Crackles in the Early Detection of Asbestosis[1,2]

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SUMMARY We studied 386 workers exposed to asbestos to assess the value of chest auscultation by a trained technician in detecting asbestosis as defined by previously reported clinical, physiologic, and roentgenologic criteria. The presence and degree of crackles were assessed at preselected basilar lung sites by a technician whose performance was validated by comparison with computer-generated time-expanded waveforms of tape recordings of lung sounds. Asbestosis was present in only 2.8% of the total population, but it was present in 8.6% of those with over 25 yr or more of employment. The technician correctly identified all the workers in whom the diagnosis was most certain, that is, those with all criteria positive. The overall true positive rate was 55%. The majority (94.8%) of those with no abnormal criteria were correctly classified. Auscultation by an objectively validated technician can be a useful noninvasive method for screening industrial populations exposed to asbestos.

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Introduction

Minimal interstitial pulmonary fibrosis caused by the inhalation of asbestos can be difficult to detect (1, 2). Symptomatology is subjective and pulmonary function studies are often nonspecific. Roentgenographic manifestations of early interstitial disease are often difficult to distinguish from normal shadows (1–3), and observer variability in interpretation of radiographs is also a problem. Discontinuous adventitious lung sounds (crackles, rales) have been recognized as prominent features of pulmonary asbestosis (4–6) and are thought to be an early finding (7–9). Although chest auscultation is regarded as highly subjective, recently developed technology has brought the promise of objective quantification of lung sounds. One such method, called time-expanded waveform (TEW) analysis, consists of tape recordings of sounds for analysis by a computer. Amplitude is then plotted versus time, with a time axis of 800 mm/s or more, allowing visualization of minute details of pulmonary sounds (10). Because TEW analysis provides documentation of the presence of crackles, it can be used to train technicians in auscultation (11). Monitoring of exposed workers by auscultation is attractive because it is noninvasive and inexpensive. The purpose of this investigation was to quantify the relationship between the prevalence of crackles assessed by a technician, whose performance had been objectively validated, to other criteria for asbestosis in exposed workers.

Methods

The 386 workers included in this study were exposed to asbestos during the manufacture of paper and insulation materials and in a shipyard. Lung sounds were recorded at 4 preselected basilar sites during breathing with the mouth open while the worker was in a sitting position. Workers were asked to breathe slightly more deeply than the usual tidal breathing as in standard clinical practice. These sites were the right and left bases in the midscapsular line, the right midclavicular line, and the left anterior axillary line. The number of crackles was estimated at each auscultation site using a scale ranging from 0 (none) to 3.0 (indicating many), and a weighted crackle score (WCS) was then calculated. Scores from the right and left bases posteriorly were doubled and added to the scores from the anterior sites. The resulting WCS ranged from 0 to 18. Lung sounds were recorded at the time of auscultation, and selected tape recordings were analyzed for frequency content and TEW analysis with and without 800-Hz filtered sound. These were compared with the independent observations of a trained technician.

For this assessment, worker identification was masked by use of code numbers. Comparison of the WCS was made by 2 observers who interpreted the TEW analyses while simultaneously listening to the sounds. The technician's results were also compared with the pulmonary physician's listening during the surveys. The Kappa statistic was calculated according to the method of Fleiss (12). Kappa is a numerical method of separating agreement from chance association, and it varies from 0 (no agreement) to 1.0 (complete agreement). For interpretation of the intermediate values, we employed the criteria of Landis and Koch (13): a Kappa value of 0.81 to 1.0 indicates almost perfect agreement, 0.61 to 0.80 indicates substantial agreement, 0.41 to 0.60 indicates moderate agreement, and 0.4 and below indicates slight to poor agreement.

Other data were collected using a questionnaire on respiratory history and occupational exposure, a physical examination including independent observations on lung sounds by 2 or more chest physicians, chest roentgenographic readings according to the ILO scheme, and detailed pulmonary function testing (14). Asbestosis in these exposed workers was considered to be present when 3 or 4 of the following criteria were present: (*1*) radiograph showing irregular opacification of a profusion of 1/2 or more, (*2*) single-breath diffusing capacity less than 80% predicted, (*3*) vital capacity less than 80% predicted, and (*4*) crackles at 2 or more basilar sites.

Results

Asbestosis by our criteria was present in only 2.3% of the workers and did not occur in workers with less than 11 yr of exposure. In the 93 workers with over 25 yr of employment, 8.6% were considered to have asbestosis. The prevalence of abnormal findings in each of these criteria is shown in table 1. In general, the prevalence of these criteria increased both with exposure and with age, as is expected in populations wherein age and duration of exposure are closely correlated (figure 1). Pleural abnormalities also showed a similar relationship to duration of exposure and age (figure 2).

