# What is the Appropriate Radiation Level for Evacuations?

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## Abstract

This commentary reviews the international radiation protection policy that resulted in the evacuation of more than 90,000 residents from areas near the Fukushima Daiichi NPS and the enormous expenditures to protect them against a hypothetical risk of cancer. The basis for the precautionary measures is shown to be invalid; the radiation level chosen for evacuation is not conservative. The actions caused unnecessary fear and suffering. An appropriate level for evacuation is recommended. Radical changes to the ICRP recommendations are long overdue.

## Commentary

It is very upsetting to read about the on-going fear and hardship suffered by the more than 90,000 residents, who were evacuated from areas surrounding the Fukushima Daiichi Nuclear Power Station (NPS) in Japan, and the enormous economic penalty, including the $55 billion increase in the cost of fossil fuel imports in 2011, due to the shutdown of almost all of the other NPSs (WNA 2012). As of December 1, more than 230,000 people have been screened with radiation meters (IAEA 2011). The "deliberate evacuation area" was based on a projected radiation dose of 20 milliSievert (mSv) per year (METI 2011a, IAEA 2012). The goal aims to keep additional radiation exposure below 1 mSv annually, particularly for children (METI 2011a, 2011b). And a plan for assistance to the residents affected has been developed (METI 2011b).

Japan is complying with international radiation protection recommendations that are based on the International Commission on Radiological Protection (ICRP) policy of maintaining exposure to nuclear radiation as low as reasonably achievable (ALARA). However, the very precautionary measures are highly inappropriate.

As described by Edward Calabrese (2009), the International Committee on X-Ray and Radium Protection was established by the Second International Congress of Radiology in 1928 to advise physicians on radiation safety measures, within a non-regulatory framework. Radiation protection was based on the "tolerance dose" (permissible dose) concept. The initial level was 0.2 roentgen[1] (R) per day in 1931, based on applying a factor of 1/100 to the commonly accepted average erythema dose of 600 R, to be spread over one month (30 days).[2] It was used as a means to determine the amount of lead shielding needed. Any harm that

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[1] The "equivalent dose" that corresponds to an exposure of 1 R depends on the energy of the x- or γ-radiation and the composition of the irradiated material. For example, if soft tissue is exposed to 1 R of γ-radiation, the dose would be approximately 9.3 mSv (Henriksen and Maillie 2012).

[2] In September 1924 at a meeting of the American Roentgen Ray Society, Arthur Mutscheller was the first person to recommend this "tolerance" dose rate for radiation workers, a dose rate that could be tolerated indefinitely (Inkret et al 1995). This level corresponds to 680 mSv/year.

might occur from exposures below the tolerance level was acceptable. However, geneticists strongly believed the theory that the number of genetic mutations is linearly proportional to radiation dose, that mutagenic damage was cumulative and that it was harmful. They argued that there was no safe dose for radiation; safety had to be weighed against the cost to achieve it.

To avoid adverse effects, early medical practitioners began to control their exposures to x-rays. For example, the British X-ray and Radium Protection Committee was formed in 1921. A study of those who joined a British radiological society revealed a significant health benefit (Smith and Doll 1981). Table 1 shows the ratio of observed/expected numbers of deaths of pre-1921 radiologists (in social class 1) and the ratio of post-1920 radiologists. A reduction from 1.04 to 0.89 is apparent for all causes of death and from 1.44 to 0.79 for cancer deaths. Note that the pre-1921 radiologists had a 44% higher cancer mortality than other men in social class 1, while the post-1920 radiologists had a 21% lower cancer mortality.

