Assessing the Biohazard Potential of Putative Martian Organisms for Exploration Class Human Space Missions

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Abstract

Exploration Class missions to Mars will require precautions against potential contamination by any native microorganisms that may be incidentally pathogenic to humans. While the results of NASA's *Viking* biology experiments of 1976 have been generally interpreted as inconclusive for surface organisms, the possibility of native surface life has never been ruled out and more recent studies suggest that the case for biological interpretation of the *Viking* Labeled Release data may now be stronger than it was when the experiments were originally conducted. It is possible that, prior to the first human landing on Mars, robotic craft and sample return missions will provide enough data to know with certainty whether or not future human landing sites harbor extant life forms. However, if native life is confirmed, it will be problematic to determine whether any of its species may present a medical risk to astronauts. Therefore, it will become necessary to assess empirically the risk that the planet contains pathogens based on terrestrial examples of pathogenicity and to take a reasonably cautious approach to bio-hazard protection. A survey of terrestrial pathogens was conducted with special emphasis on those pathogens whose evolution has not depended on the presence of animal hosts. The history of the development and implementation of *Apollo* anti-contamination protocol and recent recommendations of the NRC Space Studies Board regarding Mars were reviewed. Organisms can emerge in nature in the absence of indigenous animal hosts and both infectious and non-infectious human pathogens are theoretically possible on Mars. The prospect of Martian surface life, together with the existence of a diversity of routes by which pathogenicity has emerged on Earth, suggests that the possibility of human pathogens on Mars, while low, is not zero. Since the discovery and study of Martian life can have long-term benefits for humanity, the risk that Martian life might include pathogens should not be an obstacle to human exploration. As a precaution, however, it is recommended that EVA suits be decontaminated when astronauts enter surface habitats when returning from field activity and that biosafety protocol approximating laboratory BSL 2 be developed for astronauts working in laboratories on the Martian surface. Quarantine of astronauts and Martian materials arriving on Earth should also be part of a human Mars mission and this and the surface biosafety program should be integral to human expeditions from the earliest stages of the mission planning.

Key words: Mars, biosafety, native microorganisms, human missions

Introduction

One of the principle reasons why Mars may become the next target for human exploration is the prospect of native microbial life there, a prospect which has been thrust into a more palpable reality after the recent astonishing discovery of large amounts of ice under the planet's surface (8, 47), as well as evidence from NASA's Mars Exploration Rovers (MER) that large bodies of liquid water may have existed on the surface in the past (17, 41). However, the possibility of finding native microbial life on Mars is also one of the potential risks that human explorers may face upon arrival at the planet's surface. The level of caution that astronauts will need to take while conducting extravehicular activities (EVAs) at the Martian surface and while working with regolith, rocks, ice, permafrost, and other Martian materials will depend on the following two general factors:

1) Whether or not extant life forms exist and are situated in places accessible to human crews. Areas accessible to astronauts may include surface and near surface regolith, rocks, ice, permafrost, and transient liquid water or brine oases resulting from seepage from underground sources.

2) The risk that a Martian biosphere, if present, might include species that could be potential human pathogens.

Evidence for possible Martian Surface life

Short of knowing whether or not potentially harmful organisms exist on Mars, the robotic study of the Martian environment with *in situ* instruments and the study of Martian meteorites can help to direct research efforts in determining if Mars is indeed a living planet, and help us to begin to characterize Martian life if it is found to exist, before the arrival of human crews. However, it may turn out that human intervention on the Martian planetary surface is needed to facilitate the confirmation of these studies.

