

# Toxic Potential of Mineral Dusts

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**In this outline of the most prominent factors involved in particle toxicology, we highlight the differences in the toxic potential among airborne particles and describe what is known about the most notorious toxic agents, such as silica and asbestos. The various biological paths and, consequently, the different outcomes in the health risks associated with inhaled, micron-sized particle and fibers, as well as inhaled nanoparticles, are explained on the basis of form, size, and surface reactivity. The most relevant surface properties addressed here are the potential for free radical generation, the adsorption of endogenous molecules, and the degree of hydrophilicity or hydrophobicity of the various materials.**

KEYWORDS: toxicity, surface reactivity, silica, asbestos, nanoparticles

## PARTICLE TOXICOLOGY

Mineral dusts may severely damage human health. "Particle toxicology" refers to a branch of toxicology dealing with solid particles that enter the body mainly through the upper airways. This field is a distinct area of study because *particle toxicants* act differently than *molecular toxicants*. Particle toxicants come in contact with living matter at their surfaces; hence most mechanisms of interaction are governed by surface chemistry. The surface state of a particle is determined by its history: mechanisms of dust generation, weathering, processing and contaminants. Consequently, materials with the same bulk composition may exhibit quite different surface reactivity and, hence, toxicity.

### Not All Dusts are Equally Toxic

The toxicity of some mineral dusts has been known since very ancient times. Agricola, writing in *De Re Metallica Libri xii* (1556) on the mines in Bohemia, reported, "The dust, which is stirred and beaten up by digging, penetrates into the windpipes and lungs, and produces difficulty in breathing ... If the dust has corrosive qualities, it eats away the lungs and implants consumption in the body. In the Carpatian mines, women are found to have married seven husbands, all of whom this terrible consumption has carried away." Hippocrates' description of the metal digger who breathes with difficulty and Pliny's mention of protective devices to avoid dust inhalation suggest that the danger was known even to the ancient Greeks and Romans.

When we breathe, we introduce airborne particles into the lungs. The nature and amount of these particles depend on where we live and on our working conditions. Obviously, the lower the extent of exposure (duration of exposure and toxicant concentration), the lower is the mineral burden in

our body, and the better it is for our health. Not all mineral particles, however, are equally toxic. Silicosis, the most ancient recognized occupational disease, is caused exclusively by exposure to crystalline silica (Harley and Vallyathan 1996), and today many people are still dealing with the effects, sometimes fatal, of exposure to asbestos (Tweedale 2002).

Both silica and asbestos have some toxic features that they do not share with almost any other mineral dust. In spite of numerous experimental studies in the field, such features

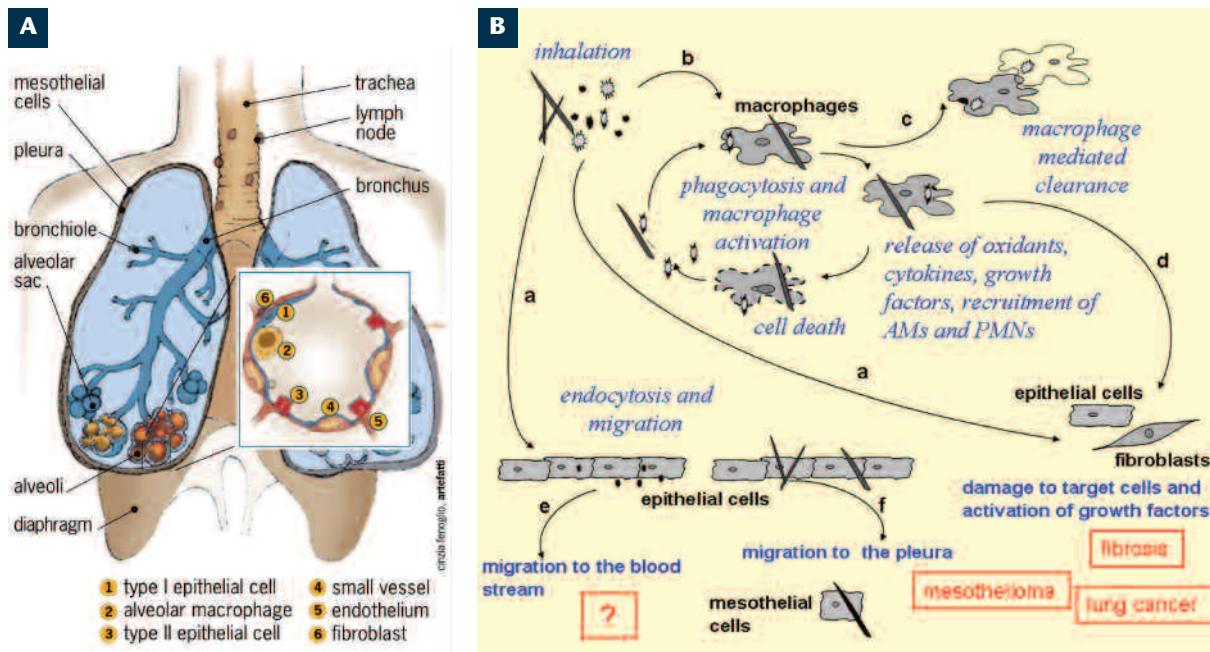
and their mechanisms of action have not yet been fully clarified. Meanwhile, questions arise on the toxic potential of many other dusts, both natural and engineered, to which we might be exposed. Therefore, detailed knowledge of what makes a mineral particle toxic is urgently needed not only to understand the cause of well-known diseases, but also to predict which minerals might be dangerous and to develop inactivation procedures for those whose toxicity is well known.

