British Journal of Industrial Medicine 1987;44:673-681

Development, radiological zone patterns, and importance of diffuse pleural thickening in relation to occupational exposure to asbestos

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ABSTRACT The radiographic appearance of the lateral pleura was divided into an upper, a middle, and a lower zone. Bilateral changes of the pulmonary layer of the pleura (diffuse pleural thickening) within the upper pleural zones were found in 863 (71%) of 1204 workers exposed to asbestos and in 249 (40%) of 622 non-exposed controls. Downwards along the chest wall this ratio of 7:4 increased progressively up to 10:1 at the lower parts of the pleura. Bilateral diffuse pleural thickening in at least two adjacent zones on each side was found in 652 (54%) of exposed and in only 86 (14%) of unexposed subjects. The difference was even more striking when comparing bilateral involvement of all three zones (28% and 3% respectively). Unilateral change was rare (4·8% and 7·8% respectively) and often due to causes other than exposure to asbestos. Pleural findings were the earliest radiographic features detectable associated with former exposure to asbestos. Bilateral diffuse thickening in at least two adjacent zones on each side seems to be a striking feature and an early indication of former occupational asbestos damage. Modifications of the International Labour Organisation 1980 classification are proposed.

Diffuse pleural thickening after exposure to asbestos has been well known to the pathologist for nearly 100 years.[1 2] The clinical evaluation of this feature started much later, with the advance of radiology,[3-7] but a broader knowledge of its frequency and significance did not come until the introduction of the high kilovolt technique for investigating the chest.[1 8]

Although international publications covering this topic have increased tremendously, many diagnosticians show little or only a superficial interest in this common feature of the objectively recordable sequelae of exposure to asbestos.[9-20] None the less, since 1968 the International Labour Organisation (ILO) in Geneva has developed a semiquantitative recording of pleural changes and added it to the International Classification of Pneumoconioses.[21 22] This pleural part of the scheme provides recording facilities by special numbers and letters for diffuse pleural thickening for the side (R/L), the length (0, 1, 2, 3, measured in quarters of the chestwall), and the width (a, b, c, measured in millimeters) of the pleural shadows.

There is little information, however, on the validity of this recording system. In 1983 in a preliminary investigation we analysed whether these facilities were efficient enough to correlate—with some degree of reliability—pleural changes with asbestos and other fibre dust exposures. Evaluation of 1031 German workers exposed to asbestos indicated that nearly all hitherto existing codes of the formula "RL1a" and many of "RL2a" were epidemiologically irrelevant.[23]

The present study describes pleural changes in radiographs of 1204 individuals with an occupational exposure to asbestos from the medical surveillance in 1982 and compares them (retrospectively and in a non-blind manner) with films of 622 randomly selected controls with no known asbestos history. Several variables are included in the analysis. The purpose of this study was to identify distribution patterns of diffuse pleural thickening after exposure to asbestos and to give proposals for a revision of the pleural part of the ILO 1980 classification.[22]

Accepted 10 November 1986

Table 1 *Main characteristics of groups A and B*

	Group A: No (%)	*Group B: No (%)*	*Significance of difference A:B*
Men	1093 (90·8)	382 (61·4)	
Women	111 (9·2)	240 (38·6)	p < 0·001‡
Age:			
Median	42	39	
Range	16–70	15–73	
–20	12 (1·0)	73 (11·7)	
–30	198 (16·4)	127 (20·4)	
–40	295 (24·5)	132 (21·2)	
–50	438 (36·4)	126 (20·3)	
–60	233 (19·4)	100 (16·1)	
>60	28 (2·3)	64 (10·3)	p < 0·001§
Ethnic origin:			
German	1033 (94·1)	577 (92·8)	
Turkish	71 (5·9)	45 (7·2)	NS‖
Years since first exposure to asbestos:			
Median	10		
– 5	303 (25·1)	—	
–10	359 (29·8)	—	
–15	213 (17·7)	—	
–20	118 (9·8)	—	
–25	91 (7·6)	—	
–30	71 (5·9)	—	
>30	49 (4·0)	—	
Thorax deformity:			
Barrel shaped	98 (8·1)	75 (12·1)	
Bell shaped	91 (7·6)	53 (8·5)	
Others	12 (1·0)	6 (1·0)	NS‖
Overweight*	231 (19·3)	97 (15·6)	NS‖
ILO: emphysema	15 (1·2)	9 (1·4)	NS‖
Former thoracic trauma†	33 (2·7)	36 (5·8)	NS‖

*Exceeding 30% more than the Broca index. †Or any reason for pleural thickening other than asbestos exposure. ‡Adjusted for age. §Adjusted for sex. NS ‖ Not significant, adjusted for age and sex.

Materials and methods

POPULATION

Radiographic films of two groups were chosen: a survey group of unselected individuals occupationally exposed to asbestos from different geographic regions (group A) and a non-exposed control group (group B). The main characteristics of the groups are presented in table 1.

