“Martian Dust Toxicity: Should We Believe the Headlines?”

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Environmental Sciences Branch Chief
NASA-Johnson Space Center
“Toxic Mars: Astronauts Must Deal with Perchlorate on the Red Planet”

“Staying Healthy on the Red Planet”
A chemical found in Martian soil might make it more dangerous to establish a permanent settlement there.

“Mars mission dangers set out”
Planners of the first human mission to Mars will have to worry more about hexavalent chromium – the toxic waste in the movie Erin Brockovich – than about hostile Martians. To assess that danger, NASA should measure levels of hexavalent chromium in Martian dust, says a new report from the US National Research Council.

“Mars Red Dust Could Be Most Deadly Thing Humans Will Face One Day”

‘The Martian' just scratches surface of danger on Mars

If the amount of perchlorate that’s in the soil of Mars were in your backyard, the EPA would turn your yard into a Superfund site. The perchlorate level of Mars is thousands of times higher than the highest limit that’s acceptable for human exposure.
“I think dust is probably one of our greatest inhibitors to a nominal operation on the Moon. I think we can overcome other physiological or physical or mechanical problems except dust.”

Gene Cernan, Apollo 17 Technical Debrief
Properties of Mineral Dusts Relevant to Toxicity

- **Form**
  - Size
  - Fibrous habit (e.g. asbestos)

- **Crystallinity**
  - Crystalline silica is highly toxic, amorphous silica generally not.

- **Micromorphology**
  - Sharp edges
  - Fractured surfaces
  - Surface defects
  - Poorly coordinated ions

  \[
  \text{Surface Reactivity}
  \]

- **Poor Solubility in biological fluids**
  - Biopersistence

- **Additional chemical components within the matrix**
Lunar Dust Investigations

- 2005 formation of the “Lunar Airborne Dust Toxicity Assessment Group” (LADTAG)
- 2005-2013: Extensive Lunar Dust Investigations by Toxicologists/Geologists
- Intratraecheal and inhalation exposures to actual lunar material with rats. Extensive attempts to restore and reflect native surface reactivity.
- NASA adopted $0.3 \text{ mg/m}^3$ for lunar dust as a permissible exposure limit (PEL).

Toxicology

- How will crew be exposed to lunar dust (risk assumptions)?
- How toxic is lunar dust relative to well-studied reference dusts?
- What is the toxicity of lunar dust in rats, and how would those findings relate to crew exposure standard?

Geology

- What is a “representative” lunar dust for LADTAG purposes?
- What properties of lunar dust need to be characterized?
- How should lunar dust be prepared for toxicity testing?
Human Research Program

Lunar Dust Exposure Standard Language
(NASA Standard 3001 Vol. 2)

Take-Aways: (1) Relative Toxicity
Quartz (0.1 mg/m$^3$ PEL) > **Lunar Dust** (0.3 mg/m$^3$ PEL) > Titanium Dioxide (15 mg/m$^3$ PEL)

Take-Aways: (2) Surface Reactivity
Surface Preparation Did Not Appreciably Affect Toxicity!

6.4.4.2 Lunar Dust Contamination [V2 6053]

The system **shall** limit the levels of lunar dust particles less than 10 μm in size in the habitable atmosphere below a time-weighted average of 0.3 mg/m$^3$ during intermittent daily exposure periods that may persist up to 6 months in duration.

Rationale: This limit was established based on detailed peer-reviewed studies completed by the Lunar Airborne Dust Toxicity Assessment Group (LADTAG), and is specific to the conditions relevant to the lunar surface (i.e., this standard would not necessarily be applicable to other missions). The standard assumes that the exposure period is episodic, and is limited to the time before ECLSS can remove the particles from the internal atmosphere (assumed as 8 hours post-introduction). Although the standard is being conservatively applied to all inhalable particles (all particles ≤10 μm), it is most applicable to dusts in the respirable range (≤2.5 μm) that can deposit more deeply into the lungs. Studies show that the particle size of lunar dust generally falls within a range of 0.02-5 μm.
Anticipating Martian Dust Experience

