

Table 16. Epidemiologic studies of bronchitis in workers exposed to silica dust

Reference and country	Study design, cohort, and followup	Subgroup	Bronchitis cases in subgroup*	Risk measure (OR [†])	95% CI	Adjusted for smoking	Comments
Clark et al. [1980], United States	Cross-sectional study of bronchitic symptoms in 249 white male taconite miners; mean age was 49 with ≥20 yr of exposure to taconite dust. Control group of 86 men with no history of exposure to taconite mine dust.	80 dust-exposed smokers with cough all day	24%	— [‡]	—	Yes	Note that subgroups represent bronchitic symptoms—not cases. 33 controls were employees of a school; however, occupations of the other controls were not reported. Occupational dust exposures to the control group may have contributed to the similar or higher prevalences of bronchitic symptoms in that group.
		52 dust-exposed nonsmokers with cough all day	1%	—	—		
		24 nondust-exposed nonsmokers with cough all day	1%	—	—		
		32 nondust-exposed smokers with cough all day	16%	—	—		
		80 dust-exposed smokers with phlegm all day	18%	—	—		
		24 nondust-exposed nonsmokers with phlegm all day	1%	—	—		
		32 nondust-exposed smokers with phlegm all day	37%	—	—		

See footnotes at end of table.

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Reference and country	Study design, cohort, and followup	Subgroup	Bronchitis cases in subgroup*	Risk measure (OR [†])	95% CI	Adjusted for smoking	Comments
Cowie and Mabena [1991], South Africa	Cross-sectional study of 1,197 black, male underground gold miners aged 28–76 with 25.1 yr since first exposure (mean). 857 miners had chronic silicosis.	Miners with chronic sputum production and “high” dust exposure	—	1.8 [§]	1.19–2.69	Yes	62% of miners who smoked and 45% of miners who never smoked had “chronic bronchitic symptom complex.”
		Miners with 24 pack-yr of smoking exposure and chronic sputum production	—	3.7	2.62–5.23**		“High” and “low” dust exposure categories were based on qualitative assessments of underground mine dust exposure and occupation. Authors stated that bronchitic symptoms may also have been related to underground mining exposures other than respirable quartz dust.

See footnotes at end of table.

(Continued)

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Reference and country	Study design, cohort, and followup	Subgroup	Bronchitis cases in subgroup*	Risk measure (OR [†])	95% CI	Adjusted for smoking	Comments	
Holman et al. [1987], Australia	Cross-sectional study of 1,363 male, current gold miners (51% were underground miners) aged 20 to >60. 53% of the cohort worked underground 1–19 yr.	Total cohort	14% ^{††}	—	—	Yes	ORs were based on comparison with nonminers and were adjusted for effects of smoking and age.	
		Miners with chronic bronchitis: 1–9 yr of underground gold mining	—	1.8	1.0–3.3			
		10–19 yr of underground gold mining	—	2.5	1.2–5.2			
		≥20 yr of underground gold mining	—	5.1	2.4–10.9			
Kreiss et al. [1989b], United States	Community-based cross-sectional study of 389 male residents of Leadville, CO. 281 (72.2%) of the sample had worked at the local molybdenum mine. Mean yr of exposure: 9.3. Mean age of cohort: 44.	Underground miners with >10 yr of employment:				Yes	ORs were based on comparison with residents having no history of occupational dust exposure. Nearly half (49%) of personal samples for quartz exposures among the miners exceeded the NIOSH REL of 0.05 mg/m ³ (total number of samples was not reported).	
		With chronic cough	—	0.84	0.37–1.90			
		With chronic phlegm	—	0.93	0.42–2.06			

See footnotes at end of table.

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Reference and country	Study design, cohort, and followup	Subgroup	Bronchitis cases in subgroup*	Risk measure (OR [†])	95% CI	Adjusted for smoking	Comments
Ng et al. [1992b], Singapore	Cross-sectional study of 85 granite quarry workers with "high" dust exposure and 154 quarry workers with "low" dust exposure (see comments); mean age was 42. Mean duration of employment was 13.7 yr. Comparison group of 148 male postal workers with no exposure to granite dust; mean age was 40.	Quarry workers with "high" dust exposure:				Yes	No quantitative exposure concentrations for dust or silica were reported: granite quarry rock drillers and rock crushers were assumed to have "high" silica exposure; and administrative workers, truck drivers, vehicle maintenance workers, and loader operators were assumed to have "low" silica exposure. Results were adjusted for effects of age.
		All (85)	9	— ^{‡‡}	—		
		Nonsmokers (34)	2	— ^{§§}	—		
		Ex-smokers (5)	—	—	—		
		Current smokers (46)	7	— ^{§§}	—		

See footnotes at end of table.

