

CHAPTER 8

FIBROGENIC EFFECTS AND CHEMICAL CHARACTERIZATION OF COAL AND MINERAL SLAGS USED AS SAND SUBSTITUTES

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INTRODUCTION

Abrasive blasting is the high-velocity bombardment of a surface by a substance propelled either by hydraulic or pneumatic pressure or by centrifugal force. The abrasive blasting processes are used extensively in cleaning and preparing surfaces prior to other operations, such as painting. The principal substance used for abrasive blasting has been silica sand, and the health hazard of human exposure to crystalline silica has been well documented [1].

Because of the health hazard associated with its use, in 1950 Great Britain banned the use of silica sand as an abrasive blasting material [2]. This was followed by efforts to restrict the use of sand for abrasive blasting purposes in Germany and the Netherlands, which led to research in Germany to find less toxic substitute abrasive blasting materials [3]. In considering candidate materials as substitutes for silica sand, three criteria were used: (1) the materials should have a free silica content of less than 1%; (2) the material should possess good abrasive properties; and (3) the materials should be

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competitive economically with sand. Mineral slags such as copper slag and chromium slag were found to have these desired properties [3].

The mineral slags are metallurgical waste products resulting from smelting operations in which metals such as copper, nickel, chromium, etc. are recovered. In the smelting process, a two-phase liquid system exists with a molten slag phase floating on top of molten metal. The molten slag is drawn off and run into water to convert it to a frit, which can be conveniently handled for disposal purposes. As the fritting process usually produces a hard, small, sharp particle, many of the frits were found to have abrasive properties. In the United States, mineral slags, primarily copper, are used in abrasive blasting operations. These are marketed under various trade names such as Kleenblast® and Monoclean®.*

In addition to mineral slags, large quantities of a wet-bottom boiler slag produced in certain types of coal-fired electric utility boilers in the United States have been used as abrasive blasting materials. This slag is formed during the burning of a powdered coal that produces an ash with a relatively low melting point. During the burning process, this molten ash falls to the bottom of the furnace as a viscous liquid, which is then allowed to drop into water where it frits. The resulting product is a hard, black solid with less than 1% free silica and is an excellent abrasive blasting material. These slags are marketed under various trade names such as Black Beauty® and Stanblast®.*

The potential adverse health effects of exposure to these coal and mineral slags were not investigated prior to their usage in commerce. The National Institute for Occupational Safety and Health (NIOSH) has initiated studies to assess the biological activity of the slags. One study investigating the fibrogenic effects of a coal slag and a copper slag has been completed [4]. A second study is currently underway to determine the fibrogenic and carcinogenic effects of two copper slags and one nickel slag. A third study, in which eighteen coal and other mineral slags were chemically characterized, has recently been completed [5]. The results of these three studies will be summarized in this chapter.

CHEMICAL CHARACTERIZATION OF COAL AND OTHER MINERAL SLAGS [5]

Eighteen slag samples were characterized, with twelve being derived from coal, five from copper smelting operations and one from a nickel smelter.

*Mention of commercial products or concerns does not constitute endorsement by the National Institute for Occupational Safety and Health.

Four of the coal slags were commercial products; the remaining eight were obtained directly from coal-fired power plants and their commercial availability is unknown. Three of the copper slags were from primary smelters, two of which were from the same smelting operation and ore source but processed at different times (1976 and 1977). These two slags were commercial products. The utilization of the third primary copper slag is unknown. The remaining two copper slags were from a secondary smelting operation and were obtained from a commercial supplier—one sample in 1974, the other in 1978. The utilization of the nickel slag in commerce is unknown.

The slag samples were analyzed by atomic absorption spectrophotometry (AAS) and proton-induced X-ray fluorescence (PIXE). Beryllium, sodium, magnesium and aluminum analyses were performed by AAS. All elements from silicon (atomic number 14) through uranium (atomic number 92) were analyzed simultaneously by PIXE.

All the slag materials analyzed are silicates, whose principal metallic components are sodium (0.2–3.2%), magnesium (0.5–2.2%), aluminum (0.9–7.1%), potassium (0.1–3.4%), calcium (0.2–13.6%) and iron (3.3–23.0%). The trace element concentrations for the slags are given in Tables I–III. The values presented represent the average of two analyses with the standard deviation. All other elements were present below PIXE detection limits.

The analytical results indicate that the slags contain varying quantities of potentially hazardous elements. These elements include beryllium, chromium, nickel and arsenic, all of which are considered by NIOSH as carcinogens or suspect carcinogens [6].

In general, the coal slags contain the lowest concentrations of the suspect carcinogens (Table I). However, nine of the twelve coal slags analyzed do contain beryllium, ranging from 7 to 48 $\mu\text{g/g}$. Chromium was found in only four coal slags ranging from 110 to 200 $\mu\text{g/g}$, while ten coal slags contained nickel in concentrations of 18 to 70 $\mu\text{g/g}$. Arsenic in 4–18 $\mu\text{g/g}$ quantities was found in five coal slags. The coal slag with the highest arsenic content (18 $\mu\text{g/g}$) was the only coal slag that also contained lead, 20 $\mu\text{g/g}$.

The trace element concentrations of the primary copper slags (Table III) are very dependent on the ore being smelted. Primary copper slags Nos. 1 and 2 were from the same ore sources but were processed at different times. The trace element concentrations of these two slags are nearly identical, with no beryllium, chromium or nickel being detected in either sample and nearly equal amounts of arsenic (32 and 34 $\mu\text{g/g}$) present in both samples. However, primary copper slag No. 3, which was from a different ore source and smelter, contained large amounts of chromium (340 $\mu\text{g/g}$) and arsenic (1450 $\mu\text{g/g}$). No beryllium or nickel was detected in this sample, but a large amount of lead (1220 $\mu\text{g/g}$) was found.

Table I. Coal Slag

Element	No. 1	No. 2	No. 3	No. 4	No. 5	No. 6
BE	29±3	7±3	48±3	24±3	30±2	29±3
Ti	10,000±2,000	5,300±200	5,300±300	4,900±600	3,400±600	3,400±400
V	400±100	270±80	320±80	330±70	180±50	190±50
CR	200±40	<100	<120	<120	<150	<150
MN	600±100	<200	<200	<200	390±80	360±90
Ni	70±10	<40	70±20	70±10	40±10	51±8
CU	49±8	21±4	50±10	22±5	8±2	<6
Zn	140±30	36±4	190±6	86±8	87±3	67±3
Ga	9±2	9±3	9±3	10±2	<6	<8
As	10±2	<8	18±2	7±2	<4	5±2
Se	<2	<6	<4	<4	<4	<2
Rb	85±3	61±5	108±4	87±6	65±3	64±3
Sr	780±10	540±10	295±8	223±5	218±4	210±10
Sc	1,700±500	500±100	600±200	800±200	600±200	600±200
Y	36±5	45±4	52±6	43±6	40±9	35±3
Zr	178±10	189±8	186±8	150±5	145±4	147±4
Nb	13±2	24±3	21±5	14±4	12±2	12±2
Mo	<8	<8	<18	<6	<12	<4
Ba	1,840±100	400±100	900±200	510±100	400±150	400±100
Pb	<12	<15	20±4	<10	<10	<6

Table II. Summary of the Analyses for the Twelve Coal Slag Samples

Element	Number of Coal Slags Containing the Element	Range of Values (µg/g)
Be	9	7-48
Ti	12	2,300-10,000
V	6	180-400
Cr	4	110-200
Mn	6	170-600
Ni	10	18-70
Cu	11	8-70
Zn	12	13-190
Ga	8	6-27
As	5	4-18
Se	1	5
Rb	12	31-108
Sr	12	210-4,600
Sc	7	400-1,700
Y	12	34-65
Zr	12	145-270
Nb	12	10-24
Mo	1	11
Ba	12	400-9,900
Pb	1	20