Table 1 - Observed and expected numbers of deaths from cancer and all other causes among radiologists who entered the study prior to 1921 or after 1920

| Cause of death | Observed (O) and expected (E) numbers of deaths | | | | | |
|---|---|---|---|---|---|---|
| | Entry prior to 1921 | | | Entry after 1920 | | |
| | O | E | O/E | O | E | O/E |
| All causes | 319 | (1) 334.42 | 0.95 | 411 | 541.77 | 0.76*** |
| | | (2) 308.03 | 1.04 | | 461.14 | 0.89* |
| | | (3) 327.97 | 0.97 | | 469.97 | 0.87** |
| All neoplasms | 62 | (1) 49.11 | 1.26* | 72 | 114.93 | 0.63*** |
| | | (2) 43.07 | 1.44** | | 91.07 | 0.79* |
| | | (3) 35.39 | 1.75*** | | 68.65 | 1.05 |
| Other causes | 257† | (1) 285.31 | 0.90* | 339† | 426.84 | 0.79*** |
| | | (2) 264.96 | 0.97 | | 370.07 | 0.92 |
| | | (3) 292.58 | 0.88* | | 401.32 | 0.84** |

(1) Based on rates for all men in England and Wales.
(2) Based on rates for social class 1.
(3) Based on rates for medical practitioners.
† includes one death with unknown cause.

*P < 0.05 ⎫ One sided in
**P < 0.01 ⎬ direction of
***P < 0.001 ⎭ difference.

After the bombing of Hiroshima and Nagasaki in World War II and the start of the nuclear arms race, geneticists greatly amplified their concerns that exposure to radiation in medical products and atomic bomb fall-out would likely have devastating consequences on the human population's gene pool. Hermann J. Muller was awarded the Nobel Prize in 1946 for his discovery of radiation-induced mutations. In his Nobel Prize Lecture of December 12, he argued that the dose-response for radiation-induced germ cell mutations was linear and that there was "no escape from the conclusion that there is no threshold" (Calabrese 2011c, 2012).

There was great controversy and extensive arguments during the following decade regarding the past human experience, the biological evidence and the strong pressures from Muller and

many other influential scientists who migrated from science to politics. The International Committee for Radiation Protection and the national organizations changed their radiation protection policies in the mid-1950s. They rejected the tolerance dose concept and adopted the concept of cancer and genetic risks, kept small compared with other hazards in life. The belief in low-dose linearity for radiation-induced mutations was accepted. The acute exposure, high-dose cancer mortality data from the Life Span Study on the Hiroshima-Nagasaki survivors was taken as the basis for predicting the number of excess cancer deaths to be expected following an exposure to a low dose of radiation or to low level radiation. However, the biology is very different from this picture. Professional ethics require a proper scientific foundation for estimating health risks (Jaworowski 1999, Calabrese 2011a).

Throughout the 20th century, an enormous amount of research has been underway in biology, on genetics and on the effects of radiation on DNA. A very important article, a commentary by Daniel Billen, was published in the Radiation Research Journal (Billen 1990), which is highly relevant to the great concern about the cancer or genetic risk from radiation. Permission was received from Radiation Research to republish it here (appended).

The Billen article points out that "DNA is not as structurally stable as once thought. On the contrary, there appears to be a natural background of chemical and physical lesions introduced into cellular DNA by thermal as well as oxidative insult. In addition, in the course of evolution, many cells have evolved biochemical mechanisms for repair or bypass of these lesions."

Spontaneous DNA damage occurs at a rate of ~ $2 \times 10^5$ natural events per cell per day. Compare this with the damage caused by nuclear radiation. The number of DNA damaged sites per cell per cGy is estimated to be 10-100 lesions, 100 to be conservative. A radiation level of 1 mSv delivered evenly over a year would cause on average less than 10 DNA damaging events per cell per year or 0.03 events/cell/day. **This is 6 million times lower than the natural rate of DNA damage that occurs in every person.** And this information has been known for more than 20 years.

The radiation in the environment around the Fukushima Daiichi NPS is shown in Figure 1 (MEXT 2011). It is interesting to note that the radiation received by the plant workers, Table 2 (JAIF 2012), did not exceed the tolerance level specified in 1931 for radiologists.

Table 2 - Radiation Exposures of the NPS Workers from 2011 March 11 until December 31

| Number of Workers | Radiation Dose (mSv) |
| --- | --- |
| 135 | 100 - 150 |
| 23 | 150 - 200 |
| 3 | 200 - 250 |
| 6 | 250 - 678 |
| 167 | |

Recently, Calabrese discovered that Muller had evidence in 1946 that contradicted the linear dose-response model at low radiation levels.  Muller did not mention this in his Nobel Prize lecture, suggesting that he still wanted the change in radiation protection policy to proceed, from the tolerance dose concept to a linear-no-threshold risk of cancer and congenital malformations (Calabrese 2011b, 2011c, 2012).