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Reference and country	Study design, cohort, and followup	Subgroup	Bronchitis cases in subgroup*	Risk measure (OR [†])	95% CI	Adjusted for smoking	Comments
Rastogi et al. [1991], India	Cross-sectional study of 240 male and 102 female agate grinders and chip-pers, and 116 male and 33 female controls with nondusty occupations. The mean duration of exposure was 10 yr for males and 8.9 yr for females.	Chronic bronchitis:				Yes	Association between dust exposure and chronic bronchitis may not have been detected because the control group included workers who may have occupational exposure to respirable silica dust (e.g., rickshaw-pullers and sweepers). High prevalence of tuberculosis in agate workers and controls may have masked an association for bronchitis.
		Male:					
		Agate workers	3.75/100	—	—		
		Controls	4.58/100	—	—		
		Female:					
		Agate workers	0	—	—		
		Controls	9.1/100	—	—		
		Acute bronchitis:					
		Male:					
		Agate workers	9.1/100	—	—		
Controls	5.17/100	—	—				
		Female:					
		Agate workers	9.8/100	<i>P</i> <0.05	—		
		Controls	0	—	—		
Samet et al. [1984], United States	Cross-sectional study of 192 male, current underground uranium miners aged <40, 40–59, and ≥60. 145 miners (76%) mined ≥10 yr underground.	Miners with chronic cough:				Yes	Chronic cough and chronic phlegm were not associated with duration of silica exposure in multiple logistic regression analysis (results were not reported).
		10–19 yr of mining	14.1/100 ^{***}	—	—		
		≥20 yr of mining	22.7/100 ^{***}	—	—		
		Miners with chronic phlegm:					
		10–19 yr of mining	31.9/100 ^{***}	—	—		
		≥20 yr of mining	36.6/100 ^{***}	—	—		

See footnotes at end of table.

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Reference and country	Study design, cohort, and followup	Subgroup	Bronchitis cases in subgroup*	Risk measure (OR [†])	95% CI	Adjusted for smoking	Comments
Sluis-Cremer et al. [1967], South Africa	Community-based, cross-sectional study of chronic bronchitis in 827 male residents who were aged >35 and who lived in Carletonville, a South African town with four gold mines.	Residents w/chronic bronchitis:				Yes	“Dust-exposed” was defined as self-reported occupational exposure in a “scheduled dusty area” of a mine. A significant difference existed between the prevalence of chronic bronchitis in dust-exposed smokers and nondust-exposed smokers ($P<0.01$). No significant difference existed between dust-exposed and nondust-exposed nonsmokers or ex-smokers.
		Dust-exposed:					
		Smokers	199/394 (51%)	—	—		
		Nonsmokers	22/168 (13%)	—	—		
Nondust-exposed:	Smokers	45/161 (28%)	—	—			
	Nonsmokers and ex-smokers	7/104 (7%)	—	—			
Wiles and Faure [1977], South Africa	Cross-sectional study of chronic bronchitis in 2,209 underground gold miners (race not reported) aged 45–54 with ≥10 yr of employment. 653 were ex-miners for ≥1 yr.	138 miners in highest cumulative dust exposure group:				Yes	Prevalence of chronic bronchitis increased with increasing mean dust concentration ($P<0.001$) and with cumulative dust exposure in nonsmokers ($P<0.05$), ex-smokers ($P<0.05$), and smokers ($P<0.001$).
		Nonsmokers	2/14 (14%)	—	—		
		Ex-smokers	4/31 (13%)	—	—		
		Smokers	47/93 (51%)	—	—		

*Number of cases unless otherwise indicated.

[†]Abbreviations: CI=confidence interval; NIOSH=National Institute for Occupational Safety and Health; OR=odds ratio; REL=recommended exposure limit.

[‡]Dash indicates *not reported*.

[§]Compared with miners having “low” dust exposure.

^{**}Compared with miners having 0 pack-yr.

^{††}Estimated prevalence.

^{‡‡}Risk measure was not reported, but $P<0.01$ compared with controls.

^{§§}Risk measure was not reported, but $P>0.05$ compared with controls.

^{***}Standardized to the overall distribution of cigarette smoking.

Table 17. Loss of lung function (FEV₁)* associated with cumulative exposure to respirable granite dust

Reference and country	Study design, cohort, and followup	Subgroup	Loss of FEV ₁			Comments
			Observed (estimated ml/yr)	Predicted (ml per mg/m ³ ·year)	Adjusted for smoking	
Eisen et al. [1995], United States	Longitudinal study of 618 white male granite workers hired after 1940, aged 25–65; employed 14.7 yr (mean), and followed 1970–1974 for annual pulmonary function testing [Eisen et al. 1983]. Quartz content of dust was 11% [Hosey et al. 1957].	Nonsmokers	34–72	—	Yes	Significant dose-response ($P < 0.05$) was observed in the “dropout” group but not in the “survivor” group or the total cohort [Eisen et al. 1983]. After 1940, granite dust concentrations in Vermont granite sheds were <10 million particles per cubic foot (mppcf), or a respirable silica concentration of about 0.075 mg/m ³ [Davis et al. 1983].
		Smokers	53–69	—		
		Nonsilicotic nonsmokers	—	4 [†]		
						Predicted loss based on results of linear regression models.
Theriault et al. [1974b], United States	Cross-sectional study of 792 male, current granite shed workers aged 25–65. Quartz content of dust was 9% [Theriault 1974a].	Granite dust exposure	1.6 ^{‡,§}	3 [§]	Yes	Predicted loss based on results of multiple regression analysis. Exposure-response relationship found between cumulative dust exposure and cumulative quartz exposure and loss of FEV ₁ .
		Quartz dust exposure	1.5 ^{**}	2.9 [§]		

*Forced expiratory volume in 1 second.

