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Small particles - Big problem

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Our lungs are exposed to a variety of respirable particles in a whole host of settings from the outdoor environment to the work place and in our homes. The biological effects of different particle types, such as asbestos fibres and quartz have been widely studied for many years, but recently a new class of particles has become the focus of research interest throughout the world, 'ultrafine' particles.

Our lungs are exposed to a variety of respirable particles in a whole host of settings from the outdoor environment to the work place and in our homes. The biological effects of different particle types, such as asbestos fibres and quartz have been widely studied for many years, but recently a new class of particles has become the focus of research interest throughout the world, 'ultrafine' particles. Ultrafine particles are defined as particles which have a diameter of less than 100 nm. Such ultrafine particles are increasingly used for industrial and high-tech applications and are also the by-products of combustion of fuels such as diesel oil. In fact, the diesel engine is the main source of ultrafine particles in environmental pollution. In our homes, ultrafine particles are also generated by processes such as gas cooking. Hence, the potential health effects of ultrafine particles are of interest to us all.

The important health effects of ultrafine particles were first recognised through experiments in which experimental animals were exposed to particles of different sizes. For example, respirable titanium dioxide particles (diameter 200 nm) known to be harmless in humans, causes little damage to the lung in experimental animals. However, by comparison, an ultrafine version of titanium dioxide (diameter 20 nm) causes a severe inflammatory reaction in the lungs indicating that they cause lung damage. Similarly in experiments performed using carbon black and ultrafine carbon black, the ultrafine particles induced a much greater inflammatory reaction than the larger carbon black particles. The results of these types of study clearly demonstrate that particles which are similar in chemical composition differ enormously in their ability to damage the lung and that ultrafine particles are highly damaging. Figure 1 demonstrates the magnitude of the difference in size between particles produced in traditional dusty trades such as coal mining or quarrying and the size of the ultrafine particle. Figure 4 shows that for a given airborne mass of particles, the number of particles increases dramatically as the particles sized decreases into the ultrafine range. This huge size difference provides several likely clues as to why ultrafine particles are so harmful to the lung. In addition we can look to the mechanisms by which the body normally removes foreign material from the lung to find an explanation.

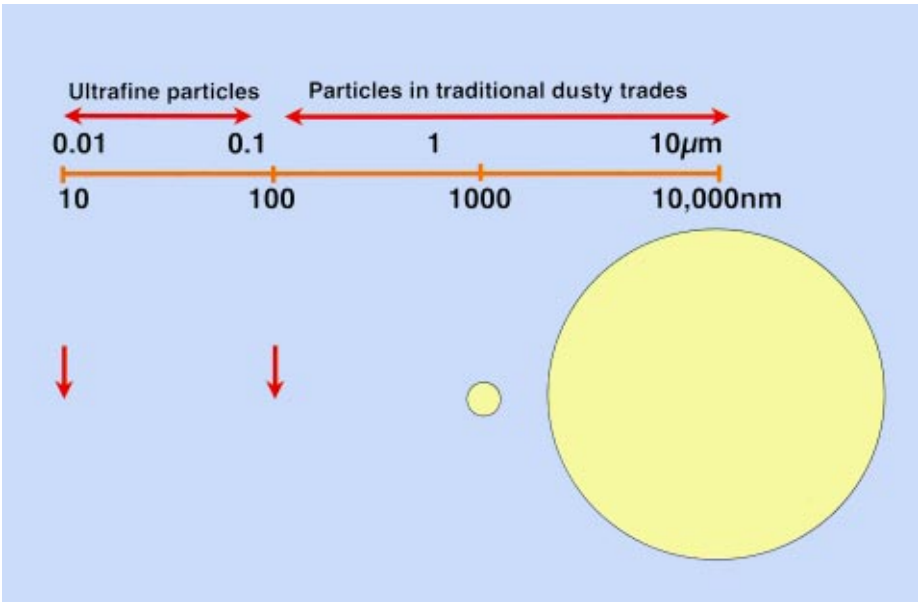

Figure 1. The relative size of particles which occur in various dusty trades compared with ultrafine particles such as those produced by the combustion of diesel oil.

The lung consists of a network of branching 'bronchial' tubes which terminate in a large number of alveolar sacs (figure 2). These tubes are well protected by an 'escalator' comprising a thin layer of mucus that traps particles and is wafted out of the lung. This is quite an effective defence, even against ultrafine particles and most particles which deposit there are cleared out.

