## **Radiation Hormesis Overview\***

T. D. Luckey

#### Abstract

Evidence of health benefits and longer average life-span following low-dose irradiation should replace fear, "all radiation is harmful," and "the perception of harm" as the basis for action in the 21<sup>st</sup> century. Hormesis is the excitation, or stimulation, by small doses of any agent in any system. Large doses inhibit. "Low dose" is defined as any dose between ambient levels of radiation and the threshold that marks the boundary between biopositive and bionegative effects. That threshold negates the "linear no threshold" (LNT) paradigm. This overview summarizes almost 3,000 reports on stimulation by low-dose irradiation.

"Hormesis with Ionizing Radiation" presented evidence of increased vigor in plants, bacteria, invertebrates and vertebrates. Most physiologic reactions in living cells are stimulated by low doses of ionizing radiation. This evidence of radiogenic metabolism (metabolism promoted by ionizing radiation) includes enzyme induction, photosynthesis, respiration and growth. Radiation hormesis in immunity decreases infection and premature death in radiation exposed populations. Increased immune competence is a major factor in the increased average life-span of populations exposed to low-dose irradiation. "Radiation Hormesis" presented evidence for radiation hormesis in major physiologic functions of vertebrates. Evidence of radiation hormesis in reproduction emphasizes the safety of low-dose irradiation. "Low-Level Radiation Health Effects: Compiling the Data" summarizes recent papers on radiation hormesis.

During the previous decades, statistically significant evidence showed that whole body exposures of humans to low doses of ionizing radiation decreased total cancer mortality rates. This is based on information compiled from 7 million person-years of exposed and control workers in nuclear shipyard and atomic bomb plants in Canada, Great Britain and the United States. Other human experiences with unusual exposures confirm radiation hormesis in cancer mortality. A variety of external sources are beneficial. Internal sources (plutonium, radium and radon) are also effective.

The conclusions have both personal and national significance. Ionizing radiation is a benign environmental agent at background levels. We live with a subclinical deficiency of ionizing radiation. Low doses of ionizing radiation significantly decrease premature cancer death. Health benefits should replace risk and death as the guide for safe exposures to ionizing radiation. Safe supplementation with ionizing radiation would provide a new plateau of health.

k	key Words
C	lancer
E	lealth
E	Iormeses
I	nmunity
L	ife-span
N	Juclear Workers
P	lutonium
R	ladium
R	ladon
R	Reproduction

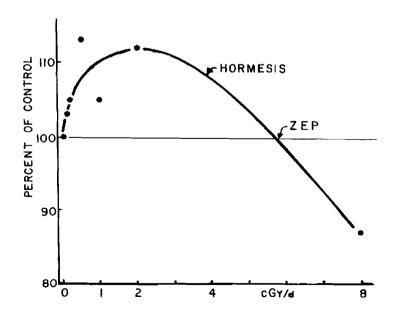
<sup>\*</sup>Taken from a lecture given at ICONE-7, Tokyo, April, 1999. The author acknowledges with thanks the critical reading of this manuscript by Pauline Luckey and Dan Crockett.

#### INTRODUCTION

At the end of the 19<sup>th</sup> century and early in this century, low doses of radiation, mostly radium and x-rays, were considered to be medical marvels. Doctors throughout the world utilized ionizing radiation to treat a variety of diseases. They soon learned that excess exposures caused erythema and cancer. High and low doses of ionizing radiation elicit opposite reactions (Figure 1). Excess radiation is harmful; the opposite effect, induced by low doses added to ambient levels, is beneficial. The salient point is: a threshold exists between biopositive and bionegative effects. The threshold, called zero equivalent point (ZEP), is the dose at which the effects mimic characteristics of the control receiving background levels of ionizing radiation. This, in turn, defines "low dose" as any dose between controls at background levels of radiation and the ZEP.

This threshold, ZEP, negates the linear no threshold (LNT) concept, which guides most national and international agencies. The base for LNT is harm from excessive doses of ionizing radiation. The concept includes interpolation to zero. This promulgates "fear of harm" from all radiation. Except for cytology and cells in culture, artificial systems which lack participation from whole body faculties (particularly the immune system), there is no reasonable or scientific proof of LNT at low doses of ionizing radiation. Official agencies interpolate between high doses and ambient levels of radiation to guestimate what the effects might be at low doses. These agencies consider the perception of harm to be more important than overwhelming scientific evidence showing that stimulation with low doses is a general rule in biology. Stimulation by low doses of many agents has been discovered, called

*Figure 1.* Growth in x-ray exposed mice fitted to a theoretic curve.<sup>[2]</sup> Radiation hormesis includes any dose between ambient levels of radiation and the thresh-hold dose. Results at the two high points were statistically significant, p < 0.01. Other data shows the threshold dose for chronic exposures is about 10Gy/y.<sup>[8]</sup>



different names, and withstood the test of time in many disciplines (Table 1).<sup>[1]</sup> *Hormology* (the study of excitation) provides a major rule of biology: small doses are stimulatory; large doses depress. The following summary indicates the consistency and diversity of data supporting radiation hormesis.

The thesis is clear. There is *no risk* and considerable benefit from chronic, whole body exposures to low doses of ionizing radiation. The evidence shows national and international agencies promulgate harm when they severely restrict exposures to ionizing radiation. Their goal should be health.

#### EARLY STUDIES

The 1200 reports summarized in "Hormesis With Ionizing Radiation" validate radiation hormesis.<sup>[2]</sup> Statistically significant results with microorganisms, plants, invertebrates, and experimental animals demonstrated radiogenic metabolism (metabolism promoted by ionizing radiation) is an important life function. Low-dose irradiation of microorganisms induced increased respiration, enzyme induction (adaptation), metabolism, resistance to killing doses, and cell division. Chronic whole body exposures to low doses of ionizing radiation increased reproduction, growth, maturation and development, resistance to disease, resistance to lethal doses of radiation, and average life-span (Table 2). Radiation hormesis in immunity is especially important.

