

**Human Research Program
Human Health Countermeasures Element**

Evidence Book

Risk of Renal Stone Formation

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I. PRD Risk Title: Risk of Renal Stone Formation

Description: Kidney stone formation and passage has the potential to greatly impact mission success and crewmember health for long-duration missions. Alterations in hydration state (relative dehydration) and bone metabolism (increased calcium excretion) during exposure to microgravity may increase the risk of kidney stone formation and it is unclear which mitigation strategy would be the most effective.

The Risk of Renal Stone Formation, as currently written in the Human Research Program Requirements Document (PRD), should also highlight that spaceflight- induced changes in urine biochemistry are conducive for stone formation.

II. Executive Summary of Evidence for Risk

The formation of renal stones poses an in-flight health risk of high severity, not only because of the impact of renal colic on human performance, but also because of complications that could possibly require crew evacuation such as hematuria, infection, and hydronephrosis. Evidence for risk factors comes from urine analyses of crewmembers documenting changes to the urinary environment that are conducive to increased saturation of stone-forming salts – the driving force for nucleation and growth of a stone nidus. Furthermore, renal stones have been documented in astronauts after return to earth and in one cosmonaut during flight. Biochemical analysis of urine specimens provided indications of hypercalciuria and hyperuricemia, reduced urine volumes, and increased urine saturation of calcium oxalate and calcium phosphate. A major contributor to the risk for renal stone formation is bone atrophy with increased turnover of the bone minerals. Dietary and fluid intakes also play major roles in the risk because of the influence on urine pH (more acidic) and volume (lower). Specific assessments in Skylab crewmembers indicated that calcium excretion increased early in flight (by 10 days) and almost exceeded the upper threshold for normal excretion (i.e., 300 mg/day in males) in some crewmembers during Skylab missions. Other crewmember data documented reduced intake of fluid and reduced intake of potassium, phosphorus and magnesium in the diet. Hence, data from both short-duration and long-duration missions indicate that space travel induces risk factors for renal stone formation that continue to persist after flight; this risk has been documented by reported kidney stones in crewmembers.

III. Introduction

Nephrolithiasis is the condition marked by the development of renal stones. Renal stones are aggregates of crystals that are formed in supersaturated urine (urine is usually supersaturated in terms of its salt components). Hypercalciuria is a characteristic of the skeletal adaptation to space, and contributes to the increased supersaturation of urine such as with calcium phosphate or calcium oxalate. However, whether a renal stone forms in supersaturated urine depends upon other risk factors. The presence of these aggregates in the renal collection or excretion system can potentially result in renal colic, hematuria, infection, and can obstruct urine flow to cause hydronephrosis. A renal stone formed during a spaceflight mission could cause acute illness with loss of that crewmember to the mission.

To date, there has been one reported episode of an in-flight renal stone occurrence. This renal stone formation occurred in a cosmonaut whose experience is described in detail in *Diary of a Cosmonaut: Two hundred eleven days in space* by Valentin Lebedev. A recent survey of renal stones in US astronauts has revealed a total of 14 episodes of kidney stones (Pietrzyk, 2007). Some of these episodes occurred in the preflight period (n=5) with the balance (n=9) having occurred in the postflight phase. The time period for the onset of symptomatic stone formation following return ranged from 9-120 months after landing. Six of the nine postflight episodes had occurred after 1994, which corresponded with the extended durations of space shuttle missions to 12 days. A total of 12 astronauts formed kidney stones with two astronauts having multiple episodes; both male (n=10) and female (n=2) astronauts were afflicted

Given the severity of the risk for renal stone formation, it is important to characterize the spaceflight conditions that promote nephrolithiasis in order to take appropriate steps to mitigate the risk. The primary risk factors for renal stone formation in space are the increased excretion of calcium due to bone atrophy and lower urine output. Other contributing risk factors include dehydration, diet (high sodium, high animal proteins), low urinary citrate, genetics, and environmental derangements (ambient temperatures). These factors can contribute to increased urinary supersaturation of salts, low urine pH, and reduced urine volumes – favorable conditions for crystallization.

