Studies of Radium-Exposed Humans: The Fallacy Underlying a Major "Foundation of NCRP, ICRP, and AEC Guidelines for Radiation Exposure to the Population-at-Large"

by

John W. Gofman and Arthur R. Tamplin

Division of Medical Physics (Berkeley)
and
Bio-Medical Research Division
Lawrence Radiation Laboratory (Livermore)
University of California

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Introduction

The guidelines which specify the maximum limits of exposure of humans to ionizing radiation from peaceful uses of atomic energy represent a set of numbers having as great an impact upon the future of the human race as any set of numbers ever could. Therefore, society must demand, as an item of the very highest priority, that such guidelines be absolutely above reproach and question, for the consequences of error can even mean the deterioration of the human race on earth.

Recently we have attacked the Federal Radiation Council Guidelines for such exposure on the grounds that if everyone received the Guideline dosage, some 16,000 additional cases of cancer plus leukemia would occur each year in the United States (1)(2).

It is the purpose of this communication to demonstrate that one of the purported major foundations of guidelines established by the ICRP, the NCRP, and the FRC is totally without basis in fact and rests upon the overtly erroneous interpretation of some otherwise extensive careful observations on humans. We refer to the belief that a threshold (practical or absolute) was demonstrated through the studies of radium dial painters, chemists exposed to radium, and persons receiving radium or related alpha emitters medically.

The chief proponent of the belief that the data accumulated through the study of such individuals leads to a valid "threshold" below which no injury occurs is Professor Robley D. Evans of the Massachusetts Institute of Technology. Dr. Evans is to be commended for a beautiful series of investigations extending over 30 years which have greatly increased our knowledge concerning radium and its effects upon man. However, we shall develop the evidence here to prove that Dr. Evans' conclusions from his own and from other data are totally erroneous with respect to demonstrating or even suggesting a "safe threshold" of ionizing radiation.

We can best start this evaluation by a series of quotations of Professor Evans, quotations of such deep consequence as to possibly affect the future of every living human and those unborn.

Quotation 1 (Reference 3)

"The effects of skeletally deposited radium and mesothorium are of immediate relevance here. These studies have provided the permissible body burden for radium in humans. It is the only NCRP, ICRP, Atomic Energy Commission permissible dose based directly upon observations on humans, and is the pivot or reference point for the permissible burdens of plutonium and of strontium-90."

Quotation 2 (Reference 4)

"It is my conviction that there does exist an absolute threshold and a practical threshold for inhaled radon daughters, below which these nuclides are innocuous."

Quotation 3 (Reference 5)

"Thus it will be seen that the present RPG of 0.1μC Ra contains a large safety factor and would appear to be a satisfactory value even if applied to large populations."

Quotation 4 (Reference 6)

"In the present series of hearings this committee has been exposed to the conservative, oversimplified, incorrect, linear and non-threshold model of radiation carcinogenesis."

These represent four quotations of great assurance and of far-reaching implications. We shall now, through analysis of the data upon which Professor Evans bases these conclusions, demonstrate that the conclusions implied in these quotations are not correct, and are in no way supported by the evidence upon which they rest.

The Experimental Observations

This analysis will address itself to the data concerning the occurrence of cancer (carcinomas plus sarcomas) in persons carrying various measured residual body burdens of radium. Evans has presented the data for one series of cases (269 persons in all) with the occurrence of cancer in individuals in relationship to the residual radium burden (5). Hasterlik has presented an entirely separate series (264 women, some 36 years after occupational exposure to radium) with the occurrence of cancer in individuals in relation to residual radium burden (7). These data are reproduced in Table 1 (Evans data) and Table 2 (Hasterlik data). As Evans correctly pointed out, there is remarkably good agreement between

the two sets of data (8). However, we must add there is remarkably good further agreement in the fact that neither set of data supports the conclusions drawn by Evans.

Table 1 (Reference 5)

Data for 269 cases where a pure radium equivalent (residual burden in μC Ra) was estimated (Dial Painters, Chemists, plus medically treated persons).