The relationship between the tech-

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TABLE 1

SELECTED RESULTS IN 386 ASBESTOS-EXPOSED WORKERS

	Number	Percent
VC < 80% pred	47	12.2
DL < 80% pred	61	15.8
Radiographic UICC 1/2 or more	14	3.6
1/1 or more	29	7.5
Bilateral rales on routine auscultation by MD	24	6.2
Weighted Crackle Score		
3 or more	31	8.0
2 or more	51	13.2
Asbestosis		
Criteria Positive: 0	289	74.9
1	63	16.3
2	23	6.0
3	7	1.8
4	4	1.0

Definition of abbreviations: VC = vital capacity; DL = diffusing capacity; MD = physician.

nician's auscultatory findings and the number of asbestos criteria found in individual workers is presented in table 2. The technician correctly identified all the workers in whom the diagnosis was most certain, that is, those with 4 of 4 positive criteria. The majority of those (94.8%) with no abnormal criteria were also correctly identified. If the crackles heard by physicians were omitted from the assessment to avoid the possibility of circular reasoning, the results were similar.

The technician identified 80% of those with all 3 of the remaining criteria. The observations of the technician while recording at the industrial site correlated well with interpretations of waveforms (table 3). The epidemiologic diagnosis of asbestosis related poorly to symptomatic and roentgenologic evidence of obstructive disease (table 4). The weighted crackle score (WCS) was associated with pack-years of cigarette smoking (table 5) but related poorly to the diagnosis of bronchitis with obstruction, as defined by the combination of a history of productive cough plus a coexistent forced expiratory volume in one second of 70%. The interaction of smoking history, years of exposure, and crackle index was statistically evaluated using logistics regression, using both a trichotomous and dichotomous response variable (15, 16). Using the trichotomous response variable, age appeared to be the most significant effect, and the smoking-asbestos interaction was nonsignificant. The effect of asbestos exposure was present only when comparing a WCS of 3+ with a WCS of 0,

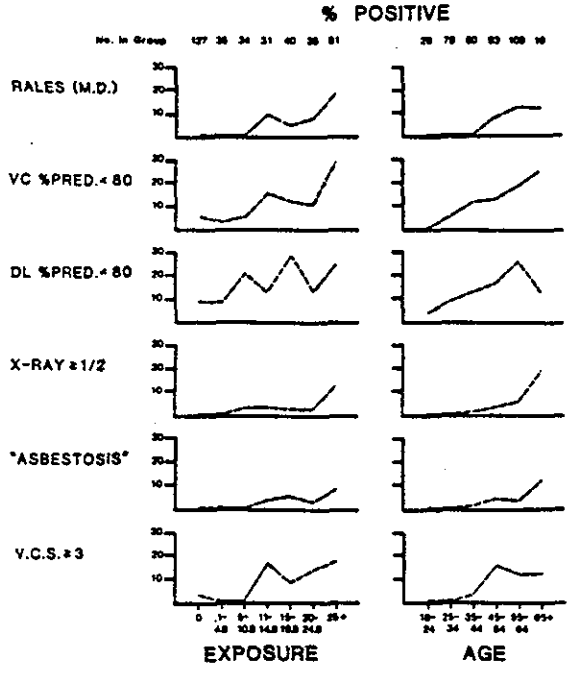

Fig. 1. Relationship of the weighted crackle score and of abnormalities consistent with pulmonary asbestosis and our diagnosis of asbestosis to duration of exposure and age in 386 asbestos-exposed workers. In general, an increasing prevalence is seen with increasing exposure for each of the criteria and for asbestosis. The weighted crackle score (WCS 3+) also shows a similar exposure and age relationship. For definition of abbreviations, *see* table 1.

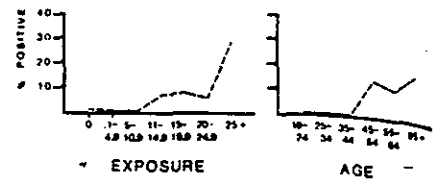

Fig. 2. Pleural thickening and/or calcification shows an increase in prevalence with increasing exposure and age, as expected in a population with exposure to asbestos.

suggesting that there was no asbestos-related differences between a WCS or 1 or 2 and a WCS of 0. The effect of smoking was more difficult to interpret. The smoking effect was present only when comparing a WCS of 1 or 2 with a WCS of 0. The results suggest the WCS of 1 or 2 may be the result of smoking, but a WCS of 3+ is associated with asbestosis.

