations as the main endpoint, an experiment to assess the dose-effect relationship in the residents of high level natural radiation areas of Ramsar was carried out. A cytogenetical study was performed on 21 healthy inhabitants of the high level natural radiation areas and 14 residents of a nearby control area. Preliminary results showed no positive correlation between the frequency of chromosome aberrations and the cumulative dose of the inhabitants.
- **Hematological Alterations.** It has been reported that in mice and rats total body exposure to moderate doses decreases the number of circulating erythrocytes, platelets, granulocytes, lymphocytes etc. However, data on hematopoieses as a result of exposure to very low doses of ionizing radiation are scarce. Hematological parameters such as counts of leukocytes (WBC), lymphocytes, monocytes, granulocytes, red blood cells (RBC), hemoglobin (Hb), hematocrit (Ht), MCV, MCH, MCHC, RDW, PLT, and MPV were studied in all of the individuals. The results of this study indicated that there was no any statistically

significant alteration in hematological parameters of the inhabitants of HLNRAs of Ramsar compared to those of the neighboring control area.

- **Immunological Changes.** It is well known that high doses of ionizing radiation suppress the activity of the immune system. On the other hand, the low-level whole body irradiation (WBI) can enhance the immunological response. To assess whether relatively high doses of natural radiation can alter humoral immune parameters, an experiment was conducted on the inhabitants of HLNRAs of Ramsar, permanently living in houses with elevated levels of natural radiation. Immunological factors such as the concentration of serum immunoglobulins of IgA, IgG, IgM and C3, C4 components of the complement system in healthy donors from HLNRAs and a neighboring NBRA were studied. Preliminary findings indicate that there is a slight increase in IgA and IgG levels of the inhabitants of HLNRAs compared to those of matched controls. IgM, C3, and C4 complements were in the normal range. In spite of the fact that the increase in IgA and IgG were not so marked to show probable enhanced immunological capability, it can be concluded that relatively high doses of natural radiation are not immunosuppressive. More research is needed to clarify the immunological alterations induced by different levels of natural radiation.
- **Radioadaptive Response** It has been shown that in high level natural radiation areas (HLNRAs) of Ramsar, the blood cells of inhabitants whose cumulative radiation doses were 170 times higher than of those living in a nearby control area (2,550 mSv and 15 mSv respectively) were significantly more radioresistant to chromosomal damage when subjected to 1.5 Gy challenge dose (Ghiassi-nejad et al. 2002, Mortazavi et al. 2002, Mortazavi 2002). The relationship between the degree of AR (as indicated by the k-value[2]) and cumulative lifetime dose is an important finding. The AR of the residents of Iranian HLNRAs is more pronounced at higher cumulative doses, except for 2 residents, whose cumulative doses are much higher than those of the others (Mortazavi et al. 2002).

The results of the adaptive responses observed in the residents of high level natural radiation areas of Ramsar are summarized here:

- Individuals whose cumulative radiation doses were up to 950 mGy, showed a significant AR after exposure of their cultured lymphocytes to 1.5 Gy gamma radiation . These doses are much higher than those received by astronauts during a six-month space mission that has been reported to be 90 mGy absorbed dose and 180 mSv equivalent dose. The radiation dose of these astronauts ranged 95-455 mGy (Testard et al. 1996).

[2] The k-value is the coefficient of induced adaptive response (k) that shows the magnitude of the adaptive response and can be calculated as the ratio of the observed frequency to the expected frequency of chromosome aberrations.

- There is a controversy over the induction of AR in resting cells (Cai and Liu 1990, Shadley et al. 1987, Azzam et al. 1992). Ramsar results showed that high levels of natural radiation might enhance radiation-resistance in non-cycling lymphocytes. Since the majority of the lymphocytes in the body are in the resting phase of the cell cycle (G_0), any implication of AR strongly depends on the possibility of induction of AR in G_0 stage.
- ARs have been usually observed in experiments by exposing the cells to a low dose radiation in the range of 10-100 mGy. These doses are considerably lower than the lifetime doses that induced AR in the inhabitants of HLNRAs of Ramsar.
- It was suggested that aging could cancel the AR (Gadhia 1998). This is contrary to findings in Ramsar population which show that aging does not influence the induction of AR.

The cumulative doses and the magnitudes of the induced adaptive response in cultured lymphocytes of residents of Ramsar HLNRAs are shown in Figure 2.