How can ICRP recommendations still be based on protecting against genetic risk at this level, when human suffering and economic costs are so great?  The ICRP has been progressively tightening its recommendations for occupational and public exposures, from 50 and 5 mSv/year (ICRP 1958) to 20 and 1 mSv/year (ICRP 1991).  Instead of ALARA, the radiation level for evacuation should be "as high as reasonably safe," AHARS (Allison 2009, 2011). For nuclear accidents, the 20 mSv/y level could be raised 50 times higher to 1000 mSv/y, which is similar to the natural radiation levels in many places (Jaworowski 2011).  And when low-dose/level radiation stimulation of the biological defences against cell damage and cancer is considered (Luckey 1991, UNSCEAR 1994, Cuttler 1999, Pollycove and Feinendegen 2003, Tubiana et al 2005, Cuttler and Pollycove 2009), Figures 2 and 3, there is no reason to expect any increase in cancer risk.  It is very difficult to understand why the ICRP recommendations have not changed accordingly.  There would have been no need for this evacuation.

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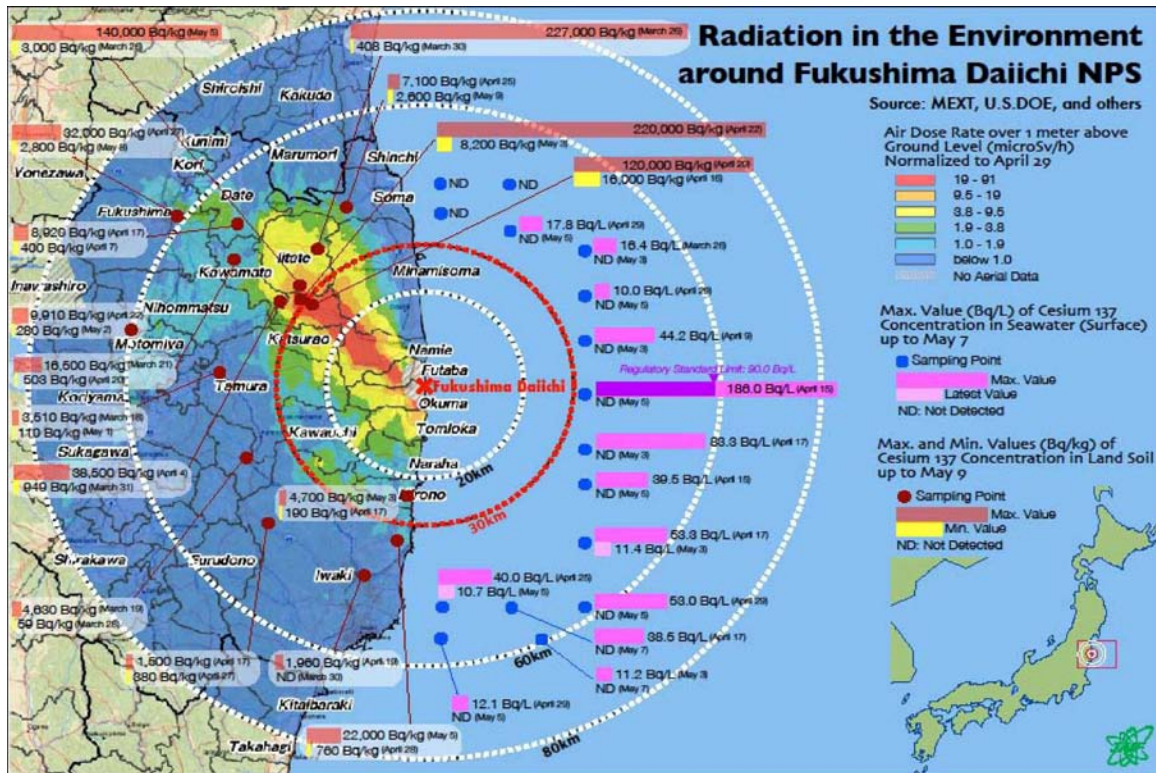
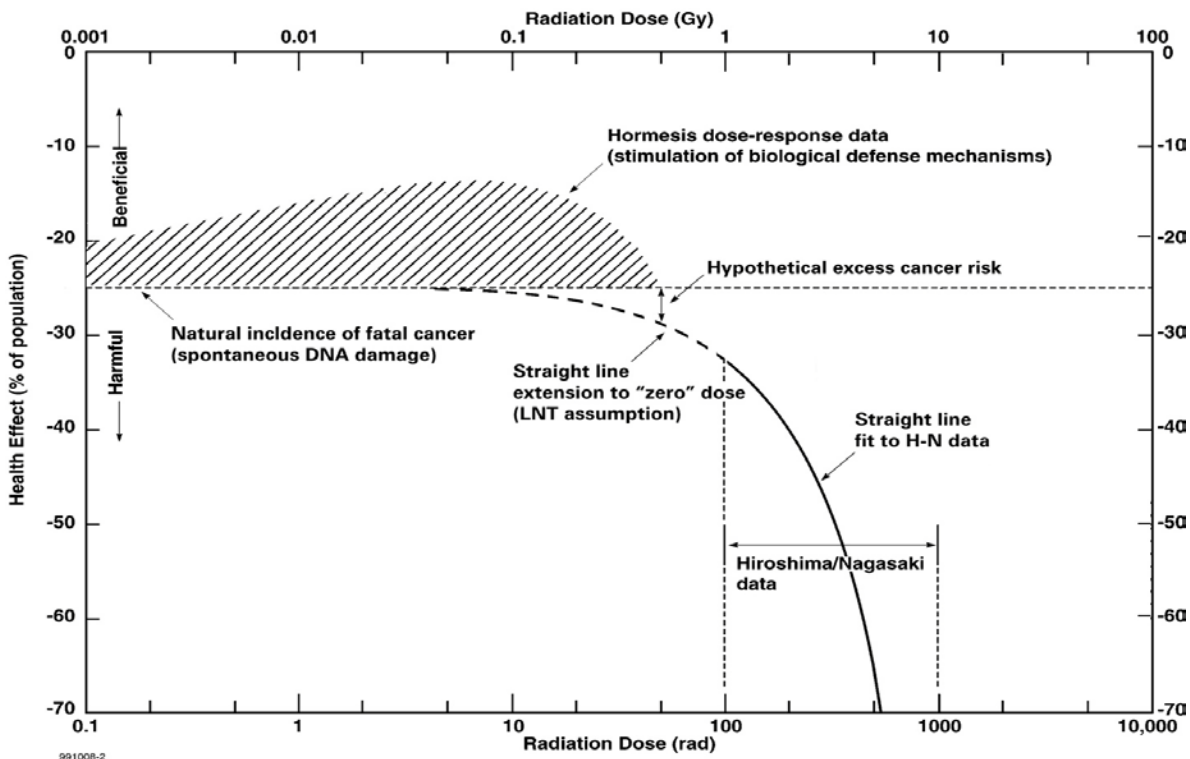Figure 1 - Radiation in Environment around Damaged Fukushima Daiichi NPS (MEXT 2011)