	μC Ra equivalent residual		
No. of Cases	Dose Range	Median Dose	Number of Cancers
42	<0.001	<0.001	0
61	0.001- 0.01	0.0055	0
80	0.01 - 0.1	0.055	0
32	0.1 - 1.0	0.55	3
40	1.0 - 10.0	5.5	14
14	10.0 -100.0	55	2

Table 2 (Reference 7)

Data for 264 women (~ 36 years after occupational exposure)

	μC Ra equivalent residual		
No. of Cases	Dose Range	Median Dose	Number of Cancers
23	<0.001	<0.001	0
36	0.001-0.01	0.0055	0
102	0.01 -0.1	0.055	0
62	0.1 -1.0	0.55	3
41	>1.0 (1-10)	5.5	14

Analysis of Both Sets of Data

The hypotheses that have been set forth by Evans, exemplified in the quotations above, are:

(1) These data indicate that there exists a threshold value below which radium deposition in the skeleton does not produce cancer in humans.

(2) These data indicate that the linear model of radiation carcinogenesis is incorrect.

Let us approach both of these hypotheses, since they are closely related. At first glance, it is to be noted, in these extremely small series

of humans, that none of the observed cases of cancer occurred in any of the dosage ranges below 0.1 μC Ra residual burden in either series of cases. We can admit even further that in the Evans series (Table 1), the lowest dosage where a cancer occurred is 0.6 μC, and in the Hasterlik series, the lowest dosage with cancer is 0.45 μC. But such a first glance observation does not even remotely resemble an analysis and does not bear at all upon the validity of the Evans hypotheses listed above. We must, therefore, proceed with an analysis.

(a) Analysis of the Evans data (Table 1)

The first step is to determine the probability of finding cancer in these subjects in relationship to dose of residual Ra burden. This can be done either using only the group of cases (1.0-10.0 μC Ra) with the largest number of cancers, since it is most reliable, or by using all the data for groups where cancers occurred (0.1-1.0, 1.0-10.0, 10.0-100.0 μC Ra). We shall do the analysis both ways, for the sake of completeness.

For the group of cases with burdens of 1.0-10.0 μC Ra there were 14 cases of cancer out of 40 total persons.

$\frac{14}{40}$ is, therefore, the probability of cancer for a median dose of 5.5 μC Ra.
So, per μC Ra, $\frac{14}{40 \times 5.5} = 0.064$ is the probability of cancer.

Expressed alternatively, 6.4 cases per 100 people are found for a burden of 1 μC Ra.

Now, we can look at the three low dose ranges where no cancers were observed. The linear thesis would expect, for such low dosages, 6.4 cases per 100 persons per μC Ra residual burden.

The 0.01-0.1 μC Ra range

We have 80 persons in this group with a median residual burden of 0.055 μC Ra.

For 80 persons, therefore, our expectation is:

$$\left(\frac{80}{100}\right) \times (6.4) \times (0.055) = 0.28 \text{ cases of cancer expected.}$$

Cancer in humans cannot occur as fractional cases. Therefore, in our group of 80 persons, occurrence can be 0 cases, 1 case, 2 cases, etc. If our expected number of cases is 0.28, then there are at least 72 chances out of 100 of observing 0 cases. So the probabilities are strongly in favor of observing 0 cases, which happened.

Conclusion: The data are completely consistent with the linear thesis and completely consistent with the absence of any threshold "safe" dose in this range.

The data provide nothing at all to indicate we should accept either of Dr. Evans hypotheses.

The 0.001-0.01 μC Ra range

We have 61 persons in this group with a median residual burden of 0.0055 μC Ra.

For 61 persons, our expectation is:

$$\left(\frac{61}{100}\right) \times (6.4) \times (0.0055) = 0.021 \text{ cases of cancer expected.}$$

With this expectation, there are at least 98 chances out of 100 that 0 cases would be observed. So the probabilities are extremely strong in favor of observing 0 cases, which happened.

Conclusion: The data are completely consistent with the linear thesis and completely consistent with the absence of any threshold "safe" dose in this range of Ra burdens, also.

The data afford no support whatever to either of Dr. Evans hypotheses.