[†]In dropout group (i.e., subjects lost to followup). No predicted loss in survivor group.

[‡]Per dust-year (i.e., granite shed dust exposure of 0.52 mg/m³ for 40 hr/week for 1 yr).

[§]Included silicotics.

**Per quartz-year (i.e., quartz dust exposure of 0.05 mg/m³ for 40 hr/week for 1 yr).

Table 18. Epidemiologic studies of emphysema in workers exposed to silica dust

Reference and country	Study design, cohort, and followup	Subgroup	Number of emphysema deaths or cases in subgroup	Risk measure	95% CI*	Adjusted for smoking	Comments
Becklake et al. [1987], South Africa	Unmatched case-control study of 44 autopsied white gold miners with emphysema \geq grade 2.0 (i.e., moderate or marked emphysema) and 42 controls without emphysema. Miners and controls were aged 51–70 at death (1980–1981).	Miners who smoked 20 cigarettes/day before 1960	— [†]	30.3 [‡]	7.0–141.0	Yes	The presence of emphysema at autopsy was not associated with the presence of silicosis.
		Miners aged 70 at death	—	26.8 [‡]	2.0–327.0	No	Deaths during 1980–1981 may not be typical of deaths in the total cohort of South African gold miners.
		Miners who worked 20 yr in occupations with “high” dust exposure	—	12.7 [‡]	3.0–52.0	No	
Chatgidakis [1963], South Africa	Prevalence study of 800 consecutive autopsies of white gold miners conducted between January 1957 and October 1962.	Miners with silicosis and emphysema	297	44.58 [§]	— ^{**}	No	Degree of emphysema was not related to years of service. Pulmonary diffuse emphysema increased significantly with incidence and degree of silicosis and with age.

See footnotes at end of table.

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Table 18 (Continued). Epidemiologic studies of emphysema in workers exposed to silica dust

Reference and country	Study design, cohort, and followup	Subgroup	Number of emphysema deaths or cases in subgroup	Risk measure	95% CI*	Adjusted for smoking	Comments
Cowie et al. [1993], South Africa	Random sample of 70 black underground gold miners selected for computed tomography lung examination from 1,197 participants in a cross-sectional study conducted in 1984–1985.	Miners by emphysema grade:				Yes	Presence and grade of emphysema were associated with silicosis ($P<0.002$; $P=0.006$) and smoking ($P<0.02$; $P=0.01$) but were not associated with years of underground mining.
		Grade 0 (no evidence)	22	—	—		
		Grade 1 (<25% of lung affected)	38	—	—		
		Grade 2 (25%–50% of lung affected)	10	—	—		Low agreement (i.e., 37/70) between computed tomographic and radiologic assessments of silicotic nodule profusion categories.

See footnotes at end of table.

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Table 18 (Continued). Epidemiologic studies of emphysema in workers exposed to silica dust

Reference and country	Study design, cohort, and followup	Subgroup	Number of emphysema deaths or cases in subgroup	Risk measure	95% CI*	Adjusted for smoking	Comments
Hnizdo et al. [1991], South Africa	Retrospective cohort study of the relationship of emphysema with lung function changes in 1,553 white gold miners aged ≥ 40 with autopsy examination between 1974 and 1987 and panacinar, centriacinar, or a mixed type of emphysema.	Miners who worked 20 yr in occupations with "high" dust exposure up to age 45	—	3.5 [‡]	1.7–6.6	Yes (in some analyses)	<p>Logistic regression model showed significant association between</p> <ul style="list-style-type: none"> • centriacinar emphysema and silicosis ($P < 0.001$), • emphysema and years of employment in a high-dust occupation for miners who smoked, • age and emphysema, and • average number of cigarettes smoked/day and emphysema. <p>Possible misclassification of emphysema type.</p>

Table 18 (Continued). Epidemiologic studies of emphysema in workers exposed to silica dust

Reference and country	Study design, cohort, and followup	Subgroup	Number of emphysema deaths or cases in subgroup	Risk measure	95% CI*	Adjusted for smoking	Comments
Hnizdo et al. [1994], South Africa	Retrospective cohort study of relationship of emphysema with lung function in 242 white gold miners who were life-long nonsmokers, were aged ≥ 45 at death, and had an autopsy examination during 1974–1990.	Nonsmoking miners with moderate emphysema	4	—	—	Yes (all study subjects were nonsmokers)	For nonsmokers, degree of emphysema at autopsy was not associated (i.e., $P > 0.05$ in multiple regression model) with years of gold mining, cumulative dust exposure, parenchymal silicosis, or lung function impairment after adjusting for age at death.

*Abbreviations: CI=confidence interval; OR=odds ratio.

†Dash indicates *not reported*.

‡OR for emphysema \geq grade 2 at autopsy.

§Chi-square value (comparing silicotic miners with emphysema to silicotic miners without emphysema).