- <1 to 5μm, average 3.2μm for suspended dust
- Martian gravity- 3/8th of Earth gravity
- While the thin atmosphere (1% of earth atmosphere in density) holds particles to a lesser degree than on earth.
  - the lack of moisture leads to long atmospheric residence-time for suspended particles
- In a habitat, larger particles will settle more than what was observed on the moon, but less than what we experience on Earth.
Dust Storms

Global storms estimated to occur every 10 years. May homogenize the soil surface more than on earth.
### Recent Missions that Provided Data on Martian Soil

<table>
<thead>
<tr>
<th>Mission</th>
<th>Year</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathfinder, Sojourner Rover, Ares Vallis (~3 months)</td>
<td>1997</td>
<td>Alpha particle X-ray spectrometry, elemental analysis</td>
</tr>
<tr>
<td>Mars Exploration Rover, Equator Opportunity/Spirit Rovers (Opportunity still working!)</td>
<td>2004</td>
<td>Elemental analysis</td>
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<td></td>
<td></td>
<td>Geologic confirmations</td>
</tr>
<tr>
<td>Phoenix Lander, Polar Site (~5 months)</td>
<td>2008</td>
<td>Wet Chemistry Lab, Confirmed pH~8.3, perchlorate confirmed</td>
</tr>
<tr>
<td>Mars Science Lab (MSL) Curiosity Rover at “Rocknest”, Gale Crater+ (4yrs+)</td>
<td>2012</td>
<td>First to use X-ray diffractive analysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“Regolith is similar to Hawaiian volcanic ash”, perchlorate reaffirmed</td>
</tr>
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![Sojourner](Image1.png) ![View from Curiosity](Image2.png)
Human Research Program

Sojourner (Pathfinder)

Opportunity

Curiosity (MSL)

Sojourner (Pathfinder)
Are We Starting From Scratch With Martian Dust?
State of Our Knowledge

- While we know a fair amount about composition, we haven’t returned any actual Martian dust. Thus, we have some limitations in our knowledge (including toxicity assessment).

- There have been efforts to develop reasonable Martian regolith simulants (including JSC Mars-1, which consisted of Hawaiian volcanic ash). Improvements in simulant engineering are underway by NASA experts, which should result in even more representative surrogates.
  - Perchlorate was not adequately represented in JSC Mars-1, but is unlikely to be a major factor in respiratory-system toxicity
  - Other changes/refinements?

- From LADTAG we observed that lunar dust simulants (Arizona volcanic ash) were surprisingly representative of actual lunar dust both from a chemical and toxicity perspective.
  - This increases our confidence in the merit of future simulant work
• JSC Toxicology has conducted some preliminary rodent studies that related Martian and lunar simulant toxicity, which suggest that Martian dust is reasonably “in family” with lunar dust (unlikely to be less toxic, and potentially slightly greater in toxicity).

Lam et al. 2002 study (predated LADTAG) with mice related relative pulmonary toxicity of lunar dust simulant and Martian simulants. 90 day exposures, intratracheal instillation.

<table>
<thead>
<tr>
<th>Dust</th>
<th>Dose dust/mouse</th>
<th>macrophages</th>
<th>inflammation</th>
<th>edema</th>
<th>fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lunar Soil Simulant</td>
<td>1 mg</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Mars-1</td>
<td>1 mg</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Quartz (Recognized silicosis hazard)</td>
<td>1 mg</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

LOGIC: If ultimate Martian PEL will not exceed 0.3 mg/m³, and you know percentage composition of dust constituents, you can conservatively estimate upper-bound on constituent exposure potential for risk assessment purposes.
Chromium Perchlorate
Trivalent chromium is an essential nutrient, applicable to proper carbohydrate metabolism, and has relatively low toxicity.

In contrast, hexavalent chromium can cause serious respiratory system damage, and is a known human carcinogen (Group A) associated with lung, nasal, and sinus cancer.