### The Fate of an Inhaled Particle

Depending upon their aerodynamic diameter, inhaled particles migrate to the alveoli in the deep lung if they are not retained in the upper airways (FIG. 1A). In the alveolar space, depending upon the form, size, chemical composition, and surface state of the particles, several events may follow (FIG. 1B).

The particles may damage type I epithelial cells, the flat cells constituting the wall of alveoli through which gaseous exchanges occur. The particles will also trigger immune defences, causing signals to be sent to alveolar macrophage (AM) cells, which are in charge of engulfing (phagocytosing) and ridding the body of any foreign substances. If they are successful (clearance), there will be no harm; if not, the activated macrophage will eventually die, releasing into its surroundings the particles and many other substances, including factors to recruit new immune-defence cells (AM and polymorphonuclear leukocytes, PMN). A continuous cycle of recruitment and cell death will be established, which causes sustained inflammation that lasts as long as the particle resides in the lung. The causes of the inflammation are the substances released during AM activation—ROS (Reactive Oxygen Species), cytokines, and growth factors—all of which contribute to damaging the surrounding epithelial cells and stimulating abnormal growth of fibroblasts, for example. In the long term, the consequences might be lung cancer and fibrosis.

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**FIGURE 1** (A) Schematic representation of the respiratory tract; the inset shows details of the alveolus. Drawing courtesy of Cinzia Fenoglio, Artefatti, Mannheim, Germany. (B) Effects of size, shape, and surface reactivity on the fate of inhaled particles. Inhaled particles reaching the alveoli come into direct contact with epithelial cells; toxic particles may react directly, with consequent cell damage (path a). The immune system is activated, with alveolar macrophages (AMs) attempting to eliminate the foreign body (path b). Smooth, unreactive particles are removed from the alveolar region by AMs (clearance, path c), while others—typically long fibers and particles with sharp edges—can stress AMs, which eventually die, releasing oxidants, cytokines, and growth factors. AMs and PMN (polymorphonuclear leukocytes) are recruited. A continuous cycle of recruitment and cell death is established, in which products released by AMs damage and/or promote abnormal growth of cells (path d). Phagocytosis is less efficient with nanoparticles, and direct damage of cells is favored (path d). Nanoparticles may overcome the epithelial layer and reach other organs via blood circulation (path e). Fibers like asbestos may reach the pleura and cause mesothelioma (path f).

If the particles have a fibrous habit, the mechanism of the body's response is partly the same as described above; however, shorter fibers will be engulfed by the AMs more easily and removed, whereas longer ones, which AMs cannot engulf successfully, will cause severe damage to both macrophages and epithelial cells, causing fibrosis (asbestosis) and lung cancer. Furthermore, fibers—particularly if they are rigid, long, and thin—may migrate to the pleura, the membrane that covers the lungs, and cause mesothelioma, a fatal neoplasia of pleural mesothelial cells. Mesothelioma may also occur in the peritoneum, the membrane that covers the abdominal organs. Mineral fibers such as asbestos, erionite, and, as recently discovered, fluoro-edenite are the only proven causative agent of this type of cancer.

Inhaled nanoparticles follow somewhat different routes. They are much less likely to be taken up by AMs and, because of their size, they may escape from the lung, travel with circulating blood, and interact directly with various organs. Based on their fate in the body, we may group toxic dusts as follows:

- micron-sized mineral particles
- mineral fibers
- nanoparticles

We will describe briefly the most relevant examples of toxic minerals and highlight open questions concerning their mechanism(s) of action at the molecular scale.

## Which Physicochemical Properties Are Relevant to Toxicity?

### Form, crystallinity, micromorphology

A fibrous habit is relevant to toxicity. In the case of silica, crystallinity is a determinant (little damage is caused by amorphous silica). Other features, such as sharp edges, fractured surfaces, surface defects, and poorly coordinated ions, are comprised in the term “micromorphology”, and govern the surface reactivity and, hence, toxicity of all mineral particles.