***In Situ* Studies**

To date, the only *in situ* searches for native Martian life forms were carried out by the Viking 1 (VL1) and Viking 2 (VL2) landers, which arrived on Mars in 1976. VL1 and VL2 each carried a gas chromatograph – mass spectrometer (GC/MS), designed to search for organic matter in regolith samples as well as three biology experiments, each designed to test samples for a particular kind of fundamental metabolic activity that Martian microorganisms, if present, may or may not have possessed (21). Since each type of metabolic activity tested was only a possible and not a necessary signature for life, a negative result to any or all of the three experiments would not have necessarily implied a lifeless surface. On the other hand, a positive result to any of the three experiments, even with negative results to the other two, would have been evidence for life. The rationale and outcome of the three biology experiments and the GC/MS studies are summarized below:

The Pyrolytic Release (PR) Experiment: This experiment (18) asked whether microorganisms capable of taking in gases from the Martian atmosphere and converting them (possibly with the help of sunlight) to biologically useful organic compounds were present in the Martian soil. Although statistically significant amounts of organic matter were found to have been produced in the soil from carbon dioxide (CO_2) and carbon monoxide (CO), the amounts produced were too low to meet the pre-launch criteria for life. Therefore, the PR investigators concluded that these findings were the result of non-biological chemical activity.

The Gas Exchange Experiment (GEx): This experiment (36) asked whether microorganisms capable of releasing and/or taking in gases were present in the Martian soil. The general concept of this experiment was to supply the soil with a wide range of compounds in concentrated solution and to scan for changes in the concentrations of a wide range of gases; depending on what sort of changes in the gases occurred, the existence of Martian microbial metabolism might be revealed. Because this instrument used gas chromatography to detect changes, its sensitivity was significantly less than that of the other two biology instruments, which were based on the detection of radioactivity from chemically converted ^{14}C-labeled compounds. The most significant finding of this experiment was a release of oxygen from the soil. However, since this release occurred in samples that were unheated prior to testing as well as in samples

heated to 140° C, which destroy putative living organisms, the results have been attributed to non-biological chemical activity.

The Labeled Release (LR) Experiment: This experiment (24) asked whether microorganisms capable of taking in food - a dilute solution containing small organic compounds - and chemically converting it to gases, were present in the Martian soil. When the Martian soil samples were treated with the nutrient solution, gas was released only by those samples that were not heated prior to testing. The results of the LR at both Viking landing sites met the pre-launch criteria for life.

The GC/MS: Although this instrument package was not designed to search directly for life, it was expected that microorganisms on Mars could be found living only in the presence of a medium containing organic building blocks. Additionally, it was expected that any life forms, present in the soil samples that were heated in ovens before being scanned by the mass spectrometer, would yield detectable amounts of organic matter on pyrolysis. The GC/MS findings were negative in samples taken from both Viking landing sites (5).

Based largely on the failure of the GC/MS to detect organic matter in Viking samples, the consensus of the Viking science team was that life on the surface at the two landing sites was unlikely, despite the positive LR results (22). The LR principal investigator, however, has maintained the view that the Viking findings are consistent with the presence of surface microorganisms at both landing sites (25). Additionally, it is now known that to yield a positive GC/MS result, the samples examined by Viking would have had to contain the organic matter equivalent of some 30 million or more bacteria-size cells per gram of soil (14). Since the LR was capable of detecting concentrations of organisms several orders of magnitude lower than 30 million per gram of regolith, and since certain classes of organic compounds if present would have been missed by the Viking GC/MS (3) it now appears that there was never any conflict between the LR and GC/MS results. Surface tests using GC/MS instruments with capabilities exceeding those of the Viking GC/MS might therefore reveal the presence of organic matter. The European Space Agency's (ESA) Beagle 2 lander, lost during an attempt to land on Mars in December, 2003, carried such a GC/MS as well as an instrument capable of detecting atmospheric methane (CH_4) –a gas that subsequent to the Beagle's loss was in fact detected by ESA's orbiting Mars Express (12). Because CH_4 in the Martian environment quickly oxidizes to form CO_2 and water, the Mars Express data suggest a replenishing CH_4

source, perhaps biological, and if methanogenic microbes exist on Mars, it is conceivable that the ^{14}C-containing gas released in the Viking LR experiment was CH_4.