Exposure concerns generally are focused on industrial situations (e.g., electroplating) where long-term exposure to mist may result in serious health effects (“chrome holes”). There is significant uncertainty regarding whether these types of exposures are relevant to hexavalent chromium particulate exposures that are more environmentally-relevant.

Speculation is that there is/was an oxidative environment on Martian surface, and that would mean that there may be more hexavalent chromium than would be expected on earth surface. There is not consensus on this!
Chromium Exposures

• Chromium Data

<table>
<thead>
<tr>
<th>Mission/Source</th>
<th>Conclusion</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mars Pathfinder</td>
<td>0.2% ± 0.1% total chromium (~2,000 mg/Kg, ppm)</td>
<td>Wanke et al. 2001</td>
</tr>
<tr>
<td>Curiosity</td>
<td>0.4-0.5% chromium (III) oxide (Cr₂O₃), 0.3% as Cr (~3,000 mg/Kg, ppm)</td>
<td>Blake et al 2013 Morris et al. 2015</td>
</tr>
</tbody>
</table>

• Comparison: most native soils on earth tend to have 10-100 mg/Kg total chromium, with essentially no Cr⁺⁶ component,

• Hawaiian volcanic soils ~0.1%, 1,000 mg/Kg Total Cr (D. Ming JSC ARES)
**Trivalent Chromium Risk Assessment**

Exposure Scenario: 1.5 years, 24-hr exposures (may overestimate exposure potential)
Dust Exposure: 0.3 mg/m$^3$ (assumed for planning purposes based on Lunar Dust PEL)
Chromium content: 0.3%

0.3 mg/m$^3 \times 0.3\% = \textbf{0.0009 mg/m}^3 \textbf{ daily exposure as Cr}^{+3}$

**Non-cancer Hazard Assessment:**

<table>
<thead>
<tr>
<th></th>
<th>Interim NASA Spacecraft Maximum Allowable Concentration (180 day)</th>
<th>Interim NASA Spacecraft Maximum Allowable Concentration (1000 day)</th>
<th>Safety Margin Relative to Health-based Exposure Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insoluble Cr$^{+3}$</strong></td>
<td>0.025 mg/m$^3$</td>
<td>0.005 mg/m$^3$</td>
<td>At least 5x margin</td>
</tr>
</tbody>
</table>

*SMACs derived by JSC Toxicology Group based on findings of Derelanko et al. (1999). This intermediate duration study observed mild lung hyperplasia/inflammation in rats exposed to trivalent chromium through nose-only inhalation for 13 weeks (6h/day, 5d/wk). A human equivalent LOAEL of 0.43 mg/m3 was calculated and a 3 fold uncertainty factor for the minimal LOAEL/NOAEL, along with a factor of 3 for extrapolation from humans to animals. This result was extrapolated to address a continuous exposure scenario over the longer spaceflight exposure durations.*
Hexavalent Chromium Risk Assessment
(Shown for Purposes of Demonstration only)

Exposure Scenario: 1.5 years, 24-hr exposures (may overestimate exposure potential)
Dust Exposure: 0.3 mg/m³ (assumed for planning purposes based on Lunar Dust PEL)
Chromium content: 0.3%
Hexavalent fraction: 2% (bounding estimate based on analogies to Fe⁶⁺ speciation, Ming/Morris, 2016. Also, in family with NRC 2002 assumption).

\[0.3 \text{ mg/m}^3 \times 0.3\% \times 2\% = 0.00002 \text{ mg/m}^3 \text{ daily exposure as Cr}^{\text{VI}}\]

Non-cancer Hazard Assessment:

<table>
<thead>
<tr>
<th>USEPA Reference Concentration, RfC (Glaser et al., 1990, Malsch et al., 1994)</th>
<th>NASA SMAC</th>
<th>Safety Margin Relative to USEPA Exposure Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr⁶⁺ Particle</td>
<td>0.0001 mg/m³</td>
<td>Not Set</td>
</tr>
</tbody>
</table>