### Surface reactivity

The surfaces of both covalent and ionic solids exhibit sites, generated by the interruption of the bulk structure of the mineral, that may react with biological molecules. Freshly ground, abraded, indented, and defective surfaces often expose surface charges, dangling bonds (i.e. surface-bound radicals), and poorly coordinated ions, all of which may covalently react or contribute to adsorbing biomolecules at the cell membranes. In some cases such reactions may cause deleterious effects on cells (Fubini and Otero Aréan 1999).

Such reactivity may be modified by the presence of surface contaminants. One example is the adsorption of polyaromatic hydrocarbons (PAH) at the surface of asbestos fibers, which has been considered to be one of the causes of the synergistic effects observed between cigarette smoke and asbestos as lung carcinogens (Kane 1996). The mechanism involves the generation of ROS during the metabolism of PAH and is similar to what has been described for PAH adsorbed on atmospheric particulates (Marano et al. 2007).

**FREE RADICAL GENERATION** Among all possible reactions, free radical generation is the most strongly implicated in the mechanisms of toxicity. When in contact with biological fluids, many dusts generate free radicals via various mechanisms (Fubini and Hubbard 2003; Schoonen et al. 2006). Free radicals released in proximity to target cells may severely damage membrane and cell functions. Mutations in DNA caused by free radicals constitute one of the first steps towards cancer. Moreover, free radicals may interfere with macrophage-derived ROS and RNS (reactive nitrogen species), producing more toxic entities. The most common mechanisms of free radical generation are:

- the reaction of endogenous hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) with surface-bound transition metal ions leading to the generation of highly reactive hydroxyl radicals (HO•).
- a surface-driven, homolytic rupture of a C–H bond, with generation of carbon-centered radicals in the target molecule (peptides, proteins, etc.)

Conversely, some carbon-based nanoparticles—fullerenes, carbon nanotubes—act as radical quenchers (Lin et al. 1999; Fenoglio et al. 2006). Whether this is beneficial or triggers new toxic mechanisms in vivo is still unclear.

**DEGREE OF HYDROPHILICITY/HYDROPHOBICITY OF THE SURFACE** Hydrophilicity originates in polar chemical functionalities (e.g. SiOH) or under-coordinated metal ions at the surface (Fubini et al. 1993). The distribution of such sites determines the degree of hydrophilicity/hydrophobicity, which is one of the determinants for phospholipids and protein adsorption (which protein will be selectively fixed at the surface, to what extent, etc.) and, in turn, perturbation of cell membranes and cell adhesion. A thermodynamic approach to explain the interaction of several metal oxides with cell membranes has recently been proposed (Sahai 2002). Clearance of particles is also governed by the degree of hydrophilicity (FIG. 1). In the case of nanoparticles, hydrophobicity favors clumping and aggregation in aqueous media (carbon nanotubes are the typical case), whereas hydrophilic nanoparticles, aggregated in air, behave in a complex way in body fluids depending upon size and shape (Parsegian 2006).

#### *Solubility in biological fluids*

“Biopersistence” defines the time of residence of a given particulate material in the body; this time depends upon the effectiveness of the mechanisms of clearance (e.g. mucociliary escalator or macrophages mediate clearance) and solubility. Obviously, the longer the particle remains unaltered in the critical biological compartment, causing stress to cells and tissues, the greater the extent of any adverse effect. Solubility in the body is strongly influenced by the complex composition of fluids encountered by the particles: drastic differences in pH, in ionic strength and composition, and in organic molecule contents (e.g. proteins, aminoacids, antioxidants) are present among intracellular and extracellular fluids. Plumlee et al. (2006) provide a complete description of factors that may influence the biopersistence of mineral particles in the various compartments of the body.

## **MICRON-SIZED MINERAL PARTICLES**

### ***Silica: The Cause of the Oldest-Recognized Occupational Disease Still Has Aspects To Be Unveiled***

#### *Health effects of silica*

Silicosis, the most ancient occupational disease, is not caused by all types of silica, but only by a subset of its crystalline polymorphs, namely quartz, tridymite and cristobalite. The high-pressure forms, coesite and stishovite, are less toxic and may even be inert. Lung cancer (IARC 1997) and some autoimmune diseases have also been associated with exposure to silica. In spite of a massive body of work since the early 1950s on the pathogenicity of silica-related diseases, there is no consensus on the mechanism of action of crystalline silica particles at the molecular level. Several physicochemical features have been hypothesized to cause silica pathogenicity, but none of these can explain the available toxicity data (Fubini 1998a). Recent studies show that numerous particle features, such as free radical generation, hydrophilicity and metal impurities, are involved in

overall toxicity, and each acts at different levels in the pathogenic process. For more details, see a recent issue of the *Journal of Environmental Pathology, Toxicology and Oncology* (volume 20/1, 2001), which is completely devoted to silica pathogenicity.

