Occupational medicine implications of engineered nanoscale particulate matter

The imminent nanotechnology revolution promises dramatic advancements in science, technology, medicine and society as a whole. First generation products containing engineered nanoscale materials are already appearing in the marketplace, while more sophisticated products are being developed in laboratories around the world. Researchers and manufacturing employees are potentially exposed to dispersible nanoscale particulate matter via inhalation, ingestion and skin contact. Preliminary research indicates that in some cases nanoparticulate matter may be more toxic than other forms of the same or similar material. Application of the classical tools of occupational medicine and industrial hygiene is hampered by the lack of consensus guidelines for medical monitoring, exposure assessment, and exposure control.

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By Richard J. Kelly

INTRODUCTION

A revolution is underway in academic and industrial laboratories and factories around the world, where developments in nanotechnology promise a huge range of benefits for science, technology, and society. More than evolutionary, new nanoscale materials will likely prove revolutionary in many fields. This revolution will have a dramatic impact in engineering, materials sciences, chemistry, computer technology, aerospace, medicine and biological sciences, as well as a wide range of manufacturing. Potential applications of these new materials are wide open to innovation.

"Nanotechnology" is most generally defined as the intentional manipulation of matter to form novel structures with one or more dimension or features less than 100 nm. In the broadest sense nanotechnology includes work at the nanoscale in the fields of inorganic and organic chemistry, biochemistry, engineering, electronics and materials science.

While many of the points in this review may be applicable to the entire field of nanotechnology, I will focus on *engineered dispersible inorganic nanoparticulate matter*, hereafter referred to as *nanoparticles*. Nanoparticles less than 100 nm in two or three dimensions, are not attached to a substrate, not part of a larger structure and can be inhaled, ingested or contaminate the skin. They are distinct from naturally occurring environmental ultrafine particles and incidentally produced nanoparticles such as diesel soot, although some engineered structures are also found in air pollution.[1]

The first generation of "passive" nanoscale materials is now appearing in industrial and consumer products. This includes carbon nanotubes in composite materials used to make sporting equipment, nanoclays in cements and plastics, metals oxides in batteries, paints and sunscreens and fluoropolymers in stain repellant clothing.

Second generation "active" nanomaterials are being developed in laboratories around the world and a few are on the verge of commercialization. Medicine, in particular, is predicted to benefit tremendously from these more advanced materials. Third and fourth generation materials, which include the holy grail of nanotechnology, molecular manufacturing, are still largely beyond the horizon at this time.

Nanoparticle behavior is often strikingly different from the behavior of the chemically similar material of larger particle size. These new properties form the basis for the optimistic claims of nanotechnology pundits. The toxicity of new nanoparticles may also vary qualitatively or quantitatively from that of similar materials at the micro- or macro-scale. To date, limited evidence suggests that some materials are uncharacteristically toxic at the nanoscale.

Employees involved in the development, production, distribution and use of these nanoparticles are already potentially exposed to materials of uncertain toxicity. The pubic is also exposed, through the use of topical sunscreens and cosmetics and ulti-

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Table 1. Elements used in engineered nanoparticles[4].

Elements used in engineered nanoparticles		
Aluminum	Antimony	Barium
Bismuth	Boron	Cadmium
Calcium	Carbon	Cerium
Chromium	Cobalt	Copper
Dysprosium	Erbium	Europium
Gadolinium	Gallium	Germanium
Gold	Hafnium	Holmium
Indium	Iridium	Iron
Lanthanum	Lead	Lithium
Lutetium	Magnesium	Manganese
Molybdenum	Neodymium	Nickel
Niobium	Nitrogen	Osmium
Oxygen	Palladium	Platinum
Potassium	Praseodymium	Promethium
Rhodium	Rhenium	Ruthenium
Samarium	Scandium	Silicon
Silver	Sodium	Strontium
Sulfur	Tantalum	Technetium
Terbium	Thulium	Tin
Titanium	Tungsten	Vanadium
Ytterbium	Yttrium	Zinc
Zirconium		

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mately through the breakdown of other nanomaterial-containing consumer products.

The challenge to occupational health professionals is to prevent the development of disease in employees handing these novel nanomaterials despite the lack of toxicological information, consensus exposure standards, air sampling methodologies and medical monitoring protocols. This is particularly difficult in R&D laboratories, where completely novel materials are developed and processes change frequently.

SOURCES OF CONCERN

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of chemistries used for nanoparticles is vast, as shown in Table 1.[2] Possible structures are almost unlimited, as suggested by Figure 1 which reveals the many different nanoparticles possible for just one chemistry (zinc oxide). In effect, nanoscale structures may be thought of as entirely new chemicals with regard to their potential toxicity.

Unfortunately, it is very apparent that discerning the toxicity of engineered nanoparticles will not be a simple task, as details of chemistry, crystalline structure, morphology, contaminants, size and many other factors must be considered.[3–5] The emerging field of "nanotoxicology" has experienced growing pains due to methodo-

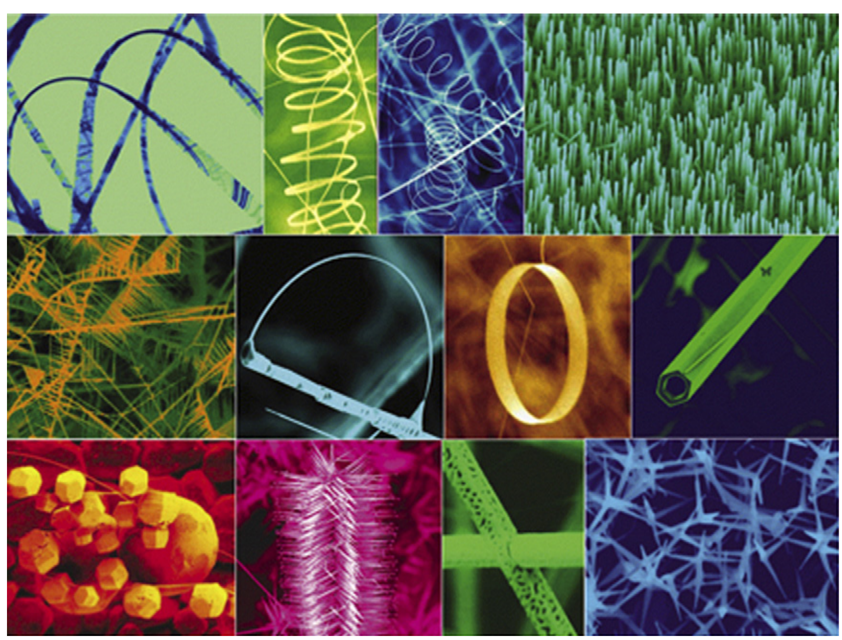

Figure 1. The many forms of nanoscale zinc oxide may pose diverse health effects.[8]