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Trace Analyses ($\mu\text{g/g}$)

No. 7	No. 8	No. 9	No. 10	No. 11	No. 12
<8	<6	27±4	<4	40±3	33±4
7,100±700	2,300±300	3,100±400	3,600±700	4,300±300	3,300±400
<400	<200	<200	<200	<180	<180
<100	110±30	130±40	180±40	<210	<180
290±80	170±30	<140	240±60	<180	<200
26±7	18±5	45±8	20±5	<60	33±9
70±4	27±6	13±3	28±5	52±4	12±4
35±3	13±4	105±7	30±3	51±6	100±9
8±3	6±2	<4	<4	27±5	13±3
4±1	<10	<4	<4	<10	<6
<2	<2	<4	5±1	<4	<6
31±8	80±3	75±3	34±5	54±4	68±30
4,600±200	1,710±20	433±9	3,600±200	1,460±20	530±10
<1,800	<800	<400	<1,600	<600	400±100
37±5	40±10	34±3	41±4	65±6	45±2
270±3	170±10	146±6	240±10	184±9	146±5
12±2	14±3	14±4	10±3	14±3	11±3
<6	<6	<8	<4	<6	11±4
4,700±300	4,200±200	1,200±100	9,900±800	1,900±100	710±100
<8	<6	<8	<10	<10	<12

The secondary copper slags contained the largest quantities of beryllium (125–180 $\mu\text{g/g}$), chromium (2100–2400 $\mu\text{g/g}$) and lead (6600–8900 $\mu\text{g/g}$). While little variation in trace element concentrations was seen in the two analyzed samples, it would normally be expected that such slags would vary considerably in composition as various scrap metal sources would be used in the smelting operations that generate these slags.

The one nickel slag examined was found to contain significant amounts of chromium (3700 $\mu\text{g/g}$) and nickel (1400 $\mu\text{g/g}$).

INITIAL ANIMAL STUDY [4]

The purpose of the initial animal study was to assess the fibrogenic potentials of coal and copper slag dusts in the lungs of rats exposed to a single high-dose intratracheal instillation of the test material. Four dust samples were tested in this study. Two were commercial grit slag samples, one derived from coal ash and one from the ash of a primary copper ore smelter. The third sample, a respirable airborne dust sample, was collected onsite at a coastal shipyard during an abrasive blasting operation using the above-mentioned commercial copper slag as the abrasive medium. The results of

Table III. Mineral Slag Trace Analyses ($\mu\text{g/g}$)

Element	Copper Primary Smelter No. 1	Copper Primary Smelter No. 2	Copper Primary Smelter No. 3	Copper Secondary Smelter No. 1	Copper Secondary Smelter No. 2	Nickel Primary Smelter
Be	<40	<6	<6	125 \pm 10	180 \pm 10	<6
Ti	1,200 \pm 100	1,200 \pm 100	1,800 \pm 300	1,500 \pm 400	1,500 \pm 100	250 \pm 70
V	<80	<80	<180	160 \pm 50	<80	<60
Cr	<60	<40	340 \pm 90	2,100 \pm 300	2,400 \pm 100	3,700 \pm 200
Mn	1,700 \pm 100	2,000 \pm 100	<400	2,400 \pm 400	1,400 \pm 200	1,100 \pm 100
Ni	<18	<18	<20	2,200 \pm 300	2,240 \pm 70	1,400 \pm 100
Cu	1,340 \pm 20	1,460 \pm 40	4,200 \pm 400	6,400 \pm 700	5,000 \pm 200	17 \pm 2
Zn	141 \pm 4	133 \pm 4	26,000 \pm 2,000	52,000 \pm 6,000	18,900 \pm 500	75 \pm 2
As	32 \pm 10	34 \pm 2	1,450 \pm 60	<40	<40	<2
Se	<6	<4	<8	32 \pm 7	18 \pm 5	<2
Br	10 \pm 2	9 \pm 1	<10	<14	<12	5 \pm 1
Rb	10 \pm 2	9 \pm 1	<12	<8	<6	<2
Sr	208 \pm 4	188 \pm 8	151 \pm 10	120 \pm 10	77 \pm 5	5 \pm 1
Sc	<800	<1000	500 \pm 100	500 \pm 200	<400	<200
Y	20 \pm 2	18 \pm 1	<8	27 \pm 9	<20	<2
Zr	300 \pm 20	50 \pm 4	69 \pm 6	850 \pm 50	264 \pm 8	15 \pm 2
Nb	<4	<6	<6	24 \pm 7	19 \pm 5	<2
Mo	<4	<6	480 \pm 10	240 \pm 10	160 \pm 20	<2
Sn	<18	<20	60 \pm 10	1,000 \pm 60	1,260 \pm 30	15 \pm 5
Sb	40 \pm 10	<18	500 \pm 40	<40	<20	<12
Ba	550 \pm 90	470 \pm 80	<80	500 \pm 100	700 \pm 200	<60
Pb	9 \pm 3	<6	1,200 \pm 70	6,600 \pm 500	8,900 \pm 100	<4

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chemical analyses performed for these three slag samples are shown in Table IV. The fourth sample, a laboratory quartz standard (Min-U-Sil,* Pennsylvania Glass Sand Corp.), served as a positive control for the induction of fibrosis. The two commercial slag samples were ball-milled for 16 hours to reduce their particle size. The airborne copper slag sample and the Min-U-Sil sample were used without further size reduction. The particle size distributions for each of the test materials, as determined by scanning electron microscopy, are summarized in Table V.

The test animals for this study were male, Caesarian-derived, Sprague-Dawley rats (Harlan Industries, Inc.) of 200 ± 10 g body weight, which were divided into five equal treatment groups as shown in Table VI. The rats in the four dust-treated groups were given a single intratracheal instillation of 20 mg of the appropriate test material. The control rats were given instillations of

Table IV. Chemical Analysis of Slag Test Materials ($\mu\text{g/g}$)—Initial Animal Study

Element	Copper	Copper-Airborne	Coal
Na	1,030	1,650	3,520
Mg	25,400 (2.54%)	22,000 (2.20%)	10,500 (1.05%)
Al	45,600 (4.56%)	38,600 (3.86%)	10,800 (1.08%)
Si	138,000 (13.8%)	120,000 (12.0%)	169,000 (16.9%)
Ca	158,000 (15.8%)	128,000 (12.8%)	63,000 (6.30%)
Mn	360	3,600	730
Fe	150,000 (15.0%)	204,000 (20.4%)	139,000 (13.9%)
Cu	2,020	2,850	52
V	160	160	160
Zn	260	2,700	126
Mo	11	35	28
Co	52	60	29
Pb	12	890	15
As	34	52	33
Be	1.3	1.5	9.7
Ni	26	240	65
Cd	0.07	6	0.08
Cr	61	564	121
Sn	58	57	16
Ag	0.92	2.4	<0.08
Ba	490	480	1,590
Hg	<0.008	0.42	0.018
Se	<2	<2	<2
B	170	390	320
Free Silica	<2,000	<3,000	<2,000

*Mention of commercial products or concerns does not constitute endorsement by the National Institute for Occupational Safety and Health.