#### *A long-lasting debate on the variability of the crystalline silica hazard*

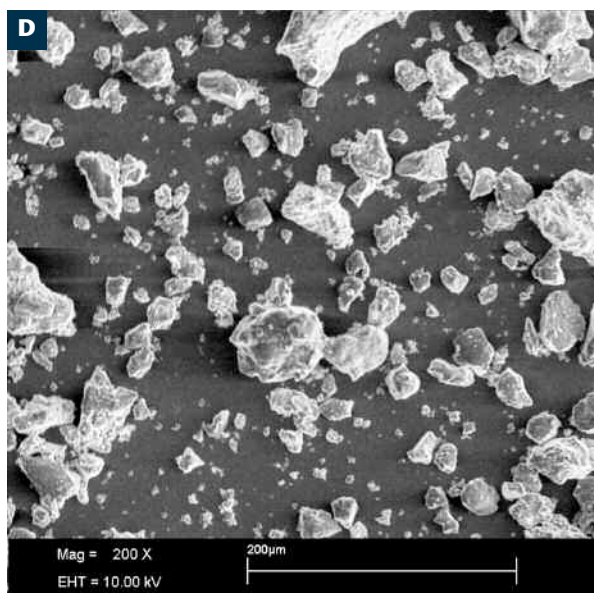
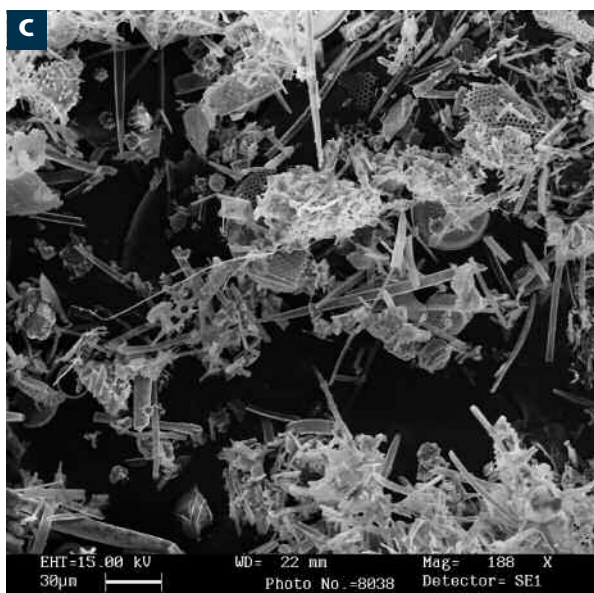
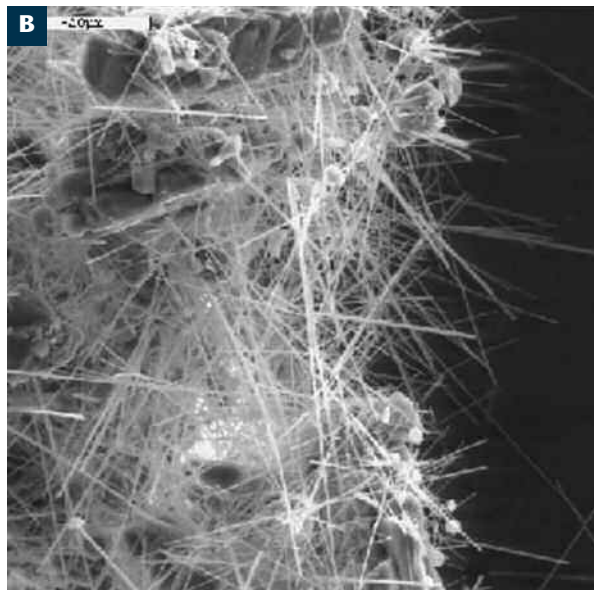
Carcinogenicity to humans due to crystalline silica was not proven in all industrial circumstances examined, and therefore the International Agency for Research on Cancer, while classifying quartz and cristobalite in class 1 (carcinogenic to humans), also stated, “Carcinogenicity may be dependent on inherent characteristics of the crystalline silica or on external factors affecting its biological activity or distribution of its polymorphs” (IARC 1997). The “inherent characteristics” of the silica may be accounted for by the state of the external surface (defects, chemical functionalities, etc.) or by the origin of the sample, while the “external factors” suggest that contact, association or contamination by substances other than silica might activate (or blunt) silica carcinogenicity. The term “variability of quartz hazard” (Donaldson and Borm 1998; Fubini 1998b) has since been adopted by the scientific community, and several studies devoted to determining what makes a silica particle toxic have been carried out. These studies show how several cellular responses related to toxicity and various inflammatory and fibrosis markers are not exhibited upon exposure to all silica dusts, and they also show that these responses are extremely variable among the different species of silica. For example, these properties were observed to vary not only among different polymorphs, but also among different dust sources. Variation was also observed among surface modifications of the same specimen, and even within dusts of a single polymorph, apparently from the same source (Daniel et al. 1995; Bruch et al. 2004; Fubini et al. 2004). While the various effects elicited by these particles are regulated by different properties (Bruch et al. 2004), they all appear to be inhibited by surface modifications obtained by using the well-known silicosis antidotes, the polymer PVPNO and aluminium salts (Albrecht et al. 2002; Knaapen et al. 2002). These observations underscore the critical role played by the surface of the particles in the mechanism.