The <0.001 μC Ra range

We have 42 persons in this group with a residual burden of <0.001. To favor Dr. Evans, let us use 0.001 as the median burden.

For 42 persons, therefore, our expectation is:

$$\left(\frac{42}{100}\right) \times (6.4) \times (0.001) = 0.0027 \text{ cases of cancer expected.}$$

With this expectation, there are at least 997 chances out of 1000 that 0 cases would be observed. So the probabilities are enormously in favor of observing 0 cases, which happened.

Conclusion: The data are completely consistent with the linear thesis and completely consistent with the absence of any threshold "safe" dose in this range of Ra burdens, also.

No support is obtained for either of Evans hypotheses.

Summarizing, we can state, for all dosages below 0.1 μC Ra, there is not a shred of scientific evidence that should lead anyone to accept either of Dr. Evans hypotheses. If evidence favoring his hypotheses exists, it certainly must be elsewhere than the data he has provided

from persons with residual Ra burdens. The linear thesis and the absence of any "safe" threshold emerge totally unscathed from this analysis. They are not proved by this analysis, but there is no suggestion whatever that they are incorrect, in contrast to Dr. Evans claim. (see Quotation 4, above)

(b) Analysis of the Hasterlik data (Table 2)

The procedure of analysis of these data is identical with that provided above. For the group of cases with burdens of 1.0-10.0 μC Ra there were 14 cases of cancer out of 41 total persons.

$\frac{14}{41}$ is, therefore, the probability of cancer for a median dose of 5.5 μC Ra residual burden.

So, per μC Ra, $\frac{14}{41 \times 5.5} = 0.062$ is the probability of cancer.

This means 6.2 cases of cancer per 100 people are found for a residual burden of 1.0 μC Ra. This is spectacularly good agreement with the value 6.4 found for the Evans cases.

We can go through each individual group now as previously, and the results of such analysis are presented in Table 3.

Table 3

Analysis of Expectation vs. Observation in the Hasterlik Series of Cases

(These are the groups where 0 cancers were observed)

No. of Cases	Dose Range	Median Dose use	Expected No. of Cancers	Probability of observing 0 Cancers in this series
23	<0.001	0.001	0.0014	998 out of 1000
36	0.001-0.01	0.0055	0.012	99 out of 100
102	0.01 -0.1	0.055	0.35	65 out of 100

Clearly, from these analyses, we can state the data are completely consistent with the linear thesis and completely consistent with the absence of any "safe" threshold range of Ra burden.

These analyses provide nothing at all to indicate we should accept either of Dr. Evans hypotheses.

(c) Analysis Based upon Use of All Cancer Cases to estimate the probability of cancer per μC Ra

In order to explore every possible way of analyzing the data to see if any support can be developed for Evans hypotheses, we thought it worthwhile to estimate the cancer probability by using all groups where

cancer did occur. Using both the Hasterlik data and the Evans data, we have the combined totals shown in Table 4.

Table 4

Combined Data for Estimation of Cancer Probability Associated with Residual Ra Burden (Hasterlik + Evans data)

No. of Cases	Dose Range	Median Dose	No. of Cancers Observed
94	0.1- 1.0	0.55	6
81	1.0- 10.0	5.5	28
14	10.0-100.0	55.0	3

To estimate the probability of cancer per μC residual Ra burden, utilizing all cases, we need first the average burden for the overall group of persons.

$$\text{Average Burden} = \frac{(94)(0.55) + (81)(5.5) + (14)(55.0)}{94 + 81 + 14} = \frac{1267.2}{189} = 6.7\ \mu C$$

Therefore, probability of cancer per μC Ra burden is:

$$\frac{6 + 28 + 3}{(189)(6.7)} = \frac{37}{(189)(6.7)} = 0.029$$

But this is much lower than the 0.064 we used above. Therefore, if we used 0.029 as the probability of cancer per μC Ra, the analysis would lead to the conclusion that it is even far less likely that any support for Evans hypotheses exists within these data.

Lastly, we may exclude the people with the very high Ra residual burdens (10-100 μC Ra) on the grounds that a very high prior death rate may have left an unrepresentative group.

