Toxicology

John T. James

Chapter Overview

This chapter describes the many sources of air pollution that can affect crew health and performance, either immediately or later because of a subtle toxicological injury. Management of the risk of airborne exposure entails a risk analysis so that our limited resources can be targeted to managing the greatest risks. Major risks include excess offgassing from polymeric material, accumulation of anthropogenic pollutants, leaks from systems and payloads, pyrolysis events, external compounds and, under some conditions, celestial dusts. The risk of crew exposure from such sources is managed by suitable containment of the potential toxicants, a robust air revitalization system, air pollutant monitoring, and personal protective equipment for high-risk activities or contingencies. Standards that define safe exposures during space flight have been uniquely defined for contingency situations and for prolonged exposures.

Learning Objectives

- 1. Review the challenges of managing spacecraft toxicological threats affecting human health and performance.
- 2. Review the evidence-based monitoring strategies for air pollutants, including combined exposures.

Introduction

This chapter begins in the mid-1990s, with the dawn of the era of permanent human occupation of space stations orbiting the Earth, and envisions a future when humans will again

J.T. James, MA, PhD (\boxtimes) Medical Sciences Division, NASA Johnson Space Center, Houston, TX 77058, USA e-mail: john.t.james@earthlink.net

explore and reside on the moon. The lessons learned from these experiences will pave the way for human exploration of Mars and beyond. Our concern is limited to threats to air quality from harmful compounds that are an ever-present danger within any space vehicle or habitat. Microbial threats and problems associated with chemical pollution of drinking water are discussed elsewhere (see Chap. [5](http://dx.doi.org/10.1007/978-1-4939-6652-3_5)).

Humans can be viewed as one of the many systems present in a space vehicle or habitat. Like most other systems, the human system must be protected from an environment that could harm the system and cause it to fail immediately or to fail after a long latent period. A human as a system has its own set of design limitations; however, it is unique in that it interfaces with almost all other vehicle systems at one time or another and is adaptive to the environment. Perhaps the most immediate requirement for the human system to perform well is a supply of clean, respirable air (Box [4.1](#page-1-0)). One of the key requirements of such air is that it be sufficiently free of pollutants that could result in illness or incapacitation. It is the goal of this chapter to describe how NASA presently achieves this goal and plans for exploration missions.

Toxicological Risks to Crew Health and Performance

Wise management of limited resources must be strictly practiced during human space flight; however, sufficient resources must be available to control and manage *credible* threats to air quality. Identifying credible risks begins with a complete knowledge of the types of compounds proposed for use and constraining choices to compounds that perform the required function without presenting an unacceptable toxicological risk. For example, relatively non-toxic triol was chosen as the heat-exchange fluid for the Russian segment of the International Space Station (ISS) to replace the more toxic, and troublesome ethylene glycol that had been used for heat transfer within the *Mir* space station [\[1](#page-15-0)[–3](#page-15-1)]. Another important constraint is to carefully select solid

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Box 4.1

Major spacecraft atmosphere contamination constitutes a serious threat to crew health and life.

materials, especially polymers, so that their release of volatile, toxic compounds into the atmosphere is limited. For example, the amount of melamine foam permitted aboard spacecraft is constrained because of its release of methanol, which is one of the more toxic small alcohols [[4\]](#page-15-2).

Reactive chemicals find many important applications in space flight; however, it is unfortunate that reactive chemicals are also the ones that tend to be most acutely toxic. Pelletized lithium hydroxide (LiOH) effectively removes carbon dioxide $(CO₂)$ from the air because it rapidly reacts with the gas to form solid lithium carbonate. LiOH dust, if it escapes from the contained pellets, can cause eye and respiratory tract irritation because of its chemical reactivity. Combustion events can produce a "soup" of toxic reactive compounds; however, these can be limited by careful selection of materials that will not combust or, if they are burned, produce non-reactive compounds during thermal degradation. The choice of wire insulation composed of Kapton® and Teflon® for spacecraft minimizes the risk of wiring pyrolysis because these materials are resistant to combustion; however, if wire insulation comprised of these materials does burn, it can, under special conditions, produce highly reactive and toxic gases such as perfluoroisobutene and toxic fumes [\[5](#page-15-3), [6](#page-15-4)].

Selection of compounds must be made with an awareness of the potential for the environmental control system to convert some materials to more toxic compounds if they were released into the atmosphere. The use of perfluorinated alkanes has been proposed in heat exchange fluids; however, if the fluid contains highly branched perfluorinated alkanes, then these can be converted on hot catalytic surfaces, such as those present in the trace contaminant control system aboard the ISS, to highly toxic gasses [[7\]](#page-15-5). Although beyond the scope of this chapter, the ability of compounds to adversely affect the air revitalization system and water recovery systems must also be considered. Often these systems are more sensitive to the "toxic" effects of compounds than the human "system." Finally, the fundamental architecture of the vehicle or habitat must intrinsically eliminate dead air spaces. Humans confined to such spaces in low gravity situations, where there is lack of convective air movement, will be rebreathing their exhaled breath and soon experience subtle toxic symptoms of excess $CO₂$ exposure. Robust movement of air is essential.

Spacecraft Materials Offgassing

During their synthesis, polymeric materials trap volatile compounds that are released slowly from the matrix of the

polymer, and some polymers slowly decompose to release volatile decomposition products into the air. The first type of offgassing shows a pattern of steadily declining rates of release of volatile compounds as the reservoir of trapped compounds is depleted; however, offgassing from materials decomposition may provide a steady, or even increasing, level of pollutant production.

Hardware and materials to be used in space flight are tested at 50 °C to determine whether they release an unacceptable amount of pollution. In addition, whole modules outfitted with at least 75 % of the material to be launched are tested at 25 °C to estimate the aggregate pollution that will be present when the crew first enters the module on orbit and how much the load to the air revitalization system will increase. The rate of offgassing is extremely sensitive to temperature, so this must be considered when comparing estimates based on different temperatures. Excessive offgassing has presented problems for the ISS as well as during the Lunar Mars Life Support Test (LMLST) conducted at the NASA Johnson Space Center (JSC).