Renal stones come in different types, and the formation of a *specific* stone-type depends upon the presence of particular risk factors. 1) The most common renal stone, and a main component in stones of mixed composition, is calcium oxalate. This type may occur as multiple stones or may recur, can induce pain with both passage and obstruction, and is commonly caused by *treatable* metabolic disorders of hypercalciuria. 2) Similar to calcium oxalate stones, uric acid stones induce the same adverse effects but differ with their rarer occurrence (only 5% of renal stones). Uric acid stones are also translucent and, unlike the other stones, cannot be distinguished by radiographs. 3) Struvite stones are generated by infections of urease-containing microorganisms that are capable of hydrolyzing the urea in urine to carbon dioxide and ammonia. When urine pH exceeds 7.2, struvite stones may form, and the resulting obstruction can fill the renal collection system and erode into the renal tissue. Treatment is by surgical removal unless stone size is <2 cm where lithotripsy can be applied to fragment the stone. 4) Unlike other renal stones, cystine stones have a single etiology – hereditary cystinuria – where stone formation begins in childhood and can grow large enough to fill the renal collection system. 5) Finally, brushite is the name for a calcium phosphate stone, the formation of which is promoted by high urine pH and supersaturation of urine with the calcium phosphate salt. Just as on Earth, it is more cost effective to prevent stone formation during a spaceflight mission than it is to treat a crewmember (Parks, 1996). Thus, understanding the etiology for the formation of specific stone types and identifying which stones are more likely to be formed during spaceflight missions will direct the application of appropriate countermeasures for nephrolithiasis.

Diagnosing nephrolithiasis is not as difficult as distinguishing the type of renal stone. It may be possible to delineate stones by physical features. Oxalate, cystine and struvite stones have distinctive appearances (stars, wax-like eggs, tree roots, respectively), but evaluation requires recovery of the stone itself, which is not always possible. Laboratory evaluations can be used to determine risk factors for stone formation based upon saturation levels of calcium, oxalate, and uric acid measured in 24-hour urine specimens. However, assessment of pH, urine volumes, urine citrate levels (an inhibitor of stone formation) and serum creatinine levels (a marker of optimal renal function) in urine and of calcium in serum will elucidate if the

conditions were optimal for stone formation. If hypercalcemia is detected, then assay of parathyroid hormone can be used to diagnose the existence of a metabolic disorder.

Additionally, if conditions that are conducive to increased urine saturation and to stone formation are detected, then countermeasure approaches, specific for stone type, can be implemented. For example, treating hypercalciuria (> 300 mg [males] or 250 mg [females] per day) requires identifying and addressing the cause of increased urinary calcium. Pharmacological agents or dietary adjustments can suppress bone atrophy or promote renal calcium reabsorption (such as with thiazide diuretics). Avoiding foods high in oxalate (nuts, pepper, chocolate, rhubarb, spinach, dark green vegetables, fruits) and diets high in fat will reduce hyperoxaluria (>75-150 mg/day). At Johnson Space Center, <45 mg/d is considered in the range of decreased risk and > 45 mg/d as an increased risk value. Reducing the ingestion of purine-containing foods (e.g., meats) will suppress hyperuricosuria. Ingesting an oral alkali such as potassium citrate will suppress calcium oxalate crystallization (by raising pH) and provide an inhibitor of crystal aggregation and growth (by binding the calcium ion to form the soluble calcium citrate). Increasing fluid intake to increase urine volume can dilute the urinary risk factors to bring these factors under the upper limit of metastability for solubility of the stone-forming salts (Whitson, 2001a). Even persons homozygous for cystinuria can dilute out the concentration of cystine by high fluid intake. Given the constraints of mission operations, the indiscriminate application of all these countermeasures would not be an effective approach to risk management. Alternatively, the full understanding of the risk factors incurred during missions in space and knowledge of the incidence of renal stone types is warranted in order to make judicious selection of prophylactic approaches.

Recent medical research has highlighted an additive effect of potassium citrate beyond the risk of stone formation. Recent medical research has shown a positive association between the ingestion of potassium citrate and increased bone density (Pak, 2002). Potassium citrate may also prevent bone loss by providing an alkali load averting the bone resorbing effect of sodium chloride excess (Sellmeyer, 2002). There is also an effect of potassium citrate to reduce bone loss in postmenopausal women, as revealed by decreases in bone resorption biomarkers, possibly by counteracting the deleterious effect of acidemia (Marangella, 2004). Potassium citrate also improves calcium balance among patients with distal renal tubular acidosis both by increasing intestinal calcium absorption and mitigating calcium excretion (Preminger, 1987).

