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CURRENT STATUS OF THE PLUTONIUM HOT PARTICLE PROBLEM*

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Introduction

The recent revival of interest in the 'hot particle' problem, especially as regards particulate plutonium and other actinide elements in the lung, has stimulated a great deal of thought on this subject during the past several years. Non-uniformity of dose distribution has been of interest to standards-setting bodies and other groups, such as the National Academy of Sciences, and to health protectionists for many years. In fact, interest in the subject as regards alpha-emitting radionuclides predates the discovery of plutonium in 1941.

The hot particle problem has recently been brought to the attention of several federal agencies by the National Resources Defense Council, Inc. [1]. The NRDC's original petition and supporting documentation was submitted to the U. S. Atomic Energy Commission (AEC) and the U. S. Environmental Protection Agency (EPA) on February 14, 1974. Because of the Energy Reorganization Act of 1974 which resulted in the formation of the U.S. Energy Research and Development Administration (ERDA) and Nuclear Regulatory Commission (NRC), the federal response to the NRDC petition is now the responsibility of the EPA and the NRC. Although many organizations have considered the hot particle problem for decades, there has been considerable reassessment of the problem since February 1974. I should point out that no final response to the NRDC's petition has been made to date by either the EPA or NRC. There have been, however, discussions and correspondence among the involved parties and the NRDC has

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presented testimony on hot particles at AEC, EPA and ERDA hearings since submitting the petition.

The NRDC petition states (page 4) that in its view the present radiation standards when applied to hot particles are too high by a factor of 115,000. In addition, the petition states that each of the NRDC's individual members is a potential victim of exposure to hot particles. The document supporting the petition, prepared by Tamplin and Cochran, proposes that a single radioactive particle in the lung capable of delivering a local radiation dose of 1000 or more rem per year will produce local tissue damage. The local tissue damage in turn produces a risk of lung cancer of one in 2000 (5×10^{-4}). Put another way, exposure to 2000 such hot particles would produce one lung cancer.

National Radiological Protection Board's Radiological Protection Bulletin #8 (1974).

A short critical review of the NRDC petition was prepared by the United Kingdom's National Radiological Protection Board (NRPB) [2] which concludes, "It is noted that the basis of ICRP recommendations is the average radiation dose to an organ and not the number of radioactive particles in the organ. This dosimetric basis of radiological protection has been established for many years by observation of humans and experimental work with animals. A better evaluation than offered by Tamplin and Cochran would be needed for this system to be set aside in favor of the hot particle concept. Their estimate that there is a risk of cancer being generated in cells surrounding a hot particle of one in 2000 cannot be substantiated by our present knowledge."

Biophysical Society (STAIS) Report (1974)

In December 1974, the Science and Technology Advice and Information Service (STAIS) of the Biophysical Society conducted a study of the question of radiation standards for hot particles at the request of the Center for Science in the Public Interest [3]. The summary of the report written by the Committee coordinators is as follows:

> "1. The problem raised by the Natural Resources Defense Council petition of what should be the maximum permissible lung burden (MPLB) of hot particles is a valid and serious one. However, the call for a decrease in MPLB by 10^5 is exaggerated. More animal and epidemiological data are needed for a truly adequate estimate of what should be the radiation protection standard. A crucial piece of missing information concerns the distribution of particle sizes involved in the Manhattan District accident. Twenty-five individuals followed for almost 30 years have no lung cancer from 3–10 nCi plutonium in the chest. Calculations in the Tamplin and Cochran report accompanying the petition indicated that the particles were too small to be effective. Other calculations resulted in the opposite conclusion. One of the reviewers suggested an experimental reenactment of this accident (without humans present) for the purpose of measuring particle size.

"The lung burdens of 25 Rocky Flats workers exposed to plutonium fires range from one to ten times the present MPLB. No lung cancer has been detected in any of these individuals after nine years. Since there is evidence that the latent period for cancer induction after a large exposure may be as short as this, these data again suggest that the factor of 10^5 is too large.