In this case, we exclude 14 subjects with burdens of 10 μC or more, and we calculate:

$$\text{Average Burden} = \frac{(94)(0.55) + (81)(5.5)}{94 + 81} = \frac{497.2}{175} = 2.8\ \mu C$$

The probability of cancer per μC Ra residual is:

$$\frac{6 + 28}{(175)(2.8)} = \frac{34}{(175)(2.8)} = 0.069$$

But this number is so close to the 0.064 already utilized, that no material support for the Evans hypotheses will derive from its use instead of 0.064.

(d) Analysis of the Evans Series and the Hasterlik Series Combined

As Evans has correctly stated, the data from his series are in remarkably good agreement with the data of Hasterlik. In the hope that possibly, having a larger series through combining both sets of data, it might be possible to give a fairer trial to the Evans hypotheses, we have calculated the expectations using all cases from both series. As the probability of cancer per μC residual Ra burden, the mean of the values derived from Evans data and from the Hasterlik data, namely, 0.063 per μC Ra residual burden is used. The "combined" analysis is presented in Table 5.

Table 5

Analysis of Expectation vs. Observation in The Combined Series of Cases (Hasterlik + Evans).

(These are the groups where 0 cancers were observed)

No. of Cases	Dose Range	Median Dose in use	Expected No. of Cancers	Probability of observing 0 Cancers in this series
65	<0.001	0.001	0.0041	996 out of 1000
97	0.001-0.01	0.0055	0.034	966 out of 1000
182	0.01 -0.1	0.055	0.63	37 out of 100

For the dosage ranges up through 0.01 μC Ra residual burden, the answer is abundantly clear -- no support whatever for either of the Evans hypotheses. Even for the higher dose range 0.01-0.1 μC residual Ra burden, the results fall far short of acceptable support for the Evans hypotheses. If we use the minimum statistical criterion of p=0.05, the analysis shows a probability 7 times too high compared with what it would take to make us accept the Evans hypotheses. On matters of such grave importance, one certainly should insist on using p=0.01, and in this case the probability is 37 times too high compared with what it would take to argue for acceptance of the Evans hypotheses.

Again, even using the combined series, the data are consistent with the linear thesis and are consistent with the absence of any "safe" threshold of residual Ra burden.

Discussion

It is now important to return to the four quotations of Evans presented in the introduction and to show, in turn, the error in each one.

Quotation 1 (see above) claims, "these studies have provided the permissible body burden for radium in humans". The analyses presented above show that "these studies" provide nothing in the way of support for a "safe" threshold body burden with respect to cancer induction. If it is true that NCRP, ICRP, and AEC have, as Evans suggests, used these studies to decide permissible burdens of radium, plutonium, and strontium-90, they would be well advised to cease and desist from any further such use.

Quotation 2 (see above) claims it is Evans "conviction that an absolute or practical threshold exists, below which radon daughters are innocuous". A "conviction" is, of course, a strange phenomenon. It can be based upon scientific evidence, upon intuition, upon hunch, upon religious belief, or upon hope. We would be the first to defend staunchly Professor Evans' right to hold convictions based upon intuition, hunch, religious persuasion, or hope. Our analysis does not address itself to these areas. We can state that his conviction cannot rest upon scientific evidence, for our analysis shows that no such evidence exists.

Quotation 3 (see above) claims that "the RPG of 0.1 μC Ra contains a large safety factor and would appear satisfactory even if applied to large populations". This contention rests in part upon the fact that Professor Evans' studies are of residual radium burdens, and the suggestive evidence that the initial burden was probably 20 times higher. Thus, he suggests that if 0.1 μC Ra residual burden is "safe", then 2.0 μC Ra initial burden would be safe. So, he calculates that 0.1 μC Ra initial burden is "conservative". But 0.1 μC Ra initial burden corresponds to 0.005 μC Ra residual burden. In the analyses above we have demonstrated that Evans data offer no support that 0.005 μC Ra residual burden is below any kind of threshold. Therefore, there is no evidence at all to support his contention that 0.1 μC Ra initial burden is at all safe, to say nothing of being conservative.