** $P < 0.00001$.

See footnotes at end of table.

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Table 19. Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Boujemaa et al. [1994], Belgium	Cross-sectional case-control study of 116 silicotic, male underground miners with no history of diabetes, nephrolithiasis, or hypertension and 61 age-matched controls from the general population. Urine samples were tested for albumin, retinol-binding protein, and NAG. Serum samples were tested for creatinine and β_2 -microglobulin.	Silicotics	116	—†	—	Miners were examined an average of 23 yr after cessation of exposure. Mean duration of exposure was 14.9 yr. Duration of exposure and severity of silicosis were not associated with the measures of renal dysfunction. Silicotic miners had significantly higher urinary concentrations of albumin ($P=0.017$), retinol-binding protein ($P=0.0045$), and NAG ($P=0.0001$). Results were similar to those found by Hotz et al. [1995].

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Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Bovenzi et al. [1995], Italy	Case-control study of 527 patients admitted to all hospitals in Trento province 1976–1991 and discharged with diagnosis of musculoskeletal disorder or connective tissue disease. Each scleroderma case was matched by age and gender to two controls who were without the disease under study and were from the same database.	Patients discharged with diagnosis of systemic sclerosis (according to specific diagnostic criteria):				—
		Women	16	0‡	—	
		Men	5	5.20§	0.48–74.1	

See footnotes at end of table.

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Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Burns et al. [1996], United States	Population-based case-control study of 274 women with confirmed systemic sclerosis diagnosed in Michigan between 1985 and 1991 and 1,184 female controls matched by race, age, and geographic region.	Women with self-reported exposure to the following: Abrasive grinding or sandblasting	3	0.34	0.10–1.10	Adjusted for age, race, and date of birth. Systemic sclerosis was not associated with self-reported exposures to silica dust or silicone (including breast implants). Same study design was applied to Ohio women with systemic sclerosis, and results were published later in a letter [Lacey et al. 1997].
		Sculpting or pottery making	20	1.53	0.89–2.65	
		Working in a dental laboratory	3	1.52	0.44–5.26	
		Working with or near silica dust, sand, or other silica products	12	1.50	0.76–2.93	
Calvert et al. [1997], United States	Cohort morbidity study of 2,412 white, male underground gold miners employed ≥ 1 yr between 1940 and 1965 and alive on January 1, 1977.	Miners with cases of treated end-stage renal disease	11	1.37**	0.68–2.46	First epidemiologic study to examine incidence of end-stage renal disease in an occupational cohort.
		Nonsystemic††	6	4.22**	1.54–9.19	
		Systemic	4	0.80**	0.22–2.06	Subcohort of gold miners studied by Steenland and Brown [1995b]. Mean respirable silica dust exposure of this subcohort was 0.05 mg/m ³ .
		Unknown	1	1.54**	0.04–8.57	

See footnotes at end of table.

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Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Cowie [1987], South Africa	Cohort study of incidence of scleroderma in black gold miners seen by the medical service from July 1981 to June 1986.	Miners with scleroderma that met diagnostic criteria	10	81.8**	—	—
Hotz et al. [1995], Belgium	Cross-sectional case-control study of prevalence of subclinical renal effects in 86 quarry workers employed 11 to 20 months with no clinical, spirometric, or radiographic signs of silicosis. Controls were manual workers [Bernard et al. 1994] matched by smoking status, body mass index, and age. Urine samples were tested for albumin, transferrin, creatinine, β_2 -microglobulin, retinol-binding protein, silicon, and NAG. Serum samples were tested for creatinine and β_2 -microglobulin.	—	86	—	—	Same cohort studied by Bernard et al. [1994]. Quarry workers had significantly higher urinary concentrations of albumin ($P<0.0004$), transferrin ($P<0.03$), retinol-binding protein ($P<0.001$), NAG ($P<0.001$), and silicon ($P<0.0001$). Controls may have been exposed to silica dust—occupational history of controls was not reported. Narrow range of employment duration may have limited the assessment of effects.

See footnotes at end of table.

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Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Klockars et al. [1987], Finland	Cohort morbidity study of 1,026 granite workers hired between 1940 and 1971 with followup until the end of 1981 for (1) incidence of disability pension awards for rheumatoid arthritis during 1969–1981, (2) prevalence of rheumatoid arthritis on December 31, 1981, and (3) prevalence of subjects receiving free medication for rheumatoid arthritis at the end of 1981. Referent group was composed of Finnish males.	Granite workers: Awarded disability pensions for rheumatoid arthritis	17 ^{§§}	5.08 ^{***}	3.31–7.79	Mean quartz concentrations measured in the granite quarries, processing yards, and crushing plants in 1970–1972 ranged from 0.02 to 4.9 mg/m ³ .
		Receiving pensions for rheumatoid arthritis at end of study period	10 ^{§§}	—	—	1.6 recipients expected (<i>P</i> <0.001).
		Receiving free medication for rheumatoid arthritis at end of study period	19 ^{†††}	—	—	7.5 recipients expected (<i>P</i> <0.001).

See footnotes at end of table.

