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Quantification of Non-Fibrous and Fibrous Particulates in Human Lungs: Twenty Year Update on Pneumoconiosis Database

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The lungs act as a continuous sampler of respirable particulate matter in the environment. Quantitative analysis of the retained lung burden of particulate material provides important clues to exposures in individual cases as well as in epidemiological studies. Since 1980 we have developed and utilized microanalytical techniques to identify and quantify the inorganic particles retained in lungs. These results and the cumulative data in the database (initially described in 1991) have had far-ranging diagnostic and research applications. The database contains data from >900 non-fibrous particle analyses and >800 fibre analyses. In this report we summarize and highlight aspects of the database after 20 years.

Keywords: pneumoconiosis; particles; database; lungs; scanning electron microscopy; microprobe analysis; asbestos; silica; metals

INTRODUCTION

The lungs act as a continuous sampler of respirable particulate matter in the environment. Quantitative analysis of the retained lung burden of particulate material provides important clues to exposures in individual cases as well as in epidemiological studies. Since 1980 we have developed and utilized microanalytical techniques to identify and quantify the inorganic particles retained in lungs. These results and the cumulative data in the database (initially described in Abraham *et al.*, 1991) have had far-ranging diagnostic and research applications.

MATERIALS AND METHODS

Lung tissues from cytological, biopsy and autopsy sources have been analysed using scanning electron microscopy and energy dispersive X-ray spectroscopy for: (i) non-fibrous particles using *in situ* analysis with a morphometric, point counting sampling of standard paraffin sections mounted on carbon substrates (Abraham and Burnett, 1983; Abraham *et al.*, 1991); and (ii) fibrous particles using filter preparation after sodium hypochlorite digestion (Abraham *et al.*, 1988). The minimum detectable concentrations are $0.5–1.0 \times 10^6$ particles/cm^3 tissue for non-fibrous particles and $10^3–10^5$ fibres/g dry lung for fibres. Usually a stratified sampling at 4000× and 10000× for fibres is used to allow lower detection limits as well as detection of the thinnest fibres (e.g. chrysotile).

RESULTS

The major classes of non-fibrous particles include silica, aluminium silicates, metals and talc. Major fibre types include various types of asbestos, talc, other silicates and metals. The database reveals frequencies of concentration of the different particle types and particle dimensions. Results of >900 *in situ* analyses (>50000 particles) and >800 fibre analyses (>10000 fibres) are currently in the database. Findings in individual cases are compared with others in the database for histopathology and exposure correlative investigations. Dose–response relationships have been investigated. Correlations with other analytical techniques and laboratories have validated the methodology used (Abraham *et al.*, 1994). It is important to note that this methodology emphasizes individual particle analysis and the *in situ* analyt-

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Table 1. Summary statistics on total non-fibrous particle concentration ($\log_{10}$) and fraction of total comprised by several particle types (893 analyses)

	n	Mean	Min	Max	SD
Log_{10}(total)[a]	893	8.09	5.98	10.5	0.749
Silica/total	893	0.152	0.00	1.0	0.176
Aluminium silicates/total	893	0.369	0.00	1.0	0.271
Metal/total	893	0.390	0.00	1.0	0.292
Talc/total	893	0.033	0.00	0.99	0.103
Fe/total	893	0.153	0.00	1.0	0.184
Ti/total	893	0.109	0.00	1.0	0.146
Al/total	893	0.059	0.00	0.99	0.131

[a]Particle concentrations in no. particles/ml lung. Range from $<10^6$ to nearly 10^{11} indicated by $\log_{10}$ values from <6 to nearly 11.

Table 2. Particle diameter data for non-fibrous particles

	Total	Aluminium silicates	Metals	Silica	Talc
Mean	0.61	0.69	0.47	0.74	0.96
SE	0.0022	0.0046	0.0029	0.0070	0.0320
SD	0.52	0.55	0.34	0.55	1.11
Median	0.5	0.51	0.4	0.6	0.63
Minimum	0.02	0.02	0.05	0.02	0.1
Maximum	24	15	5.2	6.4	24
Count	55 115	14 629	14 487	6252	1203

All values in µm.

ical approach for non-fibrous particulates provides information on particles located in various histological compartments (Abraham and Burnett, 1983) and on particles which may be lost or altered during destructive analytical approaches, such as ashing or digestion.