Advanced techniques in biotechnology can yield new and important insights into our understanding of Martian regolith chemistry and, if life is present, regolith biology. In particular, *in situ* instruments using microarray technologies can be small, light, and highly sensitive to a wide spectrum of chemical and biochemical compounds. Array technology has enormous potential in diagnostic microbiology (1). Tiny array devices can potentially run thousands of antibody assays, protein assays, nucleic acid hybridization assays, molecular beacon assays, or a combination of any or all of these on a single 2 cm x 2 cm biochip (43). Nucleic acid assays and antibody assays can be used to recognize molecular fingerprints of hitchhiking terrestrial microbes that might otherwise produce false positive results on life detection tests, and antibody assays (immunoassays) can also be used to search for native biomolecules even if putative Martian organisms are unrelated to their terrestrial counterparts. *In situ* instruments based on these techniques can be deployed beginning with robotic landing missions planned for the next decade.

Martian Meteorite Studies

Nature has provided Earth with a current inventory of more than 30 samples of Martian rock in the form of meteorites (6, 32, 34). In a few of them – Nakhla (20, 42), EETA79001 (49), and ALH84001 (26, 45)- organic matter of extraterrestrial origin has been identified. Furthermore, ALH84001 has been found to contain three additional features in its interior that, together with the organic matter which occurs as polycyclic aromatic hydrocarbons (PAHs), has been interpreted as evidence of past life on early Mars (26, 10). These other three observations are: 3.9 billion year old globules of calcium carbonate, unusual structures appearing as microfossil-like forms (Figure 1), and magnetite crystals. The unusual structures, the PAHs, and the magnetite crystals occur within and are associated with the calcium carbonate.

Currently, the controversy centers on the origin of the magnetite crystals. Magnetite crystals are formed on Earth by two mechanisms: biogenic and inorganic. Biogenic magnetite crystals display six chemical and physical properties that have not been displayed in any inorganic magnetite population. Thomas-Keprta *et al.* described a population of the ALH84001 magnetites that display all six properties of

terrestrial biogenic magnetite and hence inferred a biogenic origin for these Martian crystals (46). While some investigators have suggested nonbiological mechanisms responsible for this population of ALH magnetites (2, 15), Thomas-Keprta, *et al.* suggest that reproducing these crystals by inorganic techniques would require methods similar to those used by magnetotactic organisms themselves (46). The continued study of Martian meteorites, in combination with advanced *in situ* studies designed to search for extant as well as fossilized life, can potentially yield valuable information related to the question or possibly answer the question of the existence of Martian life in advance of the arrival of the first human crews.

