LOW LEVEL RADIATION EFFECTS: THE MANCUSO STUDY

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The AEC/ERDA Health and Mortality Study was initiated in 1964 with Dr. Thomas Mancuso, a Professor of Occupational Health at the University of Pittsburgh. The objective of the study was to investigate the health of workers in the nuclear industry, with special attention to the possible effects, if any, of radiation exposure. Mortality was selected as the most feasible measure of health experience with ascertainment of death to be determined from Social Security Administration records. Barkev Sanders, a statistician, recently retired from that agency became part of the project, as did Dr. Alan Brodsky, a health physicist. After an early exploratory period, Hanford and Oak Ridge Laboratories were selected for study, the intention being to recreate records of all persons employed from 1944 to the present. Three control or comparison groups were chosen: persons hired at these two laboratories but not subsequently employed; siblings of employees; and a national sample drawn from Social Security rolls.

In spite of an enormous expenditure of funds (6 million dollars) over the past 14 years, no publications were generated by the project. Annual progress reports suggested that preliminary analyses indicated no detectable radiation effect, a not surprising outcome in view of the very low radiation exposures experienced by employees at those laboratories.

One oral presentation by Dr. Mancuso at an annual Health Physics Society Meeting (published in the proceedings, Richland, Washington, Nov. 2-5, 1971) also suggested the absence of a radiation effect, although he cautioned that this tentative conclusion was preliminary.

In March of 1975, Dr. Mancuso was informed that his contract was to be terminated within the following year. Alan Brodsky had already left the project. Barkev Sanders was informed by Dr. Mancuso that he was to be dropped from the project. He was replaced by Dr. Alice Stewart, a British epidemiologist and her colleague Dr. George Kneale. Within a matter of months a new analysis limited to Hanford data was prepared and presented at the Saratoga Springs meeting of the Health Physics Society (October 11-13, 1976). This new material, with some changes, was recently published in the journal, Health Physics (33, 369-385, 1977). In this publication, it was concluded that occupational radiation exposures at Hanford were associated with an increase in cancer.

This unexpected finding aroused national attention, not only in scientific circles but among governmental agencies as well. Occupational radiation protection standards have been thought to be well below levels where health effects could be detected. It was said that the nuclear industry was extemely safe and studies of radiation workers at other laboratories supported that conclusion. Radiation exposure levels at Hanford were well below permissible

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levels. These were levels so low that on the basis of all other human exposure data, no detectable effects would be expected.

Following publication of the Hanford study, Representative Paul Rogers, Chairman of a House Subcommittee, charged that Federal Energy officials had attempted to cover up the report and that the ERDA contract had been taken away from Mancuso in order to prevent publication of his findings. Dr. James Liverman, who had ordered termination of the contract, testified that there was no attempt to cover up but that the contract had been terminated for other reasons, namely:

a. "A clear lack of substantive publications appearing in referenced journals, even papers on his methodology for analysis, would have been highly useful."

b. "A reluc...ce to initiate any analyses until all data collection was complete -- clear diffibulty in studies requiring massive data bases which take a long time to compile. The reason given was that the results might be misleading; however, generally in studies like this, it is crucial that even trends -- positive or negative -- get identified early so as to guide studies more directly. Related to this point is the accusation voiced by some of suppression of data. As far as I, personally, am aware, no results of any project supported by BER funds have been suppressed by management of BER programs."

c. "A judgment by his scientific peers that the work should be limited, terminated, or another investigator selected to be the principal investigator."

d. "The need from the Agency's standpoint to insure that the records constituting this study could be preserved for posterity and be readied for transfer to new program management."

Not only in its authorship and its conclusion but in other respects too, the Health Physics paper represented a divergence from the previous style and methodology of the project. In his annual reports and in private conversation, Dr. Mancuso had emphasized the need for caution and warned against the danger of premature judgements. He had stressed the requirement that all environmental factors be carefully studied so as to remove the confounding effect of other variables. Three separate control groups were developed in order to overcome the possible errors inherent in choosing an anomalous comparison group. He had been criticized for his cautiousness and unwillingness to begin analysis until all data at all Laboratories has been weighed and considered. That had in fact been his defense for the long delay in publishing analyses.