Figure 2 - Dose-Response for Short-Duration Radiation Exposure (Cuttler 1999)
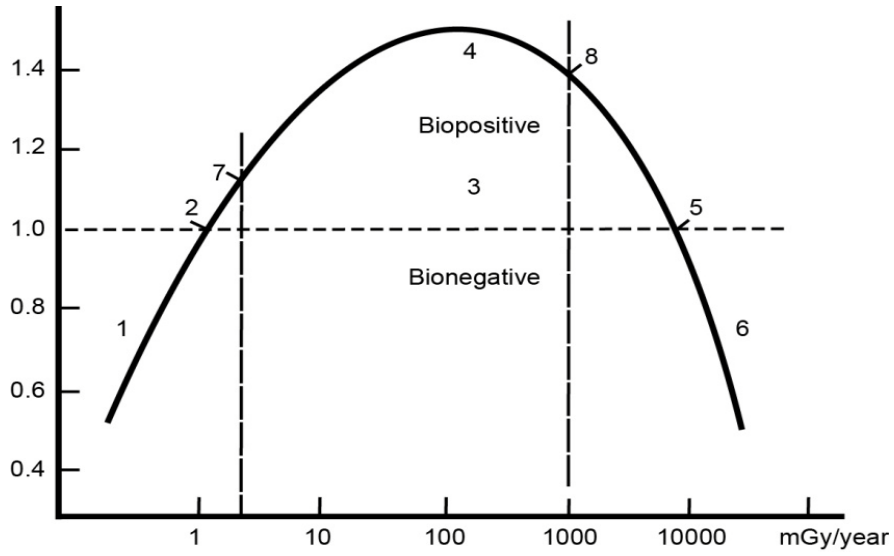
Figure 3 - Idealized Dose-Response Curve for Continuous Exposure (Luckey 1991)
1 deficient, 2 ambient, 3 hormetic, 4 optimum, 5 zero equivalent point, 6 harmful 7 ALARA, 8 AHARS

# COMMENTARY

# Spontaneous DNA Damage and Its Significance for the "Negligible Dose" Controversy in Radiation Protection

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BILLEN, D. Spontaneous DNA Damage and Its Significance for the "Negligible Dose" Controversy in Radiation Protection. Radiat. Res. 124, 242–245 (1990). © 1990 Academic Press, Inc.

One of the crucial problems in radiation protection is the reality of the negligible dose or de minimus concept (1–4). This issue of a "practical zero" and its resolution is central to our understanding of the controversy concerning the existence of a "safe" dose in radiological health. However, for very low levels of environmental mutagens and carcinogens including low doses of low-LET radiations (less than 1 cGy or 1 rad), spontaneous or endogenous DNA damage may have an increasing impact on the biological consequences of the induced cellular response. It is this issue that is addressed in this communication.

The following discussion is intentionally limited to a comparison of low-LET radiation since its effects are due primarily to indirect damage in cellular DNA brought about by OH radicals. Indirect effects of low-LET radiation under aerobic conditions are reported to account for 50–85% of measured radiation damage in cells (5, 6). High-LET radiation, on the other hand, produces unique DNA damage (7) primarily by direct effects (5) which is less likely to be properly repaired (7).

Spontaneous or intrinsic modification of cellular DNA is ubiquitous in nature and likely to be a major cause of background mutations (8), cancer (9), and other diseases (10). The documentation of this intrinsic DNA decay has increased at a rapid pace in recent years and has not gone unnoticed by contemporary radiobiologists. Setlow (11) and more recently Saul and Ames (12) summarized the findings of Lindahl and Karlstrom (13) and others (14) which suggest that approximately 10,000 measurable DNA

modification events occur per hour in each mammalian cell due to intrinsic causes.

The current radiation literature will be interpreted to show that ~100 (or fewer) measurable DNA alterations occur per centigray of low-LET radiation per mammalian cell. Therefore every hour human and other mammalian cells undergo at least 50–100 times as much spontaneous or natural DNA damage as would result from exposure to 1 cGy of ionizing radiation. Since background radiation is usually less than 100–200 mrem (1–2 mSv)/y, it can be concluded, as discussed by Muller and Mott-Smith (15), that spontaneous DNA damage is due primarily to causes other than background radiation.

## "INTRINSIC" OR "SPONTANEOUS" DNA DAMAGE

DNA is not as structurally stable as once thought. On the contrary, there appears to be a natural background of chemical and physical lesions introduced into cellular DNA by thermal as well as oxidative insult. In addition, in the course of evolution, many cells have evolved biochemical mechanisms for repair or bypass of these lesions.

Some of the more common "natural" DNA changes include depurination, depyrimidination, deamination, single-strand breaks (SSBs), double-strand breaks (DSBs), base modification, and protein–DNA crosslinks. These are caused by thermodynamic decay processes as well as reactive molecules formed by metabolic processes leading to free radicals such as OH, peroxides, and reactive oxygen species.

