

Distribution And Persistence Of Pleural Penetrations By Multi-Walled Carbon Nanotubes

R. R. Mercer¹, A. F. Hubbs¹, J. F. Scabilloni¹, L. Wang¹, V. Castranova¹, D. Porter¹

¹NIOSH, Morgantown, WV, United States of America

Rationale: Multi-walled carbon nanotubes (MWCNTs) are new manufactured nanomaterials with a wide spectrum of commercial applications. The durability and fiber-like dimensions (mean length 4.2 µm long x 49 nm diameter) of MWCNTs suggest that these fibers may migrate to and have toxicity within the pleural region.

Methods: To address whether the pleura received a significant and persistent exposure, C57BL/6J mice were exposed by pharyngeal aspiration to 80 µg MWCNTs or vehicle and the distribution of MWCNTs penetrations determined at 1, 7, 28 and 56 days after exposure. Following lung fixation and sectioning, morphometric methods were used to determine the number of MWCNT fiber penetrations of three barriers: alveolar epithelium (alveolar penetrations), the alveolar epithelium immediately adjacent to the pleura (sub-pleural penetrations) and pleural surface.

Day	Alveolar Epithelium	Subpleural Alveolar Epithelium	Pleural Surface
1	24,360 ± 7,218	60 ± 15	16 ± 4
7	10,440 ± 2,728	8 ± 4	5 ± 3
28	11,020 ± 1,437	26 ± 8	17 ± 6
56	15,909 ± 1,855	25 ± 9	13 ± 3

RESULTS: Total MWCNT penetrations in thousands of nanotubes per lung are given in the above table (mean±S.E., N=8). There was an initial and unexpected high density of penetrations in the subpleural alveolar epithelium and pleural surface one day following aspiration which appeared to decrease due to engulfment by alveolar macrophages by day 7. However, the density of penetrations increased in the sub-pleural alveolar epithelium and pleura by day 28. At day 56 approximately 1 in every 400 fiber penetrations was in either the subpleural alveolar epithelium or pleural surface. Numerous penetrations into macrophages in the alveolar airspaces throughout the lungs were demonstrated at all times but are not included in the counts presented.

Conclusions: The results document that MWCNT penetrations of the alveolar wall, alveolar macrophage and pleura are both frequent and sustained. In addition, the findings demonstrate the need to investigate the chronic toxicity of MWCNT at these sites.

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