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# Carbon nanotubes – the new asbestos?

## Exploring the occupational health and hygiene risks of carbon nanotubes

***Carbon nanotubes are already being developed for use in medicines, electronics and sports goods. But does their manufacture create new occupational health and hygiene hazards? Carole Bass explores.***

**POSTDOCTORAL** researcher Candace Tsai is operating a state-of-the-art particle analyser called a fast mobility particle sizer spectrometer (FMPS). It is housed in a beige box and weighs more than 30 kg. 'Including the cart, it will be about 90 pounds,' Tsai observes – 'about my weight'.

The University of Massachusetts Lowell invested $60,000 in the FMPS, not because of its size, but because it processes air samples at 60-times the speed of the more standard scanning mobility particle sizer. That means it can sample air for particles between about 5 and 500 nanometres – nanoparticles.

Tsai and her colleagues are among a small group of occupational health professionals worldwide who are trying to understand – and avoid – the risks of working with these tiny materials, manufactured at the scale of atoms and molecules. While nanotechnology is a fast-growing field, far more money and talent are going into developing uses for nanomaterials than into researching their health and safety risks. As a result, even the physicists and engineers whose experimental work Tsai studies have little knowledge about the potential hazards of the nanomaterials they are creating and using. When she started teaching these PhD scientists about 'nanorisks', Tsai recalls, their reaction was like anyone else's: 'They say, "I'm exposed to those nanoparticles, right? Does that mean I'm going to die?"'

The researchers were familiar, however, with the possible hazards of carbon nanotubes (CNTs), notoriously compared to one of the most toxic substances known in the workplace – asbestos. Because of their lightness, strength, and ability to conduct electricity and heat, these tiny cylinders – made from sheets of carbon a single atom thick – are among the most commonly used nanomaterials. They are also among the ones producing the most alarming results in health and safety studies, with new findings arriving every few months.

### UNPREDICTABLE BEHAVIOUR

Nanotechnology – a broad term for a range of technologies – involves creating and manipulating materials roughly in the size range 1nm–100nm. While there is no consensus on the upper limit of the nanoscale, many people peg it at 100 nanometres – 500- to 1,000-times thinner than a human hair.

At this nanoscopic scale, the high ratio of surface area to mass makes particles more chemically reactive than their bulk counterparts. And as the laws of quantum physics kick in, predictable behaviour becomes unpredictable. Nanogold turns red. Nanotitanium dioxide, used in sunscreen, turns from white to clear on the skin (and can peel the paint off metal roof shingles; Australian workers learned by accident when some of their sunscreen spilled). Nanocarbon conducts electricity far more efficiently than bulk carbon.

These novel properties are what make nanomaterials so promising, fuelling a rapidly growing global market. The US-based Project on Emerging Nanotechnologies counts more than 1,000 consumer products that claim to incorporate nanomaterials, from toothbrushes to soft toys, paint to power tools. And that does not even begin to touch the large market for nano-containing industrial materials. Carbon nanotubes are used in nanomedicine, microelectronics, and high-end sporting goods, such as bicycles and tennis rackets.

The same qualities that make nanomaterials so remarkable are also cause for concern about worker health and safety. Their tiny size means they are readily inhaled deep into the lungs and, according to some research, absorbed through the skin, and are then able to migrate into the bloodstream and organs. Although many nanomaterials are engineered from common elements and compounds, it is not clear how much of our knowledge about their health effects applies to the nano versions. That uncertainty is the reason why a March 2009 EU-OSHA report on emerging chemical hazards puts nanomaterials at the top of the list[1].

Nanoparticles are not altogether new. They can occur naturally or by accident – like the ultrafine particulates found in diesel exhaust and welding fumes. The body of occupational and environmental health research is not reassuring: the association between diesel exhaust and respiratory and heart diseases, for example, raises flags for workers exposed to similar engineered nanomaterials.