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Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Ng et al. [1993], Singapore	Cross-sectional study of subclinical renal effects in 67 granite quarry workers with no history of glomerulonephritis, urinary calculi, renal disease, diabetes, hypertension, or regular ingestion of analgesics. Workers' urine samples were tested for indicators of glomerular and tubular functions (i.e., albumin, AMG, BMG, and NAG).	Workers with low-dust-exposure jobs and no radiographic evidence of silicosis	31	—	—	Workers in the high-exposure group with ≥10 yr of employment had significantly greater ($P<0.05$) urinary concentrations of AMG, BMG, and NAG compared with workers in the low-exposure group. Quantitative dust exposure data not available. Preliminary findings were reported in Ng et al. [1992a]. Further studies are needed to define the clinical significance of AMG, BMG, and NAG as indicators of renal dysfunction in silica-exposed workers.
		Workers with high-dust-exposure jobs and <10 yr of employment	17	—	—	
		Workers with high-dust-exposure jobs and ≥10 yr of employment	19	—	—	

See footnotes at end of table.

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Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Nuyts et al. [1995], Belgium	Case-control study of occupational exposures of 16 patients diagnosed with Wegener's granulomatosis at six Belgian renal units between June 1991 and June 1993. Each patient was matched (by age, sex, and region of residence) with two controls randomly selected from lists of voters.	Patients with Wegener's granulomatosis (renal involvement) and reported occupational exposure to silica	5	5.0	1.4–11.6	Study had small sample size and was not designed specifically to examine exposure-response relationship of Wegener's granulomatosis with occupational exposure to silica. Further study is needed.
Rafnsson et al. [1998], Iceland	Population-based case-control study of residents in a district with a diatomaceous earth processing plant. Population included 8 sarcoidosis patients who were linked to a file of all past and present workers employed at the plant after it opened in 1967. 70 controls were randomly selected from the district population.	Sarcoidosis patients with occupational exposure to diatomaceous earth and cristobalite at the community plant	6	13.2	2.0–140.9	No matching of cases with controls. Mean values of personal samples of respirable cristobalite dust taken in 1978 and 1981 ranged from 0.002 to 0.6 mg/m ³ . Stratification by number of hr worked (≥1,000 hr or <1,000 hr) indicated a dose-response trend. Further study of sarcoidosis and silica exposure is needed.

See footnotes at end of table.

(Continued)

Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Rosenman and Zhu [1995]	Cohort morbidity study of men and women aged ≥ 20 and discharged from Michigan hospitals 1990–1991.	Patients with silicosis and rheumatoid arthritis:				No patients had silicosis and scleroderma.
		Women	0	—	—	
		Men	3	3.2**	1.1–9.4	
Sluis-Cremer et al. [1985], South Africa	Case-control study of silicosis in 79 white gold miners diagnosed with “definite” or “probable” progressive systemic sclerosis between 1955 and June 1984. Randomly selected control group of 79 miners in same patient index examined between May 1970 and April 1971; matched by age; without progressive systemic sclerosis.	—	79	1.18	0.26–5.38	Controlled for cumulative dust exposure. Although reported ORs suggested no association between silicosis and progressive systemic sclerosis, cases had higher cumulative dust exposure ($P < 0.001$). This study was not designed to examine the possibility of a direct association between silica dust exposure and progressive systemic sclerosis.
Sluis-Cremer et al. [1986], South Africa	Case-control study of silicosis in 157 white gold miners diagnosed with “definite” or “probable” rheumatoid arthritis between 1967 and 1979. Each case was matched by age to a control subject without rheumatoid arthritis.	Miners with “definite” rheumatoid arthritis	91	3.79***	1.72–8.36	Although the reported ORs suggested that gold miners with probable or definite rheumatoid arthritis were more likely to have silicosis as well, the study was not designed to examine the possibility of a direct association between silica exposure and rheumatoid arthritis. The results could not be explained by cumulative dust exposure or the intensity of exposure to gold mine dust.
		Miners with “probable” rheumatoid arthritis	66	1.94***	0.81–4.63	

See footnotes at end of table.

(Continued)

Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Steenland et al. [1990], United States	Population-based case-control study of occupational exposures of 325 men listed in the Michigan kidney registry and diagnosed with end-stage renal disease (excluding diabetic, congenital, and obstructive nephropathies) between 1976 and 1984. 325 controls matched by age, race, and area of residence.	Men with end-stage renal disease who reported occupational exposure to silica	87	1.67	1.02–2.74	Possible overreporting of exposure by cases.
Steenland et al. [1992], United States	Proportionate mortality study of 991 granite cutters who died after 1960 compared with causes of death in U.S. population.	Granite cutters: Arthritis deaths	17	2.01 ^{§§§}	1.17–3.21	Study included all underlying and contributing causes of mortality after 1960 and other significant conditions that were documented on the death certificate.
		Chronic renal disease deaths (ICD–9 categories 582, 583, 585, 587) ^{****}	26	2.18 ^{§§§}	1.43–3.20	

Table 19 (Continued). Epidemiologic studies of immunologic, autoimmune, and chronic renal disease (including subclinical renal changes) in silica-exposed workers

