Inhalation Toxicity Risk of Carbon Nanotubes

Lam CW, James JLt, McCluskey R and Hunter RL. “Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation.” ToxSci Advance Access published 26, 2003.

An entire molecular electronics industry is poised to take off, much of it on the back of carbon nanotubes. But new research is raising alarm. Nanotubes are highly damaging to the lungs of mice. Dr. Mae-Wan Ho calls for a moratorium until proper safeguards can be put in place.

Molecular electronics is making headlines. Much of it is based on single-wall carbon nanotubes, which have many other potential applications as strong, lightweight material in the aerospace and defence industries. Nanotubes are now manufactured in bulk. Dr. Smalley (Nobel laureate and a pioneer in carbon nanotube research) predicted that hundreds of thousands of tons of the stuff could be produced in 5 to 10 years and "in time, millions of tonnes of nanotubes will be produced worldwide every year". But enthusiasm for research and development has run way ahead of safety precaution.

Unprocessed nanotubes are very light, and could become airborne and potentially reach the lungs. Researchers in the Space and Life Sciences of NASA Johnson Space Center, Wyle Laboratories, and the Department of Pathology and Laboratory Medicine, University of Texas Medical School, in Houston, Texas, USA, investigated the toxicity of carbon nanotubes to the lungs, by introducing them into the trachea of mice under anaesthesia.

The results are alarming. Five of the mice treated with high dose of one kind of nanotubes died within 7 days. All nanotube products induced epitheliod granulomas – tumour-like nodules of bloated white blood cells in the lining of the lungs - and in some cases inflammation of the lungs at 7 days. These persisted and became more pronounced in animals that were sacrificed at 90days. The lungs of some animals also showed inflammation around the bronchi, and extensive necrosis (tissue death).

Carbon nanotubes, the researchers conclude, are "much more toxic than carbon black and can be more toxic than quartz, which is considered a serious occupational health hazard in chronic inhalation exposures."

The researchers had used nanotubes produced under different conditions containing different heavy metals. Samples of ‘raw’ and ‘purified’ nanotubes both contained iron, while a third nanotube product contained nickel and yttrium.

A suspension containing 0, 0.1 or 0.5 mg of carbon nanotubes was introduced into the trachea of the mice. As added controls, groups of mice were given a suspension of carbon black or of quartz. The mice were killed at 7days or 90days after the single treatment, in order to examine the lungs.

Nanotubes are neither water-soluble nor wettable, and all the products were extremely difficult to disperse; and ultrasound as well as heat-inactivated mouse serum had to be used.

Graphite – the most similar form of carbon to nanotubes - does not possess the electrical properties and fibrous structure of the nanotubes, and its permissible inhalation exposure limit set by the occupational safety and health administration (OSHA) is 15mg/m3 of total dust and 5mg/m3 for the 'respirable' (capable of being inhaled) fractions. It is well known that the geometry and surface chemistry of particulates can play an important role in causing lung toxicity.

All animals treated with 0.1mg per mouse of nickel-yttrium containing nanotubes showed no overt clinical signs. But 5 of 9 mice treated with 0.5mg died: 2/4 within the 7day group and 3/5 in the 90day group. All deaths occurred 4 to 7 days after receiving the nanotubes. Deaths generally preceded by lethargy, inactivity and body-weight losses. These symptoms were also seen in the high dose mice that survived. Mice in the 90day group lost 27% of their body weight by the first week. Symptoms in the two surviving mice disappeared after one week and the animals started to gain weight.

The iron-containing nanotubes (both raw and purified) did not cause deaths in the mice. Mild signs of inactivity, hypothermia, and occasionally shivering were most noticeable 8 to 12h after treatment with the raw nanotubes, and symptoms disappeared soon after this time. There were no body weight losses with the raw or purified iron-containing nanotubes.

Under the microscope, the lungs of dead animals in the high dose group showed large aggregates of particles in macrophages (large white blood cells that 'eat' foreign particles) in the alveolar space (air sac), some of the aggregates were also found in spaces between cells, forming granulomas (tumour-like nodules consisting of the bloated white blood cells). There were also signs of inflammation. Granulomas were not detected in mice given the low dose of the nickel-yttrium nanotubes. The lungs of mice given high dose of either raw or purified iron-containing nanotubes showed prominent granulomas at 7days. Most of these nodules were located beneath the bronchial epithelium (lining) and were present throughout the lung fields. Some appeared to extend into the bronchi as polyps (irregular growths) .

The granulomas consisted of macrophages laden with black particles, and had very few other white blood cells. Some of the lungs from mice given high doses of the nanotubes appeared grossly abnormal at 90 days. The lung lesions were generally more pronounced than those given the high dose at 7 days; some also had necrosis (tissue death), and extensive inflammation. Granulomas and other pulmonary lesions were also seen in some of the mice given the lose doses of nanotubes, but to a milder degree.

Heat inactivated serum did not produce any clinical signs, nor gross or microscopic lesions. The mice of the carbon black or quartz treated controls also did not show any clinical signs that could be attributed to treatment. Quartz at high dose (0.5 mg) induced an increase in the number of macrophages in the lungs, and some of these cells contained particles. Quartz also produced mild to moderate inflammation. The results for

the 7day and 90day groups were generally similar. One mouse in the 7day group had a low-grade granuloma reaction; and the mice in the high dose 90day group had increased clusters of lymphocytes surrounding the bronchi (sign of inflammation).

Purified nanotubes contained only a small amount of metal (2% by weight). Insoluble iron and iron compounds are low in toxicity, so the results strongly indicate that the nanotubes themselves induced the granulomas. Another research group had found similar results previously in rats.

The deaths of 5 mice may have been caused by nickel and yttrium in the nanotube sample, as they did not occur in the other samples of nanotubes.

One of the major effect of nanotubes is that they moved rapidly through the walls of the air sacs, in contrast to carbon black. Nanotubes are totally insoluble and non-biodegradable fibres, and it is well known that the pathogenicity of a fibre in the lungs directly correlates with its persistence.

Graphite toxicity is known as graphite pneumoconiosis, characterized by granulomas, emphysema, tissue death and hardening of the blood vessels, among other symptoms, and has been long recognized in a large number of workers involved in mining and processing graphite. But theses nanotube samples did not contain graphite.

These results show that a single exposure is enough to trigger serious effects including deaths. No safety tests have yet been carried out, especially in the longer-term, on a range of other nanoparticles used, some of them in intended medical procedures. Civil society watchdogs such as the ETC Group have called for a moratorium on nanotechnology research and development.

The present findings certainly justify a moratorium on research involving nanotubes, if not all nanoparticles, until proper safeguards can be put in place, and safety tests carried out in the meantime.

Source:
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