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Prevalence of Small Lung Opacities in Populations Unexposed to Dusts*

A Literature Analysis

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Objectives: **Despite the wide use of the International Labor Organization (ILO) system for reading chest radiographs, little information is available regarding the prevalence of abnormalities in populations unexposed to dusts. Prevalence studies of radiographic changes consistent with dust inhalation, as classified by the system, would be more meaningful if there were better understanding regarding the extent of abnormalities in unexposed populations.**

Design: **To determine small opacity prevalence in unexposed populations, a review of articles published since 1970 that used the ILO system to classify radiographs of the unexposed, either as subjects or control subjects, was performed. Criteria for inclusion in this review included ascertainment of the lack of exposure of subjects to occupational dusts, and independent reading of radiographs by at least two readers certified in the ILO system (B readers) or experienced in its use. A total of eight published articles presenting data on nine study populations were included in this study.**

Results: **The prevalence of small opacities graded 1/0 or greater varied widely, with a range from 0.21 to 11.7%. A meta-analysis of the published data yielded a population prevalence of 5.3% (95% confidence interval [CI]=2.9 to 7.7%). The prevalence was significantly greater in Europe than in North America (Europe, 11.3%; 95% CI=10.1 to 12.5%; North America, 1.6%; 95% CI=0.6 to 2.6%). A subset of the studies contained information on gender that showed greater prevalence of lung opacities in male subjects than female subjects (male subjects, 5.5%; 95% CI=3.4 to 7.6%; female subjects, 3.5%; 95% CI=1.3 to 5.8%). Based on estimated age information, the studies were divided into two strata (mean age <50 years vs ≥50 years). The age-specific pooled prevalence was higher in the studies with mean age ≥50 years than studies with mean age <50 years in both Europe (11.7% vs 9.6%) and North America (2.3% vs 0.6%). Prevalence of lung opacities remained significantly higher in Europe than in North America in each age stratum. The large difference in the prevalence between Europe and North America could not be explained on the basis of age, gender, or smoking history, although available age and smoking data are less robust.**

Conclusions: **These results indicate that a background level of opacities consistent with the radiographic appearance of pneumoconiosis exists in populations considered to be free of occupational dust exposure. Environmental and unaccounted occupational exposures, as well as reader variability, all may play a role in the determination of small opacity prevalence in these subjects and may explain the large differences between Europe and North America. Thorough ascertainments of occupational and environmental exposures are essential to determine the true significance of opacities in populations who are not exposed to dust.** *(CHEST 1997; 111:404-10)*

Key words: ILO classification; lung opacities; meta-analysis; nondusty; unexposed

Abbreviations: CI=confidence interval; ILO=International Labor Organization

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The International Labor Organization (ILO) system for the classification of radiographic abnormalities was designed to reduce variability and improve comparability in epidemiologic studies of pneumoconiosis. Nevertheless, variability in classification of radiographs continues to be apparent.[1-3] The B-reading program for applying the ILO system in the United States has been subjected to recent scrutiny in response to this documented variability.[4-6] Findings suggest that rigorous quality assurance measures are required for consistent results in

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radiographic reading. Contributing to the problem of variability are low reading volumes among most certified ILO interpreters, and use of the ILO classification for other purposes, such as medicolegal disputes.[1,6] Variability in reading may affect assessment of the unexposed as well as workers with histories of dust inhalation.

Efforts at determining the prevalence of pneumoconiosis or chest radiograph opacities must contend with the following: (1) variability inherent in the application of the ILO system; (2) disparities in data collection or presentation (*eg*, assignment of differing cutoff values for abnormal radiographs or consensus vs independent readings); (3) demographic variables, such as age and smoking history, which may affect the frequency of parenchymal opacities; and (4) real dust exposure or other environmental differences in "unexposed" populations. Cigarette smoking has been associated with increases in the prevalence of opacifications in asbestos-exposed workers.[7] Age and smoking habits have been postulated to produce radiographic parenchymal abnormalities in unexposed populations indistinguishable from occupationally related pulmonary fibrosis.[8,9] Local variations in the extent of other pulmonary diseases, such as tuberculosis, may also affect prevalence figures.[10] Patient size and chest wall thickness influence radiographic quality and observer interpretation.[8] Within the extensive literature on the dust-related lung diseases, estimates of the population prevalence of radiographic features consistent with pneumoconiosis in unexposed populations differ by nearly two orders of magnitude.[11-13]

The purpose of this study is to review the published literature on the prevalence of radiographic abnormalities that may appear consistent with pneumoconiosis in persons without known exposure to dusts. Two sources of data, which differ only in the means by which unexposed subjects were chosen for study, were available for such an analysis. The first involves studies with the direct purpose of assessing parenchymal abnormalities in populations with little or no occupational exposures to fibrogenic dusts. The second includes cross-sectional studies of asbestos workers and other occupational cohorts at risk for pneumoconiosis that used a control group of unexposed workers for comparison. Both types of studies represent a resource for the determination of the prevalence of small opacities seen on radiographic examination of unexposed populations. This information is likely to be valuable in interpreting the results of population studies designed to assess pneumoconiosis and in communicating the significance of results to affected workers.

