AUTHORS: Shvedova, A. A.; Kisin, E.; Murray, A. R.; Johnson, V. J.; Gorelik, O.; Arepalli, S.; Hubbs, A. F.; Mercer, R. R.; Keohavong, P.; Sussman, N.; Jin, J.; Yin, J.; Stone, S.; Chen, B. T.; Deye, G.; Maynard, A.; Castranova, V.; Baron, P. A.; Kagan, V. E.

TITLE: INHALATION VS. ASPIRATION OF SINGLE-WALLED CARBON NANOTUBES IN C57BL/6 MICE: INFLAMMATION, FIBROSIS, OXIDATIVE STRESS, AND MUTAGENESIS

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ABSTRACT: Nanomaterials are frontier technological products used in different manufactured goods. Because of their unique physicochemical, electrical, mechanical, and thermal properties, single-walled carbon nanotubes (SWCNT) are finding numerous applications in electronics, aerospace devices, computers, and chemical, polymer, and pharmaceutical industries. SWCNT are relatively recently discovered members of the carbon allotropes that are similar in structure to fullerenes and graphite. Previously, we (47) have reported that pharyngeal aspiration of purified SWCNT by C57BL/6 mice caused dose-dependent granulomatous pneumonia, oxidative stress, acute inflammatory/cytokine responses, fibrosis, and decrease in pulmonary function. To avoid potential artifactual effects due to instillation/agglomeration associated with SWCNT, we conducted inhalation exposures using stable and uniform SWCNT dispersions obtained by a newly developed aerosolization technique (2). The inhalation of nonpurified SWCNT (iron content of 17.7% by weight) at 5 mg/m3, 5 h/day for 4 days was compared with pharyngeal aspiration of varying doses (5-20 {micro}g per mouse) of the same SWCNT. The chain of pathological events in both exposure routes was realized through synergized interactions of early inflammatory response and oxidative stress culminating in the development of multifocal granulomatous pneumonia and interstitial fibrosis. SWCNT inhalation was more effective than aspiration in causing inflammatory response, oxidative stress, collagen deposition, and fibrosis as well as mutations of K-ras gene locus in the lung of C57BL/6 mice.