#### **RADIATION HORMESIS IN IMMUNITY AND AVERAGE LIFE-SPAN**

A century ago, Shrader showed low doses of ionizing radiation activated the immune System.<sup>[3]</sup> When infected with diphtheria bacillus, guinea pigs previously exposed to x-rays showed *no disease* while unexposed controls died with diphtheria the following day. Increased immune competence leads to decreased infection, respiratory disease and cancer. These, in turn, increase reproductive performance and average life-span. Early studies showed that exposures to ionizing radiation prior to antigen administration induced increased production of antibodies and that the high titer remained longer than that of unexposed controls.<sup>[2]</sup> Shrader's protocol of experimental infection of both radiation-exposed and control animals is most useful.

"Irradiation of the pregnant animals... and the fetuses *in utero* caused an astounding decrease of the mortality of the (virus) infected baby mice."<sup>[4]</sup> Recent research on radiation hormesis in immunity has now been summarized.<sup>[5]</sup>

Average life-span is an important parameter for the health benefits of low-dose irradiation. Early results with the flour beetle, Tribolium confusum, showed the maximum life-span was obtained with exposures to x-rays of about 150 cGy/d.<sup>[2]</sup> These results were amply confirmed. Results of one experiment prompted health physicists to suggest the radiation limit for humans should be 15 rem (15 cSv), one tenth of the amount which increased average life-span 120% of controls in mice fed uranium, then called "tube dust" or "Manhattan dust."<sup>[6]</sup> Since wartime secrecy permitted no publication of the details of these experiments, the report of Lorenz showing increased average life-span in mice (Figure 2), rats and Guinea pigs was greeted with flawed interpretation and disbelief.<sup>[7]</sup> This graph exposes the misinterpretation to conclude that control mice have longer

YEAR	DISCIPLINE	AUTHOR	CONCEPT		
1500 BC	Medicine	Hatshepsut	Poisons stimulate		
1000 BC	Immunization	Chou	Smallpox vaccination		
700 BC	Medicine	Sargon II		"Dual" belladonna	
400 BC	Therapy	Hippocrates	Give no fatal dose		
1540	Pharmacy	Paracelsus	The dose is everything		
1780	Medicine	Withering		Potential toxicants	
1878	Botany	Bernard		Stress builds	
				strenath	
1897	Botany	Townsend		×	
1888	Fermentation	Schulz	The Arndt-Schulz law		
1906	Bacteriology	Richet	Oligodynamic effect of metals		
1908	Psychology	Yerkes	The inverted U-curve		
1919	Radiation	Davey		Homeostatic doses	
1922	Medicine	Hahnemann	Minute doses heal		
1930	Toxicology	Maximov	Toxicants increase plant	<u>├───</u>	
1000	TOXIOOIOGy	IVIAXII II OV	growth		
1930	Therapy	Merck		Potential toxicants	
1936	Radiation	Gager			
1000	riadiation	Cago			
1936	Physiology	Selye	General adaptive syndrome	plan grown	
1900	T Hysiology	l	(GAS)		
1943	Entomology	Southam	Hormesis	<u>├</u> ────────	
1946	Nutrition	Moore		Antibiotics stimulate	
1010					
1950	Radiation	Lorenz		×	
1950	Nutrition	Briggs			
1951	Immunology	Taliaferro	Radiation enhances immunity	pionary promotant	
1959	Toxicology	Luckey	Hormoligosis	<u> </u>	
1960	Pharmacology	Townsend	The beta curve		
1961	Bacteriology	Jacob	Adaptive enzyme induction		
1974	Nutrition			Prohiotics	
1974	Agronomy				
1976	Radiation				
1976	Radiation				
1979	Immunity				
1980	Badiation				
1900	naulation				
1980	Radiation	_ <del>_</del>			
1985	Cancer				
1000	Carloo	1		-	
1988	Metabolism	Heiby	The reverse effect		
1990	Neurotoxicity	Davis	The U-shaped functions		
1996	Cell culture	Salone	Adaptive survival response		
			(ASR)		
1997	Cancer			Cytodynamic 2-stag	
				(CD2)	
1997	Chemistry			The dose is	
				everything	

 Table 1. Concepts of low-dose stimulation\*[1]

Figure 2. Average life-span in mice was significantly increased by x-ray exposure of 1.1mGy/d.<sup>[7]</sup>

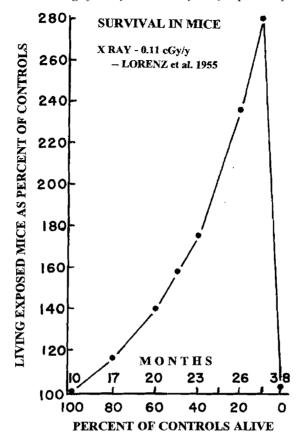


Table 2. Radiation hormesis in physiologic functions

Increased	Decreased
Mean life-span	Total mortality rate
Growth rate	Cancer mortality rate
Development rate	Cardiovascular death rate
Neurologic acuity	Respiratory death rate
Immune competence	Infections
Fecundity	Female sterility
Radioresistance	Leukemia death rate

average life-spans than the exposed mice when the *median* value was used instead of *mean or average*. The disbelief spread when major laboratories were misled by repeating the Lorenz protocols with *specific pathogenfree (SPF)* animals. Since SPF animals have no pathogens to cause infection, controls lived as long as irradiated mice and no hormesis was found. Radiation hormesis in life-span is now well accepted by those who incorporate low doses into their protocols (Table 3). Much of this research stopped about 1945, when financial support shifted to studies of harm from excess radiation.

Many of the 1000 references in "*Radiation Hormesis*" came from reports on the effects of high doses of ionizing radiation in experimental animals.<sup>[8]</sup> Recent references involve only human data.<sup>[9]</sup> Hormesis *consistently* occurred only in the lowest doses tested. Major physiologic functions (Table 1) were benefited. Early studies illustrate the safety of low-dose irradiation for different parameters of reproduction.