"2. The reviewers who looked into the quantitative aspects of the Tamplin-Cochran report all concluded that it contained exaggerations and lack of adequate reasoning (a,b, c below). This report includes interpretation of the data of others, sometimes at variance with the author's own interpretation. Two of the reviewers used existing published animal data and several biological models to estimate the probability of cancer induction in the human lung from hot particles. They conclude that the existing MPLB should probably be decreased by some factor between 40 and 10^4, but that this figure at present can only be tentative, because of the paucity of data. Another reviewer finds no reason to alter current standards.

"a) The single instance of a hand sarcoma following plutonium contamination is inadequate for a quantitative argument, especially since there was no evidence that the plutonium penetrated the skin.

"b) The single instance of supposed precancerous changes in the neighborhood of a puncture wound involving plutonium, later excised, is also not suitable for a quantitative argument, especially since there was another similar but un-excised case in which no cancer developed in 30 years.

"c) The use of the data of Albert et al. on rat skin tumors induced by fast electrons to estimate the risk from hot particles seems unjustified on four grounds: (1) The rat data involved a single dose, whereas the lung irradiation being considered is chronic. (2) Tamplin and Cochran do not cite data showing that non-uniform irradiation by beta and alpha particles is less effective than uniform radiation. (3) Previous experiments cited by the Albert groups showed no tumor production by 0.3 MeV electrons, external alpha particles and protons. (4) The hair follicle seems to be the sensitive structure for radiation-induced cancer in the skin. No similar structure has been identified in the lung, nor is there any estimate of the probability of a hot particle being close to such a structure."

National Radiological Protection Board Report R-29 (1974)

In September 1974, the United Kingdom's National Radiological Protection Board published a report entitled, "Radiological Problems in the Protection of Persons Exposed to Plutonium" [4]. The following quotations are taken from Section 9 of the report entitled "Hot Particles".

By way of introduction, the report states, "The radiological protection problems associated with insoluble particles of alpha-emitting radionuclides have been known and considered for a number of years (Dolphin, 1964) but recently public attention has been

drawn to these problems by a petition submitted to the USAEC by Tamplin and Cochran (1974) which caused comment in the national press. The problems concern the biological effect of high localised doses."

After discussing the issue, the section concludes, "In summary, there is no biological evidence available at present which suggests that "hot spots" carry a higher risk of cancer induction. Hence there is no necessity to change from the present system of using average dose to organs or tissues. However, it would be prudent to continue research into the biological effects of non-uniform dose distributions within organs."

WASH-1320 (1974)

Another report which should be consulted by those interested in the hot particle issue is WASH-1320, "A Radiobiological Assessment of the Spatial Distribution of Radiation Dose from Inhaled Plutonium," [5] which was published in September 1974 by the USAEC. The summary and conclusions of the report are as follows:

•The importance of spatial distribution of dose to radiation protection practices by national and international standards-setting organizations and the scientific community predates the discovery of plutonium. Continued examination of the radiobiological aspects of the spatial distribution of dose, especially as regards alpha-emitting particles, has not led to major changes in radiation protection standards. However, the problem is and should be continually reassessed.

•Animal studies clearly indicate that inhaled radioactive particles move from the lung to other organs and can be excreted from the body by several mechanisms. The experimental data also show that truly uniform distributions of inhaled radionuclides in lung seldom, if ever, occur. Because of the mobility of plutonium within the lung, there is some biological justification for averaging the radiation dose to the total tissue.

•Particles deposited in the lung are dynamic and mobile unless trapped, as for example, in scar tissue. Experiments have been designed to simulate the static plutonium particle and study the biological effects of truly "hot spots" of radioactivity in the lung. These and other comparative experiments of uniform and non-uniform distributions of absorbed energy from radioactive particles suggest a biological sparing effect for both acute and late responses to the non-uniform distribution. Available experimental data indicate that averaging the absorbed alpha radiation dose from plutonium particles in the lung is radiobiologically sound.