Cancer Risk Assessment:

<table>
<thead>
<tr>
<th>Exposure (mg/m³)</th>
<th>USEPA Cancer Unit Risk Factor¹ (risk per mg/m³)</th>
<th>Lifetime Exposure Cancer Risk</th>
<th>Mission-adjusted Cancer Risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00002</td>
<td>12</td>
<td>2 x 10⁻⁴</td>
<td>4 x 10⁻⁶ (risk is 25x below acceptable range)</td>
</tr>
</tbody>
</table>

*Cancer risk assessment averages the duration of exposure (1.5 yr) over a 70 yr lifetime to determine cancer risk. NASA utilizes an acceptable cancer risk limit 1 x 10⁻⁴ (1 in 10,000) when setting air/water chemical exposure limits.

¹ USEPA IRIS Database. Based on Mancuso (1975) results of respiratory system cancers in chromate-exposed workers.

*RfC incorporates a 10x uncertainty factor to ensure protection of the total range of human population including children, elderly, and population with pre-existing health conditions.
Perchlorate Context
**Perchlorates and Mars**

- **Source:** Dust in the atmosphere and soils that are high in chloride can be converted to perchlorate when exposed to UV light.
  - The conversion was reproduced in the lab using chloride-rich soils from Death Valley (Miller 2006)
  - Desert conditions would also result in limited downward migration or runoff of perchlorate deposited at the surface. Lack of moisture leads to greater stability than seen on Earth.
  - Similar elevated perchlorate found in caliche deposits in Atacama desert in Chile, lower amounts in soils from American Southwest
Perchlorate Exposure

- Perchlorate Data

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Phoenix (Polar Site) (Wet Chemistry Lab)</td>
<td>0.5% (5,000 mg/Kg, ppm)</td>
<td>Hecht et al., 2009</td>
</tr>
<tr>
<td>Curiosity (Gale Crater)</td>
<td>0.4% (4,000 mg/Kg, ppm)</td>
<td>Ming et al., 2014, Archer, 2015 contact</td>
</tr>
</tbody>
</table>

- **Comparison:** Soils in US Southwest (~0.1-10 mg/Kg)
- **Chilean caliche:** (~10-500 mg/Kg)

Lybrand et al, 2013
**Perchlorate Health Concerns**

- **Main toxic effect:** Perchlorate has been shown to interfere with normal iodide uptake by the thyroid gland.
  - Well-studied in humans due to past treatment for Graves Disease (hyperthyroidism)
  - Perchlorate is a negatively charged ion (ClO$_4^-$) that can affect thyroid function through competitive inhibition of the transport of iodide into the thyroid. Iodine is an important component of thyroid hormones T4 and T3.
    - Compensation for iodide deficiency through feedback control mechanisms. This feedback includes increased secretion of thyroid stimulating hormone (TSH).

- Greer *et al.* (2002) study where radioactive iodide uptake inhibition and thyroid health was observed in 14 day drinking water exposure with small groups of healthy adult volunteers. No observed effect level at 0.5 mg/day for thyroid uptake inhibition, with small inhibition at 1.4 mg/day, and larger inhibition at 7 and 35 mg/day. No effect on TSH or T3/T4 levels at either 0.5, 1.4 or 7 mg/day intake.

- Braverman *et al.* (2006) study observed no iodide inhibition and no thyroid effects in a 6 month oral study with small groups of human volunteers. Daily intake of 0.5 mg/day and 3 mg/day. No observed thyroid uptake inhibition and no TSH or T3/T4 impacts.

- Particulate inhalation exposures to perchlorate dust have been investigated in two published studies of ammonium perchlorate production workers (Gibbs *et al.*, 1998; Lamm *et al.*, 1999).
  - Both studies had small numbers of exposed workers and were subject to limitation of epidemiological investigations.
  - Neither study reports any significant relation of estimated perchlorate exposure to changes in thyroid hormone or TSH measures (NRC, 2005).
  - Exposures estimated at 35 mg/day
Complexity with Setting Perchlorate Health Limits

• NRC ("Health Implications of Perchlorate Ingestion", 2005)
  – Recognized no observed effect level 0.5 mg/day intake from Greer et al, 2002
  – Further reduced by 10x for sensitive human subpopulations (special concern with impacts on fetus of women who may have low iodine intake/thyroid abnormalities). Final daily limit of 0.05 mg/day.
  – NRC recognized this was a very conservative approach, and noted that much higher perchlorate intake is likely acceptable in other exposure contexts.
  “Those results have been analyzed in multiple ways, but the experimental results are clear: in healthy subjects, a dose of perchlorate of 0.5 mg/per day has no effect on thyroid radioiodide uptake or any other measure of thyroid function, and doses of 1.4-2.8 mg/per day have minimal or no effect on those measures.” (NRC, 2005, pg. 66, with doses expressed as intake)

• NASA does not have the same limitations or intent as NRC/USEPA in terms of mission!
  – Determine the highest safe level of intake for NASA crews
  – Healthy crew, pre-screened and monitored (less likely to have undiagnosed thyroid conditions)
  – Proper dietary exposure to iodine can be ensured
  – No precautions needed for fetal protection

• Beyond dust, perchlorate may be a multi-media exposure challenge given its properties
  – This is particularly relevant when assessing cumulative risk from multiple exposure sources. Perchlorate may be a perfect candidate given spaceflight resource realities!
  – Interim SMAC expressed as intake limit for perchlorate with spaceflight crews at 3 mg/day, based primarily on Braverman et al. 2006 findings, and supported by NRC conclusions and occupational studies
Special Perchlorate Considerations
Perchlorate Non-cancer Risk Assessment

Exposure Scenario: 1.5 years, 24-hr exposures
Dust Exposure: 0.3 mg/m³ (assumed for planning purposes based on Lunar Dust)
Perchlorate content: 0.5%
Inhalation Rate: 20 m³/day

0.3 mg/m³ x 20 m³ x 0.5% = **0.03 mg/day daily dose of perchlorate**

Non-cancer hazard assessment:

<table>
<thead>
<tr>
<th>Proposed Allowable Intake¹</th>
<th>Interim NASA SMAC²</th>
<th>Percent of allowable intake represented by dust inhalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perchlorate</td>
<td>3 mg/day</td>
<td>0.15 mg/m³</td>
</tr>
</tbody>
</table>

¹Based on NOAEL noted in Braverman et al. 2006 findings, and supporting studies. Actual allowable exposures for any media will depend on mission-specific cumulative exposure evaluation (air, drinking water, in-situ vegetable intake)

²Assuming only intake from dust exposure. No toxicity differences between these exposure times are expected based on research findings and perchlorate mode of action.
Example Theoretical Perchlorate Exposure Balance (3 mg/day)

- Water intake: Assuming ingestion rate of 2.8L/day at estimated perchlorate detection limit of 100 micrograms/L
- Dust exposure at 0.3 mg/m³ PEL
- Remainder allowed for crop intake
Summary and Conclusions

- Martian dust poses both new and familiar challenges to human exploration. The lunar dust work really has given us a head start on Mars.

- Risks from chromium/perchlorate:
  - **Chromium** risks are largely dependent on assumptions on the amount of chromium existing in the hexavalent form.
    - Based on preliminary geology expert feedback, this risk appears to have limited potential. Further data and/or confirmatory information may be warranted.
  - **Perchlorate** poses a real, but manageable, challenge to crew health during Martian habitation.
    - It offers some intriguing upsides, from an in-situ resource utilization perspective, as well!
    - Cumulative exposures through dust, water, and crops should be considered, if applicable.
    - Water monitoring technology for perchlorate would likely be beneficial if in-situ resources are utilized.
  - Ongoing work in evaluating other components of Martian dust to assess human health risks.