Surprisingly, quartz nanocrystals prepared under hydrothermal conditions were less toxic than larger particles, even when compared at equal mass, in experimental work by Warheit et al. (2007). This confirms that “nano” does not always mean more toxic. These hydrothermally prepared particles are smooth, with all valences satisfied by the surrounding medium, and thus quite different from the sharp particles generated by abrasion and grinding (FIG. 2D). Interestingly, two nanocrystal samples, apparently prepared in the same way, exhibited different toxicity, confirming the “variability of quartz hazard” even in silica nanoparticles.

#### *The chemical basis of variability and the most hazardous sources of silica dust*

The substantial covalence and flexibility of the Si–O bond in silica accounts for the variety of crystalline polymorphs and for the large number of amorphous silica forms. This is also reflected in the variety of surface functionalities that may be found at a silica surface: silanols (SiOH) and siloxane (Si–O–Si), which govern hydrophilicity and hydrophobicity, respectively, and surface radicals and metal ion trapping charges, which may generate free radicals (Fubini 1998a). These functionalities may react with various biomolecules, such as components of lung surfactant including dipalmitoylphosphatidyl-choline (Murray et al. 2005) and antioxidants (Fenoglio et al. 2003).





**FIGURE 2** Some minerals of concern: (A) balangeroite, a nonregulated asbestiform mineral (adapted from Groppo et al. 2005); (B) fluoro-edenite, a new carcinogen found close to the Etna volcano (Biancavilla, Sicily, Italy, adapted from Burrigato et al. 2005); (C) commercial sample of diatomaceous earth: the silica content is partly converted to cristobalite, but most of the original diatom's shape is retained; (D) cristobalite particles of mineral origin obtained by grinding. (B), (C), and (D) are scanning electron microscope images.

Freshly ground dusts contain the most reactive surface sites (Fubini 1998a). Castranova et al. (1996), in a set of experimental studies, demonstrated much higher toxicity in freshly ground particles. Conversely, it was shown that quartz is not pathogenic when associated with kaolinite (Wallace et al. 1994). Pretreatment of a highly pathogenic quartz sample with extract of either coal mine dust or kaolin significantly reduced quartz-induced inflammatory responses in rats (Stone et al. 2004). The reactivity of different types of surface sites on silica polymorphs has been modelled using *ab initio* electronic structure theory or classical molecular simulation methods. When combined with the results of experimental spectroscopic studies, these methods can provide insight into fundamental molecular-level processes (Civalleri and Ugliengo 2000; Murashov 2003; Rignanese et al 2004; Sahai and Rosso 2006).

### Diatoms and diatomaceous earth: The largest silica source in the world

Diatomaceous earth (from diatoms) is the most common silica of biogenic origin (Fig. 2C). When amorphous, it is not dangerous, but if converted into a crystalline form, it may be of concern. Various commercial dusts of biogenic origin sold under the name of Kieselguhr and Celite™, are in fact made up mainly of cristobalite, which is readily formed from the amorphous phase during processing. A significant variability in cellular response to various sources of diatomaceous earth suggests that factors other than the presence of cristobalite, such as metal impurities, hydrophobicity and free radical generation, may be involved in their toxicity (Fubini et al. 2001).

### Other Hazardous Mineral Dusts

Other dusts that may cause adverse pulmonary responses but have not been officially reported as human carcinogens include coal (coal workers' pneumoconiosis, reviewed recently in Huang et al. 2006), kaolinite, talc, and iron oxides (siderosis). The etiology (cause) of diseases that follow the inhalation of such minerals is often not well defined, because epidemiological studies are complicated by co-exposure to other minerals such as quartz and asbestos (Ross et

al. 1993). Mixed mineral dusts are present in air pollution, and their toxic potential is related to chemical composition. A study on particles from different stone quarries in Scandinavia revealed that the inflammatory potential was dependent upon the mineral composition and/or metal content (e.g. Fe, V and Cu) of the particles (Hetland et al. 2000).

Attention has been focused recently on some minerals (pyrite, forsterite, fayalite, hematite) that are reported to generate oxygenated free radicals in solution (Schoonen et al. 2006). Since free radical generation is recognized as one of the factors that contribute to the adverse effects of minerals with known toxicity (e.g. asbestos and quartz), a possible toxicity has been hypothesized for these other minerals (pyrite, forsterite, etc.) even though no adverse health effects on people exposed to these minerals have been reported.