Group A consisted of 1204 workers undergoing medical examination in 1982 with a history of occupational exposure to asbestos for at least one year. They had been exposed to nearly all types of asbestos dust generated within the German asbestos processing and handling industry, including construction industries, but there were no shipyard workers. Working conditions, duration of exposure (minimum one year), and dust concentrations could not be assessed, because the information available was inadequate. In general, individuals with less than 15 years since first exposure may be representative of plants with lower dust concentrations owing to an effective medical supervision complying with legal requirements established during this time. Those with a longer history were probably exposed to much higher dust concentrations and not so homogeneously controlled. Initially, group A consisted of more than 1300 consecutive cases, but the number decreased to 1204 after eliminating those with poor film quality (= "2," "3," and "4" for recording technical quality).

Group B consisted of 622 controls with no known occupational exposure to asbestos: 202 were first films of workers entering the asbestos industry with no previous exposure to asbestos. In addition, 420 radiographs of individuals most of whom were generally engaged in an industrial environment and a few of their clinical data were randomly selected from the archives of two large community hospitals (St George General Hospital, Hamburg, and Municipal Hospital, Luedenscheid). Films of this type and provenance were excluded when clinical information (or the films themselves) indicated pleural changes attributable to acute diseases such as pneumonia or pleurisy.

Owing to the retrospective design of this study, the films were not homogeneous in quality, exposure time, or positioning. In particular, those of group A originated from more than 90 sources (B readers).

METHODS OF INVESTIGATION

To avoid interobserver variation, which exists for pleural changes in an even wider range than for parenchymal findings,[24] all films were reread by one reader (HB) who is one of the four qualified A readers in the Federal Republic of Germany and who has been familiar with recording pleural changes for nearly four decades and who—in addition—has been

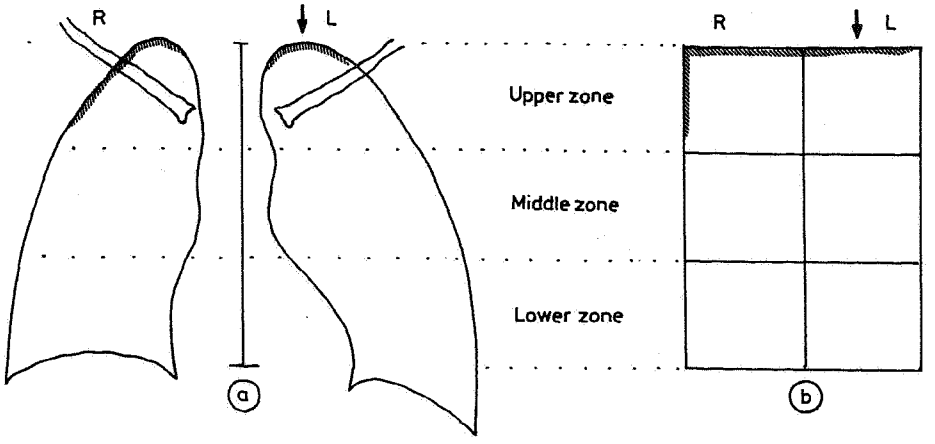


Fig 1 *Chest x ray (a), zones (b), and diffuse pleural thickening as used in this study. (b) follows scheme for lung zones and records diffuse pleural thickening compared with (a) representing different length of affected chest wall according to six zones. This offers unique opportunity of also recording localisation (zone pattern). Pleural caps (arrows) are taken as "0" = NAD when restricted to second rib (L), whereas in case of running down chest wall below clavicle upper zones were recorded as affected—that is, positive (R).*

a member of the ILO group of experts designing the last two versions of the ILO classification.[21 22]

For the purpose of this study, diffuse pleural thickening has been defined as the measurable pleural companion shadows seen in profile along the bony chest wall on straight frontal projection (solely posteroanterior films). En face findings were not recorded, since they are easily misinterpreted. For the recording of diffuse pleural thickening, the ILO scheme and the modified German system were adapted to allow for additional information on extent (length), side, and localisation. Thus the six zone scheme, as already used for recording lung appearances, was used. The information about length is given automatically in terms of affected zones: upper, middle, and lower zones (UZ, MZ, LZ) and their combinations (fig 1). Following the ILO instructions for discriminating the three lung zones of each side, the length of the bony chest wall of the lower zone is considerably greater than the length of the upper zone. As may be seen in fig 1, this modification leads therefore to a recording system of length with four different grades of extent, but one should be aware that the length of pleural thickening indicated by zones is not necessarily the same as in the original ILO grades of extent (0, 1, 2, 3 (see ILO[22])). In the upper zones symmetrical apical pleural thickening of up to 5 mm of width was recorded as not affected (fig 1, left side) whereas pleural thickening that extended below the level of the clavicles (fig 1, right side) was recorded as affected.

Other than posteroanterior films, no additional views, especially obliques—widely discussed in other publications[10 12 25]—were available to us. On the other hand, according also to our experience, obliques may increase the risk of wrong positive records of pleural thickening due to subpleural fat,[25] especially in the regions of the posterior parascapular and axillary lines as shown in many computed tomograms of the chest.