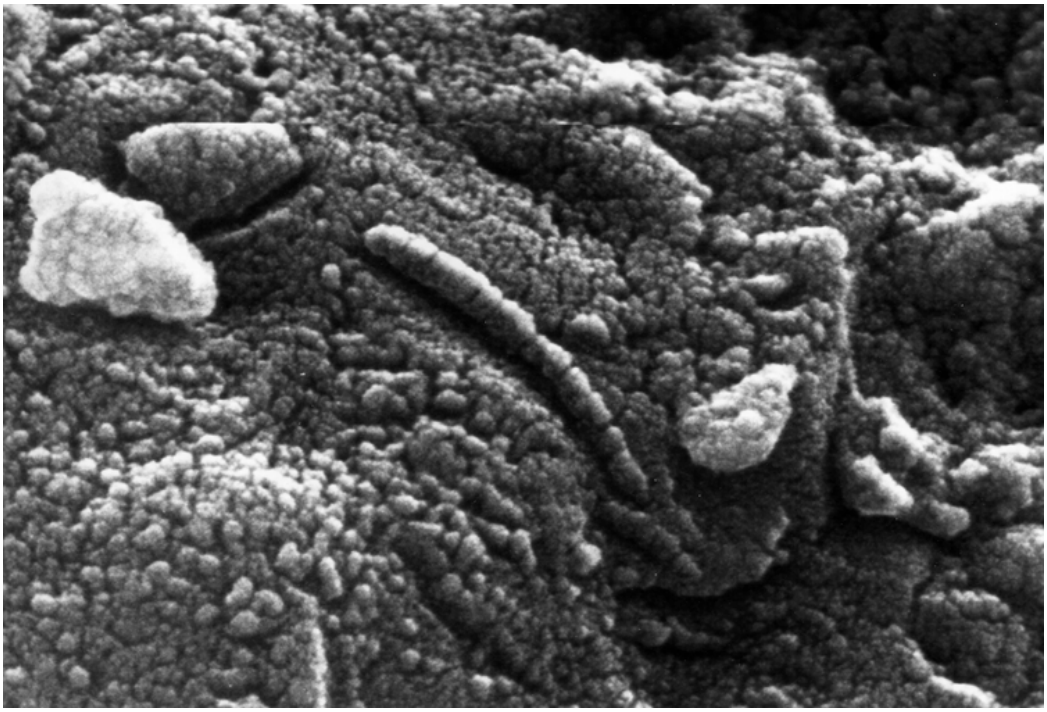

Figure 1. Scanning Electron Micrograph of features inside a carbonate granule of the Mars meteorite, ALH84001. The ovoid structure in the center of the micrograph may be a fossilized microorganism that lived on Mars 3.5 billion years ago. Image from Dr. David S. McKay, NASA Johnson Space Center.

Post Viking developments concerning Mars and life on Earth

Since the time of the Viking landings, our understanding of the history and distribution of Martian surface water has been expanding and the possibility that the Martian surface may have been wetter at some time in the past and that regions of the planet may occasionally receive liquid water from undergroud sources suggests an environment more favorable to life than thought during the time of Viking. The current surface water on Mars is now known to exist at ground level in the northern polar ice cap as well as a few meters below the surface in other areas of the planet (7). Additionally, two recent studies based on

Mars orbital data have shown that the southern polar cap also consists mostly of water ice (8, 47). A recent study of water-soluble ion content in the Martian meteorite Nakhla demonstrates high levels of chloride, sulfate, magnesium, sodium, calcium and potassium ions (38). The authors of this study suggest that these findings may indicate that the meteorite has been exposed to a brine similar to seawater that may have existed on the Martian surface in the past (38). Interpretations of extensively layered terrain as water-lain sediments (28) detected by the Mars Global Surveyor (MGS) also strengthen the case for early surface water on Mars, and could strengthen the case for ground water, frozen permafrost, and other reservoirs of trapped water on Mars today. Furthermore, another study based on MGS imaging data suggests that liquid water has seeped to the surface of the Red Planet less than one million years ago (27).

Most striking to the search for water, however, are the data sent relayed by NASA's Mars Exploration Rovers (MER) in 2004. At *Meridiani Planum*, the *Opportunity* rover discovered large quantities of jarosite, a mineral that contains iron, sulfur and trapped water, holes within rocks, suggesting that water must have once formed mineral crystals that have since fallen out of the rocks, and numerous round pebbles scattered around the surface and embedded in bedrock, indicating that they could only have been formed in the presence of water. Taken together, these observations suggest that at some point in its history, *Meridiani Planum* was completed submerged in water (41). On the other side of the planet, in the Gusev Crater, the *Spirit* rover revealed fractures in the rock, filled with minerals –a sign that water had once entered the rock (17).

Since life is more likely to exist where liquid water has recently been present, hydologically interesting regions of the planet may be astrobiologically interesting as well and may be sought as potential landing sites for robotic Mars Sample Return (MSR) and well as for piloted missions.

Also since the time of Viking, investigations into the metabolism and survival of terrestrial microbial life in a wide range of environmental habitats suggest several niches that might be supportive to life on a Mars-like planet (33). Included among these post-Viking insights is the discovery that life forms are often found living inside solid rock (23). Since the Viking landers did not look for endolithic life forms and since astronauts exploring the Martian surface will be doing precisely this, there is a possibility that astronauts will be in close contact with native Martian microorganisms, even without a definitive answer to the question of life in the regolith. It is therefore appropriate to take precautions against biological

contamination and to assess the biohazard potential that a native surface biosphere, if present, would pose to human crews.