A dichotomous model was then examined. When comparing a WCS of 0, 1, or 2 with a WCS of 3+, an asbestos effect was seen ($p = 0.06$) but no smoking effect was found. Age was shown to be highly significant ($p = 0.0099$) when there is no smoking-asbestos interaction ($p = .85$). In comparing a WCS of 0 versus 1+, a smoking effect is seen ($p = 0.024$), no asbestos effect is found ($p = 0.85$), the age effect is again highly significant ($p = 0.00026$), and no smoking-asbestos interaction is found ($p = 0.65$). The results of the dichotomous model confirm those of the trichotomous model.

Discussion

Prior to discussing the possibility of our false positives reflecting slight forms of asbestosis we will briefly review the history of crackles in asbestosis. Fifty years ago Wood and Gloyne (17) pointed out that crackles were a common feature of pulmonary asbestosis. Since that time, reports have varied as to the importance and specificity of auscultation findings. Hunter (18) said crackles occurred "sometimes" and Wyers (19) said they were "generally" present. Wyers believed that the adventitious sounds tend to be "evanescent," and that the dry crackling sounds could disappear altogether. Smither (9) believed that the crackles of asbestosis were characteristic in their sound and distribution, present first at the bases in the midaxillary lines, and tending to spread to the posterior bases. As the disease advanced, the

crackles were distributed upwards from the base at the scapular level.

The belief that crackles are an early sign is also consistent with many published reports. Crackles have been regarded as a feature of pulmonary asbestosis for over 50 yr, and even in early reports were considered to be present with minimal disease (17). Clinical features of their nature and distribution on the chest were described in some detail by Smither (9). Mitchell and coworkers (20) found crackles more closely related to duration of exposure to heat-resistant and friction composites than was vital capacity, and they recommended that chest auscultation be included as a biologic monitor of the work environment. Reported rates vary, but about half of the persons considered to have asbestosis on clinical grounds are reported to have crackles (21–23). These represent selected cases. In order to understand the strength of an association between an exposure and a health effect, it is important to know the status of all persons exposed. If only patients are studied, the effects may appear more striking than if asymptomatic persons are also included. Population-based studies, therefore, allow more precise examination of the frequency of crackles in asbestos-exposed persons. These show prevalences ranging from about 10 to 20%. Such prevalences depend on a variety of factors including the method of auscultation, the severity and duration of exposure, the age of population, the prevalence of the diseases causing crackles, etc. Nevertheless, the association between crackles and asbestos exposure is clearly established by: (*1*) high frequency in diagnosed cases, (*2*) common occurrence in exposed populations, and (*3*) increased frequency with increased duration of exposure (24, 25). Furthermore, the prevalence in control populations is low (24–27).

The correct detection of those in whom the epidemiologic diagnosis of asbestosis was most certain suggests that a trained technician can screen a group of exposed workers to estimate the prevalence of asbestosis. Despite the high true positive rate there are errors in the method. In our study, 5 of the 7 workers with 3 of 4 positive criteria were missed (false negative). Although this may represent technician error, it is known that not all those with asbestosis have crackles. Indeed, Epler and coworkers (7) reported crackles in

TABLE 2

RELATIONSHIP OF AUSCULTATION BY A TECHNICIAN TO NUMBER OF ASBESTOS CRITERIA

Number of Positive Criteria per Worker of 4 Possible Asbestosis Criteria	Weighted Crackle Score				
	0	1	2	3+	Total
0	225	34	15	15	289
1	50	5	3	5	63
2	13	3	2	5	23
3	3	2	0	2	7
4	0	0	0	4	4
Total	291	44	20	31	386

TABLE 3

TECHNICIAN VALIDATION: COMPARISON OF TECHNICIAN'S WEIGHTED CRACKLE SCORE MADE AT THE INDUSTRIAL SITE TO WAVEFORM INTERPRETATIONS OF THE SAME LUNG SOUNDS*

Waveform Interpretations	Weighted Crackle Score†		
	3 or More	Less than 3	Total
Positive for crackles	6	2	8
Negative for crackles	0	14	14
Total	6	16	22

* Kappa = 0.80; 20/22 = 90.9%.
† On-site tech observations.