Materials and Methods

A listing of articles using the ILO classification of the pneumoconioses (1971 and 1980 revisions) for either epidemiologic studies of pneumoconiosis or evaluation of unexposed subjects was obtained through a MEDLINE search covering the years from 1971 to the present. Review and cross-checking of the bibliographies of relevant articles were also performed in an effort to reduce underascertainment. In addition, indexes of journals frequently publishing studies of pneumoconiosis (*Journal of Occupational Medicine* now *Journal of Occupational and Environmental Medicine, American Journal of Industrial Medicine, American Review of Respiratory Diseases, British Journal of Industrial Medicine* now *Occupational and Environmental Medicine, Chest,* and *Scandinavian Journal of Work Environment and Health*) were systematically searched for any relevant articles that may have been missing. The articles thus obtained were examined for the presence of either (1) an occupational control group without exposure to dusts or fibers or (2) an unexposed cohort in which the prevalence of radiographic opacities was determined. Articles were selected for further review if data on one of these populations were reported.

Criteria were developed for inclusion of results in this analysis to standardize comparisons across studies. These criteria included the following: (1) some specification of the age of control subjects or the unexposed population; (2) ascertainment of the lack of exposure to fibrogenic dusts and fibers; and (3) specification that radiographs were read independently by at least two readers either certified by examination in the ILO classification ("B" readers) or specifically noted as having experience in its use. This last criterion is consistent with guidelines developed by the ILO and other organizations[14,15] for reading of radiographs in epidemiologic studies. Radiographs scored as a profusion grade of category I or greater (1/0 or higher on the ILO 12-point scale), which indicates the definitive presence of small opacities,[14] were recorded and used in this analysis.

Results from studies meeting the above criteria were compiled and a meta-analysis performed following the procedures described by Frumkin and Berlin[16] and Velanovich.[17] Briefly, the prevalence of lung opacities (P) is a random variable with a variance of P(1-P)/n. The pooled prevalence was obtained as a weighted average, where weights were assigned as the inverse of the variances. Separate pooled prevalences were obtained for European and North American study populations: younger (mean age <50 years) and older (mean age ≥50 years) populations, as well as male and female subjects. A 95% confidence interval (CI) was calculated for each prevalence estimate. Of the nine study populations, three were in Europe and six were in North America. Two recently published articles from Finland[18,19] presented data on an unexposed population and included information on gender, age, and smoking. The other two European study populations did not include female subjects.[10,20] One North American study containing two populations did not provide information on gender.[21] We used seven populations for prevalence estimation in male subjects and five populations for prevalence estimation in female subjects. One North American study had zero cases observed among female subjects.[13] To avoid deletion of this study from meta-analysis, we substituted 0.5 to the numerator to carry out gender-specific meta-analysis.

Arbitrary substitutions such as this are useful for ratio measures to avoid complete deletion of a stratum.[22] Mean age, SD, and range were estimated from the reported age data across the studies using various statistical techniques outlined by Snedecor and Cochran.[23] Based on estimated mean age, studies were categorized into two groups (those ≥50 years vs <50 years).

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Results

Among numerous studies on asbestos, silica, coal dust, and other pulmonary fibrotic disorders, only eight published reports described the prevalence of parenchymal opacities in unexposed persons and fulfilled the criteria noted above for review.[10-13,18-21] Two articles had two separate control groups within the study, with each reported separately.[13,21] Therefore, this meta-analysis contains data on nine unexposed populations reported in eight articles, including two from Zitting et al[18,19] reporting on the same unexposed population. Table 1 summarizes the source of exposed populations, number of readers, and prevalence of small lung opacities ≥1/0. The prevalence of opacities across these study populations ranged from 0.21 to 11.7%. The following methods were noted in individual studies for the resolution of interreader differences: median reading (two studies), consensus (three), average reading (one), and highest reading (one). Table 2 shows the distribution of age and smoking within European and North American studies. There were considerable variations in smoking, gender, and age distribution between studies. Because of these differences, a separate meta-analysis was performed by age and gender as well as for European and North American studies.