Such problems may also arise on other planets. It was recently reported that basaltic minerals present on the surface of the Moon and Mars produce hydrogen peroxide if ground up and placed in water (Hurowitz et al. 2007). The authors point out a possible health risk for astronauts who might inhale dust of extraterrestrial origin.

### Volcanic Ash and Other Natural Dusts

Volcanoes produce nano- to micron-sized particles, including crystalline silica, that may have toxic potential. The particles of volcanic ash are fragmented upon eruption, producing fresh, reactive surfaces that are not oxidized—a rarity in the natural environment. Epidemiological and toxicological studies show that the health risk of volcanic ash containing crystalline silica does not correlate with the crystalline silica content. This result may be due to several factors, among them the presence of other minerals, especially aluminium-containing clays (Horwell and Baxter 2006), which are known to protect against silicosis (Wallace et al. 1994). Conversely, iron in

volcanic ash may impart a high reactivity by generating hydroxyl free radicals through the Fenton reaction (Horwell et al. 2003).

Furthermore, few studies have been published on the health effects caused by long-term inhalation of dusts generated in desert areas. More research has to be done to understand the basis of the so-called desert lung syndrome, a pneumoconiosis that affects several million people in northern China (Derbyshire 2001).

## MINERAL FIBERS

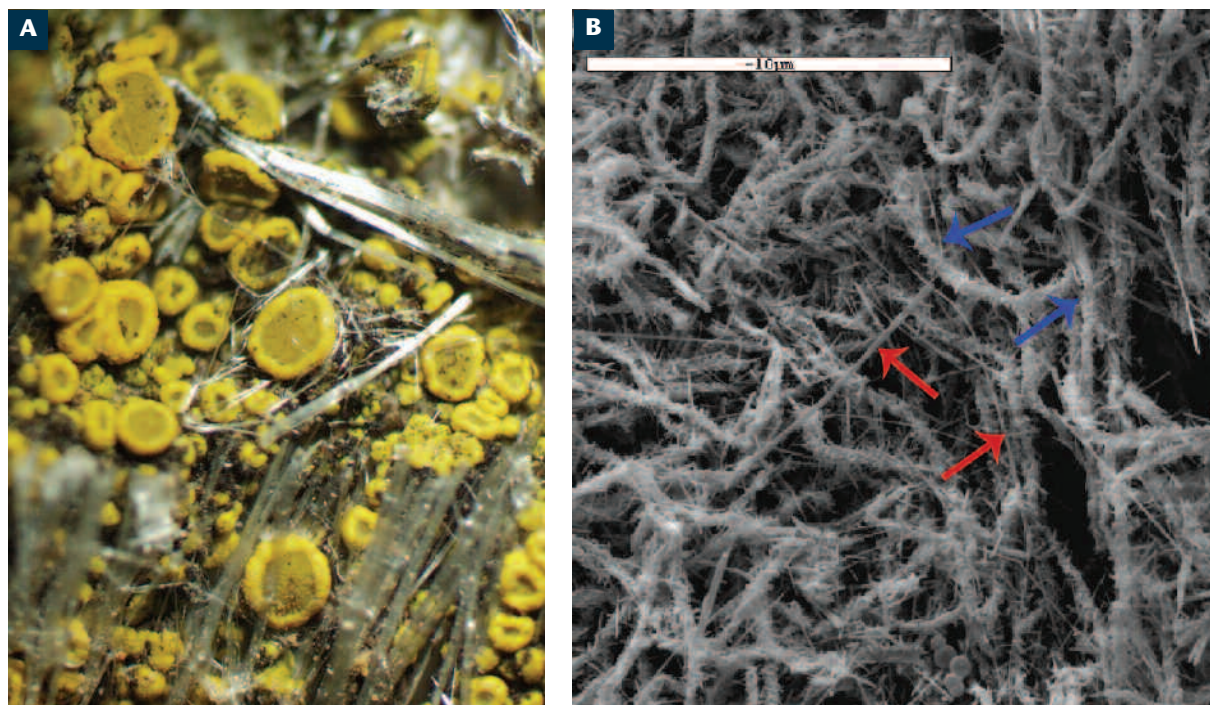
### Is a Fibrous Habit Dangerous?

For a long time, asbestos toxicity was assumed to be due simply to its fibrous habit. Consequently, all fiber types were supposed to threaten our health. A fibrous habit is an adverse feature (FIG. 1), but other characteristics must be present to render a given fiber toxic. Among the large variety of fibers to which people may be exposed, only a few are pathogenic, mostly the natural crystalline forms.