This being the case, his assertion that such a value would be satisfactory even if applied to large populations could lead, if accepted by responsible authorities, to a public health disaster unparalleled in the history of mankind.

Quotation 4 (see above) claims, "the linear, non-threshold model of radiation carcinogenesis is conservative, oversimplified, and incorrect". But our analysis shows that Evans data and his analyses do not

(a) even remotely suggest the linear, non-threshold model to be conservative,

(b) even remotely suggest the linear, non-threshold model to be oversimplified,

(c) even remotely suggest the linear, non-threshold model to be incorrect.

It is conceivable that the linear, non-threshold model of radiation carcinogenesis may be conservative, oversimplified, and incorrect. If so, this remains for future science to demonstrate. Evans' work simply does not bear upon this issue. It can be stated that the linear, non-threshold model does make excellent sense in setting Public Health Standards for radiation exposure.

It would be irresponsibility of the highest order, repugnant to any competent bio-medical scientist, to set Public Health Standards based upon a hope, unfounded in evidence, that somehow a poison will turn out to be less toxic than conservative sound estimates would indicate.

Acknowledgment

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References

(1) Gofman, J. W. and Tamplin, A. R. "Low Dose Radiation, Chromosomes, and Cancer", Presented at "1969 Institute of Electrical and Electronic Engineers Symposium: Nuclear Science", Oct. 29, 1969, San Francisco, California (To be published in IEEE Proceedings, February, 1970).

(2) Gofman, J. W. and Tamplin, A. R. "Federal Radiation Council Guidelines for Radiation Exposure of The Population-at-Large--Protection or Disaster?", Testimony presented before The SubCommittee on Air and Water Pollution Committee on Public Works, United States Senate, 91st Congress, November 18, 1969.

(3) Evans, R. D. in "Radiation Exposure of Uranium Miners", Hearings of the Joint Committee on Atomic Energy, 90th Congress, Part 1, May 9 thru August 10, 1967, p. 265.

(4) ibid p. 274.

(5) Evans, R. D. "The Effect of Skeletally Deposited Alpha Emitters in Man", Brit. J. Radiol. 39, 881-895, 1966.

(6) Reference 3, p. 274.

(7) Hasterlik, R. in "Radiation Standards, Including Fallout", Hearings of the Joint Committee on Atomic Energy, 87th Congress, Part 1, June 4-7, 1962, p. 325-331.

(8) Evans, R. D. "The Radium Standard for Boneseekers - Evaluation of the Data of Radium Patients and Dial Painters", Health Physics, 13, 267-278, 1967.

ADDENDUM

Since this manuscript was submitted, it has been called to our attention that Dr. Walter S. Snyder had already demonstrated the erroneous interpretation of Evans concerning thresholds and the linear hypothesis[1]. We are delighted to acknowledge this prior analysis, which we consider elegant and correct, by Snyder. His analysis covering 84 of the radium-exposed persons leads to the same conclusion as our analysis of the combined series of 533 radium-exposed persons in Evans' plus Hasterlik's reports. That conclusion is that Evans has not produced scientific evidence to support any safe radiation threshold, nor has he substantiated his claim that the linear model of radiation carcinogenesis is incorrect.

Evans attempted to refute Snyder's work[2]. We consider Evans' criticism of Snyder's statistical approach without merit. Whatever be Evans' comments concerning Snyder's type of analysis, we invite his refutation of our own analysis on the greatly expanded series of cases.

References for Addendum

1. Snyder, W. S. "The Bases of Standards for Radiation Protection: A Comparison of the Threshold Hypothesis and the Linear Hypothesis for the Dose-Effect Relation", in "Radiation Exposure of Uranium Miners", Hearings of the Joint Committee on Atomic Energy, 90th Congress, Part 2, May 9 through August 10, 1967, pp 1256-1260.
2. Evans, R. D. Appendix 27 "Correspondence Concerning Bases of Standards for Radiation Protection: A Comparison of the Threshold Hypothesis and the Linear Hypothesis for the Dose-Effect Relation". Ibid pp 1364-1365.