Would a Martian Biosphere Pose a Biohazard Risk?

In 1997 the National Research Council (NRC) Space Studies Board assessed the biohazard risk of putative Martian microorganisms as it relates to the issue of back contamination from an MSR mission (32). The report concluded that it is unlikely that putative Martian organisms would be capable of out-competing Earth organisms for nutrients, since Earth's microorganisms are optimally adapted to their environments as a result of billions of years of intense competition. Contamination of Earth by putative Martian microorganisms is thus unlikely to pose a risk of significant ecological impact or other harmful effects according to the study. The risk is not zero, however. Therefore, the board recommended that samples returned from Mars by spacecraft be contained and treated as though potentially hazardous unless and until sufficient knowledge of Mars and its environment becomes available (32). In considering the issue of a potential Martian biohazard in the context of a piloted mission to the Martian surface, it is appropriate to review the history of the development and implementation of the only program to date aimed at protecting astronauts and the terrestrial biosphere from possible native organisms of another world: the Apollo Quarantine Program.

Apollo Quarantine Program

In preparation for the first Apollo human landings on the Moon, the Interagency Committee on Back Contamination (ICBC) was established (19). Although the likelihood that life forms existed on the moon was considered remote, in the unlikely event that the moon did turn out to harbor organisms, the possibility that some of them might be harmful to humans or to other organisms on Earth could not be ruled out. Therefore, a program of quarantine of returning crews and containment of samples and equipment was implemented and extensive testing of lunar material for biohazardous agents was conducted to ensure the safety of all life on Earth (19, 44). The assumption of the program was that the moon harbored hazardous, replicating microorganisms. While the containment protocol was to be based on the most stringent techniques normally used for containing terrestrial infectious pathogens, the lives of the crew and those

working in contact with them were to be given a higher priority than the maintenance of the quarantine protocol. The protocol for sterilizing materials was based on the requirements for destroying the most resistant terrestrial organisms, namely spore-forming microbes.

Testing of lunar material included virology studies (analyses for replicating agents), botanical, zoological, and protozoal studies (tests on the effects of lunar material on plants, animals, and protozoa), bacteriological studies, and mycological studies (44), which were all conducted in the Lunar Receiving Laboratory (LRL), built specifically to provide the most stringent biological containment capabilities possible at the time (19). The focus of the guidelines for these studies was on the detection of those microorganisms and other biological agents (i.e. viral) requiring replication in order to be pathogenic or capable of replicating well enough in terrestrial environments to establish themselves on Earth and therefore pose a risk that they might alter terrestrial ecology. Toxicity studies were emphasized less than studies for replicating agents in the returned lunar material because any toxins present in the material, even if originally produced by organisms native to the moon, would be non-propagating and thus their effects would be self-limiting (19).

Upon return from the Apollo 11, 12, and 14 missions (the Apollo 13 astronauts did not land on the Moon), astronauts and equipment, a flight surgeon, and a recovery engineer were contained in the Mobile Quarantine Facility (MQF), located on the flight deck of the recovery ship and then flown to Houston with its occupants, who were then transferred to the LRL in building 37 at the Johnson Space Center (JSC) and quarantined for a minimum of 21 days. The MQF (Figure 2) was equipped with a filtration and negative internal pressure system, intended to protect the outer environment from any biohazardous agents located inside. To isolate them from the terrestrial environment after splashdown, the Apollo 11 astronauts wore respirators designed to filter microorganisms from expired gas and heavy biological isolation outer suits when egressing the command module until they entered the MQF (Figure 3). On the Apollo 12 and 14 missions, only the respirators and lightweight outer garments were worn to make the transition from the command module to the MQF (Figure 4). Lunar samples, film, data tapes, and medical samples were transported to the LRL outside of the MQF using special containers (19).

