The Urologist's Guide to the Galaxy

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Abstract. "Far out in the uncharted backwaters of the unfashionable end of the Western Spiral arm of the Galaxy…." Stone disease has affected mankind since earliest recorded history and will trouble us as we strive for the stars. Zero and microgravity are risk factors for urolithiasis, but the incidence is not yet known. Yet, the possible "century of space exploration" lies before us if payloads can be inexpensively offloaded from Earth's surface to orbit. The scientific publications about medical conditions of astronauts, deep water environments (submarine) and extreme conditions (Arctic and Antarctic) were reviewed to better understand the urologic risks. Actual events were next sought and any scientific data regarding therapeutic intent was carefully scrutinized. Incidence and risk potential could then be calculated and potential for intervention would then be known. The National Space Biomedical Research Institute has classified space health hazards and stone disease as "Risk 12." Combined statistics from NASA's Gemini, Apollo, and Space Shuttle flights and long-term missions such as Shuttle-Mir or Skylab fail to reveal any "disclosed" emergency stone events. One published article suggests that some cosmonauts have in fact formed stones during space missions. Detailed data from 79 U.S. space missions, involving 219 person-flights, and 175 astronauts show 23 genitourinary problems (1.2 % or 0.07 incidence for 7 days). Submarine encounters are different, however, with 1.8 to 2.6 actual emergency evacuations per 1,000 person months and 23 kidney stone events (data from all subs in U.S. Atlantic Fleet 1993-1996). Extreme environment data appears more similar to that of spaceflight (despite full Earth's gravity) with 1,967 person-years distribution showing no definite stone formation/evacuation (but 335 or 3.6% were not-specified). Pak and co-workers at the University of Texas, Southwestern have extensively evaluated the metabolic consequences of bone-mineral loss and urinary parameters associated with the increased risk of stone formation in space. Astronauts are at significantly greater risk of forming calcium oxalate, calcium phosphate and uric acid stones, and this persists for a period of time following return to normal gravity. Conflicting data exists regarding submarine and extreme environmental databases as to the "actual" space mission risks but the hazard is real. Attempts to evaluate both diagnostic and therapeutic interventions are being pursued. As the number of space visitors increases, so should the incidence of urolithiasis. Both diagnostic and therapeutic methods need to be developed coincident to our further efforts in space.

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INTRODUCTION

The title of this paper comes, of course, from the late Douglas Adams' famous work of science fiction entitled *The Hitchhiker's Guide to the Galaxy* and this is appropriate because our actual knowledge of stone formation in space is shrouded in secrecy and speculation [1]. But the science of urinary supersaturation, physiology of bone resorption, and many of the deleterious effects of prolonged zero-gravity

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exposure are well described. We are now entering what many perceive as the “The Century of Space Exploration” and it behooves those of us interested in urinary calculus disease to review our current understanding of what lies ahead, and to review related hazardous environmental experiences in order to form some realistic expectations as mankind approaches Kardashev’s level I civilization [2]. Another possible reason for this exercise for many (like the author’s) is an absolute fascination about the potential for continued space exploration, sparked by Neil Armstrong’s memorable descent upon our moon [3].

SCIENCE FICTION

“*There is no way back into the past. The choice is the Universe—or nothing.*” stated H.G. Wells. Space rock 84001 is a piece of Mars ejected an estimated 3.6 billion years ago and which landed upon this third planet from the sun at the South Pole approximately 13,000 years ago. It appears to have organic tubes that indicate the strong possibility that there was life on that planet some time ago. Our interest in space is as old as the genre of science fiction itself, and quite probably older. We are currently in the midst of intense interest in Mars and some of Jupiter’s moons as they might hold basic knowledge on the origins of life. In addition, it has been postulated that our home world is prone to periodic, and perhaps sudden catastrophic impacts, from space debris that would behoove a knowledgeable species to figure out methods of space exploration, colonization and/or expeditious transportation.

