MARTIAN DUST AND ITS INTERACTION WITH HUMAN PHYSIOLOGY: AN EMERGENCY PHYSICIAN'S PERSPECTIVE. Peter A. Sim, MD, FACEP, peteralansim@gmail.com

Introduction: Adverse health effects are to be expected when unprotected humans are exposed to significant amounts of Martian dust. Primary prevention of exposure by engineering reliable barriers (e.g., EVA suits, habitat construction, electronic dust shields, filtration of inspired atmosphere) is of critical importance. But inevitably, barriers will be compromised and exposures will occur. Because of delayed communication with Mission Control, prompt and proven medical interventions should be instituted by a self-reliant crew trained to the physician level for common, treatable-on-Mars emergencies, including dust exposures.

Astronauts have had contact with extraterrestrial dust only during the Apollo program. Harrison Schmitt experienced the noxious effect of inhaled lunar dust during Apollo 17 —"lunar dust hay fever" [1], and the abrasive, micron-sized electrostatic dust on the moon will be a significant challenge for inhabitants of a future lunar base.

Characteristics of Martian Dust: Although Martian dust has yet to be exhaustively analyzed, we do know it is abrasive, electrostatic, magnetic, highly oxidative and chemically reactive, containing known harmful ingredients like fine silicate materials, gypsum, perchlorates, and trace amounts of hexavalent chromium [Cr(VI)], arsenic, cadmium and beryllium. Based on a survey of EPA exposure risk estimates, the elements that are toxic at the lowest concentrations are hexavalent chromium (Cr VI), arsenic (As), cadmium (Cd), and beryllium (Be) [2].

It appears that Martian dust is of uniform chemical composition regardless of its location on the fourth planet. Soil analyses from three landing sites separated by thousands of kilometers are quite uniform [3]. This is likely due to the recurring global dust storms, which act like a giant mixing bowl. From multispectral imaging the average diameter of airborne Martian dust is 3.4 microns [4], and particles of this size would remain suspended in the thin atmosphere almost indefinitely at most wind speeds [5].

The respiratory system, gut, eyes, and skin are most at risk from exposure to Martian dust, and systemic absorption of toxins from any of these sites is possible. I will briefly and individually discuss the currently understood hazards and treatments of the most toxic components of Martian Dust.

Specific Toxic Effects of Martian Dust: The respirable particle average concentration of inhaled air (currently set at 1 mg/m3) must be carefully controlled, in order to be within the acceptable risk range for multiple potential toxins [6]. Pulmonary inflammation and fibrosis may result from inhalation exposure to a variety of mineral dusts, and primary prevention is key, since only symptomatic therapy is available for established disease. Inhaled silicates may eventually result in a variety of forms of silicosis, a restrictive lung disease. Gypsum inhalation may cause illness similar in pathophysiology to "black lung", or coal worker's pneumoconiosis.

Perchlorates: These compounds were first discovered in Martian soil by the Phoenix lander (May 2008), and in orders of magnitude greater concentration than found anywhere on Earth. As much as 1% of the soil's weight in some locales may be perchlorate [7]. The highly oxidized chlorine blocks thyroid function by diminishing the body's ability to absorb iodine, which is essential for thyroid hormone production. Potassium perchlorate was medically prescribed as a treatment for hyperthyroidism in the 1950's-60's, but a small number of patients developed aplastic anemia and agranulocytosis, and it was replaced with better-tolerated antithyroid agents. Medical opinion is divided on the true threat of Martian perchlorate, except for fetuses, infants and children, where hypothyroidism can result in irreversible mental impairment. Monitoring of Martian astronauts' perchlorate blood levels will be warranted.

Chromium VI: Hexavalent chromium is genotoxic, causing structural and mutagenic changes in DNA (7). Acute toxicity is a result of its strong oxidative properties. To determine if there is a substantial threat to astronauts from this compound, precise measurements of hexavalent chromium concentration in Martian dust are necessary, either in-situ or on samples returned to Earth. Assuming Cr(VI) is present at a concentration of 150 ppm in 1 mg/m3 respirable particulate matter (8), a 2 year exposure is estimated to result in a cancer risk of 5/100,000. The NRC's Committee on Precursor Measurements Necessary to Support Human Operations on the Surface of Mars places that risk in the middle of its acceptable risk range (9).

The lungs are most affected by chronic chromium exposure, resulting in a pneumoconiosis — disease due to the inhalation of dust, characterized by coughing, inflammation, and reactive fibrosis (10). Breathing hexavalent chromium increases the risk of lung cancer (especially squamous cell carcinoma) and bron-

chospasm/asthma. The permissible exposure limit (OSHA) for airborne Cr(VI) is 5 micrograms/m3 (11). An acutely toxic inhalation of chromium fumes demands evacuation from further exposure, O2, ventilatory support, albuterol for bronchospasm, and continuous positive airway pressure if noncardiogenic pulmonary edema ensues (12). Repeated ingestion of chromium VI over time is linked with oral cavity and small intestine cancers, and liver toxicity. (13). Because it is a known corrosive and may result in mucosal burns, an acute overdose (on Mars) should be addressed with gastric decontamination, but emesis is contraindicated due to possible gastric or esophageal rupture. If within 1 hour of ingestion, dilution and careful nasogastric lavage with a 10% ascorbic acid solution is indicated since ascorbate converts Cr(VI) —> Cr(III), which is nontoxic (14). Continued doses of vitamin C, 1 gram every 20 minutes x 3, preferably IV (11) are given. Since vitamin C is well absorbed orally, repeat oral doses of ascorbate might also be beneficial, if IV dosing is unavailable. Oral ascorbate has been shown to prevent chromium toxicity in rats (15). Forced diuresis with urine alkalization (to pH 7.5) enhances elimination and helps prevent acute tubular necrosis if erythrocyte hemolysis is present. IV (or oral) n-acetylcysteine (Mucomyst) in the same doses as used for acetaminophen toxicity has been shown to boost urinary elimination in an animal model (16). Chelation therapy with dimercaprol or EDTA is not effective (17).