But carbon nanotubes have been compared to an even better known hazard, one that is nearly synonymous with occupational disease: asbestos.

## LOOKS LIKE ASBESTOS ...

There are many types of carbon nanotubes: long and short, straight and crooked, single-walled and multi-walled. Some multiwalled CNTs (MWCNTs) – those with a long, straight, needle-like shape – looked enough like asbestos fibres that researchers wondered whether they would behave similarly as well.

In a 2008 study, scientists at the University of Edinburgh injected asbestos-like CNTs into the abdominal cavities of mice[2]. Inflammation of the mesothelium occurred within 24 hours; within seven days, the mesothelium developed granulomas that are a precursor to mesothelioma.

The team injected the CNTs into the peritoneum as a surrogate for the pleural cavity of the lungs because 'we were looking for a relatively quick and easy test,' one of the authors, Dr Andrew Maynard, tells *Occupational Health [at Work]*. 'Injecting stuff around the lungs is hard to do, and it's hard to interpret the data. With the peritoneum, it's much easier to deliver the stuff and to examine the tissue afterward.'

The association between MWCNTs and mesothelioma is 'still very tentative,' Maynard notes. 'That's certainly one concern: that if you inhale these things, they'll stick around for 30 years and you'll end up with cancer. But we still don't have that level of certainty. We need to carry out fairly long-range animal inhalation studies – long enough so you actually see the presence or absence of tumours.'

In the meantime, the authors warn: 'Our results suggest the need for further research and great caution before introducing such products into the market if long-term harm is to be avoided'.

The United States National Institute for Occupational Safety and Health (NIOSH) has been investigating some of the missing links in the possible CNT-cancer chain. One of those gaps is the difference between injection, which the Edinburgh study used, and inhalation – a far more plausible exposure route for workers.

In March 2009, NIOSH researchers released preliminary results from a study in which lab mice aspirated long, multiwalled CNTs suspended in liquid – a technique they said 'closely resembles inhalation of the same material suspended in the air'[3]. They found that the tubes caused fibrosis in the lungs, just as single-walled CNTs did in previous studies. Most significantly, they also found that the CNTs migrated from the alveoli to the pleura.

'It appears that after pharyngeal aspiration of MWCNT in mice that the nanotubes enter alveolar macrophages, which migrate to the lymphatic vessels,' NIOSH's Dr Vincent Castranova writes in an email to this journal. 'The macrophages containing MWCNT then migrate to lymphatics in the pleural region of the lung. Then one can observe MWCNT leaving the macrophages and the lymphatic vessels and penetrating the outer surface of the lung into the interpleural space. This was observed at one month post exposure.

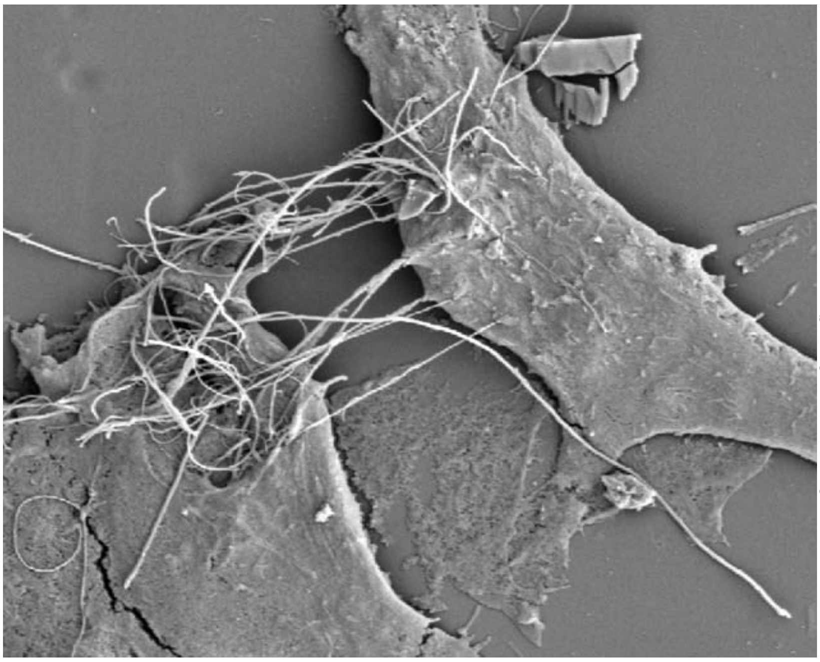

*Image courtesy of MRC Centre for Inflammation Research.*

*Scanning electronmicrograph showing mesothelial cells (in culture) exposed to carbon nanotubes.*

'It is a relatively rare but significant event,' Castranova continues. 'Until our study, no reports had shown that MWCNT could reach mesothelial cells lining the interpleural space after exposure of the lung.'

The NIOSH researchers considered these results urgent enough to release even before they were peer-reviewed or published. (Their full-length paper is currently in press[4].)

Even more recently, scientists in New Mexico published research showing how inhaled CNTs suppressed the immune systems of mice[5]. Building on previous studies, they demonstrated that the lungs of mice exposed to the highest dose signalled their spleens to activate cyclooxygenase enzymes, which suppressed immune function. Lower doses did not produce the same effect.

## UNCERTAIN EXPOSURE

Evidence of the toxicity of fibre-like CNTs is mounting and alarming. Little is known about exposure. But some studies suggest a mitigating factor: CNTs tend to clump together in clusters too large to inhale.

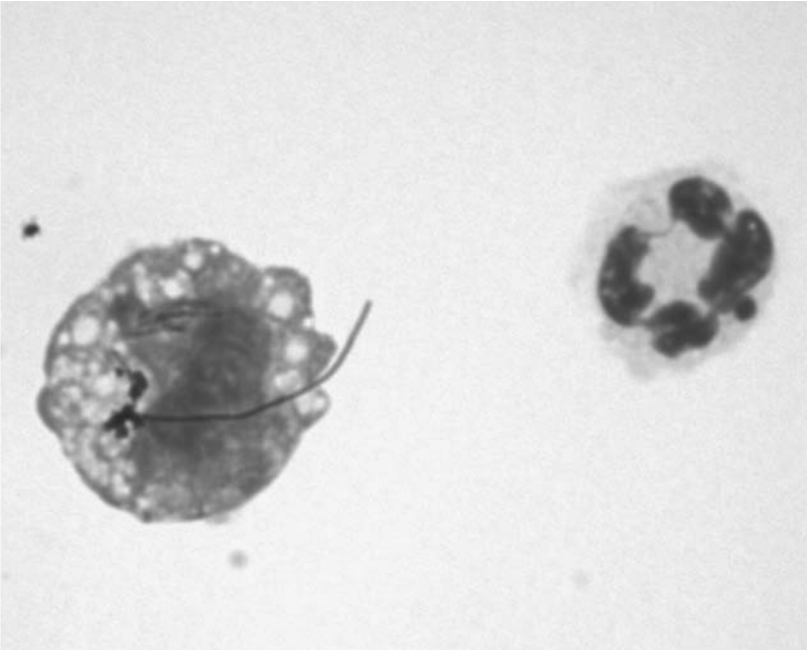

*Image courtesy of MRC Centre for Inflammation Research.*

*Cells removed from the peritoneal cavity of a mouse, which had received a 50 microgram dose of long straight carbon nanotubes. The macrophage on the left has attempted unsuccessfully to ingest some nanotubes, which are too long to be be phagocytised.*

An EU-OSHA review of scientific literature on workplace exposure to engineered nanomaterials found that inhalation 'is very limited during production because normally this process is performed in a closed reaction chamber, except in case of leaking during the process'[6]. 'Human exposure is more likely to occur after the manufacturing process,' the EU OSHA report says – 'when the reaction chamber is opened or the product is dried, or during the handling of products after their manufacture or during the reactor cleanout operation.'