Table V. Particle Size Distributions

Size Range of Test Materials (μm)	Coal Slags (%)	Copper Slags (%)	Airborne Copper Slags (%)	Min-U-Sil (%)
<0.5	40.4	25.4	26.2	45.6
≥ 0.5 -<1.0	26.0	23.2	21.4	29.9
≥ 1.0 -<1.5	14.1	14.5	12.7	11.9
≥ 1.5 -<2.0	8.2	9.6	13.1	5.8
≥ 2.0 -<3.0	6.5	10.1	13.1	5.5
≥ 3.0 -<5.0	3.5	8.4	10.1	1.3
≥ 5.0 -<10.0	1.1	5.3	3.1	0
≥ 10.0	0.1	3.3	0.4	0

Table VI. Rat Treatment Groups—Initial Study

Dust Treatment	Total Number of Rats Treated	Mortality	Total Number of Rats Sacrificed
I. Copper Slag-Airborne	60	1	59
II. Copper Slag	60	3	57
III. Coal Slag	60	2	58
IV. Positive Control (Quartz-Min-U-Sil)	60	4	56
V. Vehicle Control (Distilled Water)	60	0	60
TOTALS	300	10	290

the vehicle used to suspend the treatment dusts—distilled water. All surviving rats were sacrificed 10 months after dosing and necropsied. Complete details of the animal housing, as well as of the intratracheal instillation and necropsy procedures are given elsewhere [4].

Histopathological evaluation of lung sections from the test animals revealed that granulomas were induced by all four test materials. These granulomas were seen only in the lobes of the lungs (primarily the left lung) and in the tracheobronchial lymph nodes. This particulate was present both intra- and extracellularly within these granulomas, as well as proximal to the granulomas.

In the rats treated with quartz, large granulomas were seen. In most instances, a single granuloma occupied an entire field of view at 65X magnification (Figure 1A). All groups of the slag-treated rats showed multiple granulomas varying from 100 to 400 μm in diameter (Figures 2A

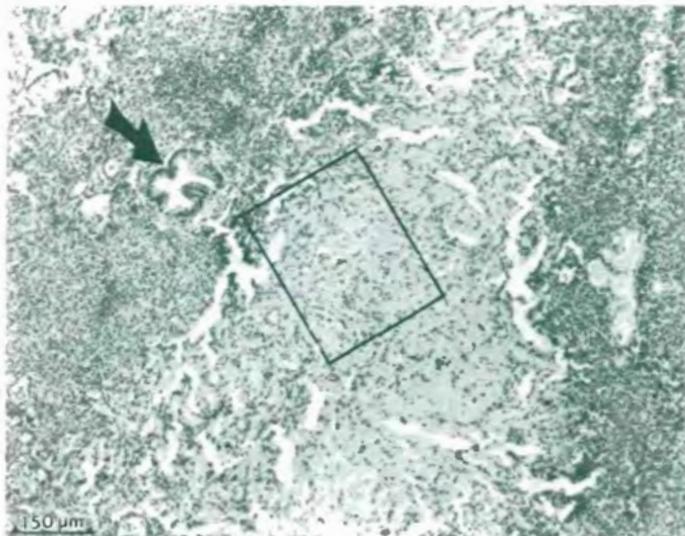


Figure 1A. Lung from a quartz-treated rat. A large hyalinized area is shown. A distorted bronchiole (arrow) in the middle of a densely cellular area composed primarily of macrophages and lymphocytes is also shown.

and 3A). There were from 6 to 10 of these small granulomas per field of view at 65X and 55X (Figures 2A and 3A, respectively).

The cell types and populations of the granulomas found in the four treatment groups varied. The quartz-induced granulomas consisted primarily of macrophages and a few lymphocytes (Figure 1A,B). Equal numbers of macrophages and lymphocytes were present in the granulomas produced by the copper slags, both the unused and airborne (Figure 2B). Macrophages, lymphocytes and foreign body giant cells were seen in the granulomas induced by the coal slag (Figures 3B and 4). All granulomas lacked a definite capsule. Internal scaffolding of fibrous tissue was present in all of the granulomas found in the lining parenchyma (alveolar region), lymph nodes and pleura.

Large accumulations of macrophages were seen in both the medulla and cortex of the tracheobronchial lymph nodes of the rats from all four dust treatment groups. These macrophages contained particulates similar in appearance to those found in the respective lungs. Particulate material was also present extracellularly in the tracheobronchial lymph nodes. The degree of macrophage accumulation and particulate deposition in these lymph nodes was similar for all four dust treatment groups.

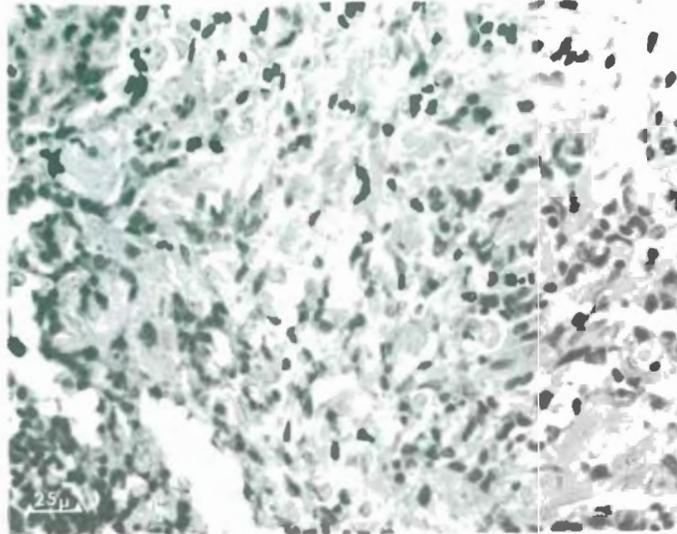


Figure 1B. Higher magnification of the indicated area in Figure 1A. Thick hyalinized bands of collagen with interspersed pyknotic nuclei are evident.

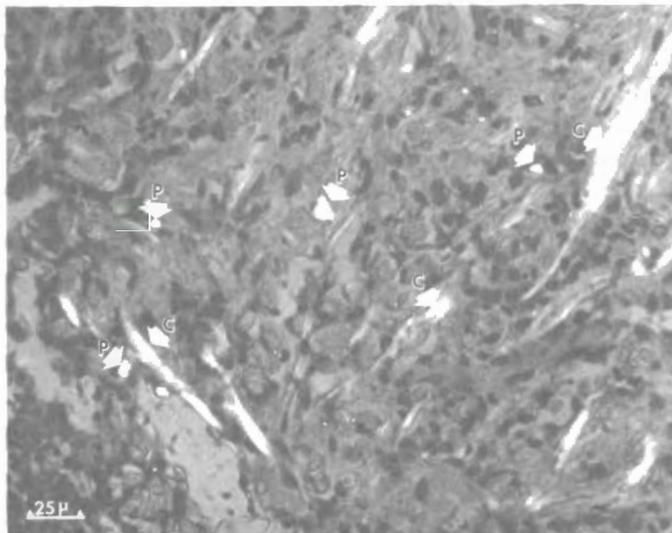


Figure 1C. Same area as shown in Figure 1B under polarized light. The birefringence of the quartz particles (P) and the collagen (C) is shown.



Figure 2A. Lung from an airborne copper slag-treated rat. Multiple granulomas are present.

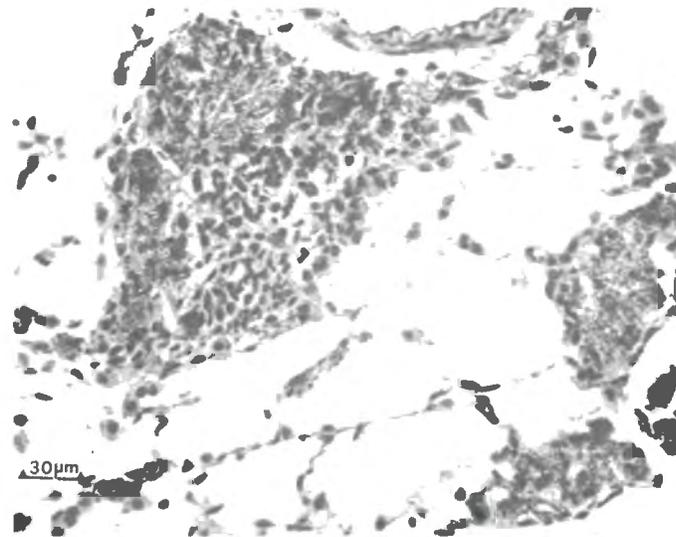


Figure 2B. Higher magnification of the indicated area in Figure 2A. The granulomas are composed primarily of macrophages, some with particulates and lymphocytes. Most of the alveolar lumens are free of particulates and particulate bearing macrophages.