Examples and summary data are presented in this report. Summary statistics for all non-fibrous particles in the database are presented in Table 1. Data on the dimensions of particles of different types are summarized in Table 2. Note that the *total* particle number also includes endogenous particles, miscellaneous silicates, gypsum, organic, etc. Note the larger particle size for talc and silica and smaller size for metals. Of special interest are the metal particles, which are often overlooked in destructive analytical methods and in methods which do not include particles <0.2 µm diameter. One can see from Table 2 that the metal particles are substantially smaller than the other major particle types. Table 3 presents the data for types of metal particles detected in the entire database (with important explanatory comments below). The figures show distributions of concentrations of non-fibrous particles (Fig. 1) and fibres detected at one of the magnifications used in the stratified sampling (Fig. 2). A different distribution of fibre types results if data from analyses at other magnifications are examined, owing to differences in detection limits and sensitivity for different fibre dimensions at differing instrument magnifications (e.g. some chrysotile and crocidolite fibres are too thin to detect at the lower magnifications).

Some examples of use of the database include the following.

- Dose–response data in New York talc miners (Abraham *et al.*, 1989), showing correlations between exposure estimates, lung burden of particulates and pathological response.
- Dose–response data in Texan sand blasters (Abraham and Wiesenfeld, 1997), showing correlations between radiological, physiological and pathological response and lung burden and demonstrating the applicability of multivariate (discriminant) analysis to lung particle burden data for correlation with workplace/practices data.
- Specific exposure association with unique histopathology in hard metal disease/giant cell interstitial pneumonia cases (Abraham *et al.*, 1991).
- Correlation of lung particle burden with lifetime exposure (age) in racing greyhounds (Schoning et al., 1997).
- Demonstration of unusual exposures by extreme lung burdens compared with database cases (e.g. aluminium welding/ship building pneumoconiosis) (Hull and Abraham, 2002).
- Determination of lung burdens in persons with no known dust exposures and normal lungs at autopsy (‘background cases’).

Table 3. Metal particulates in pneumoconiosis database

Metal	No. of cases detected	Per cent cases detected	Metal as first or only element	No. of particles	Percentage
Fe	772	85.68	Fe	4334	29.9
Ti	719	79.80	Ti	2032	20.2
Al	460	51.05	Al	2043	14.1
Cr	431	47.84	W	1477	10.2
Ni	240	26.64	Si + metal	998	6.9
Zn	221	24.53	Sn	427	2.9
Cu	195	21.64	Pb	358	2.5
Sn	191	21.20	Cr	338	2.3
Mn	161	17.87	Zn	203	1.4
Pb	151	16.76	Ni	201	1.4
W	142	15.75	Ba	169	1.2
Ba	109	12.10	S + metal	150	1.0
Zr	99	10.99	Cu	133	0.9
Ce	90	9.99	Au	118	0.8
Ag	73	8.10	Zr	116	0.8
V	64	7.10	Ag	112	0.8
Au	48	5.33			
Co	38	4.22			
Bi	35	3.88			
Hg	33	3.66			
Ta	30	3.33			
La	22	2.44			
Nd	16	1.78			
Mo	15	1.66			
I	12	1.33			
Cd	11	1.22			
Br	8	0.89			
Se	7	0.78			
Nb	5	0.55			
Os	2	0.22			
As	2	0.22			
Ru	1	0.11			
Pd					
Sr					
Tc					
Pt					

There was a total of 901 analyses (733 cases), and a total of 14487 metal particles (categorized by *first* metal listed for each particle).
Other metals (<100 particles containing listed metal as first element): Hg, Ce, Bi, Mo, Ta, Co, V, Os, Se, La, Br, Cd, Mn, Pd, Nb, Sr, Tc, As, Ru, Pt, Nd.
Total number of metal particles in the database = 14487.
Note that the order of various metals is different in the left and right tabulations. This reflects: (i) subsets of cases within the entire database, such as hard metal disease cases (accounting for the high number of W particles); (ii) metals such as Cr, Ni, Zn, Cu, Pb and Mn, which occur much less frequently as the major (first) element in an individual particle. Also note that this tabulation format does not convey information on the occurrence of more than one element in individual particles (which is often of great interest in source investigation) (Abraham *et al.*, 1997).

- Demonstration of methodological variables in results of lung fibre burden analysis.
- Comparison of lung particle types in US Navy deck grinders with results from a large database.