This Evidence Base Report will highlight the risk for renal stone formation in space by outlining the characterization of risk factors as determined in crewmembers after short duration spaceflight missions on the space shuttle. Published flight data document some of the environmental and dietary contributors to renal stone formation (e.g., high animal protein intake; high acid load). As mentioned, the primary risks for stone formation are calcium excretion with increased bone resorption and low urine volume. Thus, the risk for renal stone formation is intimately linked to hypercalciuria induced by the unbalanced bone resorption during the uncoupled bone remodeling in space. The data acquisition and analyses for the flight experiment testing the efficacy of potassium citrate as a countermeasure for renal stone formation in long-duration crewmembers was completed in 2008. Results suggest that supplementation with potassium citrate decreased the stone risk by producing a biochemical environment that was less conducive to stone formation primarily through a decrease in calcium excretion and a higher urinary pH and not due only to the citrate concentration in urine. Protection against renal stone formation in long-duration spaceflight will require a multifaceted risk-mitigation approach, including personal and family medical history, risk assessment, education, sufficient fluid intake

to increase urine volume, and dietary controls, as well as pharmacological treatment. As a result of the knowledge gained in this study, the use of potassium citrate has been approved as an operational countermeasure to reduce the risk of stone formation (Whitson et al, 2009).

IV. Evidence

A. Spaceflight Evidence

The results from specimens obtained from crewmembers who have flown in space detail the biochemical and environmental risk factors associated with the risk for renal stone formation during and after spaceflight.

1. Historical Data from Skylab

Specific assessments in Skylab crewmembers indicated that calcium excretion increased early in flight (by 10 days) and almost exceeded the upper threshold for normal excretion (300 mg/day in males) in some crewmembers during Skylab missions (Figure 4-1).

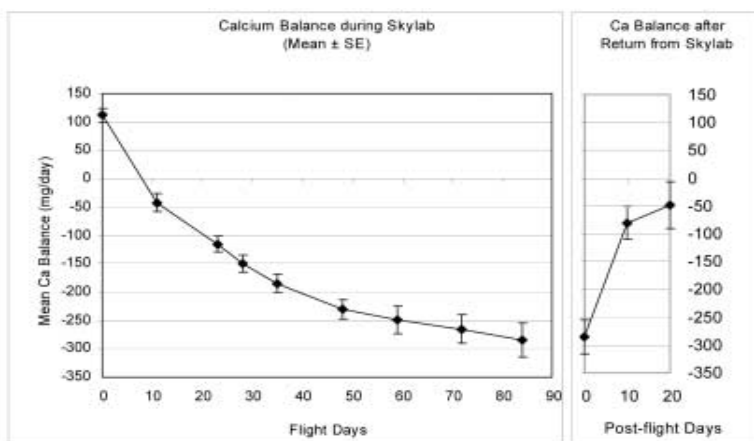


Figure 4-1. Calcium balance during and after Skylab missions. *Adapted from Rambaut and Johnston (1979)*

2. Short-duration spaceflight missions on Space Shuttle

Retrospective analysis of urinary data from U.S. Space Shuttle crewmembers was conducted in 24-hour urine specimens that were collected 10 days pre-launch (~L-10 day) and immediately post-landing. Analysis consisted of urine characteristics associated with renal stone formation and relative supersaturation of stone-forming constituents. All pre- and postflight data from Shuttle crewmembers are tabulated below (see Tables 4-1 through 4-3).

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Table 4-1. Mean Values for Urinary Biochemical Parameters in Crewmembers after Short Duration Spaceflight

| Parameter | Preflight (n=332) | Postflight (n=329) | P value | Normal Reference Values ^a |
|--------------------|----------------------|-----------------------|---------|--|
| Total Volume (L/d) | 2.1 ± 0.06 | 2.0 ± 0.06 | NS | 2-2.5 |
| <1 L/d | 13.0% | 13.1% | | - |
| <1-2 L/d | 38.9% | 46.2% | | - |
| >2 L d | 48.2% | 40.7% | | - |
| Oxalate (mg/d) | 38 ± 0.9 | 37 ± 0.9 | NS | 0-45 |
| Calcium (mg/d) | 183 ± 5.3 | 234 ± 6 | <0.05 | <300 M <250 F |
| pH | 6.05 ± 0.02 | 5.79 ± 0.03 | <0.05 | 4.5-8.0 |
| Citrate (mg/d) | 714 ± 16 | 629 ± 18 | <0.05 | > 320 |
| Magnesium (mg/d) | 116.0 ± 2.5 | 99.0 ± 2.2 | NS | 75-120 |