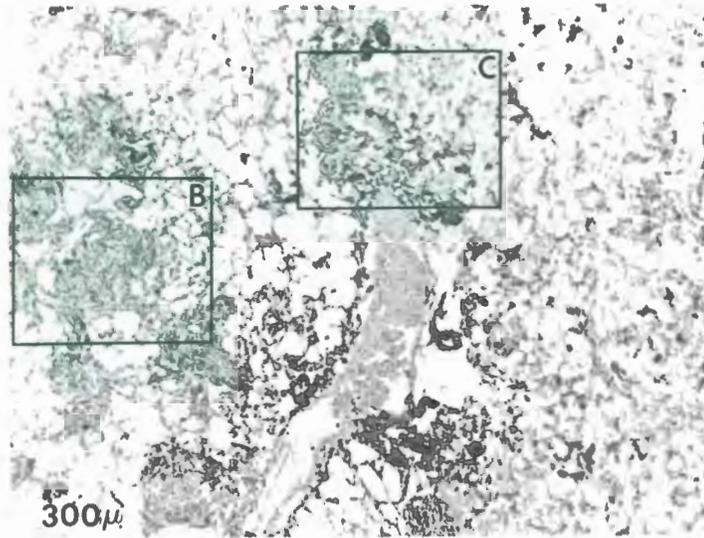


Figure 3A. Lung from a coal slag-treated rat. Multiple granulomas (left half) and marked fibrosis (right half) are shown.

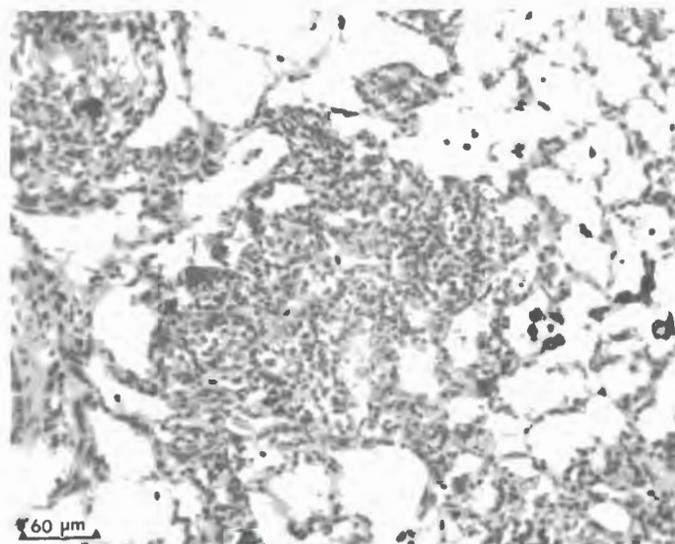


Figure 3B. Higher magnification of area (B) in Figure 3A. Both intra- and extracellular particles are found in the granulomas.

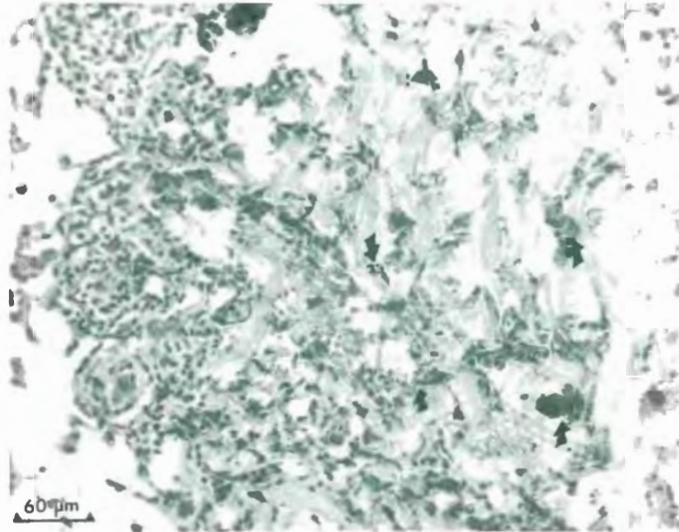


Figure 3C. High magnification of area (C) in Figure 3A. Fibrosis of alveolar walls has resulted in reduction of alveolar lumens, lack of alveolar lining epithelium and vascularity of the alveoli. Some of the particulate material present is denoted by arrows.

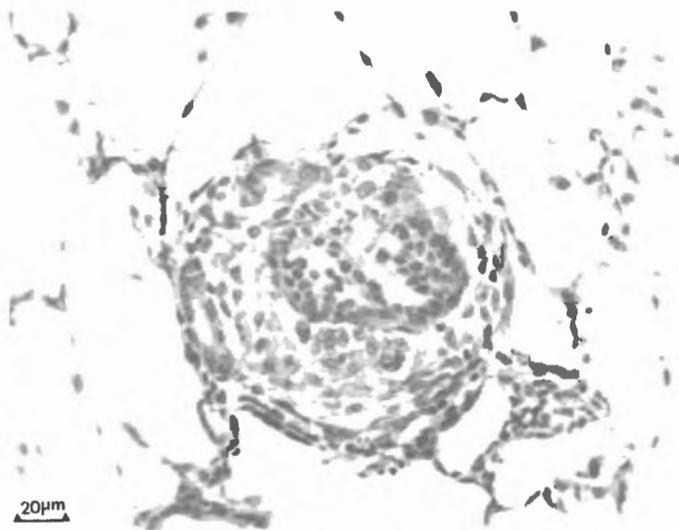


Figure 4. Lung from a coal slag-treated rat. Microgranuloma with a foreign body giant cell is shown.

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Frank fibrous tissue was apparent in the rats treated with quartz and coal slag. However, distinct differences in the locality and degree of deposition of this connective tissue was observed between these two groups. Intense collagen formation (Figures 1A,B,C), with attendant replacement and distortion of the pulmonary parenchyma, was evident in the rats treated with quartz. This marked fibrosis seen in the quartz-treated rats would be rated at 10 on a scale of 1 to 10. Quartz particles were present in the hyalinized area of the lungs (Figure 1C). Of the quartz-treated rats, 80% showed dystrophic calcification in the hyalinized areas. Calcification was also present in the pleural lesions.

The coal slag induced marked thickening of the alveolar walls due to formation of fibrous tissue that showed varying degrees of hyalinization (Figures 3A and C). This resulted in retention of the apparent alveolar architecture with reduced alveolar lumens. The fibrosis seen in the coal slag-treated rats would be rated at 4 on the scale of 1 to 10. The alveolar lining epithelium and alveolar wall capillaries were not visible by light microscopy. The fibrosing alveolar walls contained scattered macrophages filled with particulate (Figure 3C).

All tissues examined from the distilled water control rats were unremarkable.

The results of the chemical analyses performed for each of the slag samples would suggest a nonfibrogenic response in animals treated with these materials. This was proven true for the two copper slag samples; however, even though the free silica levels, as well as the levels of the major constituent elements and most trace elements found in all of the slags, were relatively similar, pulmonary fibrosis was found in the coal slag-treated group. The pulmonary fibrosis found in the coal slag-treated animals, while not as extensive as that seen in the quartz-treated animals, is significant. The pathological responses seen in the quartz-treated rats were the classical silicotic lesions, as seen by other investigators in similarly treated rats [7,8].