Reference and country	Study design, cohort, and followup	Subgroup	Number of deaths or cases in subgroup	Risk measure*	95% CI†	Comments
Steenland and Brown [1995b], United States	Mortality study of 3,328 white male gold miners employed underground ≥1 yr between 1940 and 1965 and followed for mortality from 1977 to 1990. Mortality rates of U.S. males used for comparison.	Arthritis (ICD-9 categories 711-716, 720-721) (see comments)	17	2.19 ^{††††}	1.27-3.50	Study included all underlying and contributing causes of mortality after 1960 and other significant conditions documented on the death certificate.
		Other musculoskeletal disease as well as sclerosis, scleroderma, and lupus (ICD-9 categories 710, 717-719, 722-729, 731-739) (see comments)	10	2.14 ^{††††}	1.03-3.94	Statistically significant exposure-response trend ($P<0.05$) for chronic renal disease mortality and cumulative dust exposure.
		Nonmalignant skin diseases (ICD-9 categories 690-709) (see comments)	10	2.45 ^{††††}	1.17-4.51	
		Chronic renal disease in miners in highest cumulative dust exposure category (i.e., ≥48,000 dust-days)	8	2.77 ^{††††}	1.20-5.47 ^{††††}	

*Odds ratio unless otherwise indicated.

†Abbreviations: Dash indicates *not reported*; AMG=alpha-1-microglobulin; BMG=beta-2-microglobulin; CI=confidence interval; NAG=beta-n-acetyl-D-glucosaminidase; OR=odds ratio.

‡None exposed.

§For history of silica dust exposure.

**Standardized incidence ratio (SIR).

††That is, caused by glomerulonephritis or interstitial nephritis.

†††Incidence (cases) per million black gold miners. Incidence in general population of black men of similar age (33-57) was 3.4 cases per million ($P<0.001$).

§§Disability cases.

***Rate ratio.

††††Receiving arthritis medication through national insurance plan.

†††††OR is for presence of silicosis.

§§§PMR.

****ICD-9 is the *International Classification of Diseases*, 9th Revision [WHO 1977].

†††††SMR.

††††††Reported in Steenland and Goldsmith [1995].

Table 20. Molecular epidemiology studies of biomarkers for carcinogenesis or silicosis

Reference and country	Study design and cohort*	Number of subjects	Biologic marker	Results	Comments
Bernard et al. [1994], Belgium	Belgium quarry workers who had worked <2 yr. Controls were manual workers without silica dust exposure, matched by smoking status, body mass index, and age.	86 quarry workers and 86 controls	Serum and sputum Clara cell protein (Clara cell 16)	Decreased concentrations of serum and sputum Clara cell protein in quarry workers ($P=0.04$) compared with controls.	Controls may have been exposed to silica dust. Short duration of exposure among quarry workers may have limited the analysis. Authors state that serum Clara cell 16 may be marker for toxic effects of silica particles on respiratory epithelium.
Borm et al. [1986], Netherlands	Male silicosis patients at a hospital in the Netherlands; exposed to silica for 10–38 yr. Controls were “healthy male, Caucasian blood donors” aged 50–65.	20 silicosis patients (15 coal miners, 4 ceramics workers, 1 foundry worker); 48 controls	Blood and plasma concentrations of hemoglobin, reduced and oxidized glutathione, glutathione peroxidase, and superoxide dismutase	Silicosis patients had significantly higher concentrations of red blood cell glutathione ($P<0.0001$).	Small number of subjects. Controls were not interviewed for their occupational history, and definition of “healthy” was not reported. Medication administered to patients may have been a confounder.

See footnotes at end of table.

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Table 20 (Continued). Molecular epidemiology studies of biomarkers for carcinogenesis or silicosis

Reference and country	Study design and cohort*	Number of subjects	Biologic marker	Results	Comments
Brandt-Rauf et al. [1992], Finland	Prospective study of compensated pneumoconiosis patients; 91 blood samples were collected between 1983 and 1987. Cancer cases were identified in the Finnish Cancer Registry. 4 silicotics had worked as stone workers, 1 as a stone crusher, 2 as miners, and 3 as foundry workers. 3 silicotics with lung cancer were matched by age and smoking habits with 7 controls without cancer.	46 patients: 36 with asbestosis and 10 with ILO [†] category $\geq 1/1$ silicosis	9 serum oncogene-related proteins or growth factors: growth factor PDGF-B (<i>sis</i>), TGF- β_1 , <i>ras</i> , <i>fes</i> , <i>myb</i> , <i>int-1</i> , <i>mos</i> , <i>src</i> , <i>myc</i>	7/15 asbestosis patients had <i>ras</i> (p21) oncogene, but no oncogene-related proteins were found in the 10 silicosis patients. All silicosis patients had PDGF-B (<i>sis</i>) growth factor; only 42% of asbestosis patients had PDGF-B (<i>sis</i>).	Prospective study found that 3 of the 10 silicosis patients developed cancer during the study period (1983–1987). 2 patients had bladder cancer and 1 had lung cancer. PDGF may be a possible marker for development of severe or progressive silicosis. Study results suggest different pathogeneses for silicosis and asbestosis.