#### **RADIATION HORMESIS IN REPRODUCTION**

Evidence for radiation hormesis in reproduction came as a surprise to investigators. In the study which inaugurated health physics regulations, rats fed uranium dust produced more young than controls.<sup>[6]</sup> Rats exposed to 2.5 Gy x-rays showed superovulation and superimplantation.<sup>[10]</sup> When compared with controls, sterility was reduced in humans and mice previously exposed to x-rays (Table 4).<sup>[11,12,13]</sup> Conversely, fecundity increased in lightly irradiated animals.<sup>[14]</sup> Muramatsu and associates found increased litter size (Figure 3) in a colony of gamma irradiated mice, p = 0.02. Brown reported gamma-ray irradiated rats (2 cGy/d) exhibited superior health and reproduction.<sup>[15]</sup> When compared with controls (Figure 4), females of the 12<sup>th</sup> continuously irradiated generation had 117% more litters, 157% increase in litter size, 172% increased total litter weight, 147% increased number of weaned pups, and 137% greater total weight of young weaned. Increased fecundity was confirmed (Figure 5) with colonies of 12-82 generations of irradiated rodents.<sup>[13,15,16]</sup>

In contrast with the *genetic monsters* predicted in atomic bomb victims, low doses of ionizing radiation reduced genetic abnormalities. When both parents were exposed to <40 cGy, babies born to Japanese bomb survivors had 30% fewer molecular mutations and 33% fewer chromosomal aberrations than controls.<sup>[17]</sup> Also, phenotypic abnormalities were significantly reduced in babies born of mothers who received <20 cGy (Figure 6).<sup>[18]</sup> Exposure of Japanese fathers to low-dose irradiation resulted in no significant effect on the occurrence of phenotypic abnormalities in their offspring.

#### **HUMAN CANCER STUDIES**

Recent studies have concentrated upon human cancer mortality rates. Since it accounts for over 20% of all deaths, cancer is both a family disaster and a national health problem. Total cancer mortality rates in the United States have increased (Figure 7) during the past few decades.<sup>[19]</sup> Although large doses of ionizing radiation can induce cancer, small doses of ionizing radiation reduce total cancer mortality in both animals and humans.<sup>[8,20,21]</sup> Note the ordinate for the curve in Figure 1 could represent protection from cancer; the inverse is usually used for curves showing cancer incidence, cancer deaths, or cancer death rates (as in Figure 8). Results from whole body exposures of humans to low doses of internal and external radiation are briefly summarized.

Year	Author	Radiation	Animal
1942	Stone	Uranium	Rats
1950	Lorenz	X ray	Mice
1955	Maisin	X ray	Mice
1956	Sacher	X ray	Mice
1957	Curtis	X ray	Mice
1957	Carlson	Gamma	Rats
1958	Lindop	X ray	Mice
1960	Gowen	X ray	Mice
1960	Luning	X ray	Mice
1962	Sacher	Gamma	Rats
1963	Langendorf	X ray	Rats & mice
1963	Usaec	Gamma	Guinea pigs
1967	Boche	X ray	Dogs
1968	French	Gamma	Deer mice
1969	Spalding	X ray	Mice
1969	Nishio	Gamma	Mice
1969	Nishio	<sup>137</sup> Cs	Mice
1970	Grahn	Gamma	Mice
1970	Bonham	Gamma	Salmon
1972	Grahn	Gamma	Rats
1972	Mcgregor	Gamma	Trout
1973	Tobias	A-Bomb	Humans
1975	Cahill	Tritium	Rats

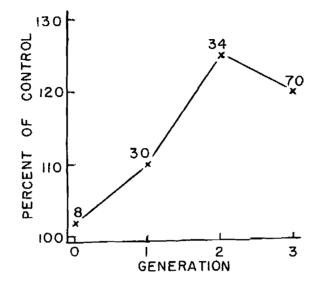
 Table 3. Low-dose irradiation increased average life-span

 Table 4. X-ray treatments decrease sterility [8]

Species	Gy	Number	Sex	Sterile*	Author
Human	0.9	644	Female	54	Kaplan
Human	2	1000+	Both	33	Hbrg
Mouse**	2	4000	Both	54	Spalding
Mouse	2.8	124	Sperm	25	Lining
Trout	0.5	11,000	Both	75	Newcomb

\* % of Control Sterility \*\* Acute exposure

*Figure 3.* Mean litter size in mice exposed to 0.43 cGy of x-rays per day through three generations.<sup>[14]</sup> The average in control mice was 5.1 young per litter. The numbers of pairs for each generation are listed.



**Figure 4.** Radiation hormesis in reproduction in the  $12^{th}$  generation of rats exposed to  $2c \text{ Gy/d.}^{[15]}$  The data compare the successive litters of 47 exposed females with 30 unexposed controls: percent of dams having litters, litter size, and weight of young weaned.

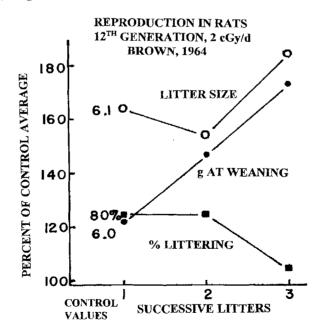
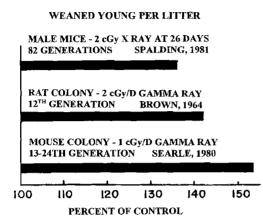


Figure 5. Reproduction in rodents is increased by irradiation of either the males or the whole colony through many generations.



**Figure 6.** Phenotypic abnormalities in Japanese babies were decreased in mothers exposed to lowdose radiation from atom bombs. The control population had 5.2 abnormalities per 100 births.