The workflow for preparation of Node 1 for launch to the ISS involved a whole-module offgassing test. According to the test procedure, the module was purged with fresh air, and then sealed for several days while samples of air were taken and analyzed. Unfortunately, just prior to the test some of the duct work in the module was replaced and adhesive was used in the repair. That adhesive had not cured before the test began and the air samples showed that high concentrations of methanol were quickly released into the air. Basically, the module was shown not to be ready for launch to ISS. Several weeks later after the adhesive had cured and the module had undergone many clean air purges, the test was repeated. The rate of production of methanol was found to be approximately 20-fold less than during the first test. The module was toxicologically acceptable for launch to ISS.

During the ground-based LMLST, 4 humans were confined in a sealed habitat for periods up to 90 days. During the 60-day phase of the testing the formaldehyde levels reached 0.25 mg/m³ by day 15 and one of the crew members reported eye and airway irritation consistent with this concentration. The test was nearly discontinued because of crew symptoms until several potential sources of formaldehyde offgassing, including colorful murals, were removed from the habitat. Crew symptoms disappeared as the formaldehyde concentration dropped below 0.2 mg/m^3 [\[8](#page-15-6)]. Studies conducted after the test ended also identified acoustic foam (melamine) and carpeting as additional sources of formaldehyde. Materials used in the habitat had not been subjected to ordinary offgas screening prior to the test; the outcome of this project demonstrated that testing for materials offgassing is an essential early step in controlling airborne pollutants.

Anthropogenic Pollutants

Human metabolic products that must be managed in a space environment include methane, hydrogen, carbon monoxide (CO), water vapor, and $CO₂$. Methane, hydrogen, and CO require catalytic filters for effective removal, water vapor is removed by condensation on cold surfaces, and $CO₂$ is removed by expendable filters or regenerable filters [[9–](#page-15-7)[11](#page-15-8)]. Methane, hydrogen and water vapor pose no toxicity threat; however, CO and $CO₂$ can be toxic if not carefully and specifically managed. Carbon monoxide is exhaled in the breath after breakdown of hemoglobin in the body and $CO₂$ is released as a result of oxidative metabolism of a variety of endogenous molecules [[4,](#page-15-2) [12](#page-15-9)]. The amount of CO released is small, so it can accumulate to toxic levels only after several weeks in the absence of any air purification; however, $CO₂$ is produced in large quantities and can accumulate to toxic levels in a few hours in the absence of its removal from the atmosphere.

Carbon dioxide is of special interest because considerable resources are required to control its concentration in the vehicle and because the appropriate levels to which control is required are not perfectly clear. Methods that can be used to control $CO₂$ include the following: LiOH canisters, solid amine beds and molecular sieve [[10,](#page-15-10) [11\]](#page-15-8). The issues associated with the adverse effects of $CO₂$ exposure are complex and have yet to be fully resolved. The human body has a considerable capacity to adapt to relatively high $CO₂$ levels; however, some data suggest that even within the apparent adaptation range, non-specific, subtle effects may occur such as headache, low energy, or mood changes [[13](#page-15-11)]. This is further compounded by the possibility that physiological changes associated with space flight (e.g., fluid shifts) may magnify some of the adverse effects of $CO₂$ exposure. Thus, the body of evidence of safe exposure levels from submariners exposed to moderately high levels of $CO₂$ may not be directly applicable to astronauts in space. Space flight $CO₂$ exposures are further confounded by the presence of areas of poor ventilation. Such areas increase the likelihood that an astronaut will be rebreathing a large portion of his exhaled breath, which has a higher level of $CO₂$ than the average level in the vehicle atmosphere. This latter concern has surfaced in reference to time spent in enclosed sleep stations where $CO₂$ would accumulate quickly if the ventilation fan failed. A study of the performance of relatively young adults has shown that exposures of 1–2 h cause worrisome deficits in the ability of test subjects to perform decision making while engaged in the Strategic Management Simulation test [[14\]](#page-15-12). Five of the nine derived measures indicated marginal or dysfunctional performance during exposures to only 2500 ppm, a concentration below levels typically found aboard the ISS.

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Escapes from Physical Containment

NASA recognizes that some compounds are sufficiently toxic that the apparatus that contains them must be 2-fault tolerant. This means that two of the containment devices could fail and the toxic compound still would not escape into the atmosphere. It is easy to imagine that constructing an apparatus with 2-fault tolerance is a challenge given the weight constraints imposed on payloads. Therefore, toxicological hazard assessments must not be made overly conservative. These assessments must also consider the behavior of the compound in the absence of gravity and the strategies available to clean up the compound if it were released. The amount considered for release is the total amount in a single containment unit at the lowest level of containment. For example, an apparatus with ten separate containment wells each containing 1 ml of a material would be assessed as if only 1 ml would escape, unless a single *plausible* failure could cause the release of the contents of more than one of the wells.

Once the toxicologist knows the amount and identity of a compound at risk for release, she must predict the behavior of the compound in the atmosphere. If the compound is a gas or a volatile liquid it will spread rapidly within the habitable volume. If it is only slightly volatile, it will spread slowly and re-condense on any cool surface. If it escapes from a pressurized system, an aerosol may form. And finally, if it is released all at once, a large spherical bleb will form and then spread by surface tension when it collides with an interior surface. For even slightly volatile compounds, the toxic hazards from the liquid and vapor forms must be considered. Generally, the ability of the environmental control and life support system (ECLSS) to remove the compound is only considered in a general way when the potential time of crew exposure is estimated. If a compound is an ionic salt, an acid, or a base, then the properties of the solution are used to predict its toxic effects. There are five levels of toxic hazard classification as shown in Table [4.1](#page-3-0) [\[15](#page-15-13)].

Broken glass is considered a level 2 toxicity hazard because of its potential to permanently damage the eye. Liquids immobilized in a matrix or permanent gel are generally not considered a toxicity hazard.

Fires and Lesser Combustion Events

Combustion events of various magnitudes are an inevitable consequence of flying in space in vehicles with chemical reactors, extremely hot surfaces, and a high density of electrical circuits. In zero-gravity conditions, convection does not remove heat from any source, so the potential for overheating requires that forced-air cooling be more robust than in an equivalent system on Earth. There has been a long, and

Toxic hazard level	Irritancy	Systemic effects	Containability and decontamination
0 (Non-) hazard (green)	No more than slight for 30 min	None	Gas, solid, or liquid that may not be containable.
1 critical hazard (blue)	Slight to moderate irritation lasting more than 30 min	Minimal	Gas, liquid, or solid that may or may not be easily contained.
2 catastrophic (yellow)	Potential for long-term contact effects; e.g. may cause permanent eye damage	None	Containable solid (dust) or liquid that can be cleaned up.
3 catastrophic (orange)	minimal to severe, but irritation does not constitute level 3 hazard	Effects on coordination, perception, memory, etc. or delayed or serious injury (e.g., cancer)	Non-volatile liquid or solid that can be cleaned up by the crew
4 catastrophic (red)	Potential for lasting contact damage and will require therapy if exposure occurs	Same as level 3	Uncontainable volatile material. Don protection immediately and leave the module, allowing the air revitalization system to decontaminate the air (or depress module).