The extent and width of pleural thickening and most parameters of the ILO 1971 and 1980 classification were recorded. In addition, the variables overweight (exceeding 30% more than the Broca-index), thoracic shape (barrel shaped, bell shaped, scoliosis), or thoracic deformities due to trauma or surgery, the time variables "period since first exposure" and "age at examination" were included in the analysis. Since it seemed possible that in the subgroup of Turkish workers some individuals might have been previously exposed to an endemic fibrous dust,[26 27] they were investigated separately. Turkish individuals in both groups were younger than in the German subpopulation (only three older than 50). In the exposed Turkish workers the period since first exposure was correspondingly shorter.

STATISTICAL ANALYSIS

Descriptive statistical methods and tests for unadjusted homogeneity of proportions were used as described in the SPSS.X statistical package.[28] In comparative analyses of proportions and life time data,[29] adjustment for confounding variables was done by using combined risk estimates[30] or maximum likelihood estimates (MLE) of the common odds ratios of

combined tables[29 31] based on algorithms modified from Thomas and Gart[29] and Thomas[32] and by using multivariate logistic models as proposed by Breslow and Day.[33] Usually, the unconditional tests have been applied. With sparse data, conditional MLE methods were additionally used to confirm results of unconditional tests. The probability distributions of risk curves were estimated by the classic method of Kaplan and Meier.[34]

Owing to inequalities in the distributions of age and sex in groups A and B, adjustments for these variables were regularly performed. This is not mentioned further in the text.

Since pleural thickening after exposure to asbestos is known to be time dependent, analyses adjusted for time are essential. By contrast with a prospective cohort study, no time intervals were available for group B that were comparable with the period since first exposure of group A. For an ad hoc substitute, age at examination was taken as the time variable for time adjusted comparison of groups A and B serving as a supplement to the unadjusted analyses of proportions.

Results

Unilateral pleural thickening was rare (table 2) and often associated with other causes of pleural thickening such as trauma (table 1). Therefore only the results of bilateral symmetrical involvement are reported. Table 2 also shows highly significant differences in typical asbestos sequelae such as plaques or pulmonary fibrosis (small opacities of a profusion of 1/0 or more), whereas obliteration of the costophrenic angle (cpa) as a possible indication for a so called asbestos pleuritis[17] is equally rare in both groups.

Table 3 shows zone patterns of bilateral pleural thickening in groups A and B. Relation to age at examination is shown in table 4. Table 5 presents the relation between zone patterns in group A and the period since first exposure. The risk estimates of developing bilateral pleural thickening in relation to time (period since first exposure for group A and age at examination for comparing group A and B) are collected in figs 2 and 3 a–f.

All these data show that bilateral pleural thickening was significantly (throughout $p < 0.0001$) more prevalent in individuals exposed to asbestos than in those unexposed. After a period since first exposure of 25 years the individuals in group A had a risk of bilateral complete (UZ, MZ, and LZ) pleural thickening of 50% (fig 2). These 25 years correspond roughly to a median age at examination of 54. At this age, only 5·2% of the individuals in group B had developed extended bilateral pleural thickening (fig 3f). By contrast, pleural thickening of the upper zones often involved individuals of the control group (fig 3a). One quarter of that group showed isolated bilateral upper zone involvement, and in another 14% it was combined with other zones. This represents a relation of

Table 2 *Case numbers of unilateral diffuse pleural thickening and of some other items of the ILO 1980 classification in both groups*

	Group A (n = 1204)	*Group B (n = 622)*	*Significance of difference p*
Unilateral pleural thickening	58	49	NS‖
Obliteration of costophrenic angle (cpa = +)	24	15	NS‖
Circumscribed pleural thickening (plaques)	215	4	$p < 0.001$
Profusion of small opacities (1/0 and more)	167	7	$p < 0.001$

‖See footnote to table 1.

Table 3 *Bilateral diffuse pleural thickening of upper, middle, and lower zones in both groups*

Zones				
Upper	*Middle*	*Lower*	*Group A No (%)*	*Group B No (%)*
0	0	0	223 (18·5)	358 (57·6)
+	0	0	224 (18·6)	166 (26·7)
0	+	0	99 (8·2)	7 (1·1)
0	0	+	5 (0·4)	5 (0·8)
+	+	0	296 (24·6)	67 (10·8)
+	0	+	1 (0·1)	— —
0	+	+	14 (1·2)	3 (0·5)
+	+	+	342 (28·4)	16 (2·6)
			1204 (100)	622 (100)
0	0	0	223 (18·5)	358 (57·6)
+	+ 0	+ 0	863 (71·7)	249 (40·0)
+ 0	+	+ 0	751 (62·4)	93 (15·0)
+ 0	+ 0	+	362 (30·1)	24 (3·9)

0, pleural thickening absent; +, present; + 0, absent *or* present.

