Medical Management of a Potentially Toxic Trialkylamine Ingestion during Spaceflight

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I have no financial relationships to disclose.

I will not discuss off-label use and/or investigational use in my presentation.
Introduction

• Need for reduction in excessive iodine consumption by astronauts

• Multiple methods for removal of residual iodine after purification aboard NASA spacecraft

• Low Iodine Residual System (LIRS)
  • developed for iodine removal aboard space shuttle
  • Initially flown on STS-95

• Case report: accidental, potentially toxic ingestion by astronauts
  • exposure to contaminated water from LIRS filtration
Introduction: LIRS

- LIRS: developed as iodine removal system for Shuttle
  - Goal: replace previous iodine removal assemblies already in use

- LIRS specs:
  - Commercially patented resin, Iodosorb II®
  - Reduces iodine concentration (heated OR chilled water)
  - Resultant iodine concentration $\leq 0.25$ mg/L
  - Historical water consumption averages: 2 L/day/astronaut
  - Iodine intake approximately 0.5 mg/day
    - Operational requirements: 0.5 mg/day from either water or food sources, maximum 1g iodine intake/day
Introduction: LIRS

• Flight Readiness:
  • Demanding timeline – need for improved systems on board

  • Contamination: 6 weeks prior to scheduled launch, LIRS cartridge found to have significant microbial contamination
    • Recommended that cartridges be sterilized before flight
    • Autoclave known to degrade effectiveness of resin
    • Sterilized with gamma irradiation (25-40 kGy)
Introduction: LIRS

• Irradiated resin sample (not LIRS flight-ready cartridge) sent for safety review
  • LIRS: considered non-critical
    • no threat to crew/mission in case of failure
  • Able to be replaced by prior systems if needed
  • Resin sample found to meet quality specifications
  • Flight-ready cartridge NEVER used for water sampling prior to flight

• LIRS launched aboard STS-95 as scheduled
  • Installed on day 2 of flight
Case Report

- Five of seven crew members consumed LIRS-filtered drinking water beginning flight day 2

- 6 hours after initial ingestion:
  - One crew member complained of malodor, abnormal taste
  - Initially complaints disregarded – “it’s just Shuttle water”
    - Other crew members using flavored drink mix – masking taste
    - Second crew member sampled non-flavored water, similarly noted abnormal odor and taste

- Official report made to Mission Control and to mission flight surgeon
  - Unscheduled private medical conference requested
Case Report

- Second gamma-irradiated flight-certified LIRS unit obtained
  - Ground-based taste test performed
  - Flight surgeon and CAPCOM sampled water
  - Abnormal taste, malodor detected
- Crew immediately advised against consuming further LIRS-filtered water
  - LIRS removed from filtration system
  - Five exposed crew members: estimated to have consumed less than 2 L of the LIRS water
- Water sample from flight-certified ground LIRS unit sent for analysis
Case Report

• Ground unit water sample:
  • Elevated Total Organic Carbon (TOC) level: 1,270 mg/L
  • Elevated tripropylamine (TPA) level: 794 mg/L
  • Elevated tributylamine (TBA) level: 176 mg/L
  • Elevated formaldehyde level: 11.4 mg/L

• Literature review
  • Possible health risk
    • Minimum adverse human dose: undefined
    • SWEG: 0.4mg/L (re: unpleasant odor, potential for decreased water consumption)
Literature Review

• Oral ingestion of trialkylamines:
  • GI mucosal absorption
  • Lipophilic distribution: brain, liver, heart, kidneys

• Liver metabolism:
  • N-oxide and N-nitrosamine compound formation
  • Omega hydroxyl- and carboxy-nitrosamine metabolites
    • Carcinogenic in rodent models
    • ? Carcinogenic in humans
  • Aliphatic side-chain oxidation and glucuronidation.
    • Hepatic/renal elimination
    • Possible injury to either organ system
Case Report

• Medical response:
  • Monitoring of liver enzymes, serum metabolites
    • Blood/urine samples collected on orbit for post-landing examination
  • Concern over the potential mission impact
    • Would the crew be able to perform critical landing operations?
    • Should the crew de-orbit ahead of schedule?
  • Crew medical officer: physician-astronaut
    • Monitored crew members throughout flight
    • No adverse effects reported

• Crew considered capable of completing flight without operational consequence
  • Mission continued uninterrupted
Post-Flight Analysis

- LIRS water:
  - TOC = 8.64 mg/L
  - TBA = 0.204 mg/L
  - TPA = 4.95 mg/L
  - Trace formaldehyde
- Estimated exposure:
  - 14-28 mg over 24 hours
  - 0.2-0.4 mg/kg/day (based on a 70 kg standard patient)
  - Approximately 25-50 times lower than that administered daily to experimental animals with resultant carcinogenic effects
Post-Flight Analysis

• On-orbit blood samples:
  • TPA levels detectable in 9/14 heparinized whole blood samples
  • TBA levels below limit of quantitation (0.5 ng/mL) in all samples

• On-orbit urine samples:
  • Elevated TPA and TBA in all exposed crew member samples
Post-Flight Analysis

• Standard post-flight clinical laboratory assays:
  • Serum:
    • No detectible trialkylamines
    • Significantly increased magnesium levels in all exposed crew members
Post-Flight Analysis

- Elevated liver enzymes in 3/5 exposed crew members
  - 2/5 exposed: elevated AST
    - All normalized by 3d post-flight
  - 1/5 exposed: elevated ALT
    - Further elevation 3d post-flight
    - Normalized by 6 months post-flight
Post-Flight Analysis

• Post-Flight NASA Anomaly Review Board
  
  • Primary cause: failure to anticipate the chemical breakdown of the resin when exposed to gamma radiation
    
    • Post-irradiation analysis focused on resin functionality
    • Analysis did NOT focus on whether irradiated resin posed any health or toxicological risk to the crew members
Post-Flight Analysis

• Misclassification of LIRS as non-critical piece of hardware
  • Multiple alternative systems readily available should the LIRS fail
    • BUT: consider possibility of crew injury from exposure

• If hardware classified as mission critical:
  • More thorough examination of all system hardware
  • Toxicological review of potential LIRS resin (rather than parallel testing of the ground-based substitute)
Operational Medical Response

• Primary concern: mission impact with incapacitation at time of landing
  • Identities of the toxicants unknown
    • Unclear whether exposure could cause significant health impacts
    • Potential for inability to perform mission-critical tasks (on-orbit and re-entry)
Operational Medical Response

• Response plan:
  • Daily private medical conferences
    • Any symptoms reviewed
    • Any signs of incapacitation
  • Flight surgeon integration with other ground support operational teams
    • Evaluate crew safety, ability to complete mission
    • Potential need for early de-orbit and return, medical evaluation
  • Crew Medical Officer
    • Physician-astronaut
    • Able to evaluate and monitor crew members, reassure ground teams
Conclusions

• Two significant issues:
  • Acute medical event during spaceflight
    • Required real-time operational medical response from the ground-based crew surgeon and medical team
  • Impact of even seemingly non-critical equipment upon mission success

• Crew members followed in Longitudinal Study of Astronaut Health (LSAH)
  • Annual physicals, life-long surveillance
  • None of the exposed crew members have suffered any adverse events related to the toxicological exposure from the LIRS equipment
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