Table 4.1 Toxic hazard levels for compounds (abridged) that could enter the atmosphere [\[15\]](#page-15-13)

sometimes tragic, history associated with space vehicles and combustion events of various magnitudes. Toxicologically speaking, a serious-looking fire (e.g., solid fuel oxygen generator [SFOG], burn aboard *Mir*) may be much less serious than an event that seems innocuous, such as the BMP (trace contaminant removal filter) burn aboard *Mir* that produced large amounts of CO. The nature of the combustion products will depend on the material combusted, the temperature of combustion, and the availability of oxygen. It may also depend on the type of fire extinguishant used to try to stop the fire. A comparison of two fires, the SFOG fire and the BMP "fire" illustrate the importance of controlling the risk of fire, yet being able to deal with one should it occur.

The SFOG fire occurred on February 23, 1997 when the ignition of a cartridge got out of control and essentially destroyed the generator. During this time, the six crewmembers that were aboard *Mir* had just finished dinner in the core module, and were preparing to get some sleep. The job of activating the final cartridge of the day fell to a cosmonaut who floated into the Kvant module where the generator resided. The fire has been dramatically described as follows:

He [the cosmonaut Lazutkin] peers at it [the generator] intently. And then suddenly, sparks fly out of the top. Before he can say or do anything, a small column of orange-pink flame shoots from the container. He flinches…Hovering in the base block table about 10 feet from where Lazutkin is marveling at the 'baby volcano' he has somehow created, Reinhold Ewald is the first to react…*Pozhar*, Ewald says, mouthing the Russian word for fire…[Somewhat later] the oxygen from the canister is obviously fueling the fire, creating a blow-torch effect. The flame is now shooting up into the air in the center of the module, flashes of sharp red and pink, at a 45 degree angle in front of him. He cannot be certain, but it seems to be 2 feet long and growing. [[16](#page-15-14)]

The story unfolds as the crew repeatedly uses fire extinguishers in an attempt to stop the fire. At last the fire dies out; they are in masks and ready to alert their ground controllers.

Box 4.2

The intensity of a fire may not correlate with the amount of toxic byproducts. The "minor" BMP smoke event produced toxic levels of CO, whereas the intense, oxygen-rich SFOG fire produced no known toxic products.

Communications with the ground were poor at the time, but the crew's words, translated from the original Russian, express the dire situation well:

So, if you hear us, I say again: We have an emergency situation on board, a fire. The solid-fuel oxygen generator cartridge caught fire. The combustion was very intense. We were able to extinguish the fire after employing a third extinguisher. The crews are wearing gas masks. The smoke content of the air is below medium…MCC people, we do not read you…The partial pressure of oxygen is 155 [mmHg]; the $CO₂$ is five and a half [mmHg]. We have nine spare gas masks. After we take off the used up gas masks, if our physical and mental state begins to deteriorate, we will don gas masks and evacuate to the [Soyuz] vehicle. The smoke content of the air is below medium; we do not know the level of CO gas.

—Transcript/translation of *Mir* air to ground 054:20:48

Although the SFOG fire was a dramatic event, the crew's description of it provides clues to why it was not a catastrophic toxicological event (Box [4.2\)](#page-3-1). The fire was being fed by the oxygen generated inside the apparatus, thus any products would tend to be thoroughly oxidized. Thus, any CO generated would be quickly converted to $CO₂$, a much less toxic compound. Furthermore, the aqueous-based fire extinguishant probably had the effect of rapidly aging the metal fumes that would be produced by the pyrolysis of the metal housing of the SFOG. Therefore, dangerous metal fumes were not an issue for the crew. Samples of air or air pollutants were taken by the crew and show that the

atmosphere was not toxicologically hazardous as one might have expected. Analyses of grab sample canisters showed that the level of carbon monoxide never exceeded 25 ppm. The crew did not report any health effects that could have been attributed to toxic exposures. The "smoke" was most likely water mist resulting from use of an aqueous-based extinguishant on a hot, sustained fire [[17\]](#page-15-15).

The *Mir* BMP combustion event occurred on February 26, 1998 when a hot regenerated filter was placed back in line prematurely and a downstream filter burned, sending a puff of smoke into the air. Because of the SFOG fire 1 year earlier, the JSC Toxicology Group had flown an experimental combustion products analyzer (CPA) to quantify CO using an electrochemical sensor in the event of a fire. This instrument indicated CO levels of several hundred ppm; however, the crew reported no immediate symptoms of exposure. However, several hours later the crew reported headaches and nausea, and they did not feel well the next morning. A grab sample container (GSC) sample taken during the event later showed that if anything the CPA was underestimating the CO concentrations, and that the crew symptoms, while delayed, were a direct result of their CO exposure. This delayed effect is clear when one compares the measured levels of CO to the estimated accumulation of carboxyhemoglobin, a biomarker of the toxic effect of reduced delivery of oxygen to the tissues. The maximum toxic effects reported by the crew occurred 5–10 h after the event, at which time the carboxyhemoglobin peaked at about 40% as estimated from the airborne concentrations of CO [\[18](#page-15-16)].

Toxicologically, the BMP event was much more serious than the SFOG fire because of the amount of CO generated. In retrospect, we had assumed that the experimental CPA was giving us misleadingly high readings after the BMP event; however, when ground-based analyses were completed and the crew symptoms considered, it was clear that crew health was seriously threatened by the presence of CO. If twice as much CO had been produced, the crew would have been exposed to a potentially lethal concentration of this dangerous, odorless toxicant.

External Sources of Pollution

Highly reactive compounds are required for many space flight operations, and these are typically located outside the cabin volume; however, these compounds can contaminate spacesuits and be brought into the habitable volume where they present a toxicological risk. Performing a toxicological hazard assessment on these materials is especially difficult for three reasons. Firstly, some materials (e.g., fuel-oxidizer reaction product [FORP]) are a poorly defined mixture of many compounds, each with unique toxic properties. Secondly, the amount of material at risk for getting on the

suit or gloves from thrusters or leaks is typically uncertain. Finally, the ability of the material to remain on the suit and be brought into the habitable space is hotly debated based on assumptions about the volatility of the material, the retention properties of the material, and the time of exposure of the contaminated area to solar heating.

