• Inhalation Hazards to Uranium Miners

This project determines the specific biological effects of exposure to known levels of uranium mine air contaminants, using both large and small experimental animals to model human respiratory disease. Lung cancer and deaths by degenerative lung disease have reached epidemic proportions among uranium miners, but the cause-effect relationships for these diseases are based on inadequate epidemiological data. This project identifies agents or combinations of agents (both chemical and radiological), and their exposure levels, that produce respiratory tract lesions, including respiratory epithelial carcinoma, pneumoconiosis, and emphysema.

INHALED RADON DAUGHTERS AND URANIUM ORE DUST IN RODENTS

Investigators:
F. T. Cross, B. O. Stuart, R. F. Palmer and J. C. Gaven
Technical Assistance:
K. C. Upton

Groups of male SPF Wistar rats were exposed to several levels of radon daughters and uranium ore dust. These studies were designed to elucidate the dependence of pulmonary disease states on radon daughter exposure rate with concurrent exposure to ore dust. Clinical and histopathological data to date indicate no significant differences among exposed animals when compared with controls.

The studies, outlined in Table 3.21, were designed to simultaneously test the roles of exposure rate and ore dust concentrations on the production and progression of lung lesions. Table 3.22, derived from Table 3.21, presents the experimental protocol for testing the influence of exposure rate. This experiment was designed to test the hypothesis that radiation delivered at very low exposure rates is more efficient in the production of cancer. Corroboration in animal studies would indicate that present-day uranium miners, who are exposed at low dose rates, are at greater risk per unit dose than the early miners whose experience was used to derive current limits.

In response to suggestions made during project reviews, radon daughter exposure levels more closely simulating those received by uranium miners were used. These will help to provide a defensible ERDA/DOE position for the current mine exposure standard of 4 WLM/yr. Our previous studies, however, indicated that high cumulative exposures are necessary to induce lung tumors in experimental animals. Exposures received by hamsters, rats and beagle dogs in those studies were about two orders of magnitude greater ($\sim 10^4$ WLM) than those reported to cause lung cancer in man. A possible explanation is that while the 120-359 WLM category (data from the epidemiology studies) may be sufficient to produce lung cancer in man, his longer life span affords more time for the carcinogenic process to proceed. High exposure rates appear to be necessary in the shorter-lived animals in order to increase the probability of lung cancer. As a result, much of the radiation may be wasted, i.e., not utilized in the formation of subsequent tumors. Not included in this explanation, however, is the suspicion that other environmental factors have not been adequately taken into account in the comparison of animals with man. Respiratory tract tumors among uranium miners are bronchogenic

TABLE 3.21. Exposures of Male SPF Wistar Rats to Radon Daughters and Uranium Ore Dust.

Expt. No.	Chamber No.[b]	Number of Animals	Exposure Rate,[a] WL ± SD	Cumulative Exposure,[b] WLM ± SD	Ore Dust Concentration mg/m³ ± SD	Condensation Nuclei Conc., 10^3/cm³ ± SD
1	1	48	882 ± 102	640 ± 93	15.0 ± 0.6	175 ± 34
1	2	48	791 ± 236	644 ± 209	3.0 ± 0.9	37 ± 27
1	3	32	490 ± 37	642 ± 48	15.0 ± 3.5	172 ± 19
1	4	32	279 ± 114	644 ± 263	15.2 ± 1.9	188 ± 41
1	5	32	Controls			
2	1	48	995 ± 52	317 ± 27	17.6 ± 2.7	236 ± 33
2	2	48	951 ± 118	322 ± 42	3.2 ± 0.8	28 ± 11
3	1	32	962 ± 88	2547 ± 233	15.6 ± 1.8	248 ± 28
3	2	32	971 ± 154	2571 ± 408	3.5 ± 0.7	36 ± 12
3	3	32	498 ± 45	~2560	17.1 ± 2.7	235 ± 29
3	5	32	Controls			

[a] The Working Level (WL) is defined as any combination of the short-lived radon daughters in 1 liter of air that will result in the ultimate emission of 1.3×10^5 MeV of potential alpha energy. The Working Level Month (WLM), as used in this report, is an exposure for 170 hours to a 1-WL concentration.

[b] See Tables 3.22 and 3.23 for chamber exposure regimen.

TABLE 3.22. Protocol of Radon Daughter Exposure Rate Versus Total Exposure in Rats.

Animal Grouping	Exposure Regimen[a]	Cumulative Exposure, WLM[a]
Experiments 1, 2 and 3 Chamber 1	1000 WL Radon Daughters 15 mg/m³ Uranium Ore Dust	320,640,2560
Experiments 1 and 3 Chamber 3	500 WL Radon Daughters 15 mg/m³ Uranium Ore Dust	640,2560
Experiment 1 Chamber 4	250 WL Radon Daughters 15 mg/m³ Uranium Ore Dust	640
Experiments 1 and 3 Chamber 5	Controls	Background

[a] Nominal values.

(specifically, in the smaller bronchi), while in the animal experiments they are bronchioloalveolar in origin. Some animal tumors also occur in the nasal epithelium. Therefore, a strict comparison of human and animal exposures required to produce tumors is not possible at this time.

Table 3.23, derived from Table 3.21, presents those experiments that will help define the role of uranium ore in the pathogenesis of lung lesions. The ore dust concentrations were chosen to maintain low fractions of unattached radon daughters (thus keeping the lung deposition sites constant), yet allow sufficient change in concentration to study the pathogenic role of the dust per se.

Most of the animals exposed according to the protocols of Tables 3.22 and 3.23 have received their exposures and are on observation for biologic effects. We have no data at this time (approximately 3 mo to 1 yr postexposure), either clinical or histopathological, that denotes a significant difference among the various exposure groups. Nearly all of the animals are still alive.

In addition to the studies described above, we are currently adjusting exposure conditions to vary the unattached fraction of the radon daughters in order to vary the site of deposition of these radionuclides; hopefully, this will produce higher doses to the region of the lung where tumors appear in man.

TABLE 3.23. Protocol of Uranium Ore Dust Exposures in Rats.

Animal Grouping	Exposure Regimen[a]	Cumulative Exposure, WLM[a]
Experiments 1, 2 and 3 Chamber 1	1000 WL Radon Daughters 15 mg/m^3 Uranium Ore Dust	320,640,2560
Experiments 1, 2 and 3 Chamber 2	1000 WL Radon Daughters 3 mg/m^3 Uranium Ore Dust	320,640, 2560
Experiments 1 and 3 Chamber 5	Controls	Background

[a]Nominal values.