No microbial life forms were recovered from the lunar material brought on the Apollo 11, 12, and 14 missions. Animal and plant species tested with the lunar material were not found to be infected with

unknown microorganisms and the crews of these missions did not develop any unknown diseases or unexplainable conditions. Therefore, the quarantine program was discontinued for returning astronauts beginning with the Apollo 15 mission. Studies on the chemical, physical and nutritional properties of the lunar material continued on samples from the first three missions as well as on samples brought to Earth on subsequent missions. Microbial growth studies using a mixture of culture media and lunar material from two regolith core tubes, taken by the Apollo 11 landing party, resulted in microbial death. The mechanism of the toxicity remains unknown. Attempts to reproduce this effect with individual samples taken from other portions of the Apollo 11 cores were unsuccessful (44).

Unfortunately, there are reports, including one by ICBC member John R. Bagby, Jr., that while the quarantine program was in effect, repeated compromises of protocol occurred (see 32 and reference therein citing Bagby, 1975). Recognizing the problems of the lunar quarantine program, the NRC report stated that many of the violations could have been avoided had the science team and lunar materials receiving program been established and integrated much earlier during the mission planning. Indeed, the NRC report concluded that early implementation of containment and receiving facilities and teams and integration with science teams during an MSR mission would likely prevent a repeat of the mistakes of the Apollo program (32). When considering a piloted mission to the Martian surface, a similar rationale should apply if there is a chance, albeit small, that astronauts may encounter potentially harmful organisms on the Red Planet. Additionally, because of the science objectives of Mars exploration, a program aimed at protecting astronauts and Earth from back contamination from Martian organisms must be integrated with a program aimed at preventing *forward* contamination to assure that Mars or samples from Mars are not contaminated with terrestrial microbes.

Figure 2. Mobile Quarantine Facility (MQF) using during the Apollo lunar program to transport astronauts from the splashdown sites to the containment facility in Building 37 at the Johnson Space Center. The MQF could be transported on the deck of an aircraft carrier as well as inside of an aircraft (44).

Figure 3. Apollo 11 astronauts walking from the recovery helicopter to the Mobile Quarantine Facility (MQF). The astronauts are wearing special heavy biological isolation outer suits as well as respirators, to filter out exhaled microorganisms. The biological isolation outer suits were not used on subsequent missions (44).

Figure 4. Recovery of Astronauts from Apollo 14. Here the astronauts can be seen wearing the respirators but not the heavy biological isolation outer suits (44).

Are Human Pathogens Possible on Mars?

In reference to a possible MSR mission, the 1997 NRC Space Studies Board report also noted that *despite the stunning diversity of Earth's microbial communities and their wide-ranging physiological and metabolic properties, only a tiny fraction of chemoorganoheterotrophic microbes produce adverse effects in host organisms….Pathogenesis is even rarer among phototrophs, lithotrophs, and autotrophs* (32). The small fraction of Earth's organisms that are pathogenic can be either infectious, causing damage only if they multiply in or on the host, or toxic, causing damage by releasing cell components or metabolic products that act as exotoxins, incidentally damaging other organisms. Infectious pathogens may be either invasive or local, while toxic effects of an exotoxin-producing microbe may or may not require that the microbe be infectious to the harmed organism. In the case of non-infectious, toxic organisms, harmful effects are produced when a vulnerable organism takes in the toxin from the environment, via ingestion or other means. In the context of an assessment of the possibility of human pathogens on Mars, we have chosen to consider non-infectious, toxic organisms as a distinct category, as compared with infectious pathogens, some of which also produce their effects via exotoxins, though released not in the external environment but on or inside the host.