The proper approach for the toxicologist to use in cases like this is to insist that propulsion experts, suit builders, and materials experts define an upper limit on the amount and kind of compound(s) that could enter the airlock from external contamination. Making worst-case assumptions for each step of the analysis can lead to unreasonably restrictive estimates of the amount of material that can be brought inside. Propellants, for example, tend to be highly toxic, thus even a small amount in the respirable atmosphere can pose a toxicity hazard in the limited volume of the airlock. One final problem stems from the need to bring a monitoring device in close proximity to the contaminated area of the suit. It is only when the contaminant evaporates and the detector inlet is brought within a few inches of the contaminated area that a monitor can indicate a contaminated area. External toxic risks that were associated with the Shuttle have been previously described [[19\]](#page-15-17). To that list, one could add unsymmetrical dimethylhydrazine and FORP for the ISS situation. Dust contamination from outside is discussed later in this chapter when exploration missions to celestial bodies are considered.

Spacecraft Maximum Allowable Concentrations (SMACS)

Defining Acceptable Air Quality for Astronauts

Many governmental and private agencies in the U.S. and abroad set environmental standards for air quality; however, none of those standards are directly applicable to the space flight situation (Box 4.3). During space flight, the crew must be able to affect self rescue if necessary, hence toxicantinduced cognitive and neurological deficits must be strictly avoided. Astronauts form a much more homogeneous and healthy population than the general public or industrial workers, so they may have a greater tolerance for exposure to toxic compounds than these other groups; however, astro-

Box 4.3

Short-term exposure standards (1 and 24 h) are needed to build flight rules for management of accidental releases into the atmosphere, and long-term standards (0.5–3 years) are needed to protect astronauts from latent effects such as cancer resulting from continuous exposures at relatively low concentrations.

nauts also experience physiological changes during space flight that could cause them to be more susceptible to the toxic actions of some compounds.

Those changes include the following: reduced blood volume, increased sensitivity to cardiac arrhythmias, immune function changes, and hematopoetic effects due to radiation exposure [\[20](#page-15-18)[–22](#page-15-19)]. Toxicants that target the same organ system as space flight effects have their allowable exposure levels reduced because of anticipated changes in susceptibility during actual missions. The factor typically used to reduce the exposure level is 3; however, because of the sudden and potentially life-threatening effects of cardiac arrhythmias, compounds that sensitize the heart to arrhythmias have their allowable exposure levels reduced by a factor of 5. Such crude factors are only a beginning in addressing the increased susceptibility of astronauts to certain air pollutants. One day it should be possible to combine our understanding of the mechanism of toxicity with our understanding of the mechanism of space flight-induced effects and deduce how the two effects interact quantitatively. This is somewhat confounded by the current goals of human space flight, which is to place humans in partial-gravity environments where the observed effects at zero gravity are expected to be significantly reduced.

Setting exposure standards is by no means a rigorous scientific undertaking. Expert judgment determines which studies ought to be used as the basis for a standard, and expert judgment then must determine the methods of extrapolation of the study findings to the predicted toxic effects on the population exposed (Box [4.4\)](#page-5-0). These fundamental limitations apply to all human exposure standards. In addition, the group setting the standard must have a clear idea of the type and magnitude of effects that ought to be prevented by the standard and to what probability. The users of air quality standards are generally not willing to state explicitly which effects can be tolerated and with what probability they might occur. Thus, when exposure standards are compared and found to be quite different, one must ask many questions before concluding that one or the other is wrong. Are the targeted exposure populations similar, are the acceptable "adverse" effects the same, are the times of exposure equivalent, and so forth? The goal, of course, is to set protective exposure standards that are not so low that resources are wasted trying to meet them. Thus, the subjective problem of

Box 4.4

Astronauts experience a spectrum of biochemical and physiological changes in space flight that could render them more susceptible to the toxic effects of some airborne pollutants.

safety margin also plays a role in standards. How much safety margin is necessary to reduce the probability of an adverse effect? Do sensitive subpopulations need to be considered?

Behavior of Compounds in Spacecraft Air

Exposure standards are typically set at a time-weightedconcentration for a specific length of time. Such a standard asserts that crewmembers exposed to an average concentration of "C" for time "T" have minimal risk of experiencing any symptoms. Many factors will play into how the standards are applied. One of the most important factors is how long the compound will remain in the atmosphere. Clearly, the "C-T" profile will not be a square wave as the standard assumes, it will be an exponentially decaying curve if the source is stopped and a mechanism exists to remove the pollutant. Even with simplifying assumptions such as uniform mixing, estimating the behavior of a compound can be difficult. The decay of CO (a slowly scrubbed gas) after its abrupt release from the BMP apparatus required 1–2 days, whereas compounds that are only slightly volatile, such as ethylene glycol, have a prolonged decay curve that can extend over a few months. Volatile compounds that are not scrubbed, such as Freon 218 (perfluoropropane), remain evenly distributed in the ISS atmosphere for months, being removed only by dilution as air turns over slowly in the ISS.

Role of the National Research Council Committee on Toxicology (NRCCOT)

Since the early 1990s NASA toxicologists have worked with outside experts assembled into a subcommittee of the NRCCOT to formulate SMACs and spacecraft water exposure guidelines (SWEGs) for spacecraft environments [[23–](#page-15-20)[25\]](#page-15-21) (Box [4.5\)](#page-5-1). Human exposure limits must not remain static because new data and new methods of risk assessment are constantly being developed. With this in mind, review and possibly revision of SMACs and SWEGs approximately every 10 years is warranted.

Box 4.5

There are five volumes of SMACs and three volumes of SWEGs extending out to values for explorationclass mission of up to 1000 days of exposure. The original effort was concluded in 2008; however, at this writing, the collaboration between NASA toxicologists and a reconstituted subcommittee will begin anew in 2014.