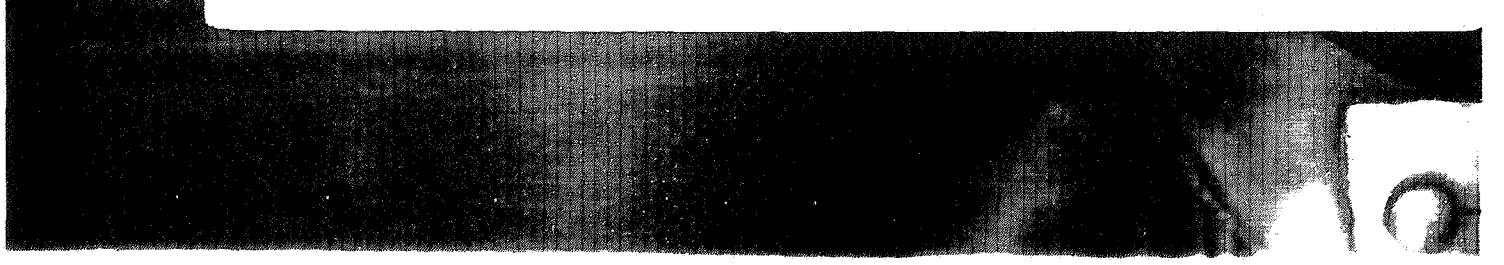


Table 4 *Zone pattern and age, both groups*

U	M	L	A/B No	Age (years) −20 A/B (%)	−30 A/B (%)	−40 A/B (%)	−50 A/B (%)	−60 A/B (%)	>60 A/B (%)
0	0	0	223/358	50/70	46/ 68	18/ 52	12/ 54	7/ 51	11/52
+	0	0	224/166	33/27	28/ 27	26/ 34	15/ 27	9/ 16	4/27
0	+	0	99/ 7	17/—	4/ 1	8/ 1	9/ 2	10/ 2	14/ 2
0	0	+	5/ 5	—/—	—/ —	1/ 1	0/ 2	0/ 1	—/ 2
+	+	0	296/ 67	—/ 3	19/ 4	27/ 7	27/ 13	23/ 25	25/16
+	0	+	1/ —	—/—	—/ —	0/ —	—/ —	—/ —	—/—
0	+	+	14/ 3	/	—/ —	0/ 1	2/ —	2/ 2	7/ —
+	+	+	342/ 16	—/—	4/ 1	19/ 5	35/ 3	49/ 3	39/ 3
No			1204/622	12/73	198/127	295/132	438/126	233/100	28/64
+	+0	+0	863/249	33/27	51/ 32	72/ 45	77/ 43	81/ 44	68/45
+0	+	+0	751/ 93	17/ 3	26/ 6	54/ 13	73/ 18	84/ 32	86/20
+0	+0	+	362/ 24	—/—	4/ 1	20/ 6	37/ 5	51/ 6	46/ 5

0, bilateral pleural thickening absent; +, present; +0, present or absent.
U, upper; M, middle; L, lower.

Table 5 *Zone pattern and period since first exposure to asbestos, group A*

Zones	Period (years) −5 No/%	−10 No/%	−15 No/%	−20 No/%	−25 No/%	−30 No/%	>30 No/%	No
No	100/ 33·0	84/ 23·4	24/ 11·3	9/ 7·6	4/ 4·4	1/ 1·4	9/ 3·0	223
U	91/ 30·0	72/ 20·1	38/ 17·8	13/ 11·0	6/ 6·6	3/ 4·2	1/ 3·0	224
M	22/ 7·3	24/ 6·1	18/ 8·5	11/ 9·3	12/ 13·2	9/ 12·7	3/ 6·7	99
L	1/ 0·4	1/ 0·3	—/ —	2/ 1·7	—/ —	—/ —	1/ 3·0	5
UM	56/ 18·5	89/ 24·8	96/ 32·4	35/ 29·7	23/ 25·3	13/ 18·3	11/ 24·4	296
UL	—/ —	—/ —	—/ —	—/ —	1/ 1·1	—/ —	—/ —	1
ML	2/ 0·7	6/ 1·7	2/ 0·9	1/ 0·8	1/ 1·1	2/ 2·8	—/ —	14
All Z	31/ 10·2	83/ 23·1	62/ 29·1	47/ 39·8	44/ 48·4	43/ 60·6	32/ 71·1	342
	303 (100)	359 (100)	213 (100)	118 (100)	91 (100)	71 (100)	49 (100)	1204

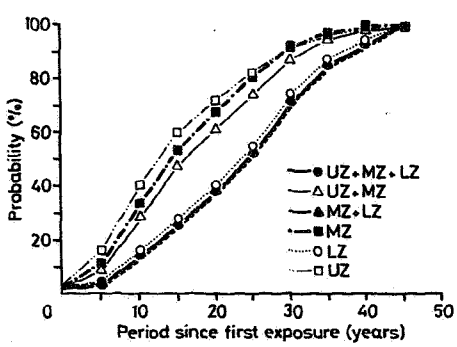
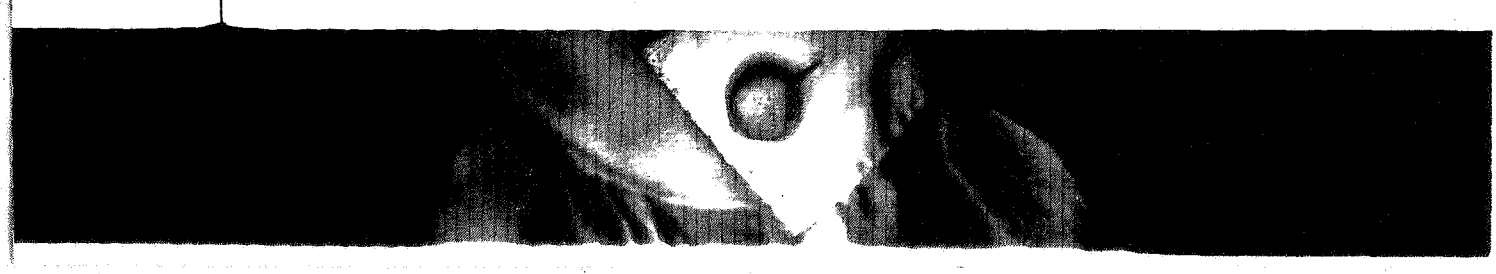


Fig 2 *Estimated risk of bilateral pleural thickening in different single or adjacent zones irrespective of involvement or no involvement of other zones. Pleural thickening at lower zones appears in median between 7 and 12 years later than pleural thickening of the upper or middle zones. As pleural thickening was recorded after and not at first appearance value of zero percent at time zero is probably not true.*

group A to B of roughly 7:4, whereas the lower zones show a relation of 10:1. Bilateral pleural thickening of the lower zones within group A developed rather late (in median 10 years later, fig 2). But it was more discriminating than thickening of the more cranial parts of the pleura (figs 3c, e, and f).

The female breasts sometimes give problems in analysing pleural shadows. Within the German subgroups A and B, no significant difference between men and women was found. This makes a reading bias improbable. In the Turkish subgroups bilateral involvement of all six zones of group B (mainly in men) occurred nearly as often as in group A ($p = 0·73$). In addition, the Turkish subgroup A developed this feature somewhat earlier than the German subgroup A.

Chest abnormalities named above or emphysema ("em") were of no significant influence, although the bell shaped thorax may cause some difficulties in diagnosing middle and lower zone involvement. With a borderline statistical significance ($p = 0·04$), a slightly



higher prevalence of "bilateral pleural thickening" was observed in overweight individuals of group A. This was expected and may be due to subpleural fat.

It was of interest to determine whether the age at onset of exposure in group A influenced the development of bilateral extended pleural thickening. From

