• 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.

INFLUENCE OF RADON-DAUGHTER EXPOSURE RATE AND URANIUM ORE DUST CONCENTRATION ON OCCURRENCE OF LUNG TUMORS

Investigators:
F. T. Cross, R. F. Palmer and R. H. Busch
Technical Assistance:
C. R. Petty, W. Skinner, J. C. Gaven and M. J. Pipes

Groups of male SPF Wistar rats were exposed concurrently to several levels of radon daughters and uranium ore dust to study the effect of these variables on pulmonary disease states. Clinical pathology data at 1 yr postexposure indicate no significant differences among exposed animals when compared with controls. Preliminary histopathologic data suggest a trend toward increasing lung tumor risk as the exposure rate is decreased (constant total dose), but the differences are not statistically significant at the 0.05 level. A similar trend occurs with decrease in ore dust concentration (except for the 2560-WLM exposure group), but these differences are also not significant at the 0.05 level. The tumor risk is significantly (0.05 level) increased as the exposure level increases from approximately 320 and 640 WLM to 2560 WLM at the high ore dust concentration (15 mg/m^3).

These studies were initiated in 1977 to test the roles of radon-daughter exposure rate and uranium ore dust concentrations on the production and progression of lung lesions. Human radon-daughter epidemiology suggests that radiation delivered at very low exposure rates is the most efficient in the production of lung 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 those early miners whose experience was used to derive current limits of exposure.

Groups of 32 or 48 male SPF Wistar rats were exposed for 30 hr/wk to several levels of radon daughters and uranium ore dust, according to the protocols in Tables 35 and 36, and were placed on a periodic sacrifice schedule for observation of developing lung lesions. The ore dust concentrations shown in Table 36 were chosen to maintain low fractions of unattached radon daughters (thus keeping the lung deposition sites constant), while allowing sufficient change in concentration to study the pathogenic role of the dust per se.

TABLE 35. Protocol for Study of Radon-Daughter Exposure Rate Versus Total Exposure in Rats

Exposure Regimen	Cumulative Exposure, WLM
1000 WL Radon Daughters 15 mg/m³ Uranium Ore Dust	320, 640, 2560
500 WL Radon Daughters 15 mg/m³ Uranium Ore Dust	640, 2560
250 WL Radon Daughters 15 mg/m³ Uranium Ore Dust	640
Controls	Background

TABLE 36. Protocol of Uranium Ore Dust Exposures in Rats

Exposure Regimen	Cumulative Exposure, WLM
1000 WL Radon Daughters 15 mg/m³ Uranium Ore Dust	320, 640, 2560
1000 WL Radon Daughters 3 mg/m³ Uranium Ore Dust	320, 640, 2560
Controls	Background

Data from approximately 75% of the animals are included in Table 37; some animals are still living, and histopathologic examinations of all dead animals have not been completed. The data indicate a trend toward increased lung tumor risk as the exposure rate is decreased, but this trend is not significant (0.05 level). The data on lung tumor occurrence are statistically significant (0.05 level) as the exposure level increases from approximately 320 and 640 WLM to 2560 WLM at the 15 mg/m^3 ore dust concentration. The data also indicate a trend toward increased lung tumor risk with decrease in ore dust concentration at the lower exposure levels, but the trend is reversed at the high (2560 WLM) level. None of these data are presently significant at the 0.05 level. Whether there is a difference in deposition site at these two dust concentrations is yet to be evaluated. We have conducted experiments which measured radon daughter burden in sections of the respiratory tract as a function of ore dust concentration and radon daughter disequilibrium; these data have not yet been analyzed.

TABLE 37. Current Summary of Primary Epithelial Tumors of the Lung

Exposure Regimen[a]			% of Examined Animals with Epithelial Tumors	% Animals Not Examined
Exposure Rate, WL	Total Exposure, WLM	Ore Dust Conc., mg/m³		
1000	320	15	3.8	45
250	640	15	9.4	0
500	640	15	12	19
1000	640	15	2.6	17
500	2560	15	44	44
1000	2560	15	25	35
1000	320	3	8.8	26
1000	640	3	12	15
1000	2560	3	5.3	39
Controls			0	30

[a] Nominal Values