ANIMAL STUDY IN PROGRESS

A second animal study is in progress in which the fibrogenic and/or carcinogenic potentials of three mineral slags are being evaluated. The test materials are three of the mineral slags listed in Table III: primary copper slag No. 3, secondary copper slag No. 2 and the nickel slag. These three slags were chosen for study because of their relatively high concentrations of suspect carcinogens. As in the earlier study, a fourth sample, Min-U-Sil quartz, was used as a positive control for the induction of fibrosis. However, the sample of Min-U-Sil used in this study was not from the same batch used in the initial study. Samples of each of the mineral slags were micronized using a Trost mill (Garlock, Inc.) to reduce their particle size. The particle size

Table VII. Particle Size Distributions

Size Range of Test Materials (μm)	Primary Copper Slag No. 3 (%)	Secondary Copper Slag No. 2 (%)	Nickel Slag (%)	Min-U-Sil (%)
<0.5	28.0	41.0	31.0	41.3
≥ 0.5 -<1.0	9.0	12.9	12.0	31.4
≥ 1.0 -<1.5	6.6	7.8	8.6	12.7
≥ 1.5 -<2.0	12.3	8.3	12.6	7.4
≥ 2.0 -<3.0	22.2	11.5	14.4	5.4
≥ 3.0 -<5.0	16.6	11.8	12.6	1.6
≥ 5.0 -<10.0	5.2	5.8	7.3	0.1
≥ 10.0	0.3	0.7	1.5	0

distributions for each of the test materials as determined by scanning electron microscopy are summarized in Table VII.

The test animals for this study are male, Caesarian-derived, Fischer 344 rats (Charles River Breeding Laboratories, Inc.) of 180 ± 15 g body weight. These animals were divided into 5 equal treatment groups, as shown in Table VIII. The rats in the four dust treatment groups were given a single, intratracheal instillation of 20 mg of the appropriate test agent. The control rats (Group 5), were given instillations of the vehicle used to suspend the treatment dusts—distilled water.

Following the exposures to the test agents, the rats are to be held for 24 months. Interim sacrifices of 10 rats per exposure group were completed at 6 months, 12 months and 18 months, with the final sacrifice at 24 months in July, 1982. The results of the histopathological evaluations for each of the four test agents for the sacrifice at 12 months are discussed below.

Table VIII. Rat Treatment Groups—Study in Progress

Dust Treatment	Total Number of Rats Treated	Number of Rats Sacrificed at			Spontaneous Deaths (up to 19 months)	Remaining Rats (19 months)
		6 Months	12 Months	18 Months		
1. Primary Copper Slag No. 3	85	10	10	10	2	53
2. Secondary Copper Slag No. 2	85	10	10	10	5	50
3. Nickel Slag	85	10	10	10	4	51
4. Positive Control (Quartz-Min-U-Sil)	85	10	10	10	14	41
5. Vehicle Control (Distilled Water)	85	10	10	10	2	53

The pulmonary reaction to quartz was most extensive. In the lobe that received most of the particulate (left lobe), 90% or more of the lung was replaced by sheets of mononuclear cells and fibroblasts with variable and usually lesser numbers of lymphocytes (Figure 5). In other lobes, discrete granulomas were seen (Figure 6) that consisted of mononuclear cells mixed with a few fibroblasts and occasionally surrounded by a few strands of collagen and/or lymphocytes. In both types of these cellular areas, fine strands of randomly distributed collagen were visible by polarized light; in a few small areas in some animals, dense collagen could be seen (Figure 7). In most of the areas not replaced by granulomas or sheets of mononuclear cells, the alveolar walls were thickened and the alveoli contained alveolar macrophages, proteinaceous material and cell debris (Figure 8). The alveolar wall cells were greatly increased in size and number, and in a few foci cuboidal and columnar cell metaplasia were evident (Figure 9). One adenocarcinoma was seen (Figure 10). Mast cells were also commonly present. Interstitial fibrosis was also present and varied in intensity from area to area in the same lobe (Figure 11).

The tracheobronchial lymph nodes were enlarged by sheets of mononuclear cells and multiple granulomas similar to those seen in the lung (Figure 12).

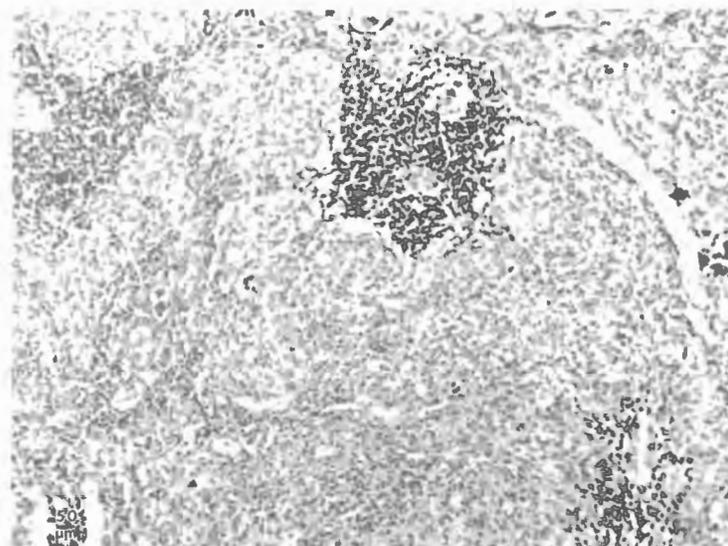


Figure 5. Lung from a quartz-treated rat (12 months post-exposure). The normal lung structure has been replaced by mononuclear cells, fibroblasts and lymphocytes. This is the most common reaction seen in the quartz-treated rats.

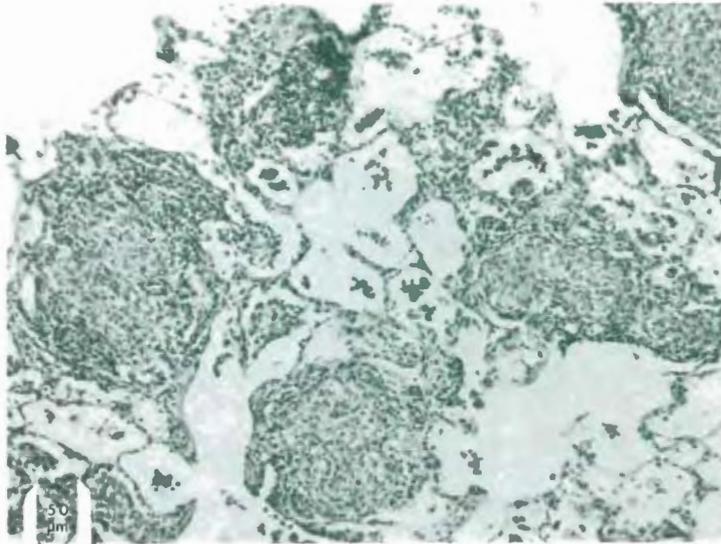


Figure 6. Lung from a quartz-treated rat. Several granulomas are shown. The granulomas are composed of primarily mononuclear cells with a few fibroblasts.