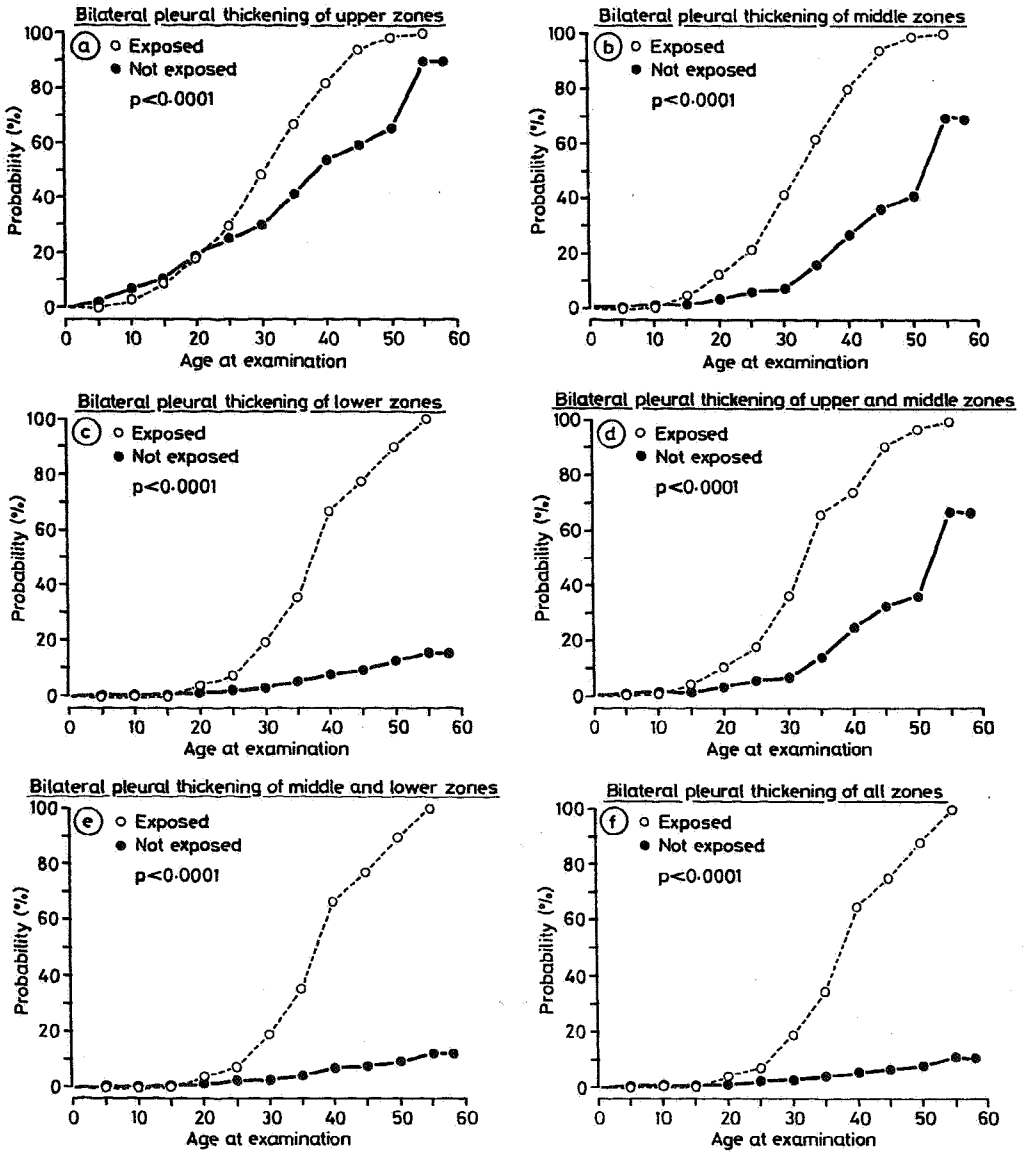


Fig 3 a–f *Estimated risk of bilateral pleural thickening in different single or adjacent zones in relation to age at examination irrespective of involvement or no involvement of other zones. Pleural thickening of upper zones is less specific and that of lower zones, which is almost always combined with thickening at the adjacent middle zones, is most specific for asbestos exposure. As pleural thickening was recorded after and not at first appearance value of zero per cent at age 15 is probably not true.*

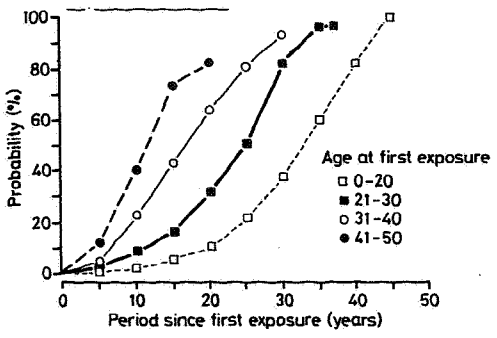


Fig 4 *Estimated risk of bilateral pleural thickening at different ages at time of first exposure ($p < 0{\cdot}0001$, after adjustment for period since first exposure: $p < 0{\cdot}0001$). First exposure at older age has a higher risk of bilateral pleural thickening of all zones. As pleural thickening was recorded after and not at first appearance value of zero per cent at time zero is probably not true.*

fig 4 it is apparent that the risk increases with age. This difference was also found after adjusting for different observation times (period since first exposure was—as could be expected—in median six years longer in the age group up to 20 years than in the group over 40).

Discussion

Our results show that bilateral diffuse pleural thickening is the most frequent[6 14 24 25] and probably the earliest detectable sequel of exposure to asbestos with the current strong legal restrictions for the asbestos industry. In the exposed group there was not a single case of parenchymal involvement that did not also have concomitant, usually advanced, diffuse pleural thickening. This may be true only for the recent conditions of low level dust exposure. Therefore, we find the assessment of pleural involvement to be of striking epidemiological importance in the medical superveillance of dust exposed populations. In this context it is noteworthy that pleural thickening may also occur in association with other types of dust exposure.[8] Nevertheless, as shown above, such diffuse pleural lesions commonly appear in unexposed populations, being more prevalent at higher ages and especially in the upper zones. On the other hand, the more impressive feature of pleural plaques is extremely rare in the unexposed group B (see table 2). Thus bilateral pleural thickening per se, although present in a much higher prevalence than plaques, discriminates exposed subjects only from a statistical point of view but not on an individual basis. This is an important difference.

As this study emphasises, however, additional information on the localisation (affected zones) permits a more specific differentiation as to whether a given pleural thickening is due to dust exposure or not: bilateral involvement of at least two adjacent zones was a characteristic feature of exposure and lower zones usually become affected later than the other parts of the pleura. Unilateral pleural thickening is, by contrast, of limited value in relation to asbestos exposure, although some association may exist to former pleuritis due to asbestos or not. Also, the involvement of the upper zones only is less significant, since this feature was found in a quarter of the unexposed population. This invalidates nearly all the readings of the codes RL1a or RL2a or both (see ILO[21 22]). In summary, this implies that the middle zones are the most important regions for the pleural sequelae of asbestos inhalation. Accordingly, the absence of bilateral pleural thickening in the middle zones with involvement of other zones instead was a rare feature in the exposed group and should therefore always suggest causes other than asbestos. This importance of middle zone involvement should be strongly considered in case the ILO "Recommendations for future research" for recording in quarters instead of sixths of the lungs should become accepted.