See footnotes at end of table.

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Table 20 (Continued). Molecular epidemiology studies of biomarkers for carcinogenesis or silicosis

Reference and country	Study design and cohort*	Number of subjects	Biologic marker	Results	Comments
Calhoun et al. [1986], United States	Healthy, male, employed granite workers (non-smokers) with no clinical or radiographic evidence of silicosis. Volunteer controls of similar age and smoking history with no history of occupational exposure to dust. All workers and controls had BAL.	9 workers and 9 controls	IgG, IgM, IgA, albumin, and total protein (all were measured in BAL fluid and serum)	No significant differences in mean serum concentrations between workers and controls. Statistically significant differences (i.e., higher concentration) between IgG, IgA, IgM concentrations and lymphocyte counts in lavage fluid of workers compared with controls.	Authors concluded that inhalation of granite dust might initiate and sustain an immune-inflammatory response.
Gáliková [1982], Slovakia	Miners, drillers, and tunnelers, half with silicosis, aged 43–81, exposed 2–30 yr. Control group of healthy blood donors aged 42–82 with no history of exposure to inorganic dusts.	40 workers and 40 controls	Serum IgG, IgM, and IgA	No difference in IgM concentration. Significantly elevated average concentration of IgG in workers compared with controls ($P < 0.001$). Significantly elevated average concentration of IgA in workers compared with controls ($P < 0.05$). No significant differences in IgG, IgM, or IgA between silicotic and non-silicotic workers.	Method of silicosis diagnosis not reported.

See footnotes at end of table.

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Table 20 (Continued). Molecular epidemiology studies of biomarkers for carcinogenesis or silicosis

Reference and country	Study design and cohort*	Number of subjects	Biologic marker	Results	Comments
Gualde et al. [1977], France	Caucasian silicosis patients (radiographic diagnosis) who had a silica-related occupation for 10–40 yr (38 gold, wolfram, and uranium miners; 35 porcelain workers; 2 quarry workers). “Normal and healthy” Caucasian controls plus second control group of porcelain workers employed 20–40 yr but with no clinical or radiographic signs of silicosis.	75 patients, 160 controls in first group, and 46 in control group of porcelain workers	27 HLA antigens (serum)	Prevalence of B7 antigen was significantly less ($P<0.05$ before correction for multiple comparisons of tested antigens) than in healthy or silica-exposed controls. No other significant differences found between silicotics and controls.	Small number of controls may have resulted in low statistical power to detect any differences after correction for multiple comparisons. Authors suggested that presence of B7 antigen may be related to resistance to development of silicosis. (See also Sluis-Cremer and Maier [1984] later in table.)
Honda et al. [1993], Japan	Japanese silicosis patients who had been sandblasters and who had radiographic evidence of silicosis. Controls were “healthy unrelated Japanese.”	46 patients, 315 controls for HLA typing, and 94, 127, 100, or 128 controls for other analyses	HLA-DQ alleles, RFLP patterns, and IGLV gene extracted from peripheral granulocytes (medium not reported)	Some HLA-DQ alleles were more frequent in silicosis patients ($P<0.05$). RFLP pattern of C4A3–C4B5 allotype and IGLV more frequent in silicosis patients ($P<0.05$).	Source and occupational history of control group not reported. Definition of “healthy” not reported. Potential confounders of exposure and immunological outcomes not reported. Authors suggested that their findings indicate that a gene for silicosis may be near the HLA-B locus. Validation of these findings is needed.

See footnotes at end of table.

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Table 20 (Continued). Molecular epidemiology studies of biomarkers for carcinogenesis or silicosis

Reference and country	Study design and cohort*	Number of subjects	Biologic marker	Results	Comments
Husgafvel-Pursiainen et al. [1997], Finland	Finnish white males with lung cancer (see comments).	5 patients with silicosis and 16 patients with asbestosis	Mutation of p53 gene and serum elevation of p53 protein (serum samples were not available for the silicosis patients)	Two of the five silicosis patients had lung tumors with DNA mutations of the p53 gene.	Subjects for study were drawn from cohort studied by Brandt-Rauf et al. [1992] (described earlier). The results of the serum tests do not support use of p53 assay by itself as a screening tool for lung cancer because only 36% of cancer cases tested positive for the mutant protein. The authors state that it may be a useful biomarker if combined with serum assays for altered oncoproteins as in the study by Brandt-Rauf [1992].
Karnik et al. [1990], India	Male slate pencil workers. Controls with no history of occupational exposure to dust or silica.	130 silica-exposed workers: 80 with ILO category 1, 2, or 3 silicosis and 50 controls	Serum IgG, IgM, and IgA	Higher concentrations ($P<0.05$) of IgG, IgM, and IgA in silicotic workers compared with controls.	Results may have been confounded by bacterial infections in some workers. Authors stated that an increase in immunoglobulin concentrations was not a marker for severity of silicosis.

See footnotes at end of table.