Infectious Organisms

While, based on the terrestrial examples, invasive capabilities will likely be rare among putative Martian microorganisms (32), we cannot be sure that they will be non-existent, nor can we depend on the following *a priori* conclusion, as expressed by a popular Mars colonization enthusiast, that *there is no evidence for the existence of macroscopic Martian fauna and flora. Without indigenous hosts, the existence of Martian pathogens is impossible* (50). In fact, not even all infectious human pathogens - let alone non-infectious pathogens - on Earth require a multicellular, macroscopic host in order to evolve harmful capabilities. July, 1976, the month that VL1 landed on the Martian surface, was also the month of the outbreak of Legionnaires' Disease at the American Legion convention in Philadelphia (13). The causative bacterium, *Legionella pneumophila*, is a facultative, gram-negative rod that is one of several human pathogens now known to be carried in the intracellular environments of protozoan hosts (16). Additionally, *L. pneumophila* can also persist, even outside of any host, as part of biofilms (30). In essence, all that a

potentially infectious human pathogen needs in order to emerge and persist in an environment is to grow and live naturally under conditions that are similar to those that it might later encounter in a human host. On Mars, these conditions might be met in a particular niche within the extracellular environment of a biofilm, or within the intracellular environment of another single-celled Martian organism. In this context, it is important to note the observation of numerous biofilms onboard the Mir space station, which were found on surfaces and within water plumbing. These films were often multi-species and included bacteria, fungi and even protozoa (37). Thus, when assessing the potential for extraterrestrial human pathogens, even in the context of a planetary biosphere that is limited to single-celled life, the possibility of infectious agents, even an invasive type, cannot be ruled out.

Locally infectious organisms, which do not multiply systemically within a host but which produce a toxin which the host can absorb, perhaps through an infected wound, may also be possible on a planet that harbors single-celled life. *Clostridia* is an example of an anaerobic genus that often lives as spores in soils and some of its species are important human pathogens, including *C. tetani* and *C. perfringens*, which are locally infectious in wounds, where they release toxins that can be life-threatening through systemic effects (*C. tetani*) or local effects (*C. perfringens*) (40).

Non-Infectious Toxic Organisms

There are terrestrial examples of organisms that are pathogenic to humans without being infectious, meaning that the organisms do not need to live or replicate on nor in humans in order to intoxicate them. For example another *Clostridia* species, *C. botulinum*, produces spores that can contaminate food that is stored under anaerobic conditions, allowing the spores to germinate. The bacteria release an exotoxin into the food which, if ingested, blocks the release of acetylcholine from presynaptic nerve endings at the neuromuscular junction (29, 39, 40). This leads to flaccid paralysis, which can be fatal. Another example is ergot alkaloid poisoning (St. Anthony's Fire), which results from the ingestion of infected grain, such as rye or barley. The organism responsible for producing the ergot alkaloids is the parasitic fungus *Claviceps purpurea*. These compounds are potent vasoconstrictors and, when ingested, can produce gangrenous ergotism leading to limb loss, convulsions and hallucinations (48).

When considering the possibility of Martian microorganisms that may naturally release coincidentally toxic substances into their native environment, a lack of shared heredity with Earth microorganisms is not relevant. Therefore, it is reasonable to consider this category of possible pathogens as more likely on Mars than that of the infectious variety, although the risk is not zero for either category.

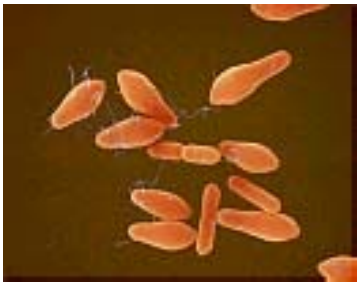

Figure 5. *Clostridium botulinum* rods at 2,000 times magnification. While the bacteria and spores themselves are harmless, they produce an exotoxin which if ingested can contaminate foods causing flaccid paralysis and death. Spores can survive for long periods in soils and water. Image from Phototake Scientific Images http://www.phototakeusa.com/results.asp?txtkeys=Disease