The literature review lists two studies that monitored different methods of handling and manufacturing CNTs. They found little or no increase in nano-sized dust, compared to background levels.

In a third study, conducted in a CNT research lab, both overall dust and airborne nanotubes did increase during handling of unrefined materials. After protective control measures were implemented, however, dust 'decreased to a nondetectable level.'

The EU-OSHA authors conclude: 'The present study suggests that the conventional industrial hygiene measures can significantly reduce exposure to airborne MWCNTs and other particulate materials in a nano research facility.'

## REGULATIONS AND RECOMMENDATIONS

Conventional industrial hygiene measures are, in fact, the main recommendation that occupational health experts have offered for working with carbon nanotubes.

'The best wisdom is to reduce exposures as low as possible and, if necessary, to wear protective equipment,' says Maynard, co-author of the Edinburgh study, who is chief science advisor at the policy research group Project on Emerging Nanotechnologies in Washington, DC. 'One of the problems is, nobody knows quite how to measure carbon nanotubes. You need an electron microscope even to see them,' he says.

As for fast mobility particle sizers – like the one Candace Tsai and her colleagues use for nanoparticles at the University of Massachusetts Lowell – 'nobody's quite sure if they work for nanotubes', says Maynard. 'They are a very unusual particle. We see some particles that are almost like gossamer threads: most of it is holes and air. So it's very hard to work out how an instrument is going to look at that.'

Partly as a result, few organisations have suggested – let alone mandated – quantitative exposure limits for CNTs. The British Standards Institute may be the first. In 2007, it proposed a 'benchmark' limit of 0.01 fibres/ml for 'fibrous nanomaterials'[7].

'When you've got a material that's harmful,' Maynard observes, 'the bottom line is, you've got to be able to say how low exposures need to be. It's not acceptable to just say: "Keep exposures low."'

In the US, NIOSH has put out interim recommendations for handling nanomaterials, as well as interim guidance for medical screening of nanoworkers[8].

In the UK, the Health and Safety Executive says that it 'views CNTs as being substances of very high concern'[9]. It notes: 'Although the recent findings only apply to some CNTs, we think a precautionary approach should be taken to the risk management of all CNTs ... If their use cannot be avoided, HSE expects a high level of control to be used.'

The US Environmental Protection Agency (EPA) went further in November 2009, proposing a rule that requires respirators, gloves, and protective clothing for workers handling carbon nanotubes[10]. The EPA cites concerns not only about potential lung damage, but also risks of dermal exposure.

Otherwise, governments have taken virtually no action to regulate nanomaterials, despite the growing evidence of potential harm. In Europe, the EU has said it thinks nanomaterials can largely be regulated as existing chemicals under its Registration, Evaluation, Authorisation and restriction of Chemicals (REACH) programme. Yet the European Parliament, in spring 2009, passed a resolution urging the EU to subject nanomaterials to closer scrutiny as new materials under REACH.

In the US and Europe, government programmes requesting that companies voluntarily share health and safety information gleaned from their nano research and manufacturing operations have largely fallen flat, with minimal participation. In April 2009, for instance, NIOSH published a formal Request for Information on carbon nanotubes, saying that the agency 'intends to evaluate the scientific data ... and develop appropriate communication documents ... which will convey the potential health risks and recommend measures for the safe handling of these materials'. Among other data, NIOSH asked for 'published and unpublished reports and findings from in-vitro and in-vivo toxicity studies', 'information on possible health effects observed in workers exposed to CNTs', 'workplace exposure data' and 'information on control measures'.

In July, NIOSH essentially admitted defeat, publishing a new notice that read, in bold letters: 'NIOSH did not receive any submissions to this request.' (NIOSH's Castranova does note, however, that his agency has received information 'through informal interactions' with industry scientists.)