### Asbestos, the Most Potent of Solid Carcinogens

Asbestos is the general industrial term encompassing six different natural fibrous silicates. Amosite [grunerite,  $(\text{Fe},\text{Mg})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$ ], crocidolite [riebeckite,  $\text{Na}_2(\text{Fe},\text{Mg})_3\text{Fe}_2\text{Si}_8\text{O}_{22}(\text{OH})_2$ ], tremolite [ $\text{Ca}_2\text{Mg}_5\text{Si}_8\text{O}_{22}(\text{OH})_2$ ], anthophyllite [ $(\text{Mg},\text{Fe})_7\text{Si}_8\text{O}_{22}(\text{OH})_2$ ] and actinolite [ $\text{Ca}_2(\text{Fe},\text{Mg})_5\text{Si}_8\text{O}_{22}(\text{OH})_2$ ] all belong to the amphibole mineral group, while chrysotile [ $(\text{Mg}_6(\text{Si}_4\text{O}_{10})(\text{OH})_8$ ] is a serpentine.

These minerals were exploited largely in the past century in industrial applications because of their versatile and unique properties. Nowadays, asbestos is associated with its potency to cause asbestosis, a debilitating and often fatal lung disease, and malignancies such as lung cancer and pleural mesothelioma, which may appear several decades after exposure.



**FIGURE 3** Fungi and lichens growing on asbestos. Metal chelators produced by some soil fungi and lichens strongly modify the chemical composition of the fibers, binding and depriving them of iron and magnesium. (A) *C. vitellina*, a lichen growing selectively on chrysotile asbestos fibers protruding from serpentinite from Balangero

(Piedmont, Italy) (adapted from Favero-Longo et al. 2005) (B) Scanning electron micrograph showing the fungal hyphae of *Oidi dendron maius* (blue arrows) intertwined with crocidolite asbestos fibers (red arrows) of various sizes (adapted from Martino et al. 2004).



It is noteworthy that a strong synergistic effect between cigarette smoke and asbestos has been proven for lung cancer but not for mesothelioma (Kane 1996).

Asbestos refinement and use is being restricted progressively or banned by several countries, including the entire European Union, which banned asbestos use in 2005. Conversely, in several developing countries, asbestos is still widely produced and used (Vogel 2005). It is noteworthy that some countries (e.g. Canada and Russia) are still producing and exporting chrysotile asbestos. The carcinogenicity of chrysotile has been a matter of hot debate during the past decades within the scientific community (Mossman et al. 1990 and related comments; Tweedale and McCulloch 2004), and the debate is ongoing. A whole book was devoted to it by the Mineralogical Association of Canada in 2001 (Nolan et al. 2001). There is general agreement that chrysotile is less potent in causing mesothelioma, but there is no clear-cut evidence of its lower toxicity in causing asbestosis and lung cancer. Epidemiological studies too, are somehow controversial (Hodgson and Darnton 2000; Tweedale 2002; Berman and Crump 2003; Terracini 2006; Hein et al. 2007). The carcinogenicity of chrysotile is nowadays unquestionable, but several studies show variability from one source of the mineral to another (Nolan et al. 2001). Another debate concerns the role played by associated contaminants on the overall carcinogenicity caused by chrysotile, since extremely pure chrysotile samples cannot be found in nature.

#### *Fiber length and toxicity: Are all sizes equally dangerous?*

The debate on the role of fiber form and length on lung toxicity started up shortly after animal testing by Wagner (1971), which showed that all forms of asbestos were potent carcinogens. At first it was assumed that carcinogenicity was attributable solely to fibrous habit. Stanton et al. (1981) stated that long (>8 µm) and thin (<0.25 µm) fibers were by far the most dangerous. The "Stanton Hypothesis" is still valid today, but other factors such as chemical composition, reactivity, and biopersistence have been found to play a major role in the ultimate toxicity of a given fibrous mineral (Kane 1996; Kamp and Weitzman 1999). Short fibers are successfully taken up by AMs and cleared out of the lung, whereas long ones undergo repeated unsuccessful phagocytosis attempts (Fig. 1).

The debate over this issue continues today. Small fibers associated with longer ones have been found in the lungs of humans (Suzuki et al. 2005). Whether the short fibers are merely the consequence of the splitting of longer fibers *in vivo*, or whether they actually contribute to the adverse response is difficult to establish. Several studies, however, suggest that all fiber sizes, to a greater or lesser extent, may contribute to asbestos toxicity (Dodson et al. 2003; Suzuki 2005). Under some circumstances (e.g. weathering and mechanical stress) chrysotile fibers split into a large number of nanofibrils; no data are available so far on their toxicity.

#### *The role of iron in the mechanism of toxicity*

Iron ions are present in all asbestos minerals, either as a stoichiometric component or substituting for Mg<sup>2+</sup>. Some surface iron ions constitute the catalytic sites where free radical and ROS generation takes place (Fubini and Otero Aréan 1999). A large portion of the scientific community, as illustrated by the exhaustive reviews appearing on the subject (Hardy and Aust 1995; Kane 1996; Kamp and Weitzman 1999), agrees on the crucial role played by iron in asbestos toxicity.