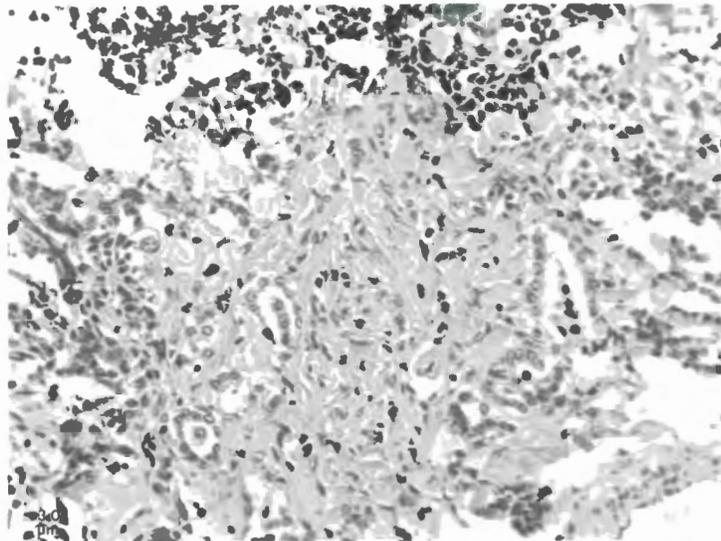


Figure 7. Lung from a quartz-treated rat. A small area with dense collagen is shown.

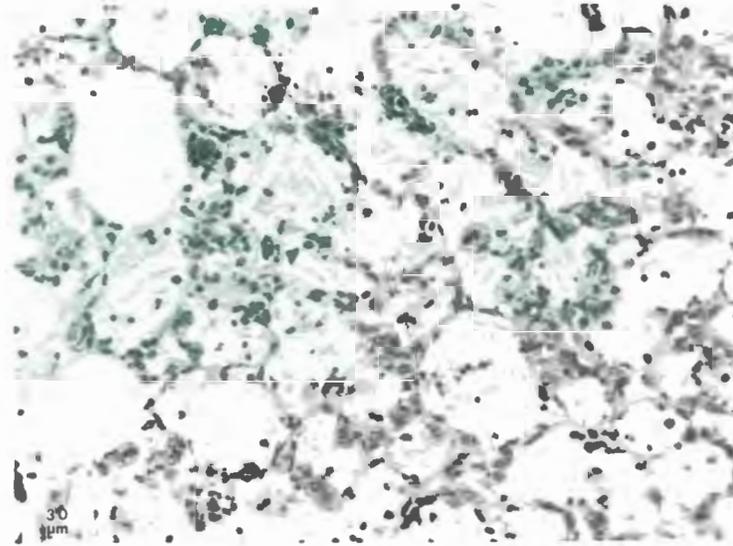


Figure 8. Lung from a quartz-treated rat. In this area, there is alveolar wall thickening. The alveoli contain macrophages, proteinaceous material and cell debris.

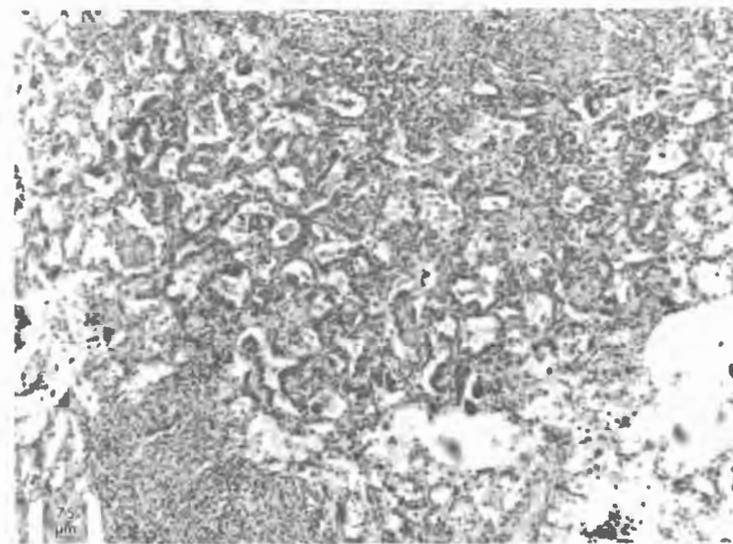


Figure 9. An area of lung from a quartz-treated rat in which there is cuboidal and columnar cell metaplasia.

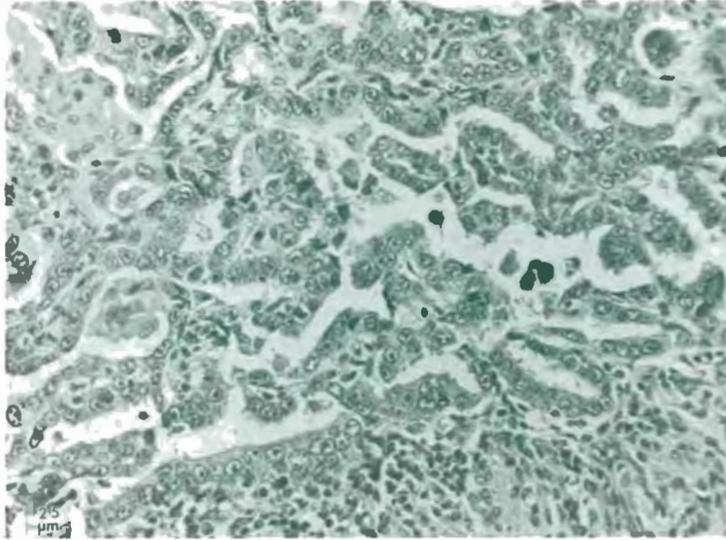


Figure 10. Lung from a quartz-treated rat showing adenocarcinoma.

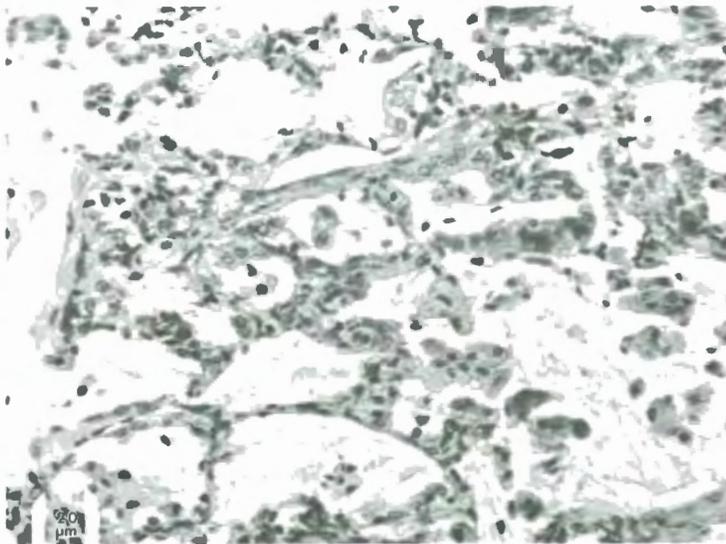


Figure 11. Lung from a quartz-treated rat showing interstitial fibrosis.

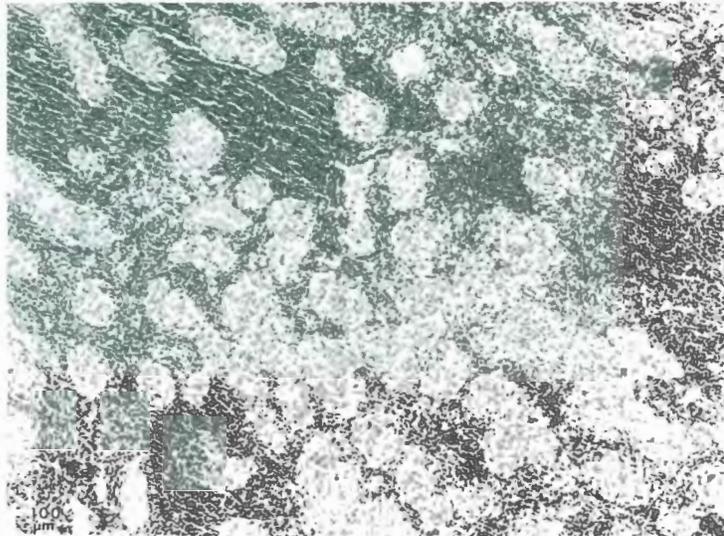


Figure 12. A tracheobronchial lymph node from a quartz-treated rat. Sheets of mononuclear cells and multiple granulomas are shown.