Our current problem with these science fiction-like endeavors is the costs of placing payloads into outer space. It has been estimated that 800 million dollars per space shuttle launch, which can carry about 27 tons, costs us about $15,000 per pound (or roughly twice the cost of gold). There are promising technologies that quite likely will solve these huge financial hurdles and allow us to rapidly and far less expensively have access to near Earth orbit. These include the Lockheed Martin X-33 VentureStar, NASA’s collaborative hypersonic scramjet, the X-43A (which recently hit Mach 10) and my personal favorite, the “space elevator.” Using nanotechnology, carbon nanotubes might be created that would allow a fixed terrestrial point on the equator to be attached to an orbiting platform that would literally run payloads into outer space at a fraction of current costs. If any of these technologies (and assuredly others not listed) manages to prove feasible, the doorway to space will become wide open and our exploration of space will shift into high gear. In fact, the probability that this might be so has prompted many scientists to prematurely call our current century “The Century of Space Exploration.”

There are many hazards to space existence for terrestrial humans. The focus of this discussion will be upon the known risks of urolithiasis formation in outer space. The published literature will be reviewed, the physiology summarized and unpublished, but widespread, speculations shall be aired. In the end, our knowledge is not exact and the methods of dealing with colic in space are unknown and as speculative as science fiction itself.

SCIENCE FACT

Early in the clinical literature of urolithiasis it was documented that humans who are incapacitated and bed ridden are prone to kidney stones. In 1922, Paul from Toronto reported on 20 cases of nephrolithiasis occurring in men aged 22 to 37 (average 28.5) who developed renal calculi following war wounds. The average time from the wound to the first symptoms of stones was 17.7 months. All patients had extensive injuries, including osteomyelitis. Most of these patients were bedridden for prolonged times [4]. Fowweather, followed by Pulvertaft, both indicated that recumbency appeared to be the critical problem associated with calcium stone formation, not the degree of trauma [5-6]. The primary event increasing the risk of nephrolithiasis appears to be an acute mobilization of calcium from the skeletal reserves [7]. In some patients, hypercalciuria may be pronounced [8]. In these patients, indwelling Foley catheterization is also common and subsequent bladder infection makes upper tract seeding commonplace. Recurrent urinary tract infection therefore changes the primary stone risk in these patients with high urinary pH with the potential for ammonium production to form struvite stones (magnesium ammonium phosphate hexahydrate) [9]. In current practice with the emphasis on early mobilization and vigorous rehabilitation, no patients except perhaps those with global trauma (i.e. multiple organ injured individuals) run this risk. One current investigation on immobilization-related hypercalemia in a mere 5 patients tried to ameliorate bone mineral loss [10]. In all of this immobilized group, the hypercalcemia during three months of observation could be reversed by administration of low dose pamidronate (10 mg). In a review by Gordon and Reinstein, a discussion of common secondary problems associated with the management of complex trauma victims revealed that urolithiasis was a significant problem. In addition, the costs in managing this secondary problem was significant [11]. It would seem reasonable, despite a paucity of published data, that immobilized patients are at higher risk and maintenance of adequate hydration would be a minimal recommendation. The use of bisphosphonates is more uncertain but indicated if hypercalcemia or urolithiasis develops. A final area of consideration is the effect of physical activity on calcium balance, calcium requirements, and upon bone mineral mass. Because of the aging population and the increasing risk of osteoporosis-induced fractures, a significant volume of research is becoming focused upon these issues. In some studies, physical activity has been noted to have a more profound role in affecting enhanced bone mineral density prior to puberty [12]. The need for greater research and the potential for physical activity itself to have an effect upon calcium balance is critical and the application of these findings to zero-gravity environments is just beginning [13].