The overall pooled prevalence was 5.3% (95% CI, 2.9 to 7.7%) for opacities graded ≥1/0. When European and North American studies were analyzed separately, the pooled prevalence for three European populations was 11.3% (95% CI, 10.1 to 12.5%). The pooled prevalence for six North American populations was 1.6% (95% CI, 0.6 to 2.6%). To evaluate whether this large difference in prevalence between Europe and North America could be explained by differences in age, gender, or smoking, we stratified studies by age category (mean age ≥50 years and <50 years) and gender. The pooled prevalence in the older age group was greater than that of the younger age group in both Europe and North America, although in each age stratum, European studies reported significantly higher prevalence of lung opacities (Table 3). In the younger age group (<50 years), the European studies had a pooled prevalence of 9.6% (95% CI, 8.2 to 11.1%) compared to only 0.6% (−0.2 to 1.4%) in the North American populations. Only one European and three North American studies could be classified in the older age group. The European study had significantly higher prevalence than the pooled prevalence of three North American studies (11.7% vs 2.3%). The gender-specific prevalence estimate showed greater prevalence in male subjects than in female subjects and this is true across European and North American studies (Table 4).

If a large European study[19] is excluded, the overall pooled prevalence drops to 2.8% (95% CI, 1.6 to 4%). This population was in the older age category. However, this particular study had the lowest prevalence of smoking among all studies presented and had a greater proportion of female subjects, demographic factors that favor lower prevalence of lung opacities. Therefore, the drop in the overall pooled prevalence when this study is excluded cannot be explained on the basis of smoking and gender. It also appears unlikely to be due to age effect alone. Three North American study populations[13,21] who were in the similar age category had significantly lower prevalence of lung opacities compared with the large European study.[19]

Discussion

The ILO system was devised to standardize reporting and comparison between observers and between studies in epidemiologic studies of pneumoconiosis.[14,24] It provides a means by which outcome

Table 1—*Prevalence of Small Opacities (≥1/0) in Subjects Unexposed to Dusts*

Published Studies, First Author (yr)	Unexposed Population	No. of Readers	No. of Opacities >1/0 (% Opacities)	N
Europe				
Glover[10] (1980)	Men chosen from electoral rolls, N Wales	3	39 (9.7%)	402
Jakobsson[20] (1995)	White collar workers from asbestos cement plant, Sweden	5	2 (6.8%)	29
Zitting[19] (1995)	Representative sample of Finnish population over age 30 yr	2	408 (11.7%)	3,494
North America				
Epstein[11] (1984)	Adults admitted to a university medical center, Philadelphia	2	22 (11%)	200
Castellan[12] (1985)	Blue collar employees in nondusty jobs, southern United States	3	3 (0.21%)	1,422
Kilburn[13] (1986)	a. Stratified sample of population in Michigan	3	3 (0.25%)	1,167
	b. Long Beach, Calif census tract	3	29 (2.1%)	1,347
Kennedy[21] (1991)	a. Employed bus mechanics, Canada	2	3 (4.5%)	66
	b. Retired grain and civic workers	2	4 (4.8%)	83

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Table 2—*Demographic and Smoking Distribution of European and North American Studies*

Published Studies*	N	Age, yr, Mean±SD (Range)†	M:F	% Current Smokers	% Current and Past Smokers
European					
Glover[10]	402	30.2 ± 16.6 (18-80)	NA‡	59	81
Jakobsson[20]	29	49 ± 5.67 (31-66)	NA	41	79
Zitting[19]	3,494	54.3 ± 13.47	1:2	17	34
North American					
Epstein[11]	200	44.2 ± 13.26 (15-84)	1:18	NA	NA
Castellan[12]	1,422	33.8 ± 12.07 (16-70)	1:1	47	61.5
Kilburn (a)[13]	1,167	42.4 ± NA (NA)	1:1	NA	69 M 50 F
Kilburn (b)[13]	1,347	51.0 ± NA (NA)	1:1	NA	60 M 40 F
Kennedy (a)[21]	66	56.2 ± 3.7 (45-67)	NA	18	73
Kennedy (b)[21]	83	69.7 ± 4.7 (56-84)	NA	13	85

*See Table 1.
†The mean age in years, SD, and range were derived statistically from the existing reports.
‡NA=not available.