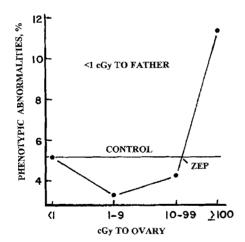
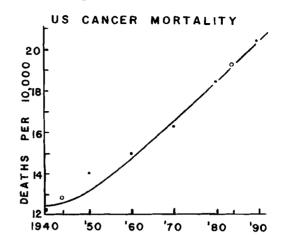
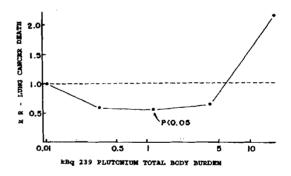


Figure 7. Cancer mortality rates in the United States increased during the national "war on cancer."<sup>[19]</sup>



**Figure 8.** Lung cancer mortality rates are reduced when Russian muclear workers were exposed to low doses of plutonium.<sup>[26]</sup> The ordinate presents the relative risk of lung cancer deaths when compared with a control population.



#### PLUTONIUM

Although plutonium occurs naturally in minute amounts in pitchblende (produced by the action of cosmic neutrons upon uranium), it was not of environmental concern until the atomic age. This "most toxic substance on earth" is one trillion times less toxic than the botulinum toxins.<sup>[22]</sup> Since the evidence, reviewed here, shows low doses of plutonium reduce lung cancer death rates, it should be considered a benign environmental agent.

To provide a standard for persons who might be exposed to plutonium in the manufacture of atomic bombs, 17 "terminally ill" patients were intravenously injected with 95 to 400 nCi of <sup>239</sup>Pu (some received the +4 citrate and some the +6 nitrate) between April 1945 and July 1947.<sup>[23]</sup> None who lived longer than nine months died with cancer (Table 5). Four lived with their plutonium 30-44 years. Another received 3.5  $\mu$ Ci of <sup>238</sup>Pu; his lifetime dose was 64 Sv. He lived with plutonium 21 years before dying of heart disease. This is evidence that *low doses* of plutonium are not carcinogenic.

Voelz and associates followed the medical history of 26 workers accidentally exposed to plutonium in 1944-45 at Los Alamos National Laboratory.<sup>[24]</sup> The standard mortality ratio (SMR) for all deaths was 0.41, for cardiovascular deaths it was 0.21, and for all cancer deaths it was 0.45. Although the small number of subjects allows no statistical significance, the data suggest plutonium exposures are beneficial. For example, Beral and associates found no leukemia deaths in 22,552 British nuclear workers who were exposed for 2-30 years to >10 mSv from either internal (plutonium, actinium or tritium) or external sources.<sup>[25]</sup>

Inhalation exposures to plutonium showed radiation hormesis for lung cancer mortality rates. Lung cancer mortality rates showed no correlation with external exposures in a study of 500 Russian plutonium workers over the course of 40 years.<sup>[26]</sup> When internal exposure was less than 0.8 Sv (6 kBq), the lung cancer mortality rate of exposed workers was significantly less, p<0.05, than controls (Figure 8).

When up to 50 years of records documenting 83,324 nuclear workers were examined, the SMR for lung cancer mortality rate was 0.14, 0.20 and 0.29, respectively, for exposed plutonium workers at Rocky Flats Nuclear Weapons Plant, Los Alamos National Laboratory and the Hanford Site.<sup>[22]</sup> The great majority of exposures were respiratory.

#### RADIUM

Early investigators knew that excessive exposures to micrograms of radium caused erythema and burns. These could eventually become cancers. However, they learned both low doses and high doses were therapeutic. Many physicians used radium extensively in medicine. The cancer produced by extensive use of the first kilogram of radium isolated (experimental, medical and dial painters) is matched by the absence of harm from the tons used (in medicine and industry, including thousands of dial painters) since 1940.

Widespread use of radium elixirs came to a sudden halt when an over-enthusiastic sportsman took about 3000 doses of *Radithor* (1  $\mu$ Ci of <sup>228</sup>Ra and 1  $\mu$ Ci of <sup>226</sup>Ra in 15 g water) in a short period of time.<sup>[27]</sup> His mediacelebrated disfigurement and death from cancer aroused public opinion and brought radiation under control of the Food and Drug Administration (FDA). Although a half million vials were sold, one death was enough. The FDA gave little consideration to the thousands of persons who took reasonable

ID	YEARS	AGE AT DEATH	cSv*	CAUSE OF DEATH
HP-9	1.2	65	52	BRONCHOPNEUMONIA
HP-4	1.4	20	46	CUSHING'S SYNDROME
HP-2	2.4	50	80	BRAIN DISEASE
HP-12	8	63	230	HEART FAILURE
HP-10	11	63	410	HEART DISEASE
HP-1	14	81	380	BRONCHOPNEUMONIA
CAL-1	21	79	6,400	HEART DISEASE
HP-8	30	71	1,000	UNKNOWN
HP-3	37	85	880	CARDIAC ARREST
HP-6	38	82	990	NATURAL CAUSE
CAL-3	44	80	155	

Table 5. Deaths in plutonium injected persons

\* Lifetime dose

doses of this elixir for various ailments. The Federal limit for  $^{226}$ Ra in drinking water is 5 pCi/L, about 5 pCi/d.

Muckerheide noted that no health problems have been found for exposures less than

50  $\mu$ Ci radium in the United States or other countries.<sup>[27]</sup> Assuming 20% absorption for one liter per person per day, it would take 137,000 years to drink enough water with 5 pCi/L to absorb 50  $\mu$ Ci of radium. Since both archeologic and genetic (maternal mitochondrial DNA) evidence suggests *Homo sapiens* originated on the shores of South Africa about 150,000 years ago, it is not surprising that the scientific community considers the FDA limit to be ridiculous.

