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TITLE: MOUSE PULMONARY DOSE- AND TIME COURSE-RESPONSES INDUCED BY EXPOSURE TO MULTI-WALLED CARBON NANOTUBES

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ABSTRACT: Carbon nanotubes (CNT) come in a variety of types, but one of the most common forms is multi-walled carbon nanotubes (MWCNT). MWCNT have potential applications in many diverse commercial processes, and thus human exposures are considered to be likely. In order to investigate the pulmonary toxicity of MWCNT, we conducted an in vivo dose-response and time course study of MWCNT in mice in order to assess their ability to induce pulmonary inflammation, damage, and fibrosis using doses that approximate estimated human occupational exposures. MWCNT were dispersed in dispersion medium (DM) and male C57BL/6J mice (7 weeks old) received either DM (vehicle control), 10, 20, 40 or 80 ìg MWCNT by aspiration exposure. At 1, 7, 28 and 56 days post-exposure, MWCNT-induced pulmonary toxicity was investigated. Bronchoalveolar lavage (BAL) studies determined pulmonary inflammation and damage was dose-dependent and peaked at 7 days post-exposure. By 56 days post-exposure, pulmonary inflammation and damage markers were returning to control levels, except for the 40 ìg MWCNT dose, which was still significantly higher than vehicle control. Histopathological studies determined that MWCNT exposure caused rapid development of pulmonary fibrosis by 7 days post-exposure, that granulomatous inflammation persisted throughout the 56-day post-exposure period, and also demonstrated that MWCNT can reach the pleura after pulmonary exposure. In summary, the data reported here indicate that MWCNT exposure rapidly produces significant adverse health outcomes in the lung. Furthermore, the observation that MWCNT reach the pleura after aspiration exposure indicates that more extensive investigations are needed to fully assess if pleural penetration results in any adverse health outcomes.