•Dosimetric models used to predict lung tumor probability in animals and human beings are biologically deficient, largely because of the lack of the required biological information. Most models are based on studies of tumor induction in irradiated rat skin and on the assumed validity of extrapolating to lung tissue. This practice is questionable for several reasons including the fact that the results of studies with rats vary with rat strains, i.e., tumor type, and that the results of comparable studies of irradiated mouse skin have not yielded results identical to the rat experiments. Thus, use of these models can lead to erroneous predictions of tumor probabilities.

•Consideration of radiation carcinogenesis mechanisms suggests that there has been no change in either the direction or strength

of data which would compel departure from the concept that average lung dose for alpha particles provides a reasonable and conservative base for radiation protection.

"Thirty years experience with plutonium in laboratory and production facilities has provided no evidence that the mean-dose lung model on which occupational radiation protection standards for plutonium are based is grossly in error or leads to hazardous practices. Data currently available from occupationally exposed persons indicate that the non-homogeneous dose distribution from inhaled plutonium does not result in demonstrably greater risk than that assumed for a uniform dose distribution. Thus, empirical considerations lead to the conclusion that the non-uniform dose distribution of plutonium particles in the lung is not more hazardous and may be less hazardous than if the plutonium were uniformly distributed and that the mean-dose lung model is a radiobiologically sound basis for establishment of plutonium standards.

The report WASH-1320 [5] was not meant to be a critique of the NRDC petition on hot particles as it addressed the main generic issue of the problem, that is, the question of the biological importance of spatial distribution of radiation dose from inhaled plutonium.

Los Alamos Scientific Laboratory Report LA-5810-MS (1974)

In November 1974, a Los Alamos Scientific Laboratory report [6] was prepared by a group of biomedical researchers with relevant plutonium research experience. This report, entitled "A Review of the Natural Resources Defense Council Petition Concerning Limits for Insoluble Alpha Emitters," represents the most detailed and comprehensive analysis of the NRDC petition available to date. The report concludes, "The preceding review has indicated that the Tamplin-Cochran conclusions are based upon a hypothesis which requires considerable extrapolation of the data upon which it is based. Later evidence, of the same nature as was used in the derivation (i.e., rat skin data), does not support the assumptions of the original model. The Tamplin-Cochran interpretation of the model not only fails to take into account the later evidence, but appears to present the hypothesis as fact. The supporting evidence on human data which they present are based upon unsupported assumptions and distortions of the words of the authors they quote. Most importantly, they fail to use or acknowledge direct evidence on the effect of radioactive particles. Such evidence indicates that the basic damage model which they use overestimates badly the carcinogenic effects of radioactive particles. We conclude, therefore, that the application of the average organ dose to the establishment of limits is still appropriate, although experimentation to narrow existing uncertainties on the effects of non-uniform dose distribution should continue."

EPA Report ORP/CSD-75-1 (1975) and WASH-1359 (1974)

The U. S. Environmental Protection Agency held hearings in December 1974 (Washington, D. C.) and January 1975 (Denver, Colorado) on the subject of plutonium standards. The question of hot particles was addressed by several persons providing testimony. Proceedings from these hearings are available in a three-volume publication [7]. A compilation of the USAEC's testimony presented at these hearings

was made available earlier in WASH-1359 entitled, "Plutonium and Other Transuranium Elements: Sources, Environmental Distribution and Biomedical Effects" [8]. These reports contain much information on the subject of the hot particle hypothesis. Also contained in WASH-1359 and ORP/CSD-75-1 is a letter from Dr. C. C. Lushbaugh concerning the incorrect interpretation by Tamplin and Cochran of his published data on a plutonium wound in the hand of a process worker. These reports also contain a report entitled "A Critique of the Tamplin-Cochran Proposal for Revision of the Current Plutonium Exposure Standards" by Dr. Roy Albert of the New York University Medical Center. The summary reads as follows:

"Largely on the basis of rat skin tumor experiments, Tamplin and Cochran propose that a single radioactive particle in the lung which delivers a local dose of more than 1000 rem per year will produce focal tissue damage and that this focal damage per se confers a risk of lung cancer of one in two thousand.