Managing Predictable Threats to Air Quality

Once we are aware of the credible toxicological risks in space flight and the acceptable levels of pollution are well defined, then we must ask how we are to manage the risks to ensure that the crew never receives a toxic exposure. This must be accomplished within tight constraints on the weight, volume, and power resources available to manage this risk. The approach that NASA has used can be viewed as a multilayered and tiered approach. If a potentially toxic compound is to be used in the vehicle, then it must be adequately contained. However, if the containment is breached, then cleanup procedures are available to limit the extent of the spill, but if the environment remains polluted for any period of time, then crew protection equipment is available to isolate the crewmembers from the polluted environment. Finally, if containment, clean up, and isolation fail, then the crew can abandon the vehicle. This is a multilayered approach.

Management of potential pollutants is also tiered. By this, we mean that nominal operation of the environmental control system will dispose of nominal loads of air pollutants with some safety margin. However, if the environment becomes suddenly polluted by an accidental release, then strategies are available to substitute contingency filters for the ordinary filters or to operate the environmental control system in a way that optimizes air purification. For example, if a fire pollutes the air, then an ambient temperature catalytic oxidizer (ATCO) filter could be substituted for nominal LiOH filters to improve removal of carbon monoxide, a major toxicant from almost all fires. In addition, the air conditioning system can be placed on full cool to capture more of the toxic pollutants that are water soluble (e.g., formaldehyde) in the vapor condensate (Box [4.6\)](#page-6-0). This is an option only if the humidity condensate can be disposed of, rather than introduced into the water purification system, which could be overloaded by the high load of water-soluble pollutants from the air.

Toxic Hazard Assessments and Containment

Risk comprises two factors: the seriousness of any adverse outcome and the probability of that outcome. These two factors offset each other in NASA's approach to the management

Box 4.6

Water-soluble air pollutants are captured by condensation during the process of water recovery from the atmosphere. Such contaminants may present a risk to the purification system and can break through to the potable water supply.

of toxic hazards. If the inherent toxicity of a substance and the amount of a substance that could be released can cause no more than a level 0 toxic hazard, then the material can be used without containment, although this is usually not practical in a micro-gravity situation. If the material is rated a level 1 toxicity hazard then the containments must be 1 fault tolerant. This means that the probability of release is the probability that two independent levels of containment fail simultaneously. If each level has a failure probability of 1/100, then the probability of escape of a level 1 substance is only 1/10,000. If the material is rated a catastrophic hazard (level 2, 3, or 4), then the apparatus containing it must be 2-fault tolerant. This means that three levels of containment must be breached before the material escapes into the cabin. Using our simple model again, with each level having a 1/100 failure rate, the probability of a catastrophic compound escaping is 1/1,000,000. It is essential that the levels of containment be demonstrated to be effective and that they are independent and workable.

During fixing operations of the Fundamental Biology Investigation (April 1995) flown aboard *Mir* 18, several drops of paraformaldehyde escaped into the environment [[26\]](#page-16-0). Paraformaldehyde is a level 2 toxicity hazard (although this rating scheme was not in use at the time) because of its ability to cause permanent eye damage by contact of the liquid with the eye, but it can be readily cleaned up with sorbent wipes (it would be rated a higher hazard if it could not be cleaned up). The liquid escaped because the bag clamps were inadequate, most likely due to inadequate training of those making the seals. The problem was somewhat compounded by failure to follow operational procedures for implementation of the outer levels of containment (glove box or mother bag) because these could be awkward as the crew fixed biological material. Thus, what should have been 3 levels of containment became at best marginal containment. Fortunately, the few drops that escaped were so small and adhered to the bag by surface tension so that none of it reached the eyes of crew members.

Personal Protection

There are key parameters that must be considered when selecting respiratory/eye protection (Box [4.7\)](#page-7-0). How long can the protection be used, are the masks universal or specific to each crew member, and how effective are they against each plausible inhalation risk?

The time that respiratory protection can be used depends on whether it is a stand-alone system or one connected into a central system of fresh air or oxygen. If a stand-alone mask is used, then its useful life is limited by its inherent capacity to produce oxygen and by the demands for oxygen made by the crew member. For example, the useful lifetime of a

Box 4.7

The last line of crew protection, other than abandoning the vehicle, is respiratory system and eye protection, although there is eye wash capability aboard U.S. vehicles. As noted previously during the SFOG fire, the crew donned Russian masks to protect themselves from inhaling potentially harmful substances.

Russian breathing mask is given as 20 min for use during intense work and 120 min at rest [\[27](#page-16-1)]. In comparison, the U.S. breathing mask aboard ISS is rated for 5 min use under intense work and 15 min at rest; however, it can be plugged into oxygen supply lines. If a mask uses filters instead of makeup air or oxygen, then the useful lifetime of the mask is controlled by the capacity of the filters to adsorb specific toxicants. Typically, activated charcoal and/or particulate filters are used in the cartridges of such masks, and these effectively remove the vast majority of pollutants; however, specific cartridges target different pollutants so one must make a judgment about the identity and concentration of the pollutant before selecting the cartridge and its useful life. If the respiratory protection system is connected into a central oxygen distribution system, then the excess oxygen that is not consumed by the crew will enter the cabin and eventually break fire protection flight rules that limit vehicle oxygen concentration.

One of the most important comparisons to make before a known toxic threat exists is to compare the ability of the vehicular environmental system to remove the pollutant within the length of time the crew will be able to use individual protection. Obviously, after a toxic release, the bulk air revitalization time ought to be less than the wear-time for crew protection. In practice this is difficult to achieve because the useful mask time is often less than 1 h, yet the time needed to make even one complete volume pass through the air scrubbers is measured in terms of many hours. For example, the U.S. trace contaminant control system (TCCS) charcoal filter has a flow of $15 \text{ m}^3/\text{h}$. Thus the Lab module, which has approximately 100 m³ free volume, would require about 14 h for a 2-volume turnover, which would still leave a substantial residual in the air even if the filter were 100% effective and the air well mixed [[27\]](#page-16-1).

Fire Extinguishants

Materials used to extinguish fires in spacecraft have been of three basic types. The Russians use an aqueous-based extinguishant in their segment of the ISS, and the U.S. uses $CO₂$ as the extinguishant in their segment of the ISS. The U.S.