variables may be reduced to a common metric across differing studies, to optimize uniformity of the reporting of results. It has been used to facilitate review and analysis of studies employing differing populations.[25] Ideally, uniformity of methods and criteria should apply across studies subject to review and analysis. It is possible, however, that these criteria are not met in ILO readings of chest radiographs. Incomplete documentation of the application of the ILO system, which may reflect inadequate implementation of standardized procedures, was noted in a recent report.[3] Misinterpretation of chest radiographs using ILO methods may lead to misdiagnosis of conditions consistent with pneumoconiosis.[2,26] Radiographic overdiagnosis should not be confused with exaggeration of prevalence; autopsy data suggest that pneumoconiosis is more prevalent than radiographs may detect.[27]

Table 3—*Stratification of Studies by Mean Age of Study Population*

Mean Age yr	Studies*	Prevalence of Opacities ≥1/0, %	Pooled Prevalence, % (95% CI)
Europe			
<50	Glover[10]	9.70	9.6 (8.2-11.1)
	Jakobsson[20]	6.80	
North America			
<50	Epstein[11]	11.00	0.6 (−0.23-1.4)
	Castellan[12]	0.21	
	Kilburn (a)[13]	0.25	
Europe			
≥50	Zitting[19]	11.70	
North America			
≥50	Kennedy (a)[21]	4.50	2.3 (1.1-3.6)
	Kennedy (b)[21]	4.80	
	Kilburn (b)[13]	2.10	

*See Table 1.

The most provocative finding of this analysis is the difference in prevalence between European and American studies. Although precise age distributions of the study populations were not available for both the European and North American study populations, an evaluation of the estimated mean ages and ranges does not indicate that the European study populations were significantly older than North American populations under consideration. Most of the study populations had an equal proportion of male and female subjects with the exception of the Zitting et al[19] study that has a significantly higher proportion of female subjects. However, as female subjects had a significantly lower prevalence of lung opacities, the difference in prevalence between Europe and North America could not be explained on the basis of gender. Similarly, the proportion of current and ever-smokers was significantly lower in the Zitting et al[19] study compared with other studies. The higher prevalence of opacifications in Europe compared with North America, therefore, cannot be explained on the basis of smoking. Confounding effects of environmental exposures, such as ambient air pollution or unaccounted occupational exposures,

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Table 4—*Prevalence of Small Opacities ≥1/0 by Sex*

Study*	Male	%	Female	%
European populations				
Glover[10]	39/402	9.7	None	
Jakobsson[20]	2/29	6.8	None	
Zitting[19]	147/1101	13.3	261/2,393	9.8
Pooled prevalence		11.2		
(95% CI)		(8.0-14.4)		
North American populations				
Epstein[11]	10/71	14.0	12/129	9.3
Castellan[12]	1/720	0.14	2/702	0.28
Kilburn (a)[13]	3/584	0.5	0.5/583	0.09
Kilburn (b)[13]	25/673	3.7	4/674	0.6
Pooled prevalence		1.3		0.4
(95% CI)		(0.27-2.4)		(−0.18-1.02)

*See Table 1.

and reader variability may contribute to the large differences in proportion of opacities between Europe and North America. Differences between unexposed control groups on the same continent may also be due to these factors. Kilburn et al[13] hypothesized that undetermined exposures, such as unrecorded work in shipyards and oil refineries, may have elevated local rates of opacities of a California population in comparison to that of their Michigan control group. Bus mechanics used as one control group may have had occupational exposure to asbestos (from brake linings) and to other dusts.[21] Studies differed substantially in definition of exposure, ranging from 3 months[10] to 5 years[12] of work in a dusty job before a subject was considered exposed.

In regard to environmental factors, Glover et al[10] surmise that the high prevalence of opacities in workers exposed to slate dust as well as in unexposed workers may be due to high rates of healed tuberculosis in North Wales. A more striking observation of pneumoconiosis in those not occupationally exposed is the prevalence of abnormalities in high-altitude villages in Ladakh, where pulmonary opacity rates of 20 to 45% presumably result from dust storms and soot from indoor kitchens.[28] Data from the Mini-Finland Health Survey show lung small opacity profusion of ≥1/0 in 14.6% of men without a past or present industrial exposure.[18,19] Variations in both work and environmental factors among differing populations are therefore likely to substantially affect the estimation of occupationally related pulmonary opacifications.

Stratification of results by mean age demonstrates an increase in prevalence of opacities ≥1/0 after the fifth decade of life. It is important to consider age-related effects on small opacity profusion.[29] For example, subjects with abnormal radiographs in one US study were older than the population mean.[12] Age, collinearly related to both dust exposure and cigarette smoke, may correlate with increased profusion of opacities in those exposed to either factor.[8] The increased prevalence of opacifications seen in older workers in this survey suggests that at least some of the variability is due to cumulative environmental exposures and perhaps age itself. Therefore, the inclusion of age data does not entirely mitigate the problem of determining whether opacifications are due to environmental exposures, as age may be a surrogate marker for exposure.