"A review of current knowledge about the relationship of tissue damage to the induction of cancer does not support the contention that tissue damage is a proximate cause of cancer; rather that tissue damage represents a parallel toxic action of carcinogens which, to some extent, may enhance the development of tumors produced by carcinogens. Since the Tamplin-Cochran proposal is based almost wholly on radiation tumor studies of the rat skin hair follicles, the decisive argument against this proposal is the evidence that focal alpha irradiation of localized regions on the hair follicle, in a pattern similar to that from a plutonium particle, is non-tumorigenic."

National Council on Radiation Protection and Measurements Report No. 46 (1975)

The National Council on Radiation Protection and Measurements (NCRP) recently released NCRP Report No. 46 entitled, "Alpha-Emitting Particles in Lungs" [9]. The report was discussed in some detail by Drs. M. Eisenbud of New York University and J. N. Stannard of the University of Rochester at the May 28, 1975, session of the Energy Research and Development Administration's public hearing concerning the Technology Research and Development Program for the Liquid Metal Fast Breeder Reactor and the Proposed Final Environmental Impact Statement on that program. The report was prepared by an ad hoc committee consisting of W. J. Bair (chairman), A. Kellerer, J. N. Stannard and R. C. Thompson and reviewed and approved by the entire NCRP Council which is comprised of approximately 70 individuals.

The NCRP report concludes that:

- a substantial body of experimental animal data indicates that particulate plutonium in the lung is no greater hazard than the same amount of plutonium distributed more uniformly throughout the lung.
- the above observation from animal data is consistent with the theoretical analysis of the microscopic distribution of energy absorption in each case.
- the current NCRP practice of averaging absorbed dose over the lung is defensible when used in conjunction with appropriate dose limits.
- more precise consideration of spatial distribution of

absorbed dose cannot be profitably used to derive permissible exposure limits until we have more understanding of the relation between dose and effect.

The report is neither an endorsement of nor a commentary on the absolute numerical adequacy of present NCRP standards for plutonium or other alpha-emitting particles.

Medical Research Council's Committee on Protection Against Ionizing Radiations-Report on the Toxicity of Plutonium (1975)

Earlier this year the United Kingdom's Medical Research Council's Committee on Protection Against Ionizing Radiations published a report entitled, "The Toxicity of Plutonium" [10]. The following is a quotation from the report on the section dealing with recommendations relating specifically to plutonium: "For many years those professionally concerned with radiological protection have been aware of the need to establish general principles for assessing the relative risks of homogeneous and inhomogeneous irradiation. As discussed in the appendix, there is no evidence that irradiation by 'hot particles' in the lung is markedly more hazardous than the same activity uniformly distributed or that the currently recommended standards for inhalation of plutonium are seriously in error." In the section of the report on hot particles, the authors state the following: "The conclusions of Tamplin and Cochran cannot be any better founded than the hypothesis on which they are based and that is too tenuous to be worth further discussion here. Tamplin and Cochran also put themselves in the difficult situation that the risk is considered to be decreased by a factor of 115,000 if a particle containing 0.1 picocurie plutonium were to break into two equal halves."