Values are Mean ± SEM; L/d – liters per day. Preflight urines collected 10 days before launch and postflight urines collected on landing following missions of <16 days. ^a JSC Clinical Laboratory and JSC Cellular and Biomedical Laboratory.

Table 4-2. Mean Values for Relative Saturation of Stone-Forming Salts in Urine from Crewmembers during Short Duration Spaceflight

| Parameter | Preflight n=332 | Postflight n=329 | P value | Normal Reference Value |
|-----------------|--------------------|---------------------|---------|------------------------------|
| Calcium Oxalate | 1.53 ± 0.06 | 2.26 ± 0.07 | <0.05 | < 2.0 |
| Brushite | 1.25 ± 0.06 | 1.00 ± 0.06 | <0.05 | < 2.0 |
| Sodium urate | 2.41 ± 0.11 | 1.42 ± 0.07 | <0.05 | < 2.0 |
| Struvite | 3.05 ± 0.83 | 3.69 ± 2.21 | NS | < 75.0 |
| uric H+ | 1.69 ± 0.08 | 2.27 ± 0.09 | <0.05 | < 2.0 |

Values are Mean ± SEM. The relative urinary supersaturations are unitless ratios determined from the activity product of the various concentrations of the urinary chemical composition and represent the saturation of the stone-forming salts and the concentration of the undissociated uric acid. The supersaturation data are expressed relative to the values from normal non-stone forming subjects and indicate the state of urinary supersaturation, a fundamental requirement for stone formation. Urinary supersaturation values < 2.0 indicate a decreased risk for calcium oxalate, brushite, sodium urate and uric acid stone formation. Values < 75.0 reflect a decreased risk for struvite stones.

Table 4-3. Prevalence of Biochemical Abnormalities in Urine in Astronauts Before and Following Short Duration Spaceflight

| Abnormality | Preflight | Postflight |
|--------------------------------|-----------|------------|
| Hypercalciuria (>250 mg/d) | 20.8% | 38.9% |
| Hypocitraturia (<320 mg/d) | 6.9% | 14.6% |
| Hypomagnesuria (<60 mg/d) | 6.0% | 15.8% |
| Urinary supersaturation (>2.0) | | |
| Calcium oxalate | 25.6 % | 46.2 % |
| Uric Acid | 32.8 % | 48.6 % |
| Brushite | 19.3 % | 13.1 % |
| Sodium urate | 44.9 % | 25.8 % |

In a series of investigations led by Peggy Whitson, Ph.D, environmental and biochemical risk factors for renal stone formation were extensively characterized for both short and longer duration missions. It was first reported that an increased risk of calcium oxalate and uric acid

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stone formation was evident immediately after spaceflight concurrent with the hypercalciuria and hypocitraturia quantified after return (Whitson et al., 1993). Further investigation, which included analysis of urine collected during flight, revealed that many of the contributing factors to renal stone formation during spaceflight were related to nutrition, urinary pH and volume output (Whitson et al., 1997). In addition, biochemical analysis of urine specimens obtained during longer Shuttle missions provided a temporal reflection of the risk indicating that the increased risk for renal stone formation occurs rapidly during spaceflight, continues throughout the mission, and persists following landing (Whitson et al., 1999). In-flight evidence from Space Shuttle missions associated the urinary supersaturations and decreased urine excretion with reduced fluid intake, and that increasing the volume of urine output effectively reduced the risk factor (that is, urine supersaturations) (Whitson et al., 2001a). However, the use of this approach as an in-flight countermeasure may not address all risk factors during a spaceflight mission. Figure 4-2a (preflight) and 4-2b (postflight) profiles display the relative risks of stone formation in a representative crew member of a Space Shuttle flight. Note that the increased postflight risk for stone formation (Figure 4-2b) corresponded i) with a larger excretion of calcium and a reduction in pH (metabolic factors); ii) with a reduction in total urine volume and increased levels of sulfate (hydration and dietary factors); and iii) with greater urine saturation for stone-forming salts (sodium urate, calcium oxalate, brushite, and uric acid stones).