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Table 20 (Continued). Molecular epidemiology studies of biomarkers for carcinogenesis or silicosis

Reference and country	Study design and cohort*	Number of subjects	Biologic marker	Results	Comments
Koskinen et al. [1983], Finland	Finnish male silicosis patients (ILO category $\geq 1/1$) who had been exposed to silica dust ≥ 10 yr. Non-silicotic controls matched by age (± 5 yr), duration of silica exposure (± 5 yr), and work environment. Additional control group of healthy Finnish blood donors.	27 patients; 27 non-silicotic, silica-exposed controls; and 900 blood donor controls	Serum HLA antigens	Higher prevalence of HLA-Aw19 in silicotics compared with non-silicotic, silica-exposed controls ($P=0.02$). Higher prevalence of HLA-Aw19 in unexposed blood donor group than in silica-exposed controls ($P=0.04$).	Authors state HLA-Aw19 may be marker for silicosis progression in Finnish population, but larger study groups are needed.
Kreiss et al. [1989a], United States	Silicotic residents from hardrock mining town in Colorado who had mined for 5–58 yr and were aged 30–59 when diagnosed with ILO category $\geq 1/0$ silicosis. Published antigen prevalences of North American whites and international whites used for comparison.	49 silicotics, 1,029 North American controls, and 1,061–1,082 international controls	HLA-A, HLA-B, HLA-DR, and HLA-DQ antigens (blood)	Significantly higher prevalence of A29 and B44 in silicotics compared with two control groups ($P<0.05$ after correction for number of antigens tested).	Population-based study design. A29 is a component of Aw19 (see Koskinen et al. [1983] above).

See footnotes at end of table.

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Table 20 (Continued). Molecular epidemiology studies of biomarkers for carcinogenesis or silicosis

Reference and country	Study design and cohort*	Number of subjects	Biologic marker	Results	Comments
Pevnitskiy et al. [1978], Russia	Male Russian patients aged 30–50 with “Stage I” silicosis who had been employed >10 yr in occupations with exposure to quartz dust (i.e., casting shop cleaners, sandblasters, and molders). Controls were “clinically healthy” Russian male blood donors aged 30–50.	32 silicosis patients and 32 controls	11 HLA antigens (6 on A locus and 5 on B locus) (serum)	Prevalence of HLA–B8 and HLA–B13 in silicotics was twice the prevalence in the control group (<i>P</i> value not reported).	Occupational history of control group not reported. Definition of “healthy” not reported. Definition of “Stage I” silicosis not reported. Small number of subjects and controls.
Sluis-Cremer and Maier [1984], South Africa	White South African gold miners who had been exposed to at least 20 “low-dust” years. Control group of Caucasian nonminers.	101 miners (45 silicotics of category $\geq 1/0$ and 56 nonsilicotics) and 279 controls	29 HLA antigens (medium not reported)	Significantly fewer silicotics had B40 antigen compared with both silica-exposed and non-exposed comparison groups (<i>P</i> =0.02).	Source of control group not reported. No significant difference was found in the prevalence of B7, which does not agree with the findings of Gualde et al. [1977] (discussed earlier).
Sobti and Bhardwaj [1991], India	Male sandstone-crushing workers. Control group of local university teachers and students.	50 workers and 25 controls	Blood: SCE and CA	Higher proportion of SCE and CA in silica-exposed workers compared with controls (2.72% versus 1.28%; <i>P</i> <0.01). More SCEs (<i>P</i> <0.01) in smokers—both silica-exposed and nonexposed.	Dust contained 50%–60% crystalline silica, 14%–16% aluminum oxide, and 4%–5% iron oxide. Possible effect of socioeconomic differences between workers and control group not accounted for. No statistical test for correlation between duration of exposure and levels of SCE and CA. Silica exposure concentrations not reported.

See footnotes at end of table.

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Table 20 (Continued). Molecular epidemiology studies of biomarkers for carcinogenesis or silicosis

Reference and country	Study design and cohort*	Number of subjects	Biologic marker	Results	Comments
Watanabe et al. [1987], Japan	Males aged 34–78, hospitalized with ILO category ≥ 2 silicosis and employed as tunnel workers or metal miners for a mean duration of 23.8 yr. “Normal” male controls aged 46–72 without silicosis.	82 patients and 25 controls	Total blood lymphocyte count and lymphocyte subsets: OKT3+, OKT4+, OKT8+, OKIa-1+ Serum IgG, IgM, IgA, IgD, and IgE	Silicosis patients with low lymphocyte counts ($\leq 1,500 \mu\text{l}$) had significantly increased IgG and IgA levels compared with controls ($P < 0.001$). Decreased number of circulating T-cells in patients.	Source and occupational history of control group not reported. Definition of “normal” controls not reported. Potential confounders of exposure and immunological outcomes not reported. Need further study of relationship of silicosis with serum immunoglobulin levels and lymphocytes.

*Studies were cross-sectional unless otherwise indicated.

†Abbreviations: BAL = bronchoalveolar lavage; CA = chromosomal aberrations; HLA = human leukocyte antigen; Ig = immunoglobulin; IGLV = immunoglobulin lambda variable chain; ILO = International Labour Organization; PDGF = platelet-derived growth factor; RFLP = restriction fragment length polymorphism; SCE = sister chromatid exchange; TGF = transforming growth factor.