Macrophages loaded with quartz particles were easily seen under polarized light. One or two areas of dense collagen were seen in some animals, and strands of collagen were dispersed throughout as in the lung. Peri-pancreatic lymph nodes contained multiple granulomas with a few quartz particles (Figure 13).

In contrast, the reactions in the lungs of the animals injected with the slags were quantitatively and qualitatively different. Lungs of animals injected with the Ni slag showed the least reaction. Dense collections of particles, many of which were birefringent, were present in alveoli in intra- or extracellular sites (Figures 14A and B). A few of the alveolar wall cells were increased in size but there was no interstitial fibrosis and there were no granulomas.

The lung tissue from animals injected with the two copper slags, however, were qualitatively similar. The particles were smaller than those seen in the Ni slag, and many alveolar macrophages were loaded with them (Figures 15A and B and 16A and B). The cellular reaction to the dust consisted of a slight to moderate increase in the size and number of alveolar wall cells, which was greater than that seen with the nickel slag but much less than that seen with the quartz. In a few foci in most of the animals, minimal interstitial fibrosis could be seen at the sites of particle deposition. This was more extensive

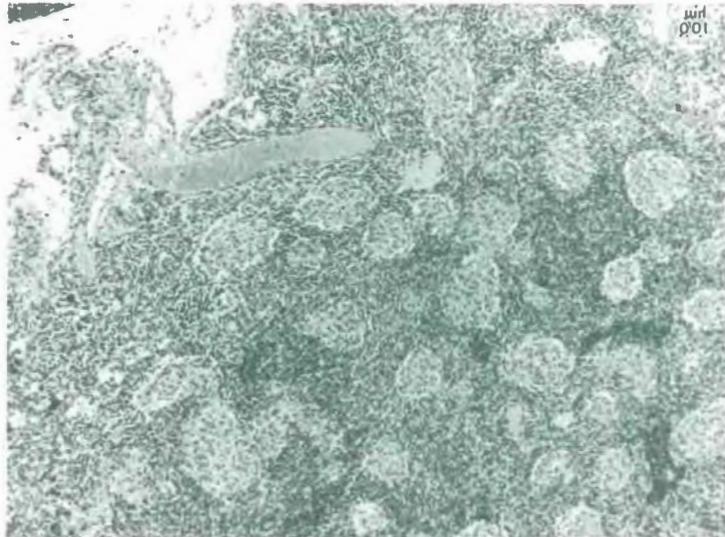


Figure 13. A peripancreatic lymph node from a quartz-treated rat. This area contains multiple granulomas.

in animals injected with secondary copper slag No. 2 and much less with both copper slags than that seen with quartz. In none of the lungs of the animals injected with the slags were there any granulomas similar to those induced with quartz or were there areas with dense collagen.

Particles were seen in the tracheobronchial lymph nodes of the animals injected with the slags, and they were usually surrounded by plasma cells.

Based on a scale of 1 to 10, the nickel slag induced a \pm reaction, primary copper slag No. 3 a 1+ reaction, secondary copper slag No. 2 a 2+ reaction, and the quartz a 10+ reaction 12 months after intratracheal instillation of the dusts. The reactions were primarily cellular. The reason for the rather small amount of collagen in the lungs of the quartz-treated rats compared to that reported by others is unknown but merits further investigation.

SUMMARY

Coal and various mineral slags are being used as substitutes for silica sand in abrasive blasting operations. These materials have been used without regard to their potential adverse health effects. Chemical analyses of eighteen coal and mineral slags has determined the presence of varying concentrations

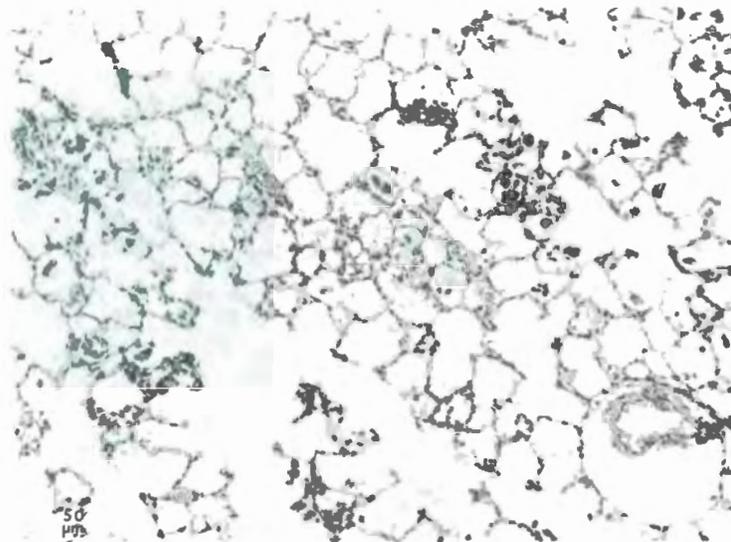


Figure 14A. Lung from a nickel slag-treated rat. The area shown is typical of these animals.

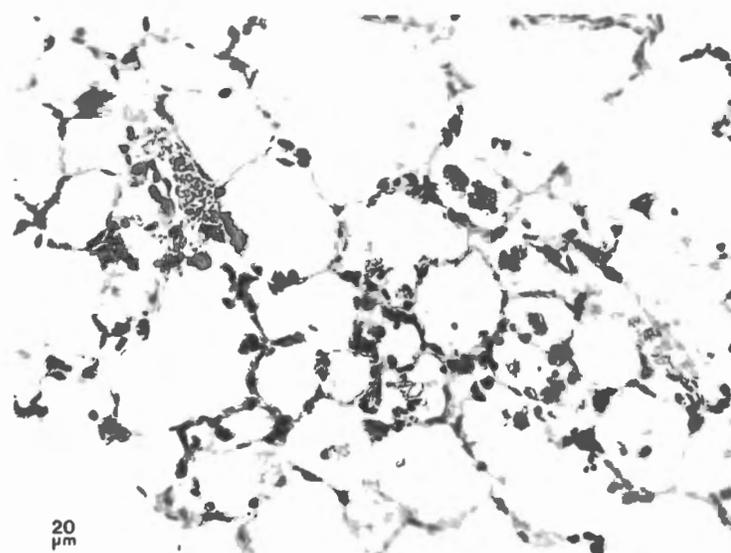


Figure 14B. A higher magnification shows collection of particles in the alveoli in both intra- and extracellular sites.

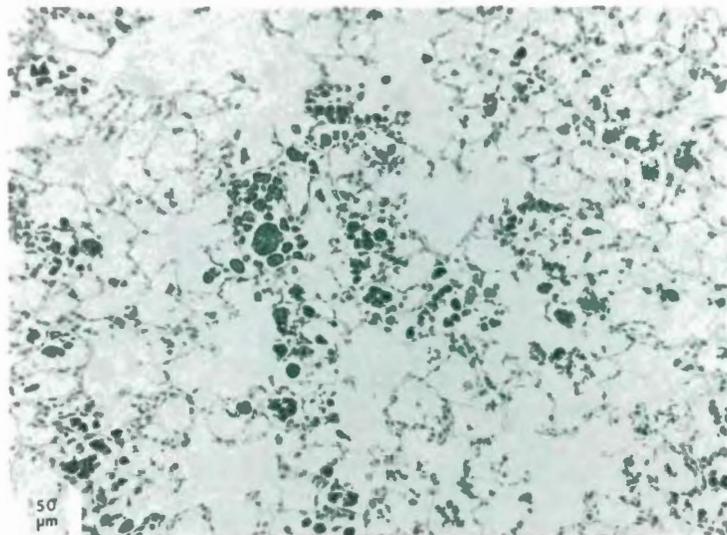


Figure 15A. Lung from a primary copper slag No. 3-treated rat. The area shown is typical for these animals.