CONCLUSIONS

Continued development of this database has enabled examination of lung particulate burden

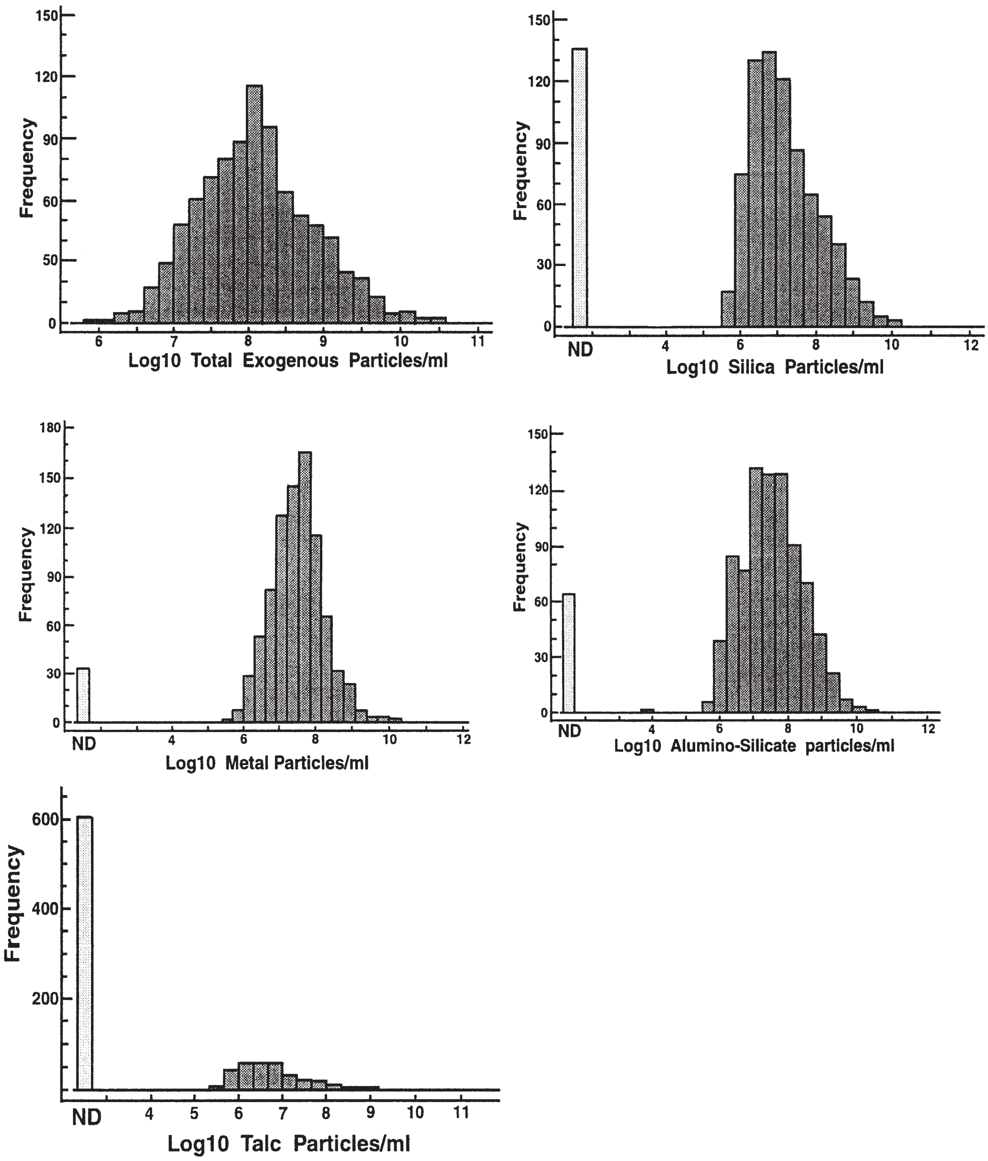

Fig. 1. Tissue section analyses: 901 analyses of 733 cases. The frequency of non-fibrous particle concentration in database cases (millions of particles/cm^3 lung). ND, analyses in which particle type was not detected.

(LPB) across hundreds of cases, with varied exposures, from the USA and elsewhere. It contains data on 'background' as well as 'exposed' populations. Relationships between exposure, histopathology and LPB are explored using multivariate statistical approaches (e.g. discriminant analysis in silicosis cases reveals clues to different employers/work practices). In some instances hypotheses regarding disease aetiology (e.g. hard metal disease and giant cell interstitial pneumonia), radiology/physiology (e.g. silicosis) and pathogenesis (e.g. persistence of Be in granulomas in chronic Be disease) are supported or rejected. Cases previously considered as 'idiopathic' may be more properly classified using such analyses and database comparisons. A major remaining goal is to make this type of database secure and available in a format accessible for multi-user access for research and diagnostic querying.