The disparity between male and female subjects seen in this review may reflect true differences in opacity development by gender; however, they are more likely related to other factors differing between the sexes such as dusty jobs or smoking, since these risks were historically higher for male subjects. Unaccounted occupational exposures, occurring in military service, part-time work, full-time work not obtained by history, or hobbies, could produce the increase in opacities seen in male subjects. The differences between male and female subjects noted in these data are an important clue that not all the variability between and within study populations is random. Some of this variability appears to reflect unaccounted dust exposure.

Only one study[10] in this review stratified results by smoking history. It demonstrated a threefold increase in abnormalities in smokers when compared with nonsmokers. The absence of quantitative data on smoking limits the ability of an analysis to determine a dose-related effect of smoking on the prevalence of small opacities in the otherwise unexposed. In a comparison between smoking and nonsmoking workers exposed to acrylamide dust, as well as in those unexposed, parenchymal abnormalities were present in 20% of smokers compared with 2.2% of nonsmokers, suggesting that smoking plays a role in

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their development.[9] Our meta-analysis is unable to determine the effect of smoking alone on unexposed populations.

Finally, the question of variability in reading of radiographs remains. Methods for resolving inter-reader disagreement varied considerably among the studies reported herein, a finding consistent with the results of a recent report.[3] A twofold prevalence range in interpretation of radiographs at lower levels of profusion is apparent from studies of interobserver variability.[1,30,31] Population median value for opacities of category 1/0 or greater in a sample of over 105,000 US Navy workers was 1.71%, but the range for 23 certified observers reading randomly distributed radiographs was 0.05 to 10.93%.[32] This range is not very different from the range in the supposedly unexposed populations reviewed in this meta-analysis, a startling similarity in view of the many shipyard and other dust-exposed workers in the Navy population. The lack of description of interpreters, their habits, and quality assurance measures in many studies[3] may be hampering the ability to accurately make comparisons between studies. A sense of uncertainty has persisted as to the degree to which interstudy differences of exposed populations reflect disparities between populations or between the chest radiograph readers.[1-6,32] This phenomenon now appears also to be true for prevalence of opacities in unexposed populations. In particular, differences in opacity prevalence between European and North American populations may be partially accounted for by reader habit differences.

A range of variation exists in the determination of the prevalence of radiographic findings in populations considered to be unexposed to fibrogenic dusts. Dependence on historic prevalence figures for the unexposed may be confusing because of this wide range. Aggregation of current data suggests that there is a background level of opacifications in populations considered unexposed. A meta-analysis shows this prevalence to average 5.3% in existing studies, but the prevalence in any given unexposed population may differ from this figure depending on age, gender, past exposure status, and geographic location. The notably high prevalence of abnormalities in European studies compared with North American studies appears most likely to be due to differences in reader habits or unaccounted exposures, rather than demographic or smoking differences.

Recommendations

Variation among studies in the reported prevalence of opacities in unexposed populations indicates that factors independent of dust exposure are operating. Age and gender differences suggest that environmental factors also play a role. The use of a control group corresponding in age, geographic location, and gender to the exposed subjects can serve as a means by which baseline prevalence of opacities can be determined within a population and the added burden of prevalence due to occupational exposure can be more accurately assessed. In addition, radiographic interpreters should be formally blinded to the exposure status of the individuals whose radiographs they read. The need for closer attention to smoking history when compiling population results, both in exposed workers and in control subjects, should be apparent in light of the persistent controversy that this issue engenders.[8,9,25] Proper ascertainment of exposures from occupational and environmental sources is suggested to reduce misclassification of subjects and the resultant bias that this may introduce.

Close attention to quality assurance measures in using the ILO system is also recommended to more accurately determine the significance of radiographic abnormalities in the dust exposed. Adherence to recommendations for multiple readers in epidemiologic studies[14,15] and thorough description of the reading process, including the means by which interreader differences are reconciled,[3] may produce data that can be better compared across studies. Continuous feedback to readers in comparison to a gold-standard reading[33] can aid in assessment of reader variability within a study. Continuous feedback also promotes adherence to more uniform reading standards.

Among these recommendations, we believe the most important to be the use of unexposed control radiographs. The presence of blindly interpreted unexposed control radiographs within an epidemiologic study can serve the role of an internal comparison for reading and aid in the control of the reading process as well as in the interpretation of results.

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