Radium dial painters provided ample evidence that bone cancers develop when exposures exceeded 10 Gy.<sup>[28]</sup> Except for breast cancer, other cancer mortality rates in radium-exposed workers show no change from the general population; and there was no dose-dependent increase in breast cancer mortality rates.<sup>[29]</sup> Leukemia deaths in female radium dial painters were much lower than expected; the SMR for 1,285 workers was 0.22.<sup>[30]</sup> The gamma ray occupational exposure of these workers was estimated to be 4 cGy/y, the average bone marrow dose was about 8 cGy/y. These results were verified when no leukemia deaths were found in female British dial painters who had worked 2-50 years with radium.<sup>[31]</sup>

The average life-span of radium-exposed persons may exceed that of the general population. Below 10 Gy there was no excess incidence of bone cancers. Excepting cancer in bone, paranasal and mastoid air cells of the most heavily exposed workers, Rowland states: "However, the great majority of exposed individuals went through life with no recognizable consequences of their exposures. They lived as long as, and apparently in as good health as, their unexposed neighbors. This fact seems to have been little appreciated and seldom mentioned, but it may be the most important finding of the entire study."<sup>[29]</sup> Among United States white female dial painters, the SMR for all causes of death, all

circulatory system disease, and cerebrovascular disease were, respectively, 0.88, p<0.05; 0.75, p<0.01 and 0.48, p<0.01.<sup>[29]</sup> British female dial painters may have had an increased life-span; the SMR was 0.90; this was not statistically significant.<sup>[31]</sup> With the exception of deaths due to cancer, the British female dial painters had an increased average life-span; the SMR was 0.81, p<0.01. When grouped by years at work, the average lifespan SMR for 0-10 years was 0.31, p=0.008; for 10-20 years it was 0.47, p=0.066; and for all, 0-50 years, the SMR was 0.72, p=0.001. Clearly, radium dial painting appeared to increase average life-span. Support for these studies stopped when beneficial results were reported.

### RADON

Radon and lung cancer have usurped the public fear previously held for genetic monsters produced by external radiation. The predicted genetic monsters did not appear and increased chromosomal aberrations were not found in Japanese exposed to low-dose irradiation from atomic bombs. There is good evidence for radiation hormesis in reproducetion and life-span in these survivors.<sup>[8]</sup> Now there is strong evidence that indicates radon reduces lung cancer deaths. Cohen's study of radon in the homes of 1700 counties accounts for 90% of the US population.<sup>[32]</sup> The results (Figure 9) provide statistically significant evidence, p<0.0001, of an inverse relationship between radon inhalation and lung cancer death. The curve was comparable for either sex, with or without smoking. Other epidemiologic factors were found to be without effect. Since decreased radon levels are associated with increased lung cancer deaths, reducing radon levels below 8 pCi/L is counterproductive. Levels below 8 pCi/L are associated with increased lung cancer deaths.

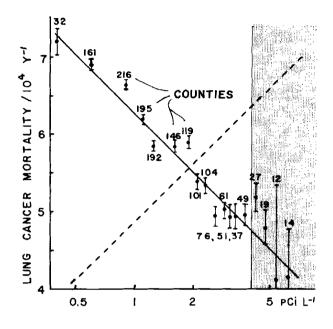
Comparable results were obtained in Britain.<sup>[34]</sup> The radon levels in Cornwall and Devon were 3.0 and 2.0 pCi/L, respectively. The SMR for lung cancer deaths for males and females in Cornwall were 0.96 and 0.91, respectively; for Devon these values were 1.02 and 1.13, respectively. Data from casecontrol studies of 1,973 lung cancers in Finland would fit the Cohen curve very well.<sup>[33]</sup> However, the lung cancer mortality rate of people living with high radon levels (11-34 pCi/L) appeared to be higher than that of the control population receiving 1.4 pCi/L.

Radon hospitals in Russia treat 1000 individuals daily for asthma, arthritis, rheumatism, immune deficiency and hormone disorders.<sup>[35]</sup> About 75% of the people respond to this treatment (Figure 10). In this study with air administered to the placebo group, the optimum therapeutic dose was 2 mSv within two weeks. These data support *testimonials* of people who frequent radon mines for health in Austria and Montana.<sup>[36,37]</sup>

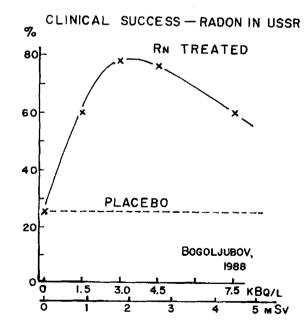
#### EXTERNAL EXPOSURES

Studies involving more than 7 million person-years (P-Y) of experience with nuclear workers provided consistent and convincing evidence that low doses of external ionizing radiation decrease total cancer mortality rates (Table 6).<sup>[20,21]</sup> The estimated lifetime dose of 152,000 exposed workers averaged 5.5 cSv above background. Radiation from most accidental exposures is either acute or diminishes to negligible amounts within a few weeks. Exposed workers were carefully matched (age, sex, sociologic factors) with over 149,000 unexposed persons working in comparable conditions. Since all workers had comparable entrance examinations, environment, management, and medical care, there was no "healthy worker effect." To

**Figure 9.** Radon decreases the lung cancer mortality rate in the United States.<sup>[32]</sup> The numbers of counties and one standard deviation are shown. The dashed line shows a federal agency interpretation of the data. The stippled area is agency recommended for remedial action.



*Figure 10.* Radon therapy was effective (ordinate) in 75% of patients in 20 years experience in Russian clinics.<sup>[35]</sup> The placebo control was air inhalation. Used with permission of CRC Press.



			Deaths/1000				
Cohort	Number	Person-years	Exp	Con	% *		
Shipyards	72,356	1,591,832	9.8	13.4	73		
Hanford	44,100	1,675,800					
Oak Ridge	8,318	291,130	20.8	34.8	60**		
Rocky Flats	5,897	165,116					
Los Alamos	14,280	457,000	17.7	20.5	86		
Canada	8,944	268,320	20.3	23.7	86		
Britain	95,217	3,237,378	2.8	9.9	28		
Totals	249,112	7,686,576			Average = 52		

#### Table 6. Nuclear workers in cancer mortality studies

EXP = exposed nuclear workers; CON = unexposed nuclear workers.

AVE - The average is weighted by the person-years for each cohort.

\* Percent of total cancer deaths in exposed compared with control workers.

\*\* Hanford, Oak Ridge and Rocky Flats are reported as one unit.

eliminate persons who had cancer or leukemia at the time of employment, deaths were not counted within the first ten and two years, respectively. When weighted according to the P-Y in each study, the total cancer mortality rate of exposed nuclear workers was only 52% that of the controls.