Particles which are deposited beyond

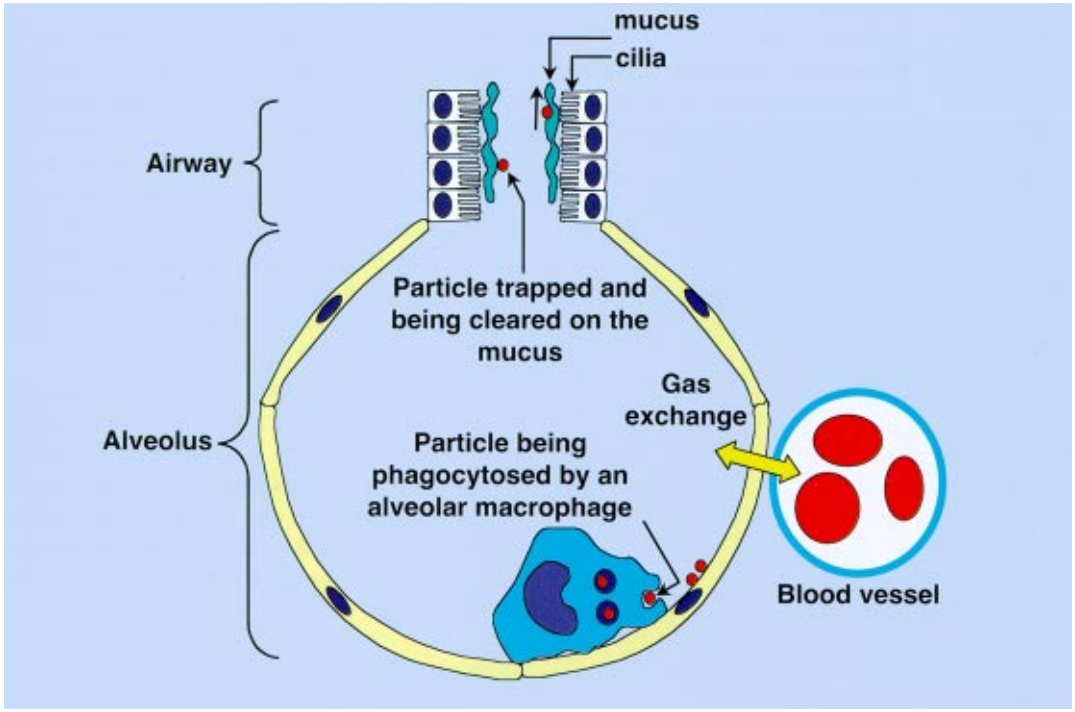

Figure 2. A diagram highlighting the mechanisms which occur to remove particles from the lung airways and alveoli. Particles are removed from the airways by an escalator system consisting of a sticky mucus which is wafted up and out of the lung by hair-like cilia. Particles in the alveolar region are engulfed by mobile macrophages which carry the particles out of the lung.

these tubes reach the alveolar part of the lung where they encounter a different defence (figure 2). A mobile cell, known as the macrophage, moves around the surface where it will engulf any particles it encounters by a process known as phagocytosis. The macrophage containing the particles leaves the alveolar region by migrating to the terminal bronchioles where it joins the mucociliary escalator to move up and out of the lung.

These mechanisms work well for non-ultrafine particles, producing an efficient mechanism for the removal of particles from the lung (unless this is prevented by harmful particles such as quartz or asbestos). In comparison with fine particles, an equal mass of ultrafine particles contains thousands more particles, which means that the macrophages must be highly efficient to remove all of the ultrafine particles that deposit in the alveolar regions of the lung (figure 3). Macrophages seem not to be able to remove ultrafine particles as efficiently as larger particles and in any case, the sheer number of particles may present an insurmountable task for the macrophages. Finally, the ultrafine particles may even damage macrophage cell functions although the mechanism by which the ultrafine particles damage macrophages remains unclear. In addition to the greater number of particles, an equal mass of the smaller diameter particles possesses a much larger surface area. These particles are known to generate highly reactive and damaging oxidant species at their surface as has been reported for other harmful dusts. This means that the ultrafine particles with their much larger surface area for the generation of such oxidants, could inhibit macrophage phagocytic function allowing particles to remain free at the lung surface to damage other cells. In addition, phagocytosis of large numbers of particles stimulates the macrophage to produce additional damaging oxidant species along with mediators which will initiate an inflammatory reaction in the lung.