The Health Physics paper as published shows none of this caution. None of these control groups were used. Nowhere are there the usual caveats about possible unrecognized confounding variables. Scholarly references to the existing literature and to the contrary findings of others are absent. There are only 6 references, two to his own work and no references to the enormous body of radiobiological literature. One has the feeling of haste in the writing of the report. Criticism of the paper falls into two categories:

1. Dose estimates. Comparisons are made between the "exposed" and "non-exposed" populations, yet the paper does not provide information on the level of radiation which would be considered "exposed". Commonly 10 millirads above background would be sufficient to produce a positive reading. Therefore, the "exposed" population is swollen with a very large number of persons who have experienced trivial exposures and a very small number of persons with considerably higher exposures, i.e., an extremely skewed distribution. The paper lacks information on the exact distribution of dose within the exposed population or among the persons with cancer and/or other causes of death. Only mean values are presented, giving the false impression that exposures were fairly uniform. One reviewer compared this usage of statistics in this way: if a population of 10 persons one of whom has an annual income of one million dollars and 9 of whom earn 100 dollars a year, the mean income of the group is $10,100 a year. The mean alone gives no indication of the disparity here.

Secondly, Dr. Mancuso had previously stressed the fact that Hanford occupational exposures are a poor reflection of total radiation exposure. Medical exposures to the work force, the subject of a publication* is not mentioned in this Health Physics paper. Nor is there any mention of occupational radiation exposures prior to or subsequent to Hanford employment, a subject which had previously been of concern to Dr. Mancuso and the subject of a previous study which had shown occupational exposures elsewhere to be as great as those at Hanford for those employees who had transferred from one laboratory to another. (Table I)

2. Methodology: The cancer epidemiologist wants to know whether radiation exposure increases the risk of cancer and the magnitude of the risk if it exists. He knows that he must be cautious in excluding the effect of other variables which may influence the risk of cancer. Since the risk of cancer rises steeply with age, age is a factor which requires careful control. In the Mancuso publication, there are no details of the ages of the living or deceased members of the exposed or non-exposed populations.

Typically, the population under study is also carefully matched by all variables known to influence cancer (such as socio-economic status, education, smoking habits) with a similar population. If exposures varied then the exposed group might be categorized by dose level on the logical assumption that a radiation effect if present would reflect a gradient from highest exposure to least. None of this appears in the Manusco report.

Although the strategy followed in the original Mancuso proposals would have provided such adjustments, the recent Health Physics paper shows use of a weaker technique known as proportionate mortality normally used when the characteristics of the population at risk are not known. The problem with proportionate mortality is that, if one cause of death is reduced, other causes will appear to be increased. One can never be certain whether any single cause of death is increased, unchanged or decreased on an absolute scale. Table II, taken from the Mancuso study, apparently shows an increase

*D. Norwood, F. L. Rising, C. W. Kirklin, A. Brodsky, B. G. Sanders, and T. F. Mancuso, "Cumulative Dose from Diagnostic Radiation," Am. J. Roetgenol, Radium Ther., Radium Ther., and Nuclear Med. CXV, 644-648, 1972.

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in cancer deaths as compared with the percentage cancer deaths among nonexposed persons. The questions then are:

1. ? Is this difference in the <u>proportion</u> of cancer deaths due to radiation or some other factor, and

2. ? Is the <u>rate</u> of cancer among exposed Hanford workers increased, decreased or unchanged

The first question is impossible to answer from the data available in the Health Physics paper since the age and occupational distribution of the two populations is not given. There is some reason to believe that the exposed population is older than the non-exposed population since the rise of radiation exposure increases with the length of employment (Table 6). Furthermore, there are occupational differences between the exposed and non-exposed groups - craftsmen and operators being more common in the former group, and managers more common in the latter group. These differences could well explain the slightly greater frequency of cancer among the deaths in the exposed group.

As to the second question of whether cancer is increased or decreased on an absolute basis in exposed Hanford workers, we are fortunate in having another analysis to which we can turn, that of Dr. Ethel S. Gilbert of Pacific Northwest Laboratories (Table 3). This table shows that when Hanford employees are carefully matched for age and years of exposure they have lower risk of death than do all U.S. males (the "healthy worker" phenomenon). We also see here that circulatory and all other diseases are even more reduced than cancers, a likely explanation of the relative increase in cancer seen in the Mancuso paper.

This material was presented by Dr. Gilbert at the AAAS meeting this month in Washington.

In examining specific cancers, Dr. Gilbert did find two sites where cancer did appear to be increased with radiation exposure, pancreas and multiple myeloma (Table 4). Neither of these cancers have been found increased in studies of other exposed populations and the meaning of this observation remains unclear, but deserves further attention.