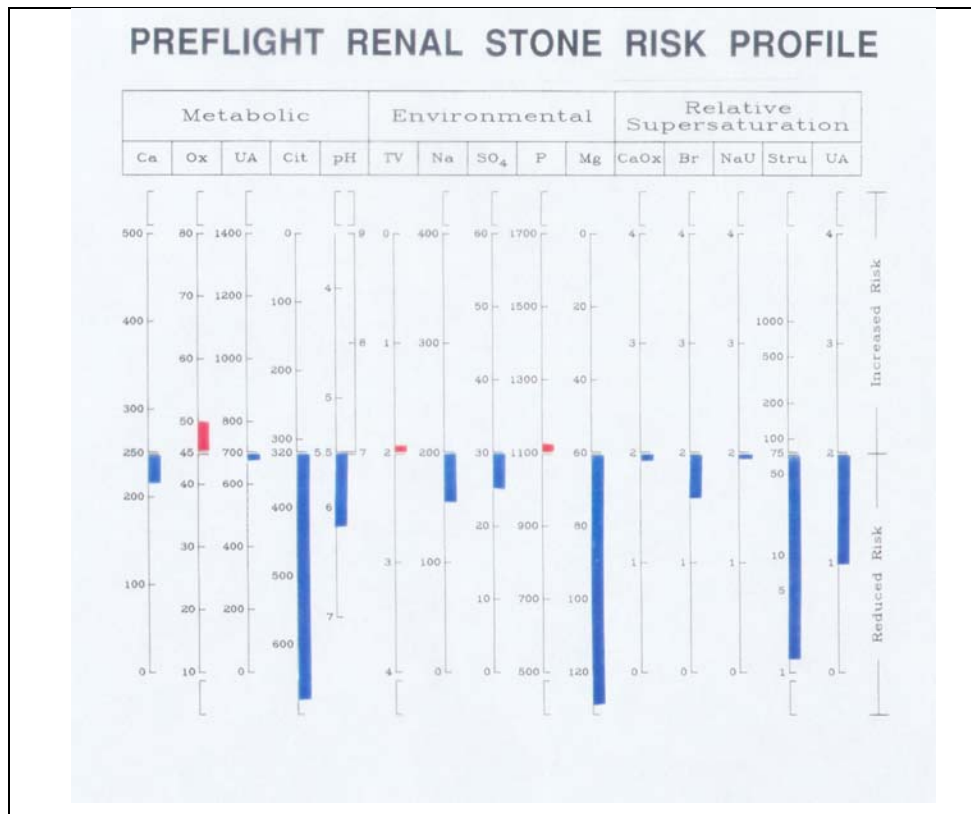


Figure 4-2a Representative preflight renal stone risk profile determined in a single crew member before a short-duration flight (i.e., Space Shuttle). BLUE bars represent decreased risk, RED bars represent increased risk.

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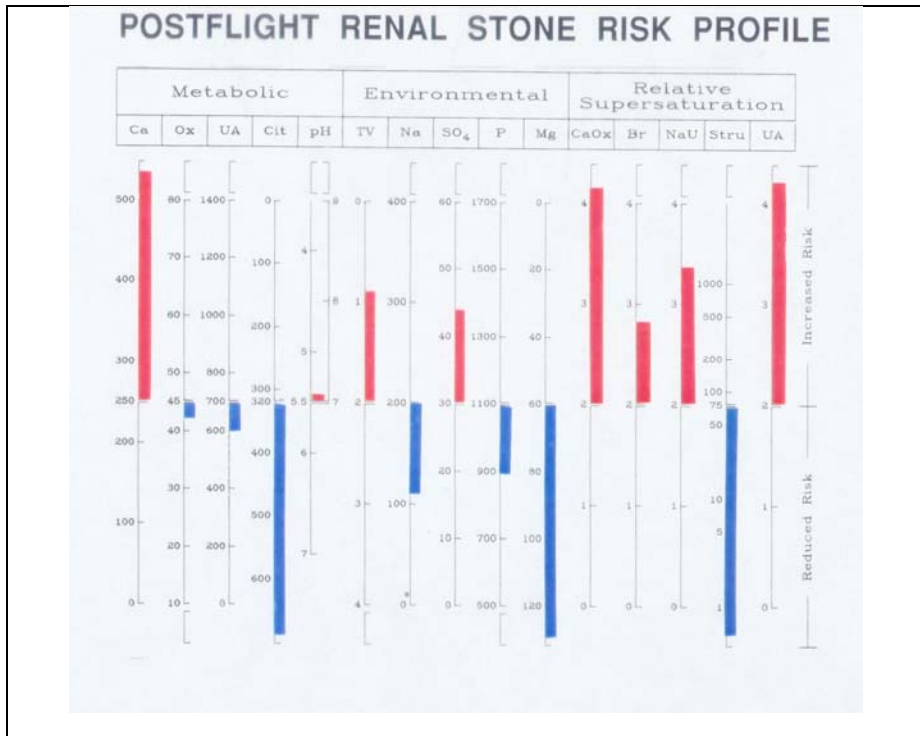