Japanese atomic bomb victims are generally considered to provide the most reliable index for the effect of acute external radiation in humans. Those exposed to lowdose irradiation had a lower cancer death rate than controls (Table 7). For every ten thousand persons exposed to 1-1.9 cGy there were 3 fewer leukemia deaths and 50 fewer solid cancer deaths than in controls.<sup>[38]</sup>

Although leukemia mortality rates increase dramatically with doses exceeding the threshold, atom bomb survivors exposed to 5-10 cSv had 5.5 fewer leukemia deaths per 10,000 persons than controls. Later studies confirm radiation hormesis in cancer mortality, leukemia mortality and average life-span of Japanese atomic bomb survivors.<sup>[17]</sup> Such results from atom bomb survivors negate the concept that *all radiation is harmful*.

Populations with unusual chronic exposures support the above results. Many generations exposed to relatively high levels of background radiation (compared with nonmedical exposures of 2 mGy/y for the US) show improved health.<sup>[20,21]</sup> This includes over 70,000 exposed (3.3 mGy/y) and 70,000 control (1.07 mGy/y) Chinese peasants, several villages in Brazil (20-35 mGy/y), the "old ones" living in the mountains of Kerala (estimated to be 10 mGy/y), villages on the coasts of Kerala (4-13 mGy/y), and Ramasar, Iran (7-480 mGy/y).

A remarkable example of radiation hormesis in cancer mortality involves people in 1360 Taiwan homes built in 1982-3; in 1992 these were found to have  ${}^{60}$ Co con-

 Table 7. Cancer deaths\* in Japanese survivors
 [38]

Dose, cSv	0 - 0.9	1 - 1.9	2 - 2.9	5 - 9.9	10 - 20	
Number	45,148	7,430	9,235	6,439	5,316	
Cancer	0	-50	56	79	32	
Leukemia	0	-3.1	-2.7	-5.5	2.8	
All cancer	0	-52	55	77	36	

\*CHANGE FROM CONTROL PER 10,000 PERSONS

taminated steel beams.<sup>[39]</sup> Assuming occupancy of eight hours per day, the average exposures were estimated to be 0.5 cSv/y with 10% receiving >5 cSv/y. The yearly cancer death rate in Taiwan was 10.5 per 10,000 people, 157 cancer deaths in 15 years. In contrast, only four persons died with cancer in the 10,000 people living 15 years in contaminated homes. The SMR for total cancer mortality in this exposed population was 0.025, an extraordinarily low value.

Fallout from a hydrogen bomb at Bikini Island covered 23 Japanese fishermen in March 1954. Whole-body exposures from gamma rays were estimated to be 200-670 cGy.<sup>[40]</sup> All had radiation sickness. One died within eight months. One died 21 years later with liver cirrhosis. None died with cancer within 25 years of their exposure. The lesson learned here and at Chernobyl is that some radiation sickness can be cured by appropriate medical care.

The Chernobyl nuclear reactor explosion revealed the depth of misguided beliefs about low-dose irradiation. Fear of radiation caused over 100,000 deaths by abortions and suicide.<sup>[41]</sup> The Nuclear Energy Agency concluded: "Nevertheless, the dose estimates generally accepted indicate that, with the exception of thyroid disease, it is unlikely that the exposure would lead to discernible radiation effects in the general population."<sup>[42]</sup> The incidence of childhood thyroid cancer increased; deaths from thyroid cancer did not increase. Of 800,000 workers involved in the cleanup, 31 died from radiation within the first four months.<sup>[42]</sup> During the first decade, no one exposed to less than 2 Gy died with cancer which could be attributed to radiation.

#### **DISCUSSION AND CONCLUSIONS**

Both animal experiments and human experiences show significant benefits from low doses of ionizing radiation from both internal and external sources. Although no mammalian data is available, radiogenic metabolism appears to be essential for health and life. Radiation hormesis in immunity is the basis for important benefits. Superior performance was found for many parameters of reproduction following low-dose irradiation of either the male or female parent, or the fetus. Increased average life-span has been found in lightly irradiated invertebrates, experimental animals and humans. Our main focus is on decreased total cancer mortality rates in humans.

There are several reasons why the results summarized here are opposite from those usually reported. Most epidemiologists and government agencies err by one or more of the following:

a) assume all radiation is harmful;

- b) include data from low-dose participants in their control cohort;
- c) have no low-dose groups in the protocol;
- d) do not use available low-dose data;
- e) do not report enough raw data to construct a dose-response curve at low doses;
- f) use a one dimensional formula or statistic which does not allow expression of beneficial effects;
- g) ignore data that does not fit the LNT dose-response curve;
- h) distort results by the use of median instead of mean or average value;
- interpolate between high doses and background levels to obtain fancied results to produce and support unreasonable regulations;
- j) assume cell functions are not subject to whole body activities;
- k) ignore increased immune competence found in exposed organisms; and
- ignore increased health and average lifespan while emphasizing risks and death. Criticisms of classic epidemiologic reports continue to be ignored.<sup>[43]</sup>

Mechanisms of radiation hormesis include:

- a) radiogenic metabolism, metabolism promoted by ionizing radiation;
- b) adaptive enzyme formation, increased DNA, RNA and membrane repair enzymes;
- c) increased immune competence, both chemical and cellular components of a very complex system; and
- d) supplementation of an "essential agent", essential according to evidence from nonvertebrates. These have been discussed.<sup>[8,9,44]</sup>

Human experiences reported during the past decade provide strong evidence showing that whole body exposures to low doses of ionizing radiation decrease cancer mortality rates. Statistically significant results from carefully controlled studies with exposed nuclear workers show that about half of all cancer deaths in the general population are premature. Since the United States has almost 600,000 cancer deaths annually, reasonable extrapolation suggests that safe supplementation with low doses of ionizing radiation would prevent about 250,000 premature cancer deaths each year. The exposure may come from either internal sources, as demonstrated with plutonium, radon and radium, or from external sources.