As is often the case with radiation, these scientific issues have now become widely publicized and politicized. Dr. Mancuso has charged that his ERDA contract was terminated because of his scientific findings (his contract was terminated prior to his recent publication). Others assume the opposite, i.e., that his scientific conclusions were influenced by "sour grapes" at his contract being ended. In any case charges have begun to fill the air. One former collaborator of Dr. Mancuso, Dr. Brodsky, has written a critique in which he attacks the "many scientific absurdities" of the Health Physics paper. The other former colleague, Barkev Sanders, has written a rebuttal, also to be published soon in Health Physics in which he concludes that no radiation effect can be detected at Hanford. Those who are anti-nuclear will adopt Manusco as a hero, and those who support nuclear power will raise their eyes to heaven and prepare for the worst. And so it goes.

TABLE I

EMPLOYEES WITH RECORDED RADIATION EXPOSURE AT HANFORD WHO LATER WORKED AT OAK RIDGE, WHERE THERE IS NO RECORD OF THEIR PRIOR RADIATION EXPOSURE AT HANFORD*

OCCUPATIONAL RADIATION IN MILLIREM

Year**	% of Offsite Radiation
1944	96.1
1945	55.3
1946	29.9
1947	27.6
1950	100.0
1951	100.0
1952	100.0
1953	100.0
1954	9.8
1955	65.2
1956	96.6
1957	100.0
1958	99.3
1961	80.5
1963	100.0
1965	86.8
1966	100.0
TOTAL	61.5

* Prepared at Oak Ridge partly from magnetic tape supplied

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TABLE II

CERTIFIED DEATHS AMONG HANFORD MALES

	% Cancers	% Non Cancers
Exposed (2184)	20:2 (442)	79.8 (1742)
Non Exposed (1336)	17.1 (228)	82.9 (1108)

(taken from Mancuso et al)

TABLE III

STANDARD MORTALITY RATIOS (SMR) FOR WHITE MALES BY LENGTH OF EMPLOYMENT

(NUMBER OF DEATHS IS GIVEN IN PARENTHESES)

	LENGTH OF EMPLOYMENT	
	<2 YEARS	2 + YEARS
NUMBER OF WORKERS	7767	13,075
CAUSE OF DEATH		
ALL CAUSES	86 (1905)	75 (2089)
ALL MALIGNANT NEOPLASMS	88 (319)	85 (414)
CIRCULATORY DISEASES	87 (839)	76 (955)
ACCIDENTS, POISONINGS & VIOLENCE	109* (243)	75 (216)
ALL OTHER CAUSES	74 (423)	65 (455)
NO DEATH CERTIFICATE	(81)	(49)

*THIS IS THE ONLY SMR PRESENTED IN THIS TABLE WHICH IS NOT SIGNIFICANTLY DIFFERENT FROM 100. ALL OTHER SMR'S ARE SIGNIFICANTLY LOWER THAN 100 AT THE .01 LEVEL.

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TABLE IV

STANDARDIZED MORTALITY RATIOS (SMR'S) FOR CRAFTSMEN AND OPERATORS EMPLOYED FOR AT LEAST 5 YEARS

(NUMBER OF DEATHS IS GIVEN IN PARENTHESES)

	OCCUPATIONAL CATEGORIES	
	HIGH EXPOSURE	LOW EXPOSURE
POPULATION SIZE	1844	1975
PERCENT WITH TOTAL DOSES >5.3 REMS	67.9	15.7
SMR FOR		
ALL CAUSES	0.65 (135)	0.76 (316)
DISEASES OF THE CIRCULATORY SYSTEM	0.67 (63)	0.78 (148)
EXTERNAL CAUSES	0.65 (20)	0.72 (26)
MALIGNANT NEOPLASMS	0.92 (46)	0.92 (68)
CANCER OF*		
STOMACH	0.32 (1)	0.98 (5)
LARGE INTESTINE	1.17 (5)	0.45 (3)
PANCREAS	2.09 (6)	0.46 (2)
LUNG	0.87 (13)	1.13 (24)
PROSTATE	0.46 (1)	2.39 (10)
RES	1.27 (7)	0.81 (6)
MYELOMA AND CERTAIN LYMPHOMAS	3.40 (3)	2.34 (3)
ALL LEUKEMIAS	0.00 (0)	0.65 (2)

*NONE OF THE DIFFERENCES IN SMR'S BETWEEN THE TWO GROUPS ARE STATISTICALLY SIGNIFICANT

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