Space Shuttle used Halon 1301 (bromotrifluoromethane) as an extinguishant. The behavior and toxicity of any extinguishant must be considered before it is employed in a specific situation. For example, the aqueous-based extinguishant used on the *Mir* SFOG fire caused the vehicle to fill with water aerosols. The water contains a high level of contaminants and these end up in the water recovery system unless that system is immediately isolated, or the captured water is discarded rather than purified. A $CO₂$ -based extinguisher can boost the nominal levels of $CO₂$ when it is used, but the increased level from one typical extinguisher is small compared to typical running levels of carbon dioxide. Water-mist fire extinguishers are presently under development for use aboard the ISS [\[28](#page-16-2)].

The situation with Halon 1301 is a little more complex. The material itself is not especially toxic with a long-term SMAC of 1800 ppm [[29\]](#page-16-3); however, it is difficult to scrub from the atmosphere and it is possible that it could decompose into toxic hydrogen bromide and hydrogen fluoride. The decomposition products are unlikely to be produced in toxic quantities unless the fire is an extremely large and hot one. We do not anticipate such a fire on orbit. The toxicity of Halon 1301 itself is a little more interesting. Halon sensitizes the myocardium to arrhythmias, and since the stress and/or microgravity of space flight also seems to do this, the space flight limit for Halon 1301 exposure has been reduced fivefold from what it would be on Earth in an unstressed situation [[29\]](#page-16-3). Nonetheless, its limit is still quite high and discharge of one container of Halon aboard a moderate-sized spacecraft would not break the exposure limits.

Bulk Air Scrubbing

Once an air pollutant reaches the atmosphere, there are a number of mechanisms for its removal. The Shuttle air revitalization system has been described in an earlier edition of this text [\[19](#page-15-17)]. The methods for removal of air pollutants aboard the ISS are much more sophisticated and have been described in detail elsewhere [\[10](#page-15-10), [11](#page-15-8)] and updated [\[27](#page-16-1)]. Table [4.2](#page-8-0) summarizes how classes of pollutants are removed from the air by intentional filtration and catalytic-reaction methods or by other factors present such as condensation in the water recovery system. The table illustrates the complex nature of the air revitalization system, which is necessary because of the complexities of the pollutants generated within the vehicle. It also provides a starting point for managing a pollution contingency because the tools available to deal with the contingency and their approximate capacities are listed. For reference, the typical free volume of a major ISS module is about 100 m^3 , so scrub times for one or two volume passes can be estimated.

Table 4.2 Pollution management aboard the ISS ([27] and communication from Jay Perry) **Table 4.2** Pollution management aboard the ISS ([[27\]](#page-16-1) and communication from Jay Perry)

CDA carbon dioxide absorber, *CDRA* carbon dioxide removal assembly, *CRK* carbon dioxide removal kit, *HCRF* harmful contaminant removal filter, *HEPA* High efficiency particulate aerosol,
RMU regenerable micropurific *CDA* carbon dioxide absorber, *CDRA* carbon dioxide removal assembly, *CRK* carbon dioxide removal kit, *HCRF* harmful contaminant removal filter, *HEPA* High efficiency particulate aerosol, *RMU* regenerable micropurification unit (BMP), *TCCS* trace contaminant control system, *CHE* condensing heat exchangers, *ATCO* ambient temperature catalytic oxidizer, *HTCO* high temperature catalytic oxidizer, *PA* phosphoric acid

At least one time, it has become necessary to abandon a portion of a vehicle and allow the air revitalization system to scrub the atmosphere. This occurred as a result of an unpredictable, rapid, thermal release of a group of pollutants that had been inadvertently accumulated on ISS Metox charcoal filters [[30](#page-16-4)]. Metox canisters are used during extravehicular activity (EVA) to scrub exhaled pollutants from inside the suit. The nominal plan was to remove the canisters from the EVA suit and regenerate them by flowing hot air through the canisters and discharging the effluent into the ISS atmosphere. Inadvertently, a pair of canisters was not desorbed immediately after EVA, and was left with a low flow of cabin air passing through them for about 6 months. This facilitated a large accumulation of pollutants on the charcoal filters inside the canisters, and when the crew attempted to regenerate the canisters, these pollutants were abruptly released into the ISS atmosphere. The crew reported a noxious atmosphere, halted the regeneration process, and took refuge in the Russian segment of the ISS until the TCCS could scrub the air in the U.S. segment to acceptable conditions. Based on analysis of returned air samples, the T value (an index of overall toxic pollution) was reduced from 5.5 to 1.5 in 30 h. T values below 1 are desirable for long-term crew exposures. Upon reentering the U.S. segment, the crew reported a faint, but easily tolerable odor.

Monitoring of Air Pollutants

Monitoring can provide valuable data for management of air quality in both nominal situations and when a pollutant has accidentally escaped into the atmosphere. Monitoring does not necessarily entail direct quantification of specific pollutants. For example, if a toxicant is contained in a pressurized system and that system maintains its pressure (we will know this by monitoring), then we know nothing has escaped.

Conversely, if a system loses a certain amount of pressure, we might be able to predict how much pollutant has been released.

Direct monitoring in the air can target the nominal condition where a broad range of pollutants are quantified at trace levels. A change in the level of background pollutants would suggest a new insidious source or a decline in function of the air revitalization system. The monitoring may be archival (i.e., samples are taken on orbit and analyzed on the ground months later) or it might be real-time *in situ* monitoring. Contingency monitoring targets specific pollutants that are at risk for suddenly creating a hazardous atmosphere because of an accident. For example, ammonia monitors have been placed aboard the ISS because of the large amount of this irritating compound that is used in the external portion of thermal loops of the U.S. segment. It is extremely unlikely that this toxic compound could reach the ISS internal volume; however, failure modes exist in which this could happen.

Compound-Specific Monitoring

The hazard associated with some compounds is sufficiently great that a specific monitor for those compounds is required. The U.S. strategy for spacecraft is to a use risk-based approach to monitoring of selected compounds that could become a health threat. Table [4.3](#page-10-0) summarizes the monitoring approach currently used aboard ISS. One of the most difficult challenges of these specific analyzers is that they must be able to indicate high pollutant levels when an accident first occurs and then follow the decrease in pollution levels as the hazardous compound is scrubbed from the atmosphere. For example, electrochemical analyzers were considered for ammonia; however, this technology could not respond to several hundred ppm of ammonia and subsequently quantify decreasing levels of ammonia over a period

Table 4.3 U.S. real-time air monitoring aboard the ISS (JSC 65129; JSC 62804, Rev. B, 2006; Carbon Dioxide Monitor Kit End Item Specification, August, 1999)

a Additional monitoring capability is provided by Russian experts. CSAS is the compound specific analyzer system

b In practice the CO sensor has a higher range than this

c Technique roughly separates length of stain into categories

Fig. 4.1 Example of a toxicitygroup panel for the date indicated. Bars that reach a value of 1.0 suggest that the risk of that effect must be given attention by the flight surgeon or crew

of several hours. Hence, detector tubes were recommended for this application because each reading is taken with a fresh tube. Monitoring in the airlock is to limit any pollutants brought into the ISS after working outside the vehicle.