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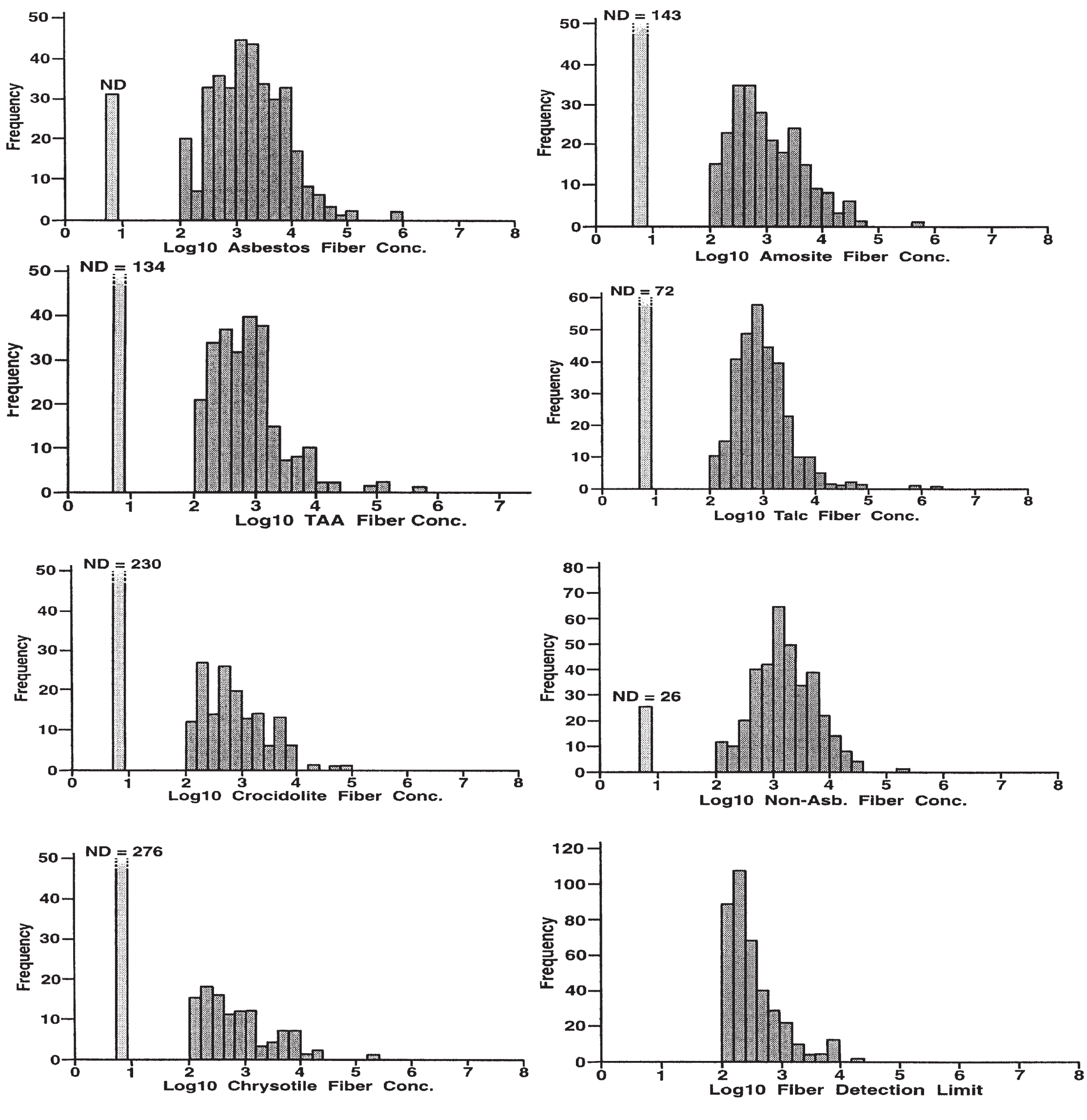

Fig. 2. Summary histograms of fibre concentrations in 418 analyses at 4000× (fibres/g wet lung). ND, analyses in which particle type was not detected; TAA, tremolite/actinolite/anthophyllite.

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