A combination of the ultrafine particles, the damaging oxidant species and the mediators secreted by the macrophage damage the nearby epithelial cells which line the alveolar spaces. These epithelial cells normally act as a barrier to prevent the entry of particles and microbes into the delicate, underlying tissues. Damage to the epithelial barrier by contact with the particles, oxidants and inflammatory mediators will allow the passage of the ultrafine particles into

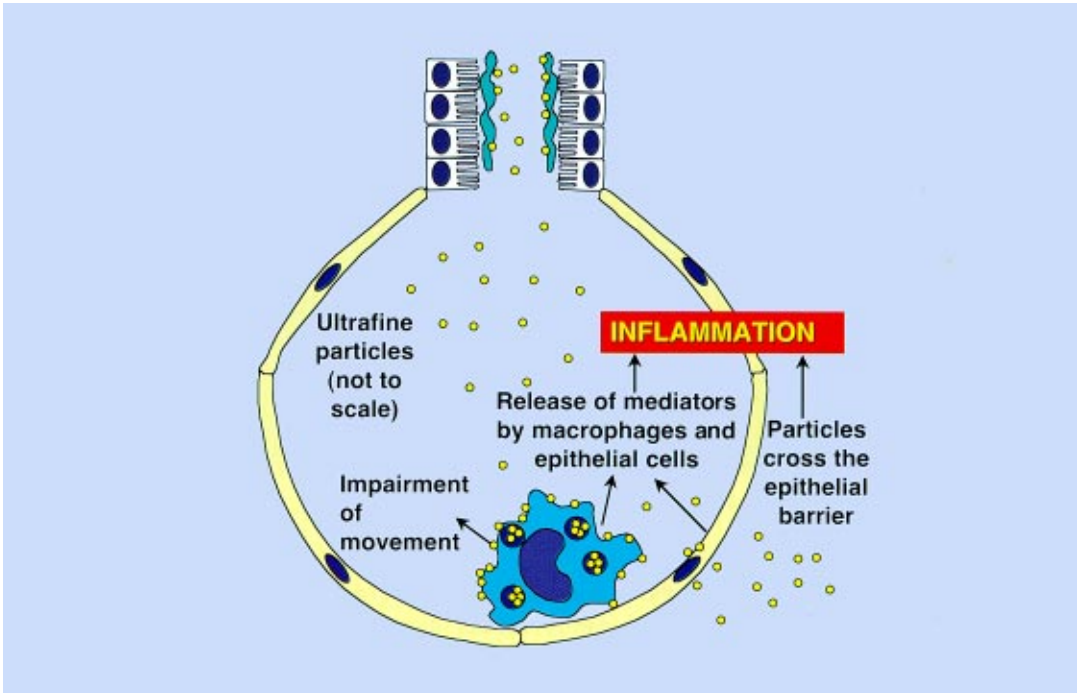

Figure 3. Exposure of the lung to ultrafine particles leads to lung damage caused by a breakdown in the mechanisms which normally remove the particles from the deep alveolar regions of the lung.

these fragile tissues. Within the tissues of the lung, the particles may continue to generate damaging oxidant species and to stimulate the production of mediators by