Broad-Spectrum Monitoring

Since many toxicological threats cannot be reasonably anticipated, compound-specific analyzers fail to address this risk. For this reason, at least in long-term missions, a broadspectrum air quality analyzer is required. Typically in a ground-based laboratory a gas chromatograph/mass spectrometer (GC/MS) is used for this purpose; however, flying such a complex instrument capable of detecting all trace compounds of interest is not yet feasible. In the early days of the ISS, a dual-channel, volatile organics analyzer using GC/ ion mobility spectrometry was used to quantify pollutants [[31](#page-16-5)]. This instrument does not have the analytical power of a GC/ MS, but it is more robust. Future broad-spectrum analyzers might use GC/MS technology, miniature mass spectrometers, IR spectrometers, or GC/differential mobility spectrometry [[32,](#page-16-6) [33\]](#page-16-7). Such monitors must operate with minimal crew involvement, be extremely reliable, require few vehicle resources, be able to deal with unknown compounds, and perform in high-contamination conditions (e.g., after a fire). They must also be no larger than a shoebox, weigh no more than a few kilograms, and demand little power. A pair of GC/ differential mobility spectrometers has been validated aboard the ISS for operational use for years to come. The instruments and their predecessor DTO versions have proven to be reliable and stable over many months [[34\]](#page-16-8).

A new paradigm has also been developed to put trace contaminant monitoring into a context that is readily understood by crew members and flight surgeons. According to this approach, the compounds in a single toxic-effect group (e.g. mucosal irritants, cardiotoxicants or neurotoxicants) are added together, each one in proportion to the applicable SMAC [\[35](#page-16-9)]. If the compound ratios added in each group are below 1, then the toxic effect is highly unlikely to occur. An example of such a panel of transformed data is given in Fig. [4.1](#page-11-0) using data from a variety of sources. The primary driver of headache risk is carbon dioxide and the primary driver of mucosal irritant risk is formaldehyde.

Celestial Dusts: Air Quality Risks Unique to Exploration Missions

Missions that return astronauts to the moon's surface or take them to an asteroid or Mars entail additional toxicological risks beyond those encountered during low-Earth-orbit flights. Missions in low Earth orbit have by no means been free of problems with dust [[36\]](#page-16-10), but the additional challenge of managing "celestial" dust during exploration missions will require informed use of resources to protect crew health and hardware. Those additional risks stem from the presence of respirable dust at the surface of those bodies and from the nature of activities that may be conducted at those surfaces (Box [4.8](#page-12-0)).

It might be possible to model mechanical properties of lunar dust, for example, with volcanic ash, but this is a poor model for the toxicological properties of lunar dust because volcanic ashes lack surface reactivity, nano-iron, and surface-condensed

Box 4.8

The natural forces that form dust on the moon, asteroids, and Mars are not like any processes on Earth, so one must be cautious in assuming that celestial dusts have an Earth-based toxicological analog.

"volatiles" that are part of lunar dust. Dust at the lunar surface is slowly "gardened" by micrometeorite bombardment and by charging effects at the day-night terminator [\[37,](#page-16-11) [38](#page-16-12)].

At this point one can only speculate what activities may occur on the lunar and Martian surfaces. The In Situ Resource Utilization (ISRU) community envisions activities that use materials present near the surface to produce oxygen, hydrogen, and water [[38\]](#page-16-12). As "industrial" activities become a reality on the surface, the potential for human exposure to dust, perhaps freshly fractured, will increase. Freshly fractured minerals on Earth often exhibit increased toxicity over the same minerals whose surfaces have been aged several months.

Lunar Dust

U.S. astronauts in the Apollo era gained first-hand experience with the tenacious and ubiquitous nature of lunar dust [[39\]](#page-16-13). Words recorded from Apollo crews are self-evident. At the lunar surface: "Almost immediately upon removing my helmet, I started to pick up symptoms that you might associate with hay fever symptoms. I never had runny eyes or nose…after about 2 h within the cabin, those symptoms gradually disappeared…After the second and third EVA… The symptoms were not nearly as strong as after the first EVA."

After leaving the moon's surface the crew's comments included:

- "After ascent orbit insertion, when the spacecraft was again subject to zero-g environment, a great quantity of dust and small particles floated free within the cabin. This dust made breathing without the helmet difficult and hazardous, and enough dust and particles were present in the cabin atmosphere to affect vision."
- "The LM was filthy dirty and it has so much dust and debris floating around in it that I took my helmet off and almost blinded myself. I immediately got my eyes full of junk, and had to put my helmet back on."
- "We had to remove our helmets from our suits to keep our eyes from burning and our noses from inhaling these small particles floating around; we just left our helmets sitting on the tops of our heads."
-
- "I could have left my helmet on, and I would have had a lot less eye and mouth irritation." "When I climbed up the tunnel I could definitely tell there was a lot of dust up in the LM and you could smell it."

Crew comments about dust during their trip home were: "On the way back, we got lunar dust in the command module. The system actually couldn't handle it; the system never did filter out the dust."

Figure [4.2](#page-13-0) illustrates how dust is kicked up on the lunar surface and Fig. [4.3](#page-14-0) shows how dust sticks to all surfaces, including the EVA suit.

Recent studies using dust returned from the lunar surface aboard Apollo 14 show that its pulmonary toxicity is intermediate between the highly toxic dust quartz and the much less toxic dust titanium dioxide (white paint pigment). Using the new technique of comparative benchmark dose modeling, investigators instilled dust into the lungs of rats and using a variety of toxicological endpoints, estimated a safe exposure level of $0.5-1$ mg/m³ for respirable-size dust if it were episodically introduced into a lunar habit over a long period of time [[40\]](#page-16-14). Nose only inhalation studies conducted for a month at 4 concentrations showed that jet-milled lunar dust at a respirable-size range caused a variety of toxic effects, including early fibrosis [[41\]](#page-16-15). From the inhalation data and using a conservative species-extrapolation factor of 3, a safe exposure estimate using benchmark dose modeling on many toxicity endpoints was between 0.3 and 0.9 mg/m³ for episodic astronaut exposures over a 6-month period [\[42](#page-16-16)]. An official exposure standard has not yet been set for lunar dust. Although the Apollo 14 dust that was used is an intermediate form between mare and highland dust, additional experiments with dust from specific, unusual areas may be necessary.