Figure 4-2b. Representative postflight renal stone risk profile determined in the same crewmember immediately following a short-duration flight (i.e., Space Shuttle). Blue bars represent decreased risk, red bars represent increased risk.

As discussed previously, a retrospective chart review for stone formation in the US astronauts (Pietrzyk, 2007) reports 14 cases of renal stone formation occurring in 12 different astronauts with 9 of those episodes occurring in the postflight period (n=7 astronauts). In addition to one in-flight stone formation in a cosmonaut, an additional cosmonaut has been identified as forming multiple urinary calculi (personal communication). Of the renal stones recovered from astronauts, 4 stones were of calcium oxalate, 1 stone was of uric acid, 1 stone was of mixed components, and 9 were of unknown composition.

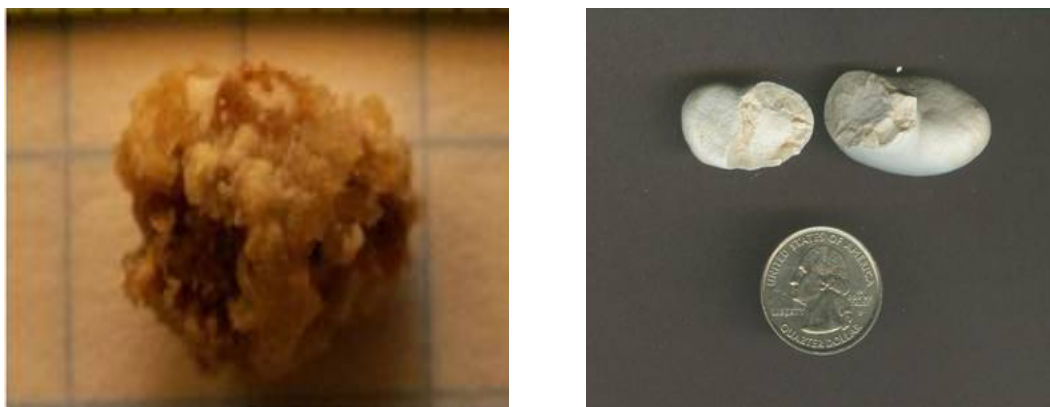


Figure 3 a,b. Microphotographs of a calcium-containing renal stones

While some of these astronauts appeared to have a history or predisposition for stone formation prior to spaceflight, unique habitability issues common to spaceflight and mission operations may exacerbate the risk for renal stone formation. These issues include food stability, preservation of food using high salt, dehydration, bone atrophy, quantity of onboard water supplies, and limited nutritional choices. It may be possible to reduce this risk by correcting operational issues; however, depending upon duration of specific mission, it may be also prudent to formulate criteria for excluding persons with pre-existing risk factors to reduce impact to mission objectives.