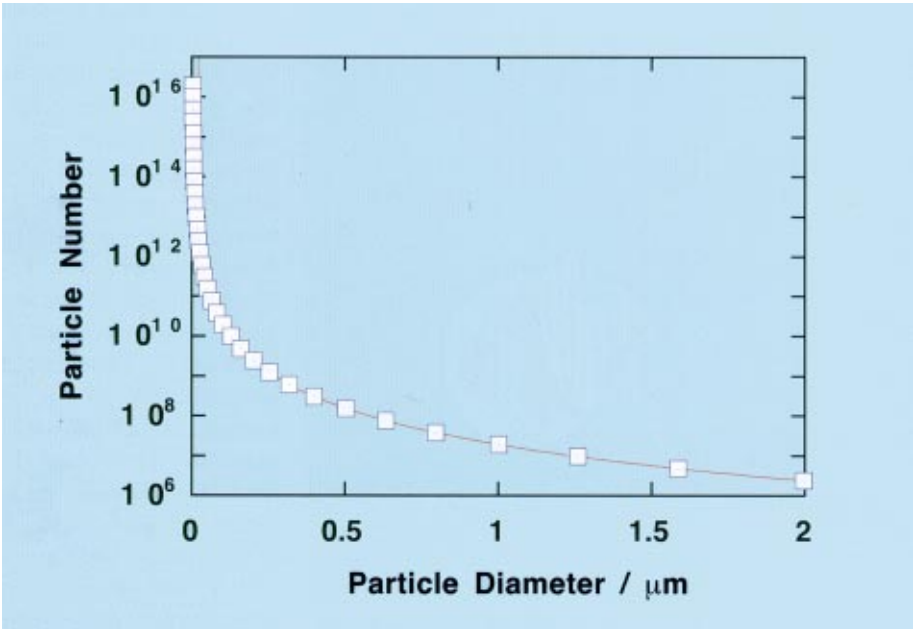

Figure 4. A graph to represent the number of individual particles which occur per ml of air when particles of different diameters are suspended at an airborne mass concentration of 10 μg/m³.

the local cells so that the damage becomes more severe and prolonged.

Damage and inflammation of this nature will potentiate certain respiratory diseases such as bronchitis and asthma. In fact, there are a growing number of reports which indicate that when the quantity of particles in the atmosphere (termed PM10, particulate•matter with a diameter of less than 10 micrometers) increase, that this is accompanied by an increase in the number of asthmatics and bronchitics exhibiting aggravated symptoms. A substantial proportion of the particle number, but not the mass of PM10 is ultrafine and this may mediate the harmful effects of PM10 (figure 5). In addition to the effects on asthmatics, an increase in PM10 has also been associated with an increase in hospital admissions for respiratory diseases and also cardiovascular diseases such as strokes and heart attacks.

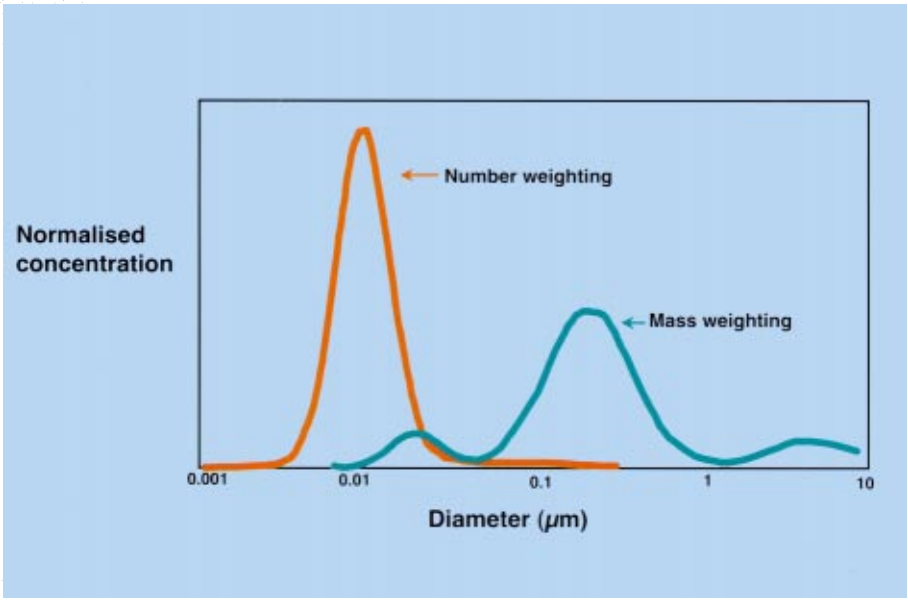

Figure 5. Typical size distribution of urban PM10

It is relatively easy to imagine how inhalation of ultrafine particles can induce damage to the respiratory system and exacerbation of respiratory diseases, however the induction of cardiovascular diseases remains less easy to understand. It has recently been discovered that a number of the mediators released by various lung cells on exposure to the ultrafine particles may increase the potential of the blood to clot, which could ultimately lead to either a stroke or heart attack.

Ultrafine particles present a fascinating challenge to those interested in how particles cause lung disease. Over the next few years ongoing research worldwide should see a much better understanding of the particles that are small in size but present a big problem to the lungs.

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Vicki Stone (BSc PhD). Having started her life in the liver, Vicki is now in the lung; half way to a haggis!