Asteroid Dust

At present NASA envisions the possibility of a mission to an asteroid, perhaps to retrieve it and study it while held in a lunar or Earth orbit. Until recently it was not clear that small asteroids, virtually devoid of any gravitational force, would have any respirable-size dust clinging to its surface. That uncertainty was resolved when the Japanese probe Hyabusa returned dust from the surface of Itokawa, much of it less than 10 μ m in diameter [\[43](#page-16-17)]. Small quantities of asteroid dust can be obtained from meteorites that have been retrieved from the Earth's surface. The link between specific types of meteorites and their asteroid counterparts is wellestablished [[43\]](#page-16-17). The dust can be obtained by grinding a small portion of the meteorite or by multiple, freeze-thaw fracturing.

Fig. 4.2 Lunar rover on the surface of the moon. The wheels kick up dust, which sticks to the EVA suit (Courtesy of NASA)

Martian Dust

The toxicological issues associated with exposure to Martian dust may be much more serious than those associated with lunar dust. Unlike moon dust, Martian dust is frequently lofted into the atmosphere in bulk quantities. Martian dust storms of global proportions have been observed from Earth and even at the local level "dust devils" traverse the landscape, churning up surface dust and dropping it in a new location. It is reasonable to expect that collisions between particles during these dust storms will break the dust into ever-smaller particles. Although the National Research Council [[44\]](#page-16-18) has expressed concern about the content of heavy metals, especially chromium, in Martian dust, the reactivity of the dust, as discovered in Viking experiments, may be of greater concern [\[45](#page-16-19)]. Martian dust also contains a large portion of iron and under some conditions quartz dust containing iron has been shown to be more toxic than quartz with much less iron content [\[46](#page-16-20)]. One can anticipate that the lunar surface expeditions will be a valuable learning experience for later stays on the Martian surface; however, the dust

problems on Mars will be substantially more difficult to manage than on the moon. Components of the dust, such as perchlorates, may also affect the toxicity of Martian dust [[47](#page-16-21)].

Case Studies from the Aeromedical Practice

Case 1

Crew members aboard a space station reported that a small puff of smoke came from the trace contaminant control system, but that nothing caught fire and they have no symptoms. A few hours later during a public affairs event the crew seems to be fine; however, about 8 h after the smoke event the crew reports that they have headaches and are nauseous. The next morning the symptoms have not resolved. An experimental instrument aboard the vehicle shows that the CO levels reached more than 400 ppm and have declined very slowly after that.

The events described are fully explained by the fact that CO at concentrations of a few hundred ppm crosses the

Fig. 4.3 Lunar dust on the rover and on the astronaut's EVA suit (Courtesy of NASA)

air-blood barrier slowly. This results in delayed formation of carboxyhemoglobin. As carboxyhemoglobin forms it restricts the ability of hemoglobin to deliver oxygen to tissues that need it, and this restriction leads to headache and nausea, but only after a delay of several hours. The carboxyhemoglobin decreases as the level of CO in the air is reduced.

Smoldering pyrolysis events in space can be especially dangerous because there is no convection to move air away from the hot area, thus there is less oxygen at the site of the smoldering event. Compared to the same event at Earth gravity, proportionally more CO is formed than carbon dioxide. $CO₂$ is much less toxic than CO. Furthermore, air revitalization systems in spacecraft are generally not designed to quickly remove bolus quantities of CO. Trustworthy monitors are now present aboard the ISS to help manage such an event should it occur there.

Case 2

The ISS crew has just discovered that there are two Metox canisters in the oven used to regenerate these filters that are used during EVAs to capture $CO₂$ and trace contaminants. They

activate the regeneration cycle and a few hours into the process the air in the U.S. segment becomes "noxious." The regeneration is discontinued and the crew takes refuge in the Russian side of the ISS. The crew remains there for 30 h while the environmental control and life support system in the U.S. segment scrubs the atmosphere. Upon reentry into the U.S. segment the crew reports a faint, but easily tolerated odor.

This event, which cost many hours of lost work time, happened because the previous crew had left un-regenerated filters in the regeneration oven after their EVA. They did not like the noise from the apparatus. Six months later the crew discovered these un-regenerated filters in the oven. What they did not know was that a slow flow of ISS air had been passing through the filters for 6 months, and the carbon beds in the Metox canisters had been accumulating large amounts of trace air pollutants. When heat was applied during regeneration, the filter beds released a bolus amount of these pollutants, causing the T value to reach almost 6 (based on analysis of a grab sample), a level easily associated with noxious air. After the 30-h stay in the Russian segment, the T value for the air in the U.S. segment was just over 1. This event illustrates the need for broad spectrum, in situ analysis of trace pollutants.

Self-Study Questions

- 1. What is the most serious type of toxic event in space flight and why?
- 2. What is the mechanism by which air pollutants enter the water recovery system?
- 3. What is the T-value concept for predicting the health effects of trace pollutants?
- 4. What is the most important anthropogenic pollutant and what are its adverse effects?
- 5. What properties of celestial dusts affect their toxicity?

Key Points to Remember

- 1. Long duration spacecraft and habitats are considered closed environments, even if some of the respirable gases are replaced rather than regenerated.
- 2. High concentrations of contaminants in a closed environment may be difficult to remove, presenting a lasting threat and possible abandonment of the vehicle.
- 3. Spacecraft atmosphere pollution can originate from predictable sources and from totally unpredictable sources.
- 4. The health effects of air pollutants must be based on the aggregate of air pollutants, not just one of the air pollutants.
- 5. Because of the physiological effects of space flight and the continuous exposures, exposure standards for human space flight must be uniquely set.
- 6. Air pollutants can contaminate the recovered water and thereby pose a threat to the water recovery system.
- 7. Pyrolysis events are the greatest immediate threat to crew health and performance.
- 8. Selection of targets for monitoring must be on a risk basis.
- 9. Celestial dusts will pose a challenging toxicological threat once prolonged exploration of these bodies commences. Martian dust will be a particularly challenging factor.

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