The report continues, "The evidence most immediately relevant to the 'hot particle' problem is human experience of lung irradiation. 'Hot particle' irradiation seems unlikely to be more carcinogenic than uniform irradiation to the same dose as is received by the tissues adjacent to the particles. Indeed the risk for uniform irradiation on any hypothesis of carcinogenesis would be larger than for localised irradiation at the same dose in proportion to the ratios of the lung masses involved, unless the sites of deposition of the particles are also the sites where the lung cells specifically sensitive to cancer induction are to be found. Current ideas suggest the opposite, that particles with long residence times are in the deep lung and the cells specially sensitive to cancer induction are in the linings of the airways. On the unlikely assumption of uniform distribution of particles and sensitive cells, if 1000 rem in a year to 64 μg of lung tissue resulted in a mean lung cancer incidence of 1/2000, the cancer risk for irradiation of 120 mg would be 100 percent, and after uniform irradiation of the whole lung of mass 1000 g to 1000 rem some 8000 separately induced lung cancers would be expected on average in each individual. There is no evidence that this happens. Parts of the lung are frequently irradiated to doses of this order in the course of radiotherapy."

This section of the report on hot particles concludes that there is at present no evidence to suggest that irradiation of the lung by plutonium particles is likely to be markedly more carcinogenic than for the case when the same activity is uniformly distributed.

The Importance of Non-Uniform Dose-Distribution to An Organ (1975)

In May 1974 a symposium entitled, "Plutonium Health Implications for Man," was held at Los Alamos, New Mexico. At that meeting, a paper was presented on the subject of non-uniform dose-distribution of plutonium, especially as regards the lung. The published report [11] reviews the data from animal experiments that are often used both for and against support of the hot particle hypothesis. Also contained in the paper are the Los Alamos hamster experiments which currently provide rather convincing evidence that the tumor probability per hot particle as postulated by the NRDC [1] is incorrect. Some consideration of biological mechanisms is contained in the paper as evidenced by the following statement:

"For cases of non-uniform exposure, as occurs for particulate plutonium, there appears to be a biological sparing effect resulting from the fact that fewer cells are exposed to the alpha radiations, and much of the alpha energy is wasted as compared with a more uniform distribution. Also, the collective defenses of the body, both local and abscopal, such as inhibition of transformed cells by normal cells and immune surveillance, are more efficient in the case of non-uniform distribution. The key to the problem may well be the number of cells that interact with an alpha particle but are not killed. For the non-uniform distribution case, there are fewer of these cells which might have the potential to form a cancer, and they would be in an environment which would tend to inhibit their division and development to proceed to form a cancer."

Suggested Reduction of Permissible Exposure to Plutonium and Other Transuranium Elements (1975)

A recent publication suggesting possible reductions for permissible exposure to plutonium considered the lung and the question of hot particles [12]. The report states that "No one knows the answer to this question at the present time. Certainly we would like to have more information. Tamplin and Cochran (*reference*) suggest that because of the very large dose (thousands of rem/y) in the vicinity of a micron size particle of ^{239}Pu lodged in lung tissue, the present q for lung ($\sim$0.015 μCi) and the corresponding values of $(MPC)_a$ for occupational exposure as well as those for members of the public should be lowered by a factor of 10^5. Perhaps they are right, but I believe they have not made a strong case for this factor simply because adequate biological data are not available and much of that which we have seems to give contradictory information."

Morgan [12] also points out that he does not believe that we have "unequivocal proof that there is or isn't a hot particle problem," but that "it certainly is encouraging that there is no clear evidence at the present time that human occupational exposure to plutonium and other transuranium elements has resulted in any form of cancer."

On the basis of other work [13] involving plutonium studies in baboons, Morgan suggests that the value of q when the total lung is the critical tissue, may be reduced by a factor of 4, but cautions that "this of course does not address the hot particle problem but rather shelves it until we have more data." Morgan also adds that this

shelving is what society has practiced for generations in the case of environmental pollutants from burning of fossil fuels.

The abstract of Morgan's paper [12] does state that "Until certain questions are answered about the particle problem, it will not be possible to set a satisfactory maximum permissible body burden for ^{239}Pu based on lung as the critical organ..."

