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

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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 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

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 × 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-
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 \( \mu \text{m} \) 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 blassters (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 1. Summary statistics on total non-fibrous particle concentration (log_{10}) and fraction of total comprised by several particle types (893 analyses)

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Mean</th>
<th>Min</th>
<th>Max</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log_{10}(total)</td>
<td>893</td>
<td>8.09</td>
<td>5.98</td>
<td>10.5</td>
<td>0.749</td>
</tr>
<tr>
<td>Silica/total</td>
<td>893</td>
<td>0.152</td>
<td>0.00</td>
<td>1.0</td>
<td>0.176</td>
</tr>
<tr>
<td>Aluminium silicates/total</td>
<td>893</td>
<td>0.369</td>
<td>0.00</td>
<td>1.0</td>
<td>0.271</td>
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<tr>
<td>Metal/total</td>
<td>893</td>
<td>0.390</td>
<td>0.00</td>
<td>1.0</td>
<td>0.292</td>
</tr>
<tr>
<td>Talc/total</td>
<td>893</td>
<td>0.033</td>
<td>0.00</td>
<td>0.99</td>
<td>0.103</td>
</tr>
<tr>
<td>Fe/total</td>
<td>893</td>
<td>0.153</td>
<td>0.00</td>
<td>1.0</td>
<td>0.184</td>
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<tr>
<td>Ti/total</td>
<td>893</td>
<td>0.109</td>
<td>0.00</td>
<td>1.0</td>
<td>0.146</td>
</tr>
<tr>
<td>Al/total</td>
<td>893</td>
<td>0.059</td>
<td>0.00</td>
<td>0.99</td>
<td>0.131</td>
</tr>
</tbody>
</table>

*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

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Aluminium silicates</th>
<th>Metals</th>
<th>Silica</th>
<th>Talc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.61</td>
<td>0.69</td>
<td>0.47</td>
<td>0.74</td>
<td>0.96</td>
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<tr>
<td>SE</td>
<td>0.0022</td>
<td>0.0046</td>
<td>0.0029</td>
<td>0.0070</td>
<td>0.0320</td>
</tr>
<tr>
<td>SD</td>
<td>0.52</td>
<td>0.55</td>
<td>0.34</td>
<td>0.55</td>
<td>1.11</td>
</tr>
<tr>
<td>Median</td>
<td>0.5</td>
<td>0.51</td>
<td>0.4</td>
<td>0.6</td>
<td>0.63</td>
</tr>
<tr>
<td>Minimum</td>
<td>0.02</td>
<td>0.02</td>
<td>0.05</td>
<td>0.02</td>
<td>0.1</td>
</tr>
<tr>
<td>Maximum</td>
<td>24</td>
<td>15</td>
<td>5.2</td>
<td>6.4</td>
<td>24</td>
</tr>
<tr>
<td>Count</td>
<td>55115</td>
<td>14629</td>
<td>14487</td>
<td>6252</td>
<td>1203</td>
</tr>
</tbody>
</table>

All values in \( \mu \text{m} \).
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.

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...
(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.

Acknowledgements—The maintenance of the database has been largely supported by the Department of Pathology, SUNY Upstate Medical University.
REFERENCES


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.