NASA-TM-111752

RENAL-STONE RISK ASSESSMENT DURING SPACE SHUTTLE FLIGHTS

Peggy A. Whitson, Ph.D.

Medical Sciences Division, NASA/Johnson Space Center

Houston, Texas

Robert A. Pietrzyk, M.S.

KRUG Life Sciences Inc., Houston, Texas

Charles Y. C. Pak, M.D.

Section of Mineral Metabolism, Southwestern Medical School

University of Texas Health Science Center, Dallas, Texas

Running Title: Renal Stone Risk During Space Flight

Correspondence: Peggy A. Whitson, Ph.D., Astronaut Office, Mail Code CB, NASA/Johnson Space Center, Houston, TX 77058. Telephone (713) 244-8950; FAX (713) 244-8873

Prepared for submission to *J. Urology*

ABSTRACT

Purpose: The metabolic and environmental factors influencing renal stone formation before, during, and after Space Shuttle flights were assessed. We established the contributing roles of dietary factors in relationship to the urinary risk factors associated with renal stone formation.

Materials and Methods: 24-hr urine samples were collected prior to, during space flight, and following landing. Urinary factors associated with renal stone formation were analyzed and the relative urinary supersaturation ratios of calcium oxalate, calcium phosphate (brushite), sodium urate, struvite and uric acid were calculated. Food and fluid consumption was recorded for a 48-hr period ending with the urine collection.

Results: Urinary composition changed during flight to favor the crystallization of stone-forming salts. Factors that contributed to increased potential for stone formation during space flight were significant reductions in urinary pH, and increases in urinary calcium. Urinary output and citrate, a potent inhibitor of calcium-containing stones, were slightly reduced during space flight. Dietary intakes were significantly reduced for a number of variables, including fluid, energy, protein, potassium, phosphorus and magnesium.

Conclusions: This is the first in-flight characterization of the renal stone forming potential in astronauts. With the examination of urinary components and nutritional factors, it was possible to determine the factors that contributed to increased risk or protected from risk. In spite of the protective components, the negative contributions to renal stone risk predominated and resulted in a urinary environment that favored the supersaturation of stone-forming salts. The importance of the hypercalciuria was noted since renal excretion was high relative to the intake. Dietary and

pharmacologic therapies need to be assessed to minimize the potential for renal stone formation in astronauts during/after space flight.

Characterizing the effects of space flight on renal-stone formation is important to the National Aeronautics and Space Administration (NASA) because of the prevalence of this disease in the general population (~20% worldwide[1]), the severity of the symptoms that would require a mission abort, and the likelihood that certain physiologic reactions to space flight could increase the risk of stone formation.

Renal stones can consist of calcium oxalate, calcium phosphate, uric acid, cystine, and struvite; more than 75% of all formed stones contain calcium. Stone formation typically is the result of hypercalciuria, hyperphosphaturia, hyperoxalauria or hypocitraturia.[2,3] Several physiologic reactions to space flight affect urine composition in ways that influence the potential for renal-stone formation. One such reaction is bone loss, manifested by increased calcium excretion and negative calcium imbalance.[4-6] The high amounts of urinary calcium noted during Gemini, Apollo, Skylab and Space Shuttle missions[4-8] logically would increase the risk of stone formation even in the absence of other physiologic or environmental factors. Other factors also present that would potentially enhance this risk include in-flight increases in urinary phosphate concentrations,[4-9]; decreased fluid intake and vomiting, which will reduce urine volume,[4] and are associated with space motion sickness (especially early in flight).[10] Citrate, a potent inhibitor of calcium-containing stones, has never been quantified during space flight, but we found it to be substantially decreased immediately after flight relative to before.[11] This same study showed that astronauts are at greater risk of forming calcium-oxalate and uric-acid stones immediately after flight,[11] but the influences of readaptation to 1-*g* could not be ruled out without in-flight measurements.

Dietary factors also play a key role in the development of renal stones. For example, high-protein diets are known to increase urinary calcium and uric acid and decrease urinary citrate.[12] Oxalate from dietary sources may be even more lithogenic than dietary calcium, especially under conditions of calcium restriction. Reducing calcium intake enhances oxalate absorption by the gastrointestinal tract, which increases calcium-oxalate supersaturation.[13] Dietary sodium also may pose risks for hypercalciuria, since high sodium intake leads to increases in urinary sodium and calcium, which elevate the risk of sodium urate and calcium-containing stones. Because many Space Shuttle foods are preserved with salt and each crewmember may select their own diet menu, sodium intake could exceed 8 grams per day, and thus could potentially exacerbate the renal-stone risk during flight. Another key factor in stone risk is low fluid intake, which is associated with low urine volume and correspondingly high concentrations of stone-forming salts. Increasing fluid intake —and thus urine volume— has been shown to bring urinary risk factors under the upper limit of metastability for solubility of stone-forming salts.[14,15]

The study reported here is the first to characterize the risk of forming renal stones during exposure to microgravity. Both urinary components and dietary factors were assