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PROPOSED EXPERIMENTS AT HANFORD ON PARTICLE PROBLEM

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In memo dated July 29, 1954 from Sturges to Bugher on above subject, mention is made of a conflict in data as regards the hazards, if any, on inhaled radioactive particles, citing the work of Taplin, Marinelli and University of Rochester (Hodge).

To my knowledge there is no conflict on this score since the concept of hazard from inhaled radioactive particles stems from the high incidence of lung cancer in European Uranium mines rather than from experimental data. Marinelli's work (Transport of Radium Sulphate from the Lung and Its Elimination from the Human Body Following Single Accidental Exposures, Radiology: 61, 903, 1953) is concerned with the clearance rate of radium sulphate beginning a number of days after exposure. He found a biological half-life in the order of 120 days. Taplin obtained information in rabbits on the rates of removal from the lung of prodigiosin powder and tagged subtilis spores (UCLA 121, 158, 195, 136). He found that much of the material was removed within a few hours. Hodge, from data on the rate of build-up of uranium in dogs' lungs during chronic exposure (UR-67), calculated the biological half-life (ca 200 days) of insoluble uranium salts in the lung. The apparent disparity between Taplin's data and the others is explained by the fact that clearance of dust from the lung is accomplished by two distinct modes: ciliary clearance from the bronchial mucosa which is accomplished in a few hours, and alveolar clearance which takes a much longer time. Marinelli and Hodge's data pertain to the latter mechanism.

The control of the lung cancer hazard from inhaled radioactive particles must be based on the answers to some fundamental questions: (a) how much radiation is required to produce lung cancer, (b) what is the fate of inhaled particles in the lung (i.e. how much is retained in the lung after inhalation and how long do the particles in the lung remain after deposition). With such information, one could calculate the expected lung dosage from airborne particles of a given size distribution and from knowledge of the carcinogenic dose of radiation, estimate the hazard. There is need for considerably more data in both

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categories, especially on the following topics:

1. What cumulative lung dose will increase the incidence of lung cancer after single inhalations of radioactive particles?
2. Same as "1" but with chronic exposure.
3. Does the cancer hazard differ when the radioactivity is deposited in the lung in relatively few large particles compared to many smaller particles (for equal total amounts of radioactivity)?
4. What is the relationship between particle size and bronchial deposition? (Those particles deposited on the bronchi will be cleared out of the lung within a few hours in contrast to those which penetrate the lung more deeply).
5. Is the carcinogenic susceptibility of the bronchial mucosa higher than that of the alveoli or pleura? (Most lung cancers in the European Uranium mines arose on the bronchial mucosa. Is this a question of susceptibility or that a greater dose is delivered to the bronchial mucosa because of bronchial deposition of inhaled radioactive particles?)
6. What materials will act as a co-carcinogen for radiation in the lung? (Tobacco smoke, chromium, arsenic, methylcholanthrene, dibenzanthracene, etc.)
7. How can the particles, once deposited, be removed more quickly?

The Hanford proposal (Project CB-572, Phase II) seems to touch on many of these problems. However, it is difficult to evaluate the proposal because of its lack of specificity in regard to the experimental details. The following questions illustrate this point:

1. Why have the numbers of dogs and monkeys been established at 20 and 8 respectively? Is this related to the expected incidence of lung cancer or lung abscesses? The latter appears to be taken as the end-point for early radiation damage. The rationale behind this is not apparent, since lung infection would be a secondary effect and dependent on a number of external circumstances. In addition, it is not the end-point of interest, namely, lung cancer.

2. What are the radiation dosages involved with the "dosage parameter of 0.1 - 4.0 ug" plutonium oxide? This is important if any generalization of the study is to be made to other materials.
3. What significance can one attach to the measure of clearance rates of particles if one does not know the particle size distribution since the two are interrelated?
4. Mention is made of a co-carcinogen producing lung cancer in combination with radioactive particles. What is the chemical nature of this carcinogen? What types of tumors and with what incidence have they been produced?
5. In what manner is the hazard from single particles of 0.03 - 3 u to be estimated?
6. What agents will be tried for "etiologic" therapy?

The use of dogs and monkeys tacitly assumes that the carcinogenic susceptibility is correlated to animal size and consequently that larger animals will more closely resemble man. A better approach, perhaps, would be to establish the susceptibility of the lung to radiation cancer, using bone as a benchmark, in a single convenient species. This data could then be transferred to man, knowing his susceptibility to bone cancer from the radium experience.

Although the "time factor" is mentioned as important, there is no provision for administering the radioactive particles over varying periods of time. It is a fact that the hazard from inhaled radioactive particles can be chronic (miners, uranium chemical operators) as well as acute (accidental exposure).

The proposed study certainly covers several areas of considerable current interest. However, the proposal itself lacks definition as to the specific lines of attack.

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