3. Long-duration during the Shuttle-Mir Missions

The results from an investigation of eleven astronauts and cosmonauts who flew on the Mir space station provided evidence of the risk for stone formation during long duration missions (Whitson et al., 2001). Data from missions ranging from 129 to 208 days suggested spaceflight and the return to Earth have acute effects on the urinary biochemistry that may favor increased crystallization in the urine. Changes previously observed during short duration Shuttle flights included a rapid increase in the supersaturation of the stone-forming salts in the urine early during the flight that continued through landing day. However, the stone-forming potential in the urine was different during and after spaceflight. During flight, an increased risk occurred for both calcium oxalate and calcium phosphate stones. Immediately after flight, however, the risk was greater for calcium oxalate and uric acid stone development, which could be attributed to low urine volumes and decreased urinary pH. In these long-duration crewmembers, there was a 47% decrease in urine volume early during the missions (< flight day 30) and a 39% lower urine output late in the mission (> mission day 60). Urinary calcium levels during the preflight period ranged from 159 mg/day to 316 mg/day, and during flight the range was 129 mg/day to 435 mg/day. During flight, 7 of the 11 crewmembers demonstrated higher in-flight urinary calcium values as compared to their respective preflight levels, and 5 of these 11 crewmembers exhibited calcium excretion greater than 250 mg/day. Data from these long duration missions suggested a similar trend, as with short duration missions, showing increased risk for calcium phosphate stone formation occurring early in-flight. These data suggested that the early phase (< 30 days) of spaceflight may generate conditions in which the risk of stone formation was greater than during the later phases of the mission. These data were consistent with the short duration Shuttle data in which both calcium oxalate and calcium phosphate risk increased.

4. International Space Station

Finally, a flight experiment (96-E057) performed during long duration missions (“Renal stone risk during spaceflight: Assessment and Countermeasure Evaluation” with PI: P. Whitson) will provide data from crewmembers of International Space Station (ISS) missions. The aim of the experiment was to evaluate the in-flight efficacy of potassium citrate as a mitigator of the formation of renal stones (particularly composed of calcium salts) during long-duration spaceflight. Potassium citrate is a known therapy for the formation of calcium oxalate, calcium phosphate, and uric acid containing stones, because of the formation of the soluble calcium citrate complex; risk factors are also alleviated by the alkalization of urine and by the reduction of physiological acid/base ratio as induced by potassium and the metabolism of citrate to carbonate. This double-blind study required crewmember subjects on Expeditions 3-6, 8, and

11-14 to consume two tablets (placebo or 20 mEq potassium citrate) with the last meal of the day every day from L-3 to R+14 days (3 days pre-launch to 14 days after return). Twenty-four hour urine specimens were collected three times during flight: early (< 35 days into flight), middle (between 36-120 days into flight), and late mission (within 30 days of undocking). All diet, fluid, exercise and medications were logged for 48 hours before and during the urine collection time to assess the potential impact from environmental factors. Urinary saturation levels were analyzed. In addition to evaluating the efficacy of potassium citrate to minimize the risk of stone formation, the results of this experiment described the renal stone forming potential in crewmembers as a function of time in space as well as the stone forming potential during the postflight period. Results of this investigation were briefly described above and recently published (Whitson. 2009)

B. Ground-based Evidence

Similar to the pharmacologic agent, potassium citrate, Potassium-*magnesium* citrate was evaluated as a countermeasure for renal stones in a flight analog experiment (Zerwekh, 2007). A double-blind, placebo-controlled study was conducted in normocalciuric human test subjects skeletally unloaded by prolonged bed rest (5 weeks) as an analog for spaceflight. Two 24-h urine collections were obtained to evaluate renal stone risk parameters and the relative saturation of calcium oxalate, brushite, and undissociated uric acid. Circulating parathyroid hormone (PTH) and vitamin D metabolite were measured in serum samples. As expected, bed rest immediately induced hypercalciuria by an increase of 50 mg/d in both groups. Subjects treated with potassium-magnesium citrate displayed reductions in the relative saturation of calcium oxalate and in the concentration of undissociated uric acid compared to placebo. PTH and vitamin D metabolites were reduced in both groups with no difference between groups in the decrements. In conclusion, potassium magnesium citrate is an effective inhibitor of renal stone formation as indicated by the reduced urine saturation of calcium oxalate and concentration of undissociated uric acid by the citrate chelation of calcium and the alkalization of pH, respectively.

V. Computer-Based Simulation Information

Late in 2008, a probabilistic analysis of renal stones in US astronauts had been initiated and development continues to be optimized by the Integrated Medical Model (IMM) team at Glenn Research Center.