TABLE 4

RELATIONSHIP OF ROENTGENOGRAPHIC EVIDENCE OF EMPHYSEMA AND SYMPTOMS OF CHRONIC BRONCHITIS TO ASBESTOSIS AND WEIGHTED CRACKLE SCORE

	Asbestosis*			Weighted Crackle Score		
	Yes	No	Total	Yes	No	Total
Emphysema†						
Yes	0	5	5	1	4	5
No	11	343	354	28	326	354
Total	11	348	359	29	330	359
Chronic bronchitis‡						
Yes	3	56	59	8	51	59
No	8	319	327	23	304	327
Total	11	375	386	31	355	386

* Asbestosis defined as 3 or 4 criteria positive.
† Emphysema defined by roentgenographic criteria.
‡ Chronic bronchitis defined by American Thoracic Society criteria.

TABLE 5

RELATIONSHIP OF SMOKING HISTORY TO WEIGHTED CRACKLE SCORE*

Smoking History (*pack-years*)	Weighted Crackle Score			
	0	1, 2	3+	Total
0–20	169 (153.4)†	27 (38.64)	12 (15.91)	208
21–40	52 (57.54)	20 (14.49)	6 (5.97)	78
41–60	32 (33.93)	9 (8.55)	5 (3.52)	46
61+	17 (25.08)	12 (6.32)	5 (2.60)	34
Total	270	68	28	366

* $X^2 = 19.35$, $p < 0.005$.
† Numbers in parentheses refer to the expected value for that cell.

only 60% in their pathologically proved cases of usual interstitial pneumonia. The magnitude of the false negative rate for each asbestos criteria was assessed by comparing the number of positives by the test with those workers positive by each of the remaining tests. The diffusing capacity was abnormal in 4 of the 5 workers positive for each of the remaining tests. Corresponding rates were 4/7 for vital capacity, 4/6 for radiograph, 4/5 for physician-crackles, and 4/5 for technician crackles. The false negative rate of crackles for the identification of asbestosis was, therefore, similar to the false negative rate for each of the other criteria, when considered separately. In any case, a false negative rate would have to be accepted for auscultation, as is true for any of the other available screening methods.

Some of the false negative results may have been due to the method we employed. Mitchell and coworkers (8) pointed out that inhalation to total lung capacity can abolish or decrease the number of fine rales heard in a subsequent inspiration. Conversely, Shirai and associates (26) have shown very high prevalences by breathholding volumes prior to deep breathing. Presumably this maneuver accentuates collapse of dependent lung regions, which reexpand on the subsequent inspiration. This is consistent with the theory that the opening of collapsed airways is the mechanism of crackle generation (28). We have also found that crackles are more common after this maneuver, particularly if the initial inspiration is performed slowly. Unfortunately, observer variability and artifacts appear to be somewhat greater, and more careful investigations will be required before this becomes an acceptable method.

The "false positives," that is, those with a WCS of 3+ but otherwise not meeting our criteria for asbestosis, are of particular interest. Possible explanations for this include: (*1*) technician error, (*2*) crackles caused by conditions unrelated to exposure, or (*3*) crackles indicating lesser degrees of disease than do the other methods employed.

Technician Error

Such error is likely small in circumstances such as this study wherein the technician is highly trained and focuses on a specific task. We evaluated the accuracy of the technician in assessing the presence, degree, and quality of crackles, using objective methods of detecting crackles by tape recordings and time-expanded waveform analysis. Indeed, the association between the observations of the technician and the waveform interpretation was over 90%; the Kappa statistic likewise was high, indicating that this was due to agreement rather than to mere association, as it was in a more extensive study of observer variation in chest auscultation (29). The accuracy of the technician in this study in classifying crackles as fine or coarse compared with the computer classifier devised by Holford (30) was 84.4% (Kappa, 0.68). Crackle measurements made on TEW analyses are illustrated in figure 3.

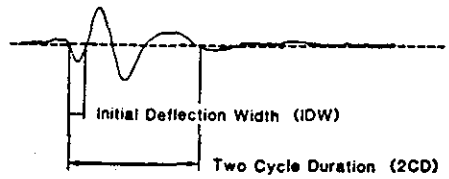

Fig. 3. A single crackle from time-expanded waveform analysis. On the basis of 2 waveform features, Holford (30) devised a classifier for separating fine from coarse crackles. The first measurement (the initial deflection width or IDW) is the time in milliseconds of the first deflection of an identifiable crackle above or below the baseline. The two-cycle duration is the time in milliseconds for 2 S-shaped waves or cycles to occur. A discriminant curve on the classifier then separates fine from coarse crackles based upon both IDW and 2CD measurements for each crackle.

