

## High Aspect Respirable Particles - Dr Craig Poland

The IOM has a long history of investigating the various aspects of how particles gain entry into the body and what harm they may cause. In relation to respiratory exposure, the respiratory system has evolved to limit the size and quantity of particles which can gain entry to the lung and clear the particles which do. The airways of the lung can be imagined as a progressively narrowing and branching system of tubes meaning that large particles that are breathed in tend to land in the larger, upper airways. From here there are effective mechanisms to deal with them so they do not reach the deep lung where they may cause a problem.

Therefore, only very small particles tend to be able to penetrate through the ever-narrowing airways into the deep lung; such particles that are small enough to gain access to the fragile tissues of the deep lung are termed 'respirable' particles or fibres. The respirable particles that do land in the deep lung encounter clearance mechanisms that rely on the action of cells (macrophages: i.e. Latin for big eaters) that are adept at handling small particles. They eat (phagocytose) the small particles and clear them as shown in figure 1. These cells are too small to deal with

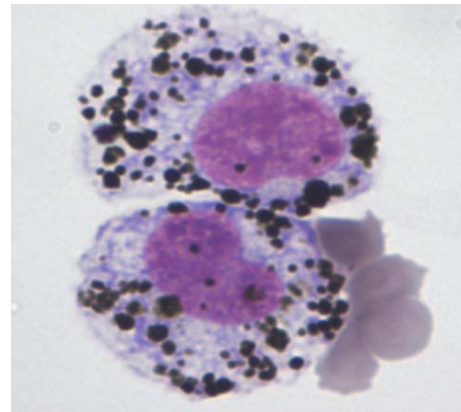


Figure 1: Specialised cells (macrophages) after 'eating' carbon particles.

larger particles (larger than  $\sim 10\text{-}20\mu\text{m}$ ) but due to the filtering effect of the airways, macrophages never see large particles. An exception to this is the ability of long fibres such as asbestos to negotiate the airways and deposit in these deep areas and cause problems for clearance. This is because the fibres are long (a high aspect) and have a very small diameter (a high length-to-width aspect ratio). In the airstream air steam the fibres travel like tiny javelins aligned in the airstream, presenting only their diameter as resistance and so are respirable in size). As shown in figure 2, the macrophages will still try and eat these long fibres and stretch along them but are unable to fully enclose the fibre and become 'frustrated' in their attempts. As the fibres are not cleared efficiently, repeated exposure and inhalation of the fibres can mean that if they don't dissolve, they can slowly accumulate in the lung. Here they may cause a

problem such as inflammation, DNA damage or scar tissue formation or other forms of disease.

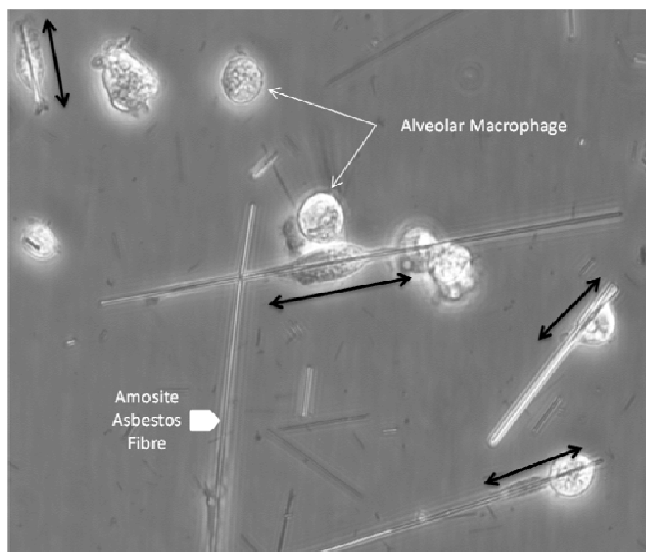


Figure 2: Macrophages attempting to 'eat' long asbestos fibres by stretching along them (black arrows) but failing to enclose them.

At the IOM we are interested in not only fibres such as asbestos which can be inhaled, but also other materials which present a similar issue of being rather large and hence causing a problem for clearance, yet still being respirable. A particular area of interest is how this may apply to the new generation of nanomaterials and whether, due to their very small size in a particular aspect (e.g. very thin) they are respirable but also have another aspect that is large enough to present the macrophages with

problems. Calculations performed by Dr. Alan Jones, an aerosol physicist at the IOM published as part of a study performed by Professor Ken Donaldson's research group at the University of Edinburgh have focused on the plate-like 'wonder' nanomaterial graphene. These calculations clearly show that graphene nanoplatelets may be respirable despite having a very large diameter even up to 30µm). The experimental aspect of the research performed by Anja Schinwald and colleagues (Schinwald et al 2011<sup>1</sup>) show that these particles, if introduced into the lungs, can cause frustrated phagocytosis and so can drive responses such as inflammation and disease.

A third form of high aspect but respirable particle may exist in the form of loosely bundled materials such as collections of carbon nanotubes. If they form a loose bundle then these may have a high aspect but be very light and so be respirable.

The concept of a unifying theory of the pathogenic action of high aspect respirable particles is an on-going area of research for the IOM and our collaborators. Such work is vital and aims to find structure : toxicity relationships which use physico-chemistry to predict toxicity, so reducing the need for toxicology testing. It is one weapon in the armoury used in risk assessment, risk management and disease prevention that will allow the safe development and use of new materials.

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<sup>1</sup> Schinwald A, Murphy FA, Jones A, Macnee W, Donaldson K. (2012) "Graphene-Based Nanoplatelets: A New Risk to the Respiratory System as a Consequence of Their Unusual Aerodynamic Properties." ACS Nano. 2012 Jan 6. [Epub ahead of print]