Cr(VI) surface exposure may damage the skin and nasal epithelium (18). Skin is washed copiously with soap and water, followed by a 10% topical ascorbic acid solution. Once skin exposure ceases, chromium-induced skin ulcerations typically heal spontaneously in weeks to months For chronic low-level exposure, the nasal septum is protected from corrosive necrosis and eventual perforation by daily nasal irrigation followed by barium or zinc ointment applied to the septum (19).

Arsenic: There is a dose-dependent correlation between various forms of cancer (skin, lung, liver, kidney, and bladder) and chronic arsenic exposure (20). A small but measurable increased risk for bladder cancer occurs at 10 ppb (the WHO recommended limit in drinking water). Acute arsenic poisoning symptoms include abdominal pain, vomiting and diarrhea (often bloody), and encephalopathy. Chronic poisoning presents with abdominal pain, diarrhea, darkened and thickened skin, numbness, heart disease, and cancer (20). For acute poisoning, dimercaptopropane sulfonate (DMPS) or dimercaptosuccinic acid (DMSA) are recommended chelating agents (21).

Cadmium: There is no known biological function for cadmium, Classified as a human carcinogen, any exposure is to be avoided. The OSHA PEL for people occupationally exposed to cadmium is 5 µg/m3 (fumes). Over-exposure may occur even in environments with trace amounts of the metal, and inhalation or ingestion is linked to cardiovascular disease, hypertension, early atherosclerosis (22), and kidney disease (23). The neurological, respiratory, gastrointestinal, and reproductive systems are also affected. It is possible cadmium interferes with hormone signaling pathways, thereby disrupting various parts of the endocrine system. Cadmium is a catalyst in forming reactive oxygen species, increasing lipid peroxidation and depleting antioxidants, glutathione and protein-bound sulfhydryl groups, as well as promoting the production of inflammatory cytokines.(24)(25)

Inhaling cadmium-containing dust can quickly lead to pulmonary and irreversible renal problems, and even death from renal failure. Acute inhalation exposure is treated in standard supportive fashion: fluids, oxygen, and mechanical ventilation if necessary.

A flu-like illness ("metal fume fever" or "the cadmium blues") results from inhaling cadmium fumes; spontaneous resolution of symptoms in about a week will occur if exposure ceases. More severe inhalation exposures may produce a pneumonitis or pulmonary edema.
Immediate poisoning, with damage to the kidneys and liver, result from ingestion. Timely emesis or gastric lavage is indicated. Activated charcoal is not effective (26).

Cadmium exposure may be measured indirectly with the urinary beta-2 microglobulin test, and monitoring astronauts' levels makes sense until the cadmium situationion on Mars is fully elucidated. Blood or urine cadmium levels provide a better evaluation following acute poisoning.

Beryllium: The Be (2+) ion, small and highly charged, easily enters cells and tissues, and appears to target cell nuclei. Because of chemical similarity to magnesium, beryllium may displace magnesium from many enzymes (among those are enzymes used for synthesizing DNA), thereby altering their function (27). Once beryllium is absorbed into the body, there is no current method for removing it (28).

Beryllium and beryllium compounds are considered Category 1 carcinogens by the International Agency for Research on Cancer. OSHA has published permissible exposure limits (time-weighted averages and peak levels). The level immediately dangerous to life and health is 4 mg/m3. Beryllium dust or powder is well known to be toxic, and acute beryllium disease presents as a chemical pneumonitis. Susceptible individuals (there appears to be a genetic component to

beryllium sensitivity) experience a cell-mediated immune response resulting in pulmonary fibrosis. Chronic beryllium disease (CBD, or Berylliosis) is an allergic response of the lungs to exposure, causing granuloma formation and a restrictive lung disease resembling sarcoidosis. Lung cancer may ultimately be induced. CBD may present over a variable period of time (week to decades), with shortness of breath, cough, chest pain, fever and weight loss being prominent symptoms.

Eye and Cutaneous Exposures to Martian Dust: Because the highly oxidative and caustic Martian dust may burn the cornea and exposed skin (similar to lye or bleach), it is essential to have ready access to prolonged eye and cutaneous irrigation. For eye irrigation, lactated Ringer's (Hartmann's) solution is preferred due to its low cost, tolerability, and close to neutral pH, but normal saline solution (or even plain water if the other solutions are unavailable) may be used to flush out debris and neutralize the pH. The skin may be washed with soap and water, followed by continued irrigation with water. Total removal and neutralization of a concentrated alkali or acid on either the cornea or dermis may take hours of irrigation. Checking the pH of the affected area with litmus paper may help to define an end point.

Conclusions: We have not completely characterized the chemical composition of Martian dust, or the concentrations of known (and possibly as yet unknown) toxic constituents. A return of dust and regolith samples to Earth for analysis would be ideal. Keeping humans and Martian dust apart, with no direct exposure, will be the goal. If barriers are breached (almost inevitably), astronauts must be equipped with the knowledge and resources to institute specific emergency response plans on their own.

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