2.5. Potential Implications of Radioadaptation in Radiation Protection

It was generally believed that the presence of AR does not mean that the low dose radiation is beneficial to living organisms (Sagan 1989, Wolff 1989). Even in its 1994 report on adaptive responses to radiation in cells and organisms (UNSCEAR 1994), after reviewing experimental and epidemiological studies showing increased longevity and lower-than-expected incidence of tumors, UNSCEAR stated that "it would be premature to conclude that cellular adaptive response could convey possible beneficial effects to the organism that would outweigh the detrimental effects of exposure to low doses of low-LET radiation". However, more recent worldwide studies on the different aspects of AR, have lead to recognition of its positive health effects, and to a more realistic assessment of the risk of radiation. The preliminary studies of the Ramsar residents (Mortazavi et al. 2001), suggest that the induced AR might have considerable implications for radiation protection, and that the chronic low dose radiation may be protective against accidental high dose radiation (Pollycove and Feinendegen 2001).

2.6. Radioadaptation and Deep Space Manned Missions

Based on Ramsar findings, it has been recently reported that adaptive response studies may have implications in radiation protection. It was proposed that individuals who failed to show an adaptive response would not be good candidates for space travel (Mortazavi et al. 2003a, Mortazavi et al. 2003b). These authors suggested that all potential crew members for a deep space mission had their adaptive response measured. The space crew should show a high magnitude of adaptive response. The chronic exposure to elevated levels of space radiation during a long-term mission can considerably decrease their radiation susceptibility and protect them against the unpredictable exposure to sudden and dramatic increase in flux due to solar flares and coronal mass ejections.

References

Azzam E.I., S.M. de Toledo, G.P. Raaphorst and R.E.J. Mitchel. Radiation-induced radioresistance in a normal human skin fibroblast cell line, In Low Dose Irradiation and Biological Defense Mechanisms (T. Sugahara, L.A. Sagan and T. Aoyama, Eds), pp. 291-294, Amsterdam: Excerpta Medica, 1992.

Band PR, Le ND, Fang R, Deschamps M, Coldman AJ, Gallagher RP, Moody J. Cohort study of Air Canada pilots: mortality, cancer incidence, and leukemia risk. Am J Epidemiol, 143(2):137-43,1996.

Barquinero J.F., L. Barrios, M.R. Caballin, R. Miro, M. Ribas, A. Subias and J. Egozcue, Occupational exposure to radiation induces an adaptive response in human lymphocytes., Int. J. Radiat. Biol. 67, 187-91 (1995).

Cai L. and S.Z. Liu, Induction of cytogenetic adaptive response of somatic and germ cells *in vivo* and *in vitro* by low dose X-irradiation. Int. J. Radiat. Biol. 58, 187-194 (1990).

Cortes F., I. Dominguez, S. Mateos, J. Pinero and JC. Mateos, Evidence for an adaptive response to radiation damage in plant cells conditioned with X-rays or incorporated tritium. Int J Radiat Biol, 57, 537-41 (1990).

Deorukhakar V.V. and B.S. Rao, Induction of gene conversion in yeast cells continuously cultured at high radiation background. Radiat Environ Biophys. 34, 185-90 (1995).

Farooqi Z.and PC. Kesavan, Low-dose radiation-induced adaptive response in bone marrow cells of mice. Mutat. Res. 302, 83-9 (1993).

Fedorenko B, Druzhinin S, Yudaeva L, Petrov V, Akatov Y, Snigiryova G, Novitskaya N, Shevchenko V, Rubanovich A. Cytogenetic studies of blood lymphocytes from cosmonauts after long-term space flights on Mir station. Adv Space Res. 27, 355-9 (2001).

Flores M.J., J. Pinero, T. Ortiz, N. Pastor, J.C. Mateos and F. Cortes, Both bovine and rabbit lymphocytes conditioned with hydrogen peroxide show an adaptive response to radiation damage. Mutat. Res. 372, 9-15 (1996).

Frigerio N.A., and Stowe R.S. Carcinogenic and Genetic Hazard from Background Radiation, in Biological and Environmental Effects of Low-Level Radiation, International Atomic Energy Agency, Vienna, Austria, pp.385-393, 1976.

Fritz-Niggli H. and C. Schaeppi-Buechi, Adaptive response to dominant lethality of mature (class A) and immature (class B) oocytes of D. melanogaster to low doses of ionizing radiation: effects in repair-proficient (yw) and repair-deficient strains (mei 41D5 and mus 302D1). Int J Radiat Biol. 59, 75-84 (1991).