Meanwhile, the research of Candace Tsai and her colleagues at the University of Massachusetts Lowell is up in the air. The state government cut funding for the university's Toxic Use Reduction Institute, through which the nano researchers have been carrying out their work, by about two-thirds for the current fiscal year. Next year's funding is even more uncertain.

Two US scientists are calling for a new approach to guarding against emerging hazards such as nanomaterials.[11] The pair, NIOSH director Dr John Howard and current NIOSH special assistant for nanotechnology Dr Vladimir Murashov, argue that their proposal, which they dub 'just-in-time risk management,' is essential not only to protect against well-known but not-yet-quantified harms, but also to allow useful technologies to flourish.

'The increasingly rapid pace of technology development has come into conflict with the slow pace of the governmental standard-setting process, thus increasing the chances that any new technology, like nanotechnology, may cause damage to workers' health before strategies based on quantitative risk assessment can be implemented,' they write. 'Developing proactive approaches to occupational risk management of emerging technologies is crucial not only to protect workers, but also to ensure that the promise of this new technology is fulfilled.'

Such an approach – which would include voluntary standards, qualitative risk assessment, and a global reach – would not be a permanent substitute for more protective regulations, the authors write. But it 'may be a critical interim measure to fill the current risk management gap before our knowledge of the emerging technology and the associated risks matures.' ■

## *CONCLUSIONS*

- **Nanomaterials** may behave differently from their bulk counterparts and therefore require additional research to determine their potential health and safety risks
- **Nanomaterials** are not a single category of material, but present different risks according to their size, shape, and composition
- **Because** of their fibre-like shape, some types of carbon nanotubes (CNTs) seem to cause an asbestos-like reaction in animal studies
- **Airborne** CNTs are difficult to measure; studies so far indicate that they clump together, making high inhalation exposures less likely
- **No** governments have adopted quantitative exposure limits for CNTs. Guidelines in the UK, US and elsewhere call for keeping exposures to a minimum by enclosing operations and, if necessary, using protective clothing and equipment
- **The** British Standards Institute proposes an exposure limit of 0.01 fibres/ml for 'fibrous nanomaterials'

*Carole Bass is a US-based journalist who writes frequently about occupational and environmental health.*

**Notes**

*1 European Agency for Safety and Health at Work. Expert forecast on emerging chemical risks related to occupational safety and health, Luxembourg: Office for Official Publications of the European Communities, 2009.*

*2 Poland CA, Duffin R et al. Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. Nature Nanotechnology 2008; 3: 423–428.*

*3 Hubbs A, Mercer RR et al. Persistent pulmonary inflammation, airway mucous metaplasia and migration of multi-walled carbon nanotubes from the lung after subchronic exposure. The Toxicologist 2009; 108(1): A2193.*

*4 Porter DW, Hubbs AF et al. Mouse pulmonary dose- and time course-responses induced by exposure to multi-walled carbon nanotubes. Toxicology 2009, in press.*

*5 Mitchell LA, Lauer FT et al. Mechanisms for how inhaled multiwalled carbon nanotubes suppress systemic immune function in mice. Nature Nanotechnology 2009; 4: 451–456.*

*6. Kaluza S, Balderhaar JK et al. Workplace exposure to nanoparticles. European Risk Observatory literature review. Bilbao: European Agency for Safety and Health at Work, 2009.*

*7 British Standards Institute. Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials. London: BSI, 2007.*

*8 National Institute for Occupational Safety and Health. Approaches to safe nanotechnology. DHHS (NIOSH) Publication no. 2009–125. Cincinnati, Ohio: NIOSH, 2009.*

*9 Health and Safety Executive. Risk management of carbon nanotubes. London: HSE, 2009, www.hse.gov.uk/pubns/web38.pdf*

*10 US Environmental Protection Agency. Proposed significant new use rules on certain chemical substances. Federal Register 2009; 74(214) (November 6): 57430–57436.*

*11 Murashov V, Howard J. Essential features for proactive risk management. Nature Nanotechnology 2009; 4: 467–470.*