#### *Detoxification of asbestos in nature*

Because of its previous widespread applications, asbestos is still present in many settings, such as abandoned mines, factories, and asbestos-cement roofing. New, environmentally friendly inactivation strategies must be found for asbestos dispersed in large tracts of soil. Soil fungi and lichens have been investigated because of their capacity to generate selective chelators, including siderophores, when exposed to asbestos (Favero-Longo et al. 2005; Daghino et al. 2005), and they have been found to modify the bulk structure of fibers and their potential to release free radicals and damage DNA (Daghino et al. 2005). Lichens grow selectively on chrysotile fibers (Fig. 3) (Favero-Longo et al. 2005), secreting oxalic and other chelating lichenic acids, which progressively extract Fe and Mg. When tested at higher concentration in the laboratory, such chelating molecules were able to transform the fibers into an amorphous, non-fibrous material (Turci et al. 2007).

#### *Asbestiform Minerals: A Potential New Hazard*

Several minerals besides those comprised in the term asbestos may crystallize with a fibrous habit. Some occur only locally and are associated with other fibers, so the impact of human exposure to this kind of fiber alone is not known. However, if these fibers become airborne as a consequence of construction work, land removal, etc., they may constitute a serious hazard for human health. A recent, multidisciplinary project has shown that balangerite [(Mg,Fe<sup>2+</sup>,Fe<sup>3+</sup>,Mn<sup>2+</sup>)<sub>42</sub>Si<sub>16</sub>O<sub>54</sub>(OH)<sub>36</sub>], a fiber typical of the Balangero mine area, shares most of the features involved in the toxicity of asbestos (Fig. 2A) (Groppo et al. 2005; Turci et al. 2005).

#### *Erionite: A Dangerous Zeolite*

Erionite [K<sub>2</sub>NaMgCa<sub>1.5</sub>(Al<sub>8</sub>Si<sub>28</sub>)O<sub>72</sub>•28H<sub>2</sub>O] is a zeolite, but compared to asbestos is equally toxic (Carbone et al. 2007). Its carcinogenic potency resides in its needle-like shape and the surface chemistry that the particle triggers in contact with biological matter. As with asbestos, the precise molecular mechanism is still partly unclear. At its surface, erionite normally contains only traces of iron, acting as a catalytic centre for free radical generation, resulting in DNA mutations and cancer.

#### *A New Toxic Fiber from Sicily*

In a rural area near the Mt. Etna volcano, Sicily, an excess of mesotheliomas was found among people who had never had an occupational exposure to asbestos. A thorough investigation found that a white dust obtained from stones close to the village of Biancavilla had been widely used to white-wash houses. Unfortunately, this dust was found to be rich in fluoro-edenite [NaCa<sub>2</sub>Mg<sub>5</sub>(Si<sub>7</sub>Al)O<sub>22</sub>F<sub>2</sub>], a new asbestiform mineral (Fig. 2B). It is likely that these fibers acted as carcinogens, like erionite and asbestos (Burrigato et al. 2005).

#### **NANOPARTICLES: A NEW HAZARD**

Nanoparticles (NPs) are not, as the media report, a toxic entity per se merely due to their size; nor are they all toxic. The potential toxicity of nanoparticles generated by new nanotechnologies has recently been strongly emphasized (Nel et al. 2006). This is in view of the large amount of engineered NPs that will soon be on the market for various purposes, including applications in biomedicine. Many particle toxicologists have moved to research on NPs, and studies on urban air pollution have been revisited to investigate whether the nano-sized fraction could be the most dangerous component. When going from micron- to nano-sized particles of the same composition (e.g. titania, carbon particles, etc.), a greater toxicity to experimental animals and

cell cultures has been reported (Oberdöster et al. 2005; Singh et al. 2007). This increased toxicity, however, is sometimes due only to the fact that a given mass of nanoparticles has larger exposed surface areas than the same mass of larger particles. This is typical of low-toxic dusts like TiO<sub>2</sub>. In this case, it can also be shown that a particular biological response elicited, e.g. the IL-8 expression in epithelial cells following stimulation with TiO<sub>2</sub> particles (Singh et al. 2007), is a surface-driven effect. However a reduction in size may also cause the generation of a large amount of reactive “edge” and “corner” sites and, consequently, a more pronounced reactivity per unit surface area. Only occasionally does a truly new reactivity arise at the nanoscale (Fubini et al. 2007). Recent experimental evidence indicating that in exposed rats some nanoparticles reached the brain through the olfactory nerve, thus overcoming the blood brain barrier, suggests quite a new scenario for nanoparticle toxicity (Oberdöster et al. 2005). The lines of action in this field are starting to be defined (Maynard et al. 2006).

Few studies are devoted to NPs in the environment as humans have always been exposed to some nano-sized particles in nature and from “anthropogenic” sources (Hochella and Madden 2005). Information on the real risk associated with exposure to nanoparticles may result from tailored studies on, for example, the effect of NP-rich volcanic emissions on the exposed population.

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