Gadhia PK., Possible age-dependent adaptive response to a low dose of X-rays in human lymphocytes. Mutagenesis. 13, 151-2 (1998).

Ghiassi-nejad M, Mortazavi SMJ, Cameron JR, Niroomand-rad A and Karam PA, Very High level natural radiation areas of Ramsar, Iran: Preliminary Biological Studies. Health Physics. 82, 87-93 (2002).

Gourabi H. and H. Mozdarani, A cytokinesis-blocked micronucleus study of the radioadaptive response of lymphocytes of individuals occupationally exposed to chronic doses of radiation. Mutagenesis. 13, 475-80 (1998).

Heimers A., Chromosome aberration analysis in Concorde pilots. Mutat Res. 467, 169-76 (2000).

Ikushima T., Chromosomal responses to ionizing radiation reminiscent of an adaptive response in cultured Chinese hamster cells. Mutation Research. 180, 215-221 (1987).

Irvine D, Davies DM. British Airways flightdeck mortality study, 1950-1992. Aviat Space Environ Med. 70(6):548-55, 1999.

Ishii K.and M. Watanabe, Participation of gap-junctional cell communication on the adaptive response in human cells induced by low dose of X-rays. Int. J. Radiat. Biol. 69, 291-9 (1996).

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

Jaworowski Z., Beneficial effects of radiation and regulatory policy. Australas Phys Eng Sci Med. 20, 125-38 (1997).

Jensen R.H., Zhang S., Wang Z., Wang W.and Boice J., Glycophorin A somatic cell mutation frequencies in residents of Tibet at high altitudes. Health Phys. 73, 663-7 (1997).

Karam PA, Leslie SA. Calculations of background beta-gamma radiation dose through geologic time. Health Phys. 77(6):662-7, 1999.

Karam P. A. (2001) Changes in background cosmic radiation dose during the history of life on Earth. Ph.D. thesis, Ohio State University.

Liu S.Z., L. Cai and S.Q. Sun, Induction of a cytogenetic adaptive response by exposure of rabbits to very low dose-rate gamma-radiation. Int. J. Radiat. Biol. 62,187-90 (1992).

Mortazavi S.M.J., M. Ghiassi Nejad and M. Beitollahi. Very High level natural radiation areas (VHLNRAs) 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).

Mortazavi S.M.J., M. Ghiassi-nejad, A. Niroomand-rad, P.A. Karam and J.R. Cameron, How should governments address high levels of natural radiation and radon? Lessons from the Chernobyl nuclear accident, Risk: Health, Safety and Environment. 13, 31-36 (2002).

Mortazavi, SMJ, Karam P.A. High Levels of Natural Radiation in Ramsar, Iran: Should Regulatory Authorities Protect the Inhabitants? Iranian Journal of Science (Germany), 2 (2): 1-9, 2002.

Mortazavi, SMJ., Risk Assessment: Extraordinary Levels of Natural Radioactivity in the Environment and the Problems Associated with Induced Radioresistance, In: Proceedings of the International Conference on Radioactivity in the Environment. Borretzen P, Jolle T, and Strand P. Eds, pp. 110-113, 2002.

Mortazavi SMJ, Cameron JR, and Niroomand-rad A. Adaptive response studies may help choose astronauts for long-term space travel, Advances in Space Research, 31 (6): 1543-1552, 2003a.

Mortazavi SMJ, Cameron JR, and Niroomand-rad A. Is the Adaptive Response an Efficient Protection Against the Detrimental Effects of Space Radiation. Proceedings of the 28th International Cosmic Ray Conference, Universal Academy Press, pp 4299-4302, 2003b.

Mortazavi SMJ, Ikushima T, and Mozdarani H. Variability of chromosomal radioadaptive response in human lymphocytes. IJRR, 1(1): 55 - 61, 2003c.

Mortazavi SMJ, Ghiassi-Nejad M, Ikushima T, Assaie R, Heidary A, Varzegar R,

Zakeri F, Asghari K, and Esmaili A. Are the Inhabitants of High level natural radiation areas of Ramsar More Radioresistant? Scope of the Problem and the Need for Future Studies. Iranian Journal of Radiology, 1(1), 37-43, 2003d.

Olivieri G., Bodycote J. and Wolff S., Adaptive response of human lymphocytes to low concentrations of radioactive thymidine, Science, 223, 594-597 (1984).

Planel H, Soleilhavoup JP, Tixador R, Richoilley G, Conter A, Croute F, Caratero C, Gaubin Y. Influence on cell proliferation of background radiation or exposure to very low, chronic gamma radiation. Health Phys.;52(5):571-8, 1987.