Without realistic concepts of health involved, risk/benefit analyses based only on death statistics are devastating to both health and industry. Most government agencies are oriented toward protection and restriction. People would be better served if they were oriented toward health and safety. The federal agency penchant for protection at any cost leads to intellectual dishonesty and disaster for health considerations. One death in 1932 inaugurated FDA strict radiation regulations. Where is consideration for 250,000 premature cancer deaths each year in the United States? Based upon the data in Table 6, safe radiation supplementation in the United States would prevent 700 premature deaths every day. These deaths preclude extensive research programs to obtain information that is already available.

The conclusion is this: *we live with a subclinical deficiency of ionizing radiation*. By ignoring the scientific data in almost 3000 reports, advisory committees and government practices have caused, and are now causing, premature cancer deaths for millions of people. We need more, not less, exposure to ionizing radiation. The evidence that ionizing radiation is an essential agent has been

reviewed.<sup>[8,20,21,44]</sup> A partial radiation deficiency can be remedied by safe supplementation with external or internal sources.<sup>[44,45]</sup> Data from exposed nuclear workers indicated a lifetime dose was about 5 cGy.<sup>[20,44,45]</sup> Since much of this was rapidly dissipated by excretion, fractionated, or chronic, doses of 5 cGy/y should be used. This would provide a safety factor of 200, considerably greater than that provided for several essential nutrients. Several populations have been exposed to more than 5 Gy/y for many generations.<sup>[44,45]</sup>

There is proven benefit and no known risk from low-dose irradiation. Health and increased average life-span, not risk and death, should be the guide for new recommendations and laws. With the exception of suicides and abortions motivated by fear, people do not die from low-dose irradiation. Concern for LNT and the *perception of harm* by regulatory agencies promotes fear of this benign environmental agent. Convincing evidence shows that safe supplementation with low doses of ionizing radiation would produce a new plateau of health.

Radiation hormesis invalidates LNT and reverses the need for counterproductive efforts to attain as low as reasonably achievable (ALARA) exposures in commercial industries and waste management programs. Nuclear industries should allow exposures up to thirty times the average background radiation levels, 2 mGy/y. A lifetime dose of 5 cGy is not only safe, it is shown to be healthful by 7 million personvears experience with exposed and carefully selected control nuclear workers.<sup>[45]</sup> The trillions of dollars estimated for worldwide nuclear waste management can be reduced to billions to provide safe, low-dose irradiation to improve our health. The direction is obvious; the first step remains to be taken.

#### References

- Luckey, T.D., "Hormesis Revisited," *RSO* Magazine, 3:20-21, 1998.
- 2. Luckey, T.D., *Hormesis with Ionizing Radiation*, CRC Press, Boca Raton, 1980.
- 3. Anon, "Experiments with X-Rays Upon Germs," *Electr. Engin.*, **22**:176, 1896.
- Mayr, A. and Paulis, S., "Unexpected Effects of Whole-Body Irradiation on the Mortality Rate of Baby Mice After an Infection with the Vesicular Stomatitis Virus (VSV)," *Zentralbl. Veterinaermed.*, 36:577-581, 1989.
- Liu, Z-S., "Ionizing Radiation Increases Immune Competence," Abstract, pp. 12-13 and 52-53, The Seventh International Conference on Nuclear Engineering Special Symposium "Radiation Health Effects: Applying Data to Standards", Tokyo, April 1999.
- Stone, R., "Health Protection Activities of the Plutonium Project," *Proc. Am. Philos. Soc.*, 90:11-19, 1942.
- Lorenz, E., "Some Biologic Effects of Long Continued Irradiation," *Am. J. Roentgenol.*, 63:176-185, 1950.
- 8. Luckey, T.D., *Radiation Hormesis*, CRC Press, Boca Raton, 1991.
- Muckerheide, J., "Low-Level Radiation Health Effects: Compiling the Data," Radiation, Science, and Health, Inc., Needham, 1999.
- Hahn, E.W. and Ward, W.F., "Increased Litter Size in the X-Irradiated During the Estrous Cycle Before Mating," *Science*, 157:956-957, 1967.

- 11. Kaplan, I.I., *Clinical Radiation Therapy*, P.B. Hoeber, New York, 1949.
- Luning, K., "Studies of Irradiated Mouse Populations," *Hereditas*, 46:668-674, 1960.
- Spalding, J.F., Brooks, M.R. and Tietjen, G.L., "Comparative Litter Reproduction Characteristics of Mouse Populations for 82 Generations of X-Irradiated Male Progenitors," *Proc. Soc. Exptl. Biol. Med.*, 166:237-240, 1981.
- Muramatsu, S., Sugahara, T, Tschiya, T and Okazawa, Y, "Effects of Chronic Low-Dose Irradiation for Three Successive Generations on the Breeding Behavior of Mice," *J. Rad. Biol.*, 8:523-531, 1964.
- Brown, S.O., "Effects of Continuous Low Intensity Radiation on Successive Generations of the Albino Rat," *Genetics*, 50: 1101-1113, 1964.
- Searle, A.G., "Effects of Low-Level Irradiation on Fitness and Skeletal Variation in an Inbred Mouse Strain," *Genetics*, 50 (Suppl): 1159-1178, 1964.
- Kondo, S., *Health Effects of Low-Level Radiation*, Kinki University Press, Osaka, 1993.
- Schull, W. J., Otakee, M. and Neel, J.V., "Genetic Effects of the Atomic Bomb: Reappraisal," *Science*, **213**:1220-1227, 1981.
- US Bureau of the Census, "Statistical Abstracts of the United States," 116<sup>th</sup> edition, Washington, DC, 1996.
- Luckey, T.D., "Radiation Hormesis in Cancer Mortality," *Int. J. Occup. Med. Tox.*, 3:175-191, 1994.