The high prevalence of pleural thickening of the upper parts of the pulmonary pleural layer in the exposed population is in striking opposition to the behaviour of asbestosis in the lung. Likewise, the rather lower and late involvement of the lower zones by contrast with the middle zones is equally surprising. An explanation of this different predilection for reactions of asbestos dust in the lung and the pleura is not apparent from this study. It is known that shorter fibres and more isometric dust particles gain the upper bronchi, whereas the longer fibres reach rather the lower parts of the lung, favouring asbestos changes in these locations.[1 8 35 36] Apparently, the short fibres are predominantly transported to the pleura through the lymph vessels. Thus the selection of the fibrous dust by the airstream may explain the described phenomena.

The differences in the reported prevalence of pleural thickening are highly influenced by national and international interobserver variation and the personal biases of the readers. Former international reading trials have shown that each reader has his own characteristic "handwriting" when recording pleural findings. For that reason reports on prevalence are difficult to compare. For our study, the films of both groups, A and B, were reread by the same reader. The range of specific personal characteristics must therefore be the same in both groups and makes the results

at least comparable between A and B, even though a possible bias cannot be excluded with certainty as the reader was not "blind" to asbestos exposure. Nevertheless, there is a remarkably higher prevalence of bilateral pleural thickening in our study than in other investigations, as for instance in that of Cordier *et al.*[13]

On the other hand, there is no doubt that training and personal exchange of knowledge and experience among readers can decrease interobserver variation. In reading pleural findings the agreement (identical records) among the four A-Readers in the Federal Republic of Germany in 1978–9 was—owing to such exchange—high (87–90% of 14 000 films.)[24] Despite some other insufficiencies of this investigation (retrospective design, no blind reading, limited number of available controls, and only vague data on occupational conditions) the striking differences between groups A and B are conclusive.

With respect to the high proportion of Turkish workers within the working population of the Federal Republic of Germany, the knowledge about endemic pleural changes after exposure to fibre dust in Turkey[26 27] made a separate analysis of individuals with Turkish ethnic origin necessary, since our files showed no exact data on the regions where they came from. The higher prevalence of diffuse pleural thickening within both Turkish subgroups A and B may be at least partially due to this precondition.

Conclusions

As figs 2–4 show, the development of diffuse pleural thickening is first obvious within the upper parts of the pleura and not in the lower zones (except after pleurisy); the speed of development is much slower in the unexposed group. This discriminates exposed and unexposed populations from a statistical point of view but not on an individual basis. The main feature of discrimination is the bilateral involvement of at least two adjacent zones; the "mandatory" involvement of the middle zones rarely occurs in non-exposed individuals.

This type of involvement requires recognition and inclusion in the pleural part of the ILO 1980 scheme in terms of pleurally affected lung zones, as already in use for recording lung appearances. The study presented shows that this method is useful and more convenient than the present recording system of extent of length and side, since it offers the hitherto lacking, but necessary, indication of localisation and therefore more reliable information. This seems particularly important since, as was shown under low level dust exposure, diffuse pleural thickening is the earliest and thus a sensitive radiological sign of the biological action of asbestos.