Shapiro (14) has recently discussed and summarized the frequency at which various kinds of spontaneous DNA damage occur. Spontaneous DNA damage events per cell per hour are shown in Table I and were estimated from the data presented by Shapiro [Table II (14)].

For single-stranded DNA of mammalian cells at least $8 \times 10^3$ damage events occur/cell/h, whereas for double-stranded DNA there were $\sim 6 \times 10^3$ damage events per hour (Table I). While the ratio of single-stranded DNA to

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## TABLE I
### Estimated Spontaneous DNA Degradation Events (Cell/h)[a]

| Reaction | Single-strand DNA | Double-strand DNA |
|---|---|---|
| Depurination | 4000 | 1000 |
| Depyrimidination | 200 | 50 |
| Deamination of cytosine | 4000 | 15 |
| Chain break resulting from depurination | — | 1000 |
| Direct chain break | — | 4000 |

[a] Calculated from Shapiro (14).

double-stranded DNA varies with phase of the cell cycle, it is reasonable to assume that double-stranded DNA is the usual configuration for most cellular DNA at any one time. From the data summarized in Table I it is not unreasonable to suggest that, at a minimum, the spontaneous DNA damage is of the order of $6-10 \times 10^3$ events/cell/h and to use $8 \times 10^3$ DNA damage events/cell/h as a reasonable average for the purpose of discussion. This allows a calculation of $1.9 \times 10^5$ spontaneous cellular DNA damaging events/cell/day or $7 \times 10^7$ per year in mammals including humans (Table II). The lifetime load of spontaneous DNA damage events per cell is then $\sim 5 \times 10^9$ if an average life span of 75 years is allowed for humans.

### DNA DAMAGE INDUCED BY IRRADIATION

Several recent reviews summarize the types and quantities of alteration of DNA in cells caused by exposure to low-LET radiation (16–18). The reader should refer to these for references to the original works from which the reviews were drawn.

The estimate of about 100 DNA events/cell/cGy used in this discussion is based on information contained in the reviews by Ward (16, 20) and assumes the molecular weight of the mammalian genomic DNA to be $6 \times 10^{12}$ Da, constituting about 1% of the cell weight.

Ward [Table II (16)] lists the amount of energy deposited in various DNA constituents/cell/Gy. From this table a total of 13.3 DNA events/cGy is calculated. His estimate of damaged DNA sites/cell/cGy is 10–100. I chose the 100-lesion estimate to make as reasonable a conservative comparison with spontaneous DNA damage as possible (Table II). This number of damaged sites would include both direct and indirect DNA damage.

### SPONTANEOUS VS INDUCED DNA MODIFICATIONS AND THEIR BIOLOGICAL CONSEQUENCES

Wallace has recently reviewed the nature of the DNA lesions caused by active oxidizing species produced both naturally and by low-LET radiation (17). Oxidizing radicals and especially OH radicals resulting from either cause produce similar types of DNA lesions (17–19). The enzymes involved in their repair are similar whether the DNA damage is produced spontaneously or by radiation. However, radiation is known to induce an error-prone repair system in bacterial cells and perhaps in mammalian cells as well (21, 22).

DNA glycosylases and endonucleases are involved in the repair of base damage. Other nucleases are available for sugar damage repair (17). Recognition of the damage site by the appropriate enzymes is dependent not on the initiating event but on the chemical nature of the end product. These end products appear to be similar whether induced by natural causes or radiation (17). It would seem reasonable to conclude that, due to common oxidizing radicals, many of the qualitative changes in DNA are quite similar for radiation-induced or spontaneous DNA damage.

