



Craig A Poland, Rodger Duffin, Ian Kinloch, Andrew Maynard, William AH Wallace, Anthony Seaton, Vicki Stone, Simon Brown, William MacNee and Ken Donaldson (2008 in press). *Carbon nanotubes introduced into the abdominal cavity display asbestos-like pathogenic behaviour in a pilot study*. Nature Nanotechnology.

Commentary on the above paper by the lead author Prof Ken Donaldson - University of Edinburgh & SnIRC

Background to the paper

Anyone who has any knowledge of the history of occupational lung disease and even most of the general public, are aware of the pandemic of lung disease caused globally by asbestos in the last century. Before and after asbestos was banned or regulated out of use, a number of other fibrous materials began to be exploited. The reason for this is that fibres have a number of useful properties. These other fibres were duly studied by particle toxicologists, alongside asbestos, and a unifying 'paradigm' emerged that explained what made some fibres harmful and others less harmful or non-harmful.

The paradigm has essentially 3 rules that must be met for any fibre to be harmful:-

Rule 1 - fibre has to be thin enough to enter the lungs (less than about 5 microns thick i.e. 5 thousandths of a mm)

Rule 2 - fibre has to be longer than the cells of the lung that usually gets rid of fibres and other dusts, thereby impeding its removal (that is longer than about 15 microns)

Rule 3 - fibre has to resist dissolving in the lung environment or the number of fibres (the dose) does not build up. In other words the fibre has to be non- biosoluble.

Only if it satisfies all 3 rules will a fibre be highly pathogenic i.e. if it is long, thin and durable in the lungs. By these rules amphibole asbestos is highly pathogenic, chrysotile asbestos much less so and insulation wools e.g. rockwool are not pathogenic. This is borne out by studies in human populations, which show exactly this pattern of health impact. Therefore the pathogenic fibre paradigm is the best 'structure: activity' model in particle toxicology; i.e. the relationship between the structure of the particle (fibre) and its toxicity is well understood.



Carbon nanotubes are an interesting new product emanating from the nanotechnology industries that comprise tubular graphene (carbon lattice) sheets – they are essentially fibrous in shape and are in large-scale industrial production already and this is set to increase rapidly. Despite warnings that carbon nanotubes should be looked at in terms of the asbestos paradigm, this has not been addressed up to the present.

How do carbon nanotubes look when superficially compared against the rules of the fibre toxicology paradigm?

a) Thinness - they are very thin, commonly 10-200nm.

b) Length - they can be long and straight, long and tangled or they can be short and tangled.

c) Biopersistence - they are very tough - essentially being composed of graphene, the same material as graphite and so are not likely to be biosoluble. In preliminary studies we have carried out, they are highly durable.

I had been involved in the development of the fibre paradigm in the eighties and early nineties and subsequently became interested in the toxicology of ultrafine and nanoparticles from the late nineties onwards. I therefore set my PhD student, Craig Poland, to specifically address the issue of carbon nanotubes and the asbestos/fibre paradigm in his project in the University of Edinburgh. The paper arose from this work and the research team included several members of [SnIRC](#) (Ken Donaldson, Vicki Stone, Anthony Seaton).

The paper

We specifically asked whether carbon nanotubes satisfied the paradigm rule regarding length – in other words were long carbon nanotube fibres harmful whilst short nanotube fibres were not. We focused on the mesothelium, the cells that line the pleura and other body cavities, since asbestos-exposed individuals develop a number of conditions of the pleura, including the tumour mesothelioma; so this seems a special target for harmful fibres.

We chose nanotubes that were long and straightish (i.e. one dimension longer than about 15 microns) and also nanotubes that were long tangled or short tangled (less than about 5 microns in any dimension). We looked at the short-term response of the mesothelium and found that only the long carbon nanotubes caused damage, inflammation and scarring. As has been shown for long amphibole asbestos, these endpoints are linked to longer term effects, like mesothelioma. The short carbon nanotubes had



no effect. We included a long and a short asbestos control - the long caused damage and inflammation whilst the short had no effect. We included nanoparticulate carbon black as a control nanoparticle, composed of graphene in particle, not tubular form -this had no effect on the mesothelium.

Our conclusions

We conclude that in terms of the toxicological rules governing fibre pathogenicity, long multiwalled carbon nanotubes satisfy the criterion of a pathogenic fibre and that short multiwalled carbon nanotubes satisfy the criterion of non-harmful. As for the other rules - carbon nanotubes are very thin and they are durable in preliminary studies that we have carried out.

The things our study didn't address, but that arise from it and that we recommend be addressed urgently in future research

- 1) Are long straight nanotubes commonly in use?
- 2) Can CNT get airborne in large quantities when they are being used in industrial settings?
- 3) If they are inhaled in quantities, do carbon nanotubes find their way to the sensitive mesothelial tissues?
- 4) Will mesothelioma or other adverse effects develop in such an exposure situation?
- 5) This work only addressed fibre-like effects and would not have detected any adverse effects caused by nanotubes acting as particles.

Summing up - this research provides evidence that MWCNT show the same toxicological behaviour as asbestos, and therefore that exposure to some types of nanotubes could carry a high risk. More research is urgently needed on the toxicology of these useful new materials and on potential exposures so we can quantify and manage the risk to exposed individuals.

Ken Donaldson
15/05/08