Toxicity of Mineral Dusts and a Proposed Mechanism for the Pathogenesis of Particle-induced Lung Diseases.

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Humans will set foot on the moon again. The lunar surface has been bombarded for 4 billion years by micrometeoroids and cosmic radiation, creating a layer of fine dust having a potentially reactive particle surface. To investigate the impact of surface reactivity (SR) on the toxicity of particles, and in particular, lunar dust (LD), we ground 2 Apollo 14 LD samples to increase their SR and compare their toxicity with those of unground LD, TiO2, and quartz. Intratracheally instilled at 0, 1, 2.5, or 7.5 mg/rat, all dusts caused dose-dependent increases in pulmonary lesions, and enhancement of biomarkers of toxicity assessed in bronchoalveolar lavage fluids (BALF). The toxicity of LD was greater than that of TiO2 but less than that of quartz. Three LDs differed 14-fold in SR but were equally toxic; quartz had the lowest SR but was most toxic. These results show no correlation between particle SR and toxicity. Often pulmonary toxicity of a dust can be attributed to oxidative stress (OS). We further observed dose-dependent and dust-cytotoxicity-dependent increases in neutrophils. The oxidative content per BALF cell was also directly proportional to both the dose and cytotoxicity of the dusts. Because neutrophils are short-lived and release of oxidative contents after they die could initiate and promote a spectrum of lesions, we postulate a general mechanism for the pathogenesis of particle-induced diseases in the lung that involves chiefly neutrophils, the source of persistent endogenous OS. This mechanism explains why one dust (e.g., quartz or nanoparticles) is more toxic than another (e.g., micrometer-sized TiO2), why dust-induced lesions progress with time, and why lung cancer occurs in rats but not in mice and hamsters exposed to the same duration and concentration of dust.