## TABLE II
### DNA Damage Events per Mammalian Cell

| Character of event | Spontaneous DNA damage events | | | DNA damage/cGy[a] |
| | Per second | Per hour | Per year | |
|---|---|---|---|---|
| Single-strand breaks | 1.4 | $\sim 5 \times 10^3$ | $\sim 4.4 \times 10^7$ | 10 |
| Double-strand breaks | | | | 0.4 |
| Depurination and/or base lesions | 0.8 | $\sim 1.5 \times 10^3$ <br> $\sim 1.25 \times 10^3$ | $\sim 1.4 \times 10^7$ <br> $\sim 1.1 \times 10^7$ | 9.5 |
| Total events | 2.2 | $\sim 8.0 \times 10^3$ | $\sim 7 \times 10^7$ | $\sim 20$ |
| cGy equivalents (1 cGy = 100 events)[b] | 0.022 | $8.0 \times 10^1$ | $7 \times 10^5$ | |

[a] From Ward (20).
[b] Since other radiation-induced DNA damage such as DNA–protein crosslinking and base modifications (18) occur, 100 events/cGy is used as a "ballpark" value for ease of comparison with spontaneous events.

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The quantity and distribution of each class of lesion may, however, differ significantly. As indicated earlier there would appear to be relatively more DNA strand breaks than other lesions resulting from spontaneous causes as compared to radiation insult. A good portion of these may result from depurination (Table I) with production of 3' OH termini ("clean ends") as part of the repair process.

Many of the DNA strand breaks caused by low-LET radiation are incapable of serving as primer for DNA polymerase (23). However, endo- and exonucleases exist which can restore these blocking ends to clean ends and allow completion of the repair process (17).

A strong correlation exists between DNA DSBs and lethality in mammalian cells for low-LET radiation. While the quantity of DSBs produced by ionizing radiation is fairly well documented, this is not true for spontaneous DSB production in mammalian cells.

In spontaneous DNA decay, formation of a DSB is likely to be the result of single-strand events occurring in close proximity on each daughter strand and leading to cohesive ends which can be repaired easily by a ligation step.

A survey of the literature on the doubling dose for mutagenesis in eukaryotes exposed to low-LET radiation indicates a range of 4 to 300 cGy and for carcinogenesis a range of 100 to 400 cGy. Using the "ballpark" value of approximately 100 DNA events/cell/cGy, this would represent a range of 400 to 40,000 induced DNA damage events per doubling dose. Using 100 cGy as the approximate doubling dose, a total of $1 \times 10^4$ DNA damage events would be required to induce mutations in numbers equal to that observed in nature. This is approximately the number of DNA events ($8.0 \times 10^3$) produced spontaneously in each cell/h (Table II).

## THE NEGLIGIBLE DOSE CONTROVERSY

The comparison of low-LET radiation-induced DNA damage with that which occurs spontaneously indicates (Table II) that a relatively large number of DNA damage events can occur spontaneously during the lifetime of mammalian and other cells.

Dose protraction over a period of weeks or months would lead to an increasing ratio of spontaneous DNA damage events to those caused by irradiation. By extrapolation from high doses and high dose rate as discussed by Ward (16, 20), 1 cGy delivered in 1 s would cause 40–50 times as many DNA damaging events per cell as that caused spontaneously during the same time span (Table II). However, 1 cGy delivered evenly over 1 year would cause (on average) less than 1 DNA damaging event per cell/day. This can be compared to $\sim 2 \times 10^5$ natural events caused per cell/day.

From these numbers, it seems reasonable to suggest that there does exist a "negligible" dose in the range of our terrestrial background annual radiation dose of $\sim 1$ mSv ($\sim 10$ DNA events/cell/year). This can be compared to the approximately $7 \times 10^7$ DNA events/cell/years produced by spontaneous causes.

Adler and Weinberg (24) have proposed that the standard deviation of the background irradiation ($\sim 0.2$ mSv) be used as an acceptable additional dose due to human activities. This would lead to $\sim 2$ additional induced DNA damaging events/cell/year as compared to $\sim 7 \times 10^7$ spontaneous DNA damage events. Considering the magnitude of the spontaneously induced DNA changes in each human cell, it is not unreasonable to predict that 0.2 mSv delivered over a year would have negligible biological consequences.

When temporal considerations are factored in, it becomes clear that spontaneous DNA damage in mammalian cells may be many orders of magnitude greater than that caused by low and protracted radiation doses, especially in the terrestrial background range of 1–2 mSv (100–200 mrem) per year. It is important that further studies on the effects of both ionizing radiations and spontaneous events on DNA decay and repair be conducted to better understand the practical health consequences of low and protracted doses of radiation (2, 9, 25).

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