Recommendations

It is prudent for human crews to explore the Martian surface with as much caution as possible. This means that a particular laboratory biosafety level (BSL) protocol (9) should be chosen as a guideline for developing appropriate criteria both for astronauts working with samples inside surface habitat laboratories and for decontamination of EVA suits of crews returning to the habitats following surface field activities. Biosafety criteria must be chosen that offer the greatest amount of protection to the astronauts exposed to the Martian materials as is feasible on Mars. However, since very small landing parties (5 – 8 astronauts) can be expected on the Martian surface during the earliest human missions and since all crew members will perform EVAs and work with Martian materials, biohazard precautions used in terrestrial laboratories intended to protect the environment outside the laboratory would make little sense while the crew is on Mars. Since the principle requirements that distinguish a BSL 3 from a BSL 2 laboratory have more to do with protection of people and the environment outside the laboratory than with protection of the lab workers themselves beyond what is possible at BSL 2 (9), we propose that the BSL 2 criteria be used as guidelines for developing a Mars surface biosafety protocol. However, in order to satisfy the science objectives of the mission, special additional precautions may be necessary in order to prevent forward contamination with terrestrial microorganisms of samples that astronauts collect and study.

A quarantine program for crews and materials arriving on Earth from Mars is also prudent as a precaution, as in the days of the Apollo lunar missions, and together with a surface biosafety protocol and an anti-forward contamination protocol should be developed from the earliest stages of the mission planning. Indeed, since robotic MSR missions will precede human missions by several years, a receiving laboratory, which will in essence amount to a BSL 5 facility (BSL 4 plus additional measures to prevent contamination of the samples by terrestrial materials or organisms), could be in operation before a human Mars program even begins. The MSR receiving facility must be quarantine capable and might then be expanded in order to accommodate the needs of returning Mars crews. While, unlike in the case of the lunar missions, the return trip from Mars may be sufficiently long so that signs and symptoms of a Mars-born disease would be apparent before arrival on Earth, this cannot be assumed. More importantly, quarantine would allow not only for rigorous testing of the Martian materials but also for close medical observation and specialized testing of returning astronauts at a level that will not be possible onboard the return vehicle. In the case of robotic MSR missions, a strategy involving a shuttle rendezvous and pickup and containment check of the MSR container before landing in White Sands, New Mexico, where the facility could be located, can be made to meet a level 5 BSL with quarantine capability, as long as provisions are made for quarantining the shuttle crew at the facility should they find the container seal to have been compromised between Mars and low Earth orbit (LEO). It may also be possible, and would be ideal, to construct a Martian receiving facility on the Moon and to conduct the quarantine there. However, this will likely be of benefit only if enough funding is available to transport appropriate staff and equipment to this natural staging point and would probably amount to, not a mere outpost, but a full lunar base.

In planning and implementing a biosafety program, it is important to never lose sight of the overall long-term objectives of an aggressive Mars exploration program in which human expeditions will play an important role. Therefore, since the risk of finding human pathogens on Mars, although not zero is probably low, it should not be a contraindication for human Mars exploration. Furthermore, for astronauts to intentionally avoid all contact with Martian microorganisms, if they exist, while exploring the planet would defeat one of the prime, and certainly the most exciting, purposes of including humans in the Mars exploration program, which is to search for life. The risk that harm may come to a human crew on the Martian surface must be balanced with the potential benefits that the discovery of Martian life may yield.

Along with the possibility that a novel organism might produce a novel toxin comes the possibility that a novel organism might produce a novel compound that is useful in medicine or benefits humanity in some other way. In fact, even toxins are sometimes harnessed for clinical use as drugs, as in the case of the two toxins mentioned above; Botulinum toxin is used clinically (as Botox) for conditions such as blepharospasm and strabismus (35), as well as for cosmetic purposes in the skin, while ergotamine and its derivatives can be used in treating conditions that include migraine headache (11), orthostatic hypotension (4), and was used in the past for uterine bleeding (48). More importantly, if life exists on Mars, it might differ at the molecular level in major ways as compared to its terrestrial counterpart and thus constitute a second datum for biology, all life on Earth amounting to the first. A study of Martian life may therefore lead to a new understanding of biology so that we may eventually come to study life, not as a special case on Earth, but more in the way that we study physics and chemistry, that is, as a fundamental property of the Cosmos.

Acknowledgements

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