Other Causes of Crackles

Numerous conditions other than interstitial fibrosis, such as chronic bronchitis, cause crackles. Our technician was carefully trained by listening to tape recordings of crackles from patients with asbestosis to facilitate recognition of these sounds. Indeed, the prevalence of crackles did not correlate significantly with the symptoms of chronic bronchitis, pulmonary function showing obstruction, or with roentgenographic evidence of emphysema. There was, however, a significant correlation between WCS 3+ and pack-years of smoking. The degree to which crackles reflect the industrial exposure rather than the effects of cigarette smoking is difficult to determine in these workers. Weiss (31) has suggested that it is important, but not all studies confirm this opinion (32). The study of Rossiter and Berry (21) is interesting in this regard. These investigators showed an interaction between smoking and asbestos exposure in the production of crepitations. In an asbestos textile factory, those who did not smoke or smoked less than 5 cigarettes per day were less likely to develop crepitations or be certified for asbestosis than those who smoked more, although the amount of asbestos exposure was similar. Clarification of this point awaits more thorough investigation of the relationship of smoking to interstitial fibrosis and more careful delineation of the differentiating characteristics of crackles in bronchitis and asbestosis. As cigarette smoking and resulting chronic obstructive lung diseases are common in industrial workers, this is an important consideration. The effect of removing persons with a ratio of forced expiratory volume in one second to vital capacity of less than 70% on the age and duration of exposure plots is shown in figure 1. These tend to strengthen the relationships.

The fine crackles of interstitial fibrosis are similar in character to those caused by congestive heart failure. The latter diagnosis can usually be readily distinguished on clinical grounds. In this regard, it is important to mention that our criteria were designed for epidemiologic screening and in no way were intended to obviate the need for careful clinical evaluation of suspected positives.

Crackles as an Early Diagnostic Sign of Asbestosis

Whether our false positives reflected lesser degrees of asbestosis than other tests is unknown. However, the average duration of exposure of the workers with high crackle scores and no other criteria was longer than that of the entire group (19.6 and 13.8 yr, respectively).

Most investigators consider crackles to be an early finding (7, 26, 33). Not all investigators have concurred. In the study of 386 ship repair workers by Selikoff and associates (34), radiologic changes were considered to be a far more sensitive index than were crackles. Some of this variation in opinion is likely related to the criteria employed. We have discussed the rationale for our choice previously (10, 35, 36). Selikoff and associates apparently considered a small opacity of 0/1 or greater or any pleural change to be evidence of asbestosis. Indeed, in an asbestos worker in the course of developing asbestosis, it is likely that microscopic changes of alveolar thickening and peribronchial fibrosis precede any roentgenologic abnormality. It is also

probable that those who develop severe asbestosis have roentgenographic progression from UICC grade 0/0 to 3/4 in a relatively orderly fashion. Our reluctance to regard the lesser UICC grades of small opacifications as prima facie evidence of an effect of asbestos is based on the reliability of such evidence. First, the early diagnosis of interstitial fibrosis has long been regarded as one of the most subjective in radiology (2, 3) (other causes for roentgenologically similar shadows include soft tissues, inadequate inspiration, etc.). Second, it is likely that a variety of other illnesses and exposures produce similar findings (previous pulmonary infection, other silicates, drugs, congestive heart failure, etc.). Third, in our studies, lesser grades of opacifications in asbestos workers could not be distinguished reliably from shadows seen on roentgenograms of the control subjects (10, 36). Decreasing the degree of disease required to classify an individual as a positive case in epidemiologic studies frequently leads to an increase in sensitivity. Unfortunately, this also often decreases the specificity or accuracy of the observation (13). The relative "earliness" of pulmonary function abnormalities, roentgenographic findings, and auscultation are all subject to this phenomenon. The relevant issue is which test or set of tests provides reliable monitoring of workers to assure, as far as practicable, their safety. In this regard, a significant advantage of auscultation is its noninvasiveness, as worker acceptance must also be considered. Roentgenograms offered by employers are frequently refused by workers because of the fear of exposure to radiation or personal considerations.

The results of these studies indicate that auscultation, by a properly trained and objectively validated technician, can be a useful method for screening industrial populations with exposure to asbestos. Although true positives may be underestimated, the false negative rate is low and the method is inexpensive. With the use of modern recording and analysis techniques, chest auscultation can be verified and permanent records can be made. Further studies of the sensitivity and specificity are warranted in view of the noninvasive nature of auscultation.

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