References

1 Otto H, Bohlig H. Morphologie und Röntgenologie der Asbestose. *Radiologe* 1985;**25**:9–21.
2 Stewart MJ. Pulmonary asbestosis. *Br Med J* 1928;ii:675–82.
3 Bohlig H, Jacob G, Müller H. *Die Asbestose der Lungen–Genese, Klinik, Röntgenologie*. Stuttgart: G Thieme, 1964.
4 Jacob G, Bohlig H. Die röntgenologischen Komplikationen der Lungenasbestose. *Fortschr Röntgenstr* 1985;**83**:515–25.
5 Kiviluoto R. Pleural calcification as a roentgenological sign if nonoccupational endemic anthophyllite-asbestosis. *Acta Radiol* 1960;suppl 194.
6 Kiviluoto R, Bohlig H. Die Pleura. In: Bohlig H, ed. *Die Staublungenerkrankungen und ihre Differentialdiagnose*. Stuttgart: G Thieme, 1964;261–7.
7 Sluis-Cremer GK, Theron CP. Radiological and pathological correlations in asbestosis in the Republic of South Africa and the United Kingdom. In: Whipple HE, ed. Biological effects of asbestos. *Ann NY Acad Sci* 1965;**132**:373–8.
8 Bohlig H, Otto H. Die pleuralen Röntgenzeichen der Pneumokoniosen. In: *Handbuch der medizinische Radiologie*. Vol IX/5b. Berlin: (in press).
9 Abelda SM, Epstein DM, Gefter WB, Miller WT. Pleural thickening: its significance and relationship to asbestos dust exposure. *Am Rev Respir Dis* 1985;**25**:9–21.
10 Baker EL, Greene R. Incremental value of oblique chest radiographs in the diagnosis of asbestos-induced pleural disease. *Am J Ind Med* 1982;**3**:17–22.
11 Begin R, Boctor M, Bergeron D, *et al*. Radiographic assessment of pleuropulmonary disease in asbestos workers: posteroanterior, four view films and computed tomograms of the thorax. *Br J Ind Med* 1984;**41**:373–83.
12 Bohlig H, ed. *Staublungenerkrankungen und ihre Differentialdiagnose*. Stuttgart: G Thieme 1964.
13 Cordier S, Theriault G, Provencher S. Radiographic changes in a group of chrysotile miners and millers exposed to low asbestos dust concentrations. *Br J Ind Med* 1984;**41**:384–8.
14 Hillerdal G. Non-malignant asbestos pleural disease. *Thorax* 1981;**36**:669–75.
15 Mattison MC. *Asbestos and asbestos related disease*. Croydon: Jupiter Press, 1983.
16 McGavin CR, Sheers G. Diffuse pleural thickening in asbestos workers: disability and lung function abnormalities. *Thorax* 1984;**39**:604–7.
17 McLoud T, Woods BO, Carrington CB, Epler GR, Gaensler EA. Diffuse pleural thickening in an asbestos exposed population: prevalence and causes. *Am J Roentgenol* 1985;**144**:9–13.
18 Wagner JC, ed. *Biological effects of mineral fibres*. Lyon: International Agency for Research on Cancer, 1980. (IARC sci publ No 30.)
19 Wain SL, Roggli VL, Foster WL. Parietal pleural plaques, asbestos bodies, and neoplasia. *Chest* 1984;**85**:707–13.
20 Whipple HE. Biological effects of asbestos. *Ann NY Acad Sci* 1965;**132**:373–8.
21 International Labour Organisation. *ILO U/C international classification of radiographs of pneumoconioses 1971*. Geneva: ILO, 1972. (Occupational safety and health series 22 (rev).)
22 International Labour Organisation. *Guidelines for the use of ILO international classification of radiographs of pneumoconioses*. Geneva: ILO, 1981. (Occupational safety and health series (rev 80).)
23 Bohlig H, Calavrezos A. Localization of pleural thickening and its correlation to asbestos dust exposure. In: Bergbau Berufsgenossenschaft, ed. *VI International pneumoconiosis conference. Bochum. 1983*. Vol 2. Bremerhaven: Wirtschaftsverlag NW, Verlag für neue Wissenschaft, 1984;890–8.
24 Bohlig H. Interbeurteiler-Variation bei arbeitsmedizinischen Vorsorgeuntersuchungen von Asbestarbeitern in der Bundesrepublik Deutschland. In: Bergbau-Berufsgenossenschaft, ed. *VI International pneumoconiosis conference. Bochum 1983*.

Vol 3. Bremerhaven: Wirtschaftsverlag NW, Verlag für neue Wissenschaft, 1984:2096–103.
25 Sargent EN, Boswell WD, Ralls WP, Markovitz A. Subpleural fat pads in patients exposed to asbestos: distinction from noncalcified pleural plaques. *Radiology* 1984;**152**:273–7.
26 Baris YI, Sahin AA, Özesmi M, *et al*. An outbreak of pleural mesothelioma and chronic fibrosing pleurisy in the village of Karain/Urgüp in Anatolia. *Thorax* 1978;**33**:181–92.
27 Saracci R. Epidemiology of groups exposed to other mineral fibres. In: Wagner JC, ed. *Biological effects of mineral fibres*. Vol 2. Lyon: International Agency for Research on Cancer, 1980:951–61. (IARC sci publ No 30.)
28 Nie NH, Hull GH, Jenkins JG, Steinbrenner K, Bent D. *Statistical package for the social sciences*. New York: McGraw Hill, 1975.
29 Thomas DG, Gart JJ. Stratified trend and homogeneity of proportions and life time data. *Comput Biomed Res* 1983;**16**:116–26.
30 Mantel N, Haenzel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959;**22**:719–48.
31 Gart JJ. Statistical analyses of the relative risk. *Environ Health Perspect* 1979;**32**:157–67.
32 Thomas DG. Exact and asymptotic methods for the combining of 2 × 2 tables. *Comput Biomed Res* 1975;**8**:423–46.
33 Breslow NE, Day NE. *Statistical methods in cancer research*. Vol 1. *The analysis of case control studies*. Lyon: International Agency for the Research of Cancer, 1980.
34 Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association* 1958;**53**:457–81.
35 Doll R, Peto J. *Asbestos. Effects on health of exposure to asbestos*. London: HMSO, 1985.
36 Elmes PC. Health hazards of short mineral fibers. In: *Proceedings of the symposium on "Short and thin mineral fibres," Stockholm, 1982*. Stockholm: Government of Sweden, 1983:163–80.