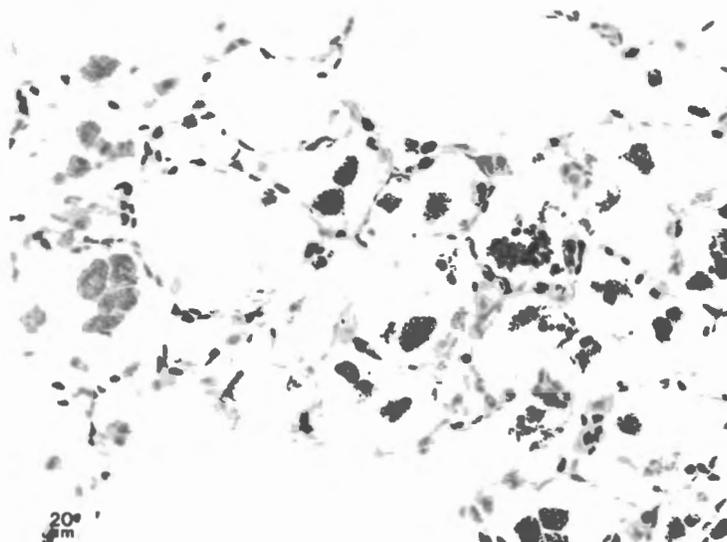


Figure 15B. A higher magnification showing numerous particulate-laden macrophages present in the alveoli.

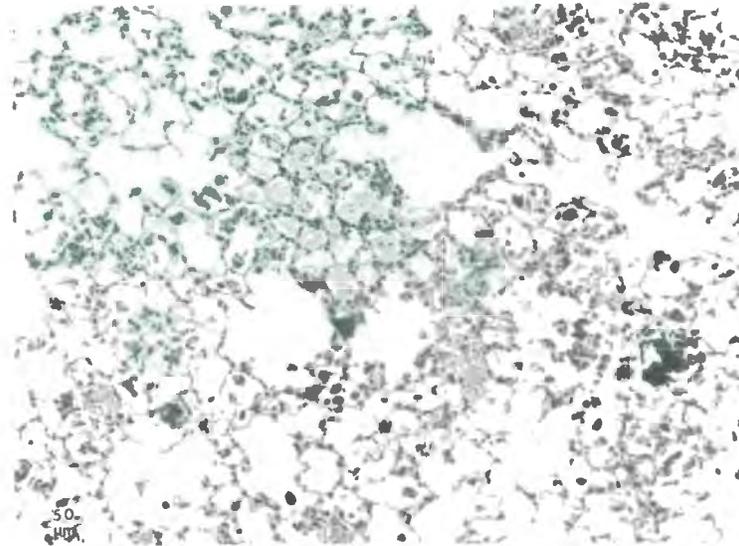


Figure 16A. Lung from a secondary copper slag No. 2-treated rat. A typical area is shown.

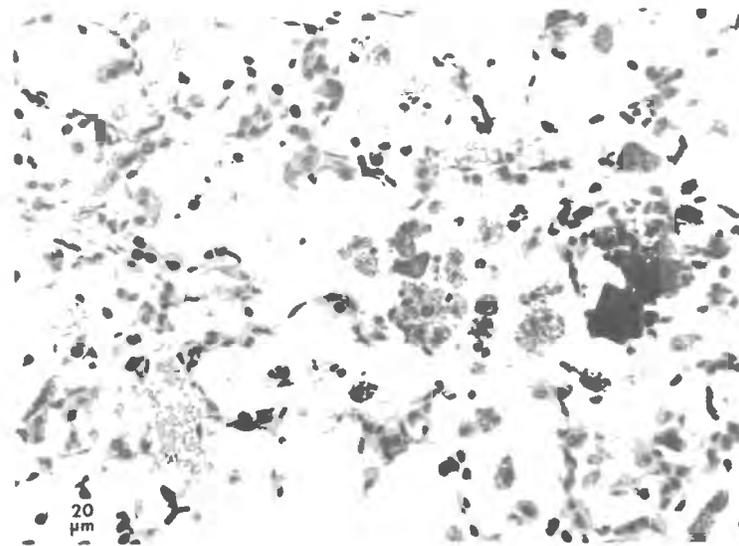


Figure 16B. A higher magnification showing some particulate-laden macrophages present in the alveoli, as well as several large particles in extracellular sites.

of suspect carcinogens such as arsenic, beryllium, chromium and nickel in these slags.

An initial study in which the fibrogenic effects of a coal and a copper slag were tested in rats by intratracheal instillation has been completed. The coal slag tested was found to be fibrogenic, while the copper slag was not. On a scale of 1 to 10, the fibrosis seen in the coal slag-treated rats was rated at 4. Fibrosis seen in quartz-treated rats was rated at 10.

A second study in which the fibrogenic and/or carcinogenic effects of three mineral slags are being tested is currently in progress. Results of the sacrifice at 12 months of 10 rats from each exposure group indicate a mild cellular reaction with each of the slags.

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DISCUSSION

Question: Did you find free silica in any of your samples?

Response: No. I might add that it's possible to get pulmonary fibrosis without any quartz. We got very beautiful fibrotic nodules from antimony trioxide by inhalation and by radiation.

Question: At the ALOSH lab in Morgantown, we looked at a case of silicosis in a rock driller. He had classical silicotic nodules in the lung, but he also had

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silicotic nodules in the spleen. I wonder if you've observed any lesions outside of the lungs? I know you said there was dust in the abdominal lymph nodes.

Response: In the rats, yes.

Question: I believe you can see coal dust in the spleens of coal miners?

Response: Yes, about 20% show significant amounts of it.

Question: At the American Thoracic Society meeting last year, there was a "round robin" on volcanic ash. Several people had used crystalline silica as their toxic control and, in fact, there were two people who looked at crystalline silica given to rats by inhalation. Each had a very different response. One of the differences seemed to be that one lab used specific pathogen-free rats and the other lab did not. Could this account for the differences you have seen?

Response: It's interesting you should mention that. When we did the study back in 1967, the rats had chronic pneumonia. It may be that chronic infection promotes the response. We know this is true in guinea pigs. More recently, we have been much more careful in the rats we accept from the supplier; in addition, the hygiene is much better now than it was back in 1967. It may be that these rats do not have any infection; consequently, the effect of the quartz takes longer, and possibly much, much longer to give the same result.

Question: We had a recent experience in our laboratory in a model of fibrogenesis using bleomycin in oxygen. We had two groups of hamsters, one of which had some acute responses to sendai virus infections. There was a dramatic synergism of the acute phase of the viral infection with bleomycin, and the animals had a greater response. I think it's a common problem that we all face. How do you see this type of study with large amounts of dust fitting in with the general question of assessing particulate toxicity? How do you interpret these data? Where does it leave you? How do you use these kinds of results?

Response: This is a screening technique very much like in vitro screening methods. We can't really give any absolutes. We can't establish a standard based on nonintratracheal injections. But you can't establish a standard based on inhalation in rats either, because a resting rat is a lot different from a working human.

Question: But you feel you can make some judgments as to the relative toxicity.

Response: Yes, definitely.

**HEALTH ISSUES
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