VI. Risk in Context of Exploration Mission Operational Scenarios

Because of the reduced level of care, renal stone disease could cause acute illness with loss of that crewmember to the mission. Therefore it is a critical requirement to have a validated countermeasure to prevent renal stone formation prior to exploration missions. Countermeasures related to space and planetary habitability are important (for example, dietary restrictions of risk factors, improved food science, and sufficient hydration). However, as previously mentioned, the primary risk factor for the formation of calcium renal stones in space is the hypercalciuria induced by bone atrophy and low urinary output. Increasing fluid intake and thereby increasing urine volume can provide favorable changes in the urinary supersaturation of the stone-forming salts. However, increased urine volume alone does not address the underlying physiological

processes that may exacerbate the in-flight stone risk including hypercalciuria, hypocitraturia, and decreased urinary pH. Operational constraints, including supplies of onboard water and the busy crew workloads, may limit the benefits of hydration to minimize the risk of stone formation. Optimal countermeasures for the risk could mitigate multiple risk factors from the bone atrophy to the saturation of urine. Ideally, a countermeasure for bone atrophy could also mitigate the risk for renal stone formation. Furthermore, research priorities related to understanding the time course of bone loss and the influence of mechanical loading on planetary surfaces (both surface activities and partial gravity) are relevant to the risk for renal stone formation during exploration missions (see the Evidence Base Report on the Risk for Accelerated Osteoporosis.) Specific scenarios for exploration missions are defined according to the duration of time in space (Table 4-4).

Table 4-4. Definition of Exploration Mission Durations.

| Duration Length | Mission Location | Transit time to Location (days) | Length of Stay (days) | Transit time back To Earth (days) |
|------------------------|-------------------------|--|------------------------------|--|
| Short | Moon | 3 | 8 | 3 |
| Long | Moon | 5 | 170 | 5 |
| Short | Mars | 162 | 40 | 162 |
| Long | Mars | 189 | 540 | 189 |

VII. Gaps

The following are relevant and identified knowledge gaps associated with the risk for renal stone formation, given the context of the current exploration mission scenarios.

- Can successful mitigation of renal stone formation be achieved 1) by providing an inhibitor of stone formation, 2) by ensuring sufficient hydration of crewmembers (avoiding increased urine saturation), and 3) by optimal nutrition (such as foods replete in citrate, low in oxalate)?
- Will an alkali-based therapy for renal stone formation (such as potassium citrate) increase the risk for brushite stones due to the increase in urinary pH?
- Stone formation in the postflight period (and the relationship to stays on other planetary surfaces and return to Earth) should continue to be monitored in order to expand the evidence-to-date, particularly with regards to the types of stones formed (to identify the specific risk factor and appropriate countermeasure), the correlation with diet, and the time course for stone formation.
- Data mining for the renal stone risk should be integrated into a bone epidemiological analysis which, in its multifactorial analysis of bone atrophy in space, would address the primary risk factors for renal stone formation as well as any recommendations for crew selection standards (critical medical criteria for an optimal crewmember to serve on exploration missions).
- What is the time course of bone loss for spaceflight durations that are > 6 months (is the increased excretion of calcium that accompanies skeletal adaptation to space attenuated over time?) Can it be monitored real-time in space?
- What factors effectively suppress bone atrophy in space and the accompanying hypercalciuria (for example, partial gravity and pharmaceutical agents)?

VIII. Conclusion

NASA's strategic goals are for a human presence for exploration class missions, which include the goals of returning to the moon and landing on Mars. With these objectives, the "human system" will experience extended exposure to the unique environments of space and the adaptive effects of human physiology to weightlessness, to partial gravity, and to the operational constraints and limitations of space habitation. The adaptive effects of space travel on human physiology are seen as an altered urinary chemical composition that occurs both during spaceflight and after return to Earth. These biochemical changes in urine are known risk factors for the formation of renal stones. As of January 2007, 14 known symptomatic medical events consistent with urinary calculi have been experienced by 12 U.S. astronauts. Although previous stone formers are at high risk to form new stones, it is not possible to predict which crewmembers will form renal stones de novo on Earth or during space missions. Thus, efforts should continue to define the risk of renal stone formation in space with countermeasures focused on the prevention of stone formation.

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XI. List of Acronyms

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| ISS | International Space Station |
| KCit | Potassium citrate |
| mEq | Milliequivalent |
| PRD | Program Requirements Document |
| PTH | Parathyroid hormone |

Risk of Renal Stone Formation