Lung Irradiation with Static Plutonium Microspheres

Experiments conducted at the Los Alamos Scientific Laboratory in which hamster lungs are exposed to plutonium containing microspheres represent an important test of the hot particle hypothesis. Data from these experiments were discussed in WASH-1320 [5] and in several Los Alamos Scientific Laboratory progress reports [14-16].

The Los Alamos experiments were discussed in considerable detail in a report presented at a conference on Experimental Lung Cancer-Carcinogenesis and Bioassays [17]. The report states:

"Our results are in definite contradiction to all simplistic models (GEESAMAN, 1968; DEAN and LANGHAM, 1969; PEREZ and COLEMAN, 1969) that assume tumor induction can be calculated solely on the basis of cellular radiation exposure. The indication is that much more complicated mechanisms are involved and that the volume of tissue irradiated is an important factor. Of the experimental exposures, only the earliest ones have been completed in the sense that the animals have lived out their normal life spans. These involved comparatively small numbers of spheres irradiating only a few percent of the total lung mass. However, 1,142 hamsters were exposed to a total of some 5,700,000 spheres in these experiments, and only 2 lung tumors were observed, which already sets a very low limit on the probability of tumor induction per particle. The additional experiments begun through 1973 will raise the totals to 1,900 animals and 160,000,000 spheres and will greatly increase the fraction of lung irradiated."

Earlier this month, the results of the plutonium microsphere experiments being conducted at Los Alamos were summarized [18] at an International Atomic Energy Agency sponsored symposium on the Biological Effects of Low Level Radiation Pertinent to Protection of Man and His Environment. The report emphasizes that the studies do not add credence to the supposition that lung tumor induction and expression from plutonium particulates can be predicted solely on the number of cells at risk and that discrete focal alpha radiation alone is not an efficient respiratory carcinogen in the hamster.

Additional Information Prepared on the Hot Particle Hypothesis

A status report on the hot particle problem was given at the summer 1975 meeting of the American Nuclear Society and appears as an abstract in the transactions of the meeting [19]. The report covers the original hypothesis and critiques of reviews of the hypothesis. The interested reader is directed to reference [19] for additional information.

National Academy of Sciences

An ad hoc subcommittee of the National Academy of Sciences' Committee on the Biological Effects of Ionizing Radiation is reviewing the problem of non-uniformity of radiation dose as it relates to lung irradiation from plutonium and other actinide elements. A report will be published in the near future.

Conclusions

What can we conclude from the information now available on the hot particle question? I believe that the majority of responsible researchers and others who have reviewed the question of lung irradiation from particulate plutonium have rejected the hot particle hypothesis as put forth by Tamplin and Cochran as being unsupportable. This is, however, an important radiobiological question which continues to command attention of researchers and radiation protection groups.

The proposed risk estimate for plutonium-induced lung cancer of 5×10^{-4} per particle cannot be substantiated on the basis of our current knowledge. In fact, careful consideration of the available data shows that particulate plutonium is not more hazardous than the same amount of plutonium distributed uniformly. Further, the data suggest that the potential hazard from plutonium increases as the dispersion throughout the lung becomes more uniform.

We have yet to learn of the official response to the petition [1] by the EPA and the NRC. Perhaps a response will be available from these agencies before the second anniversary of the petition (14 February 1976). It is unfortunate that questions of such importance require such long periods of time for response. Perhaps we could accelerate the examination process by immediately directing important issues to established organizations such as the NCRP or, on an international scale, the ICRP, to determine if the question or issue is of reasonable importance and priority to command immediate attention. There must also be judgements other than technical that enter the decision making process on a given issue and these must not be overlooked. It is difficult, however, for the lay public to have thrust upon them complex issues which have not first been evaluated by national or international organizations established to provide guidance on the issues being questioned or examined. I believe much time, money and frustration could be saved if we developed a better system for review. In some instances, questions might be identified as "non-issues" and set aside in deference to questions that may indeed require review and decision making by the technical and other components of society.

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