- Luckey, T.D., "Low-Dose Irradiation Reduces Cancer Deaths," *Rad. Protect.Manag.*, 14:58-64, 1997.
- Luckey, T.D., "Risk/Benefit Evaluation of Environmental Plutonium," *Rad. Protect Manag.*, 15:19-25, 1998.
- 23. Moss, W. and Eckhardt, R., "The Human Plutonium Injection Experiments," *Los Alamos Science*, **23**:177-233, 1995.
- Voelz, G. L. and Lawrence, J. N., "A 42-Year Medical Follow-Up of Manhattan Project Plutonium Workers," *Health. Phys.*, 61:181-190, 1991.
- Beral, V., Fraser, P., Carpenter, L., Booth, M., Brown, A. and Rose, G., "Mortality of Employees of the Atomic Weapons Establishment," *Brit. Med. J.*, 297:757-770, 1988.
- Tokarskaya, Z.B., Okladnikova, N.D., Belyaeva, Z.D. and Drozhko, E.G., "Multifactoral Analysis of Lung Cancer Dose-Response Relationships for Workers at the Mayak Nuclear Enterprise," *Health Phys.*, **73**:899-905, 1997.
- Muckerheide, J., "Low-Level Radiation Health Effects Policies and Cost/Benefits," *Trans. Amer. Nucl. Soc.*, 72:12-13, 1995.
- 28. Evans, R.D., "Radium in Man," *Health Phys.*, **27**:497-510, 1974.
- Rowland, R.E., *Radium in Humans: a Review of US Studies,* ANL/ER-3 UC-408, Argonne National Laboratory, 1994.
- Spiers, F.W., et. al., "Leukemia Incidence in the U.S. Dial Workers," *Health Phys. Soc.*, 44:1, 1983.
- Baverstock, K.F. and Papworth, D., "The UK Radium Luminizer Survey," pp.72-76 in Taylor, D.M., Mays, C.W., Gerber, G.B. and Thomas, R.G., eds., *Risks from Radium and Thorotrast*, British Institute

of Radiology, London, 1989.

- Cohen, B.L., "Test of the Linear No-Threshold Theory of Radiation Carcinogenesis for Inhaled Radon Decay Products," *Health Phys.*, 68:157-174, 1995.
- Auvenin, A., Maekelaeinen, I., Hakama, M., et. al., "Indoor Radon Exposure and Risk of Lung Cancer: a Nested Case-Control Study in Finland," *J. Nat. Cancer Inst.*, 88:966-972, 1996.
- Haynes, R.M., "The Distribution of Domestic Radon Concentrations and Lung Cancer Mortality in England and Wales," *Rad. Protect. Dosim.*, 25:93-96, 1988.
- Bogoljubov, W.M., "Clinical Aspects of Radon Therapy in the USSR," Z. Phys. Med. Balneol.Med. Klimatol., 17:58-63, 1988.
- Adam, H., ed., "Scientific Principles of the Health Treatments in Badgastein and Bad Hofgastein," Cure and Tourism Administration, Badgastein, 1991.
- Lewis, W.V., "Arthritis and Radioactivity," Peanut Butter Publishing, Seattle, 1994.
- 38. Shimizu, Y., Kato, H., Schull, W.J. and Mabuchi, K., "Dose-Response Analysis Among Atomic Bomb Survivors Exposed to Low-Dose Irradiation," pp.71-74 in Sugahara, T., Sagan, L. and Aoyama, T., eds., Low-Dose Irradiation and Biological Defense Mechanisms, Excerpta Medica, Amsterdam, 1982.
- Laun, Y.C., "Follow-Up Study of the Incident of the Cobalt-60 Radiation Contaminated Buildings in Taiwan," The RBC Pollution Prevention Society of ROC, 1998.

- Kumatori, T., Ishihara, T, Hirshima, K., Sugiyama, H., Ishii, S. and Miyokshi, K., "Follow-Up Studies Over a 25-Year Period on the Japanese Fishermen Exposed to Radioactive Fallout in 1954," pp. 33-54 in Hubner, K.F. and Fry, A.A., eds., *The Medical Basis for Radiation Preparedness*, Elsevier, New York, 1980.
- Ketchum, L.E., "Lessons of Chernobyl: SNM Members Try to Decontaminate World Threatened by Fallout," *J. Nucl. Med.*, 28:413-422, 1987.
- NEA Committee, "Chernobyl, Ten Years on Radiological and Health Impact," Nuclear Energy Agency, Cedex, Paris, 1995.
- Cohen, B.L., "Limitations and Problems in Deriving Risk Estimates for Low-Level Radiation Exposures," *J. Biol. Med.*, 54:329-338, 1981.
- Luckey, T.D., "Nurture with Ionizing Radiation," *Nutrition and Cancer*, submitted 1998.
- Luckey, T.D., "Estimation of a Minimum Yearly Radiation Allowance (MYRA)," J. Clean Technol. Environ. Toxicol & Occup. Med., 6;1052-1962, 1997.

#### The Author

**T. D. Luckey** is Professor Emeritus of the University of Missouri, Columbia and Honorary Professor of Olde Herborn University. He has a BS degree in chemistry from Colorado State University and an MS and PhD from Wisconsin University. Eight years of research in gnotobiology at Notre Dame University was followed by 30 years as professor of biochemistry, 14 years as chair, at the University of Missouri. Dr. Luckey has lectured extensively on nutrition, intestinal microecology, germ-free life, thymic hormones and radiation hormesis. In 1979, he received a Humboldt Senior Scientist Award for research in Germany. In 1984, he was knighted Ritter von Greifenstein. In 1996, he became a member of the Board of Directors of Radiation, Science and Health, an international group of independent individuals knowledgeable in radiation science and public policy.

## **RSO Magazine's Sponsors**

All material published in these pages is copyrighted by RSA Publications, a division of Radiation Safety Associates, Inc. Copyright 2003, all rights reserved.

# Sponsors and advertisers help to make these pages possible; please support them (click below to visit their websites).

Bicron Direct (<u>www.bicrondirect.com</u>) Canberra (<u>www.canberra.com</u>) Perkin-Elmer (<u>www.perkinelmer.com</u>) RSA Laboratories (<u>www.radpro.com/analysis</u>) RSA Publications (<u>www.radpro.com/publications</u>) Radiation Safety Associates, Inc. (<u>www.radpro.com</u>)