Pollycove M. and LE. Feinendegen. The Journal of Nuclear Medicine. 42, 26N-37N (2001).

Sagan LA., On radiation, paradigms, and hormesis. Science. 245, 574, 621 (1989).

Samson L. and J. Cairns, A new pathway for DNA repair in *Escherichia coli*. Nature. 267, 281-282 (1977).

Sankaranarayanan K., A. Von Duyn, M. Loos and A.T. Natarjan, Adaptive response of human lymphocytes to low level radiation from radioisotopes or X-rays. Mutat. Res. 211, 7-12 (1989).

Satta L, Augusti-Tocco G, Ceccarelli R, Esposito A, Fiore M, Paggi P, Poggesi I, Ricordy R, Scarsella G, Cundari E. Low environmental radiation background impairs biological defence of the yeast Saccharomyces cerevisiae to chemical radiomimetic agents. Mutat Res. 347(3-4):129-33, 1995.

Satta L, Antonelli F, Belli M, Sapora O, Simone G, Sorrentino E, Tabocchini MA, Amicarelli F, Ara C, Ceru MP, Colafarina S, Conti Devirgiliis L, De Marco A, Balata M, Falgiani A, Nisi S. Influence of a low background radiation environment on biochemical and biological responses in V79 cells. Radiat Environ Biophys. 41(3):217-24, 2002.

Shadley J.D. and S. Wolff, Very low doses of X-rays can cause human lymphocytes to become less susceptible to ionizing radiation, 2, 95-96 (1987).

Shadley J.D. and J.K. Wiencke, Induction of the adaptive response by X-rays is dependent on radiation intensity. Int. J. Radiat. Biol. 56, 107-118 (1989).

Shadley J.D., V. Afzal and S. Wolff. Characterization of the adaptive response to ionizing radiation induced by low doses of X rays to human lymphocytes. Radiat Res. 111, 511-7 (1987).

Shouzhi Z., Current status of space radiation research in China, In Exploring Future Research Strategies in Space Radiation Science, (H.J. Majima and K. Fujitaka, Eds), pp. 99-103, Tokyo: Iryokagakusha, 2000.

Testard I., M. Ricoul, F. Hoffschir, A. Flury-Herard, B. Dutrillaux, B. Fedorenko, V. Gerasimenko and L Sabatier, Radiation-induced chromosome damage in astronauts' lymphocytes. Int J Radiat Biol. 70, 403-11 (1996).

UNSCEAR, Sorces and Effects of Ionizing Radiation, Report to the General Assembly, United Nations Scientific Committee on the Effects of Atomic Radiation, United Nations, New York, NY, 1994.

UNSCEAR, Sources and Effects of Ionizing Radiation, Report to the General Assembly, United Nations Scientific Committee on the Effects of Atomic Radiation, United Nations, New York, NY, 2000.

Wiencke J.K., V. Afzal, G. Olivieri and S. Wolff, Evidence that the [3H] thymidine induced adaptive response of human lymphocytes to subsequent doses of X-rays

involves the induction of chromosomal repair mechanism. Mutagenesis. 1, 375-380 (1986).

Wojcik A. and H. Tuschl, Indications of an adaptive response in C57BL mice pre-exposed *in vivo* to low doses of ionizing radiation. Mutat. Res. 243, 67-73 (1990).

Wolff S., Are radiation-induced effects hormetic? Science. 245, 575, 621 (1989).

Wolff S., Afzal V., J.K. Wiencke and G. Olivieri, Human lymphocytes exposed to low doses of ionizing radiation become refractory to high doses of radiation as well as to chemical mutagens that induce double strand breaks in DNA. Int. J. Radiat. Biol. 53, 39-48 (1988).

Xin X.F., Cosmic radiation levels and the status of mortality from malignant tumors in Tibet. Chin. J. Radiat. Med. Prot. 3, 1-31, (1983).

Zeeb H, Blettner M, Hammer GP, Langner I. Cohort mortality study of German cockpit crew, 1960-1997. Epidemiology, 13(6):693-9, 2002.

Zwingmann I.H., I.J. Welle, van M. Herwijnen, J.J. Engelen, P.A. Schilderman, T. Smid and J.C. Kleinjans, Oxidative DNA damage and cytogenetic effects in flight engineers exposed to cosmic radiation. Environ Mol Mutagen. 32, 121-9 (1998).