A corollary to the immobilization-related hypercalemia and stone formation scenario is the possibility of placing humans in microgravity activity in outer space. With the advent of cooperative international endeavors such as the Space Station, plans for a manned mission to Mars, and the real probability that China might attempt a mission to the moon, these considerations have assumed a more vigorous scientific scrutiny. The physiologic changes that occur to astronauts exposed to microgravity during space flight have been increasingly investigated. Body fluid volumes, electrolyte levels, and bone and muscle undergo significant changes as the body adapts to the weightless environment. There are both short-term space missions similar to those of Gemini, Apollo, and Space Shuttle flights and long-term missions such as Shuttle-Mir or Skylab [14]. In the former short-term space missions, negative calcium balance with bone mineral loss and associated hypercalciuria was noted during Gemini, Apollo, and Space Shuttle missions [14]. Additional alterations include elevated urinary phosphate, decreased fluid intake secondary to early flight space sickness (associated nausea and vomiting) with resulting decreased urinary volume and rising formation product [15]. Citrate has been shown to fall during space flight [16]. Whitson and coworkers have demonstrated that astronauts are at greater risk of forming calcium oxalate, calcium phosphate, and uric acid stones. In follow-up investigations, this same group studied more carefully 6 male astronauts with a mean age of 42.5 (range 36- 49 years old) flying Space Shuttle missions of 11 to 16 days [16]. Urine specimens were collected before, early in the mission (2-4 days), late in the mission (10-13 days), landing day, and 7 to 10 days after landing. Nutrition recommendations were rigorously controlled. Urine volume declined during the early flight but tended to equilibrate by post flight measurements. Urine output declined by 22-52% during spaceflight. Urine pH had a tendency toward increased acidity (lower pH) which also normalized by 7-10 days post flight. Urinary calcium levels increased for all members with individual variation being large (38 to 253 mg/d). Calcium excretion continued to increase during the flight. Urinary potassium was less during the early flight and urinary citrate was lower during the flight but neither were statistically different. The relative supersaturation of calcium oxalate, brushite, sodium urate, and uric acid all rose during early space flight. The calcium oxalate and brushite supersaturations remained statistically elevated throughout the entire space flight [16].

Whitson and colleagues further speculate that dietary factors of the astronauts also play a role in risk for urolithiasis formation. Fluid restriction, protein and calorie ingestion all increase urinary calcium and uric acid concentrations while decreasing urinary citrate. Dietary sodium can also promote renal calculus disease. Diets high in potassium and magnesium may have beneficial effects [16]. Zerwekh reviewed this metabolic data and generated specific nutritional recommendations for crew members on longer space missions. Pharmacologic intervention can raise urinary volumes, diminish bone losses and prevent reductions in urine pH and citrate levels [17].

There exists one published article suggesting that some cosmonauts have in fact formed stones during space missions [18-19]. Another report from NASA's Life Sciences Division suggests this to be a real probability [20]. In Pak's earlier investigations in stone formation by astronauts, he suggested that stone risk factors among applicants for spaceflight programs were environmental in origin [21].

STONES IN SPACE

Space flight is a hazardous activity. There are published well documented investigations into the pathophysiologic problems encountered [22]. In flight medical events for U.S. astronauts during the space shuttle program from April 1981 to January 1998 show a 42% incidence of space sickness but no definite reports of urinary colic and/or urolithiasis. Medical events reported from Russia's Mir from March 1995 to June 1998 likewise fail to reveal any stone events. But space exploration and manned flights are still infrequent compared to terrestrial explorations in other hazardous environments, such as deep sea and polar. Antarctic databases on health hazards also disclose no episodes of evacuation for urinary colic. The incidence of evacuation from U.S. submarines from 1993 to 1996 reveal 23 episodes of acute colic and stone passage out of 332 total emergency evacuations.

Stone disease represents a real risk to our human habitation in micro- or zero-gravity environments. The physiology behind this increased risk is well known and preventative strategies have been developed. The fact that stones in space have not been reported does not mean that they have not occurred. Astronauts as well as pilots in general have an obvious bias against coming forward in reporting these episodes, due to the fear of being grounded. In addition, the system would find that the cost of training specific individuals might outweigh the risk of stone formation in the "highly selected" individuals and efforts to keep them flying might outweigh and justify avoiding reporting. But stone disease in space is potentially serious, especially if exploration expands and extraterrestrial work environments are created that would prolong microgravity exposure times. NASA's "Bioastronautics Roadmap" calls renal stone formation "Risk 4." [23] The National Space Biomedical Research Institute calls stone disease "Risk 12." One published article only suggests that some cosmonauts have, in fact, formed stones during space missions. Detailed data from 79 U.S. space missions, involving 219 person-flights, and 175 astronauts do demonstrate 23 genitourinary problems (1.2% or 0.07 incidence per 7 days) but no further details are available. Conflicting data exists regarding actual space mission risk and stone incidence during submarine duty, but all would agree that the risk of stone disease in space is real. Attempts to evaluate both diagnostic and therapeutic interventions are being pursued actively and the funding for such endeavors is ongoing. As mankind strives to gain access to the final frontier of outer space, hazards must be assumed and methods for adapting to these risks must be found. Arthur C. Clarke stated, "*Two possibilities exist: either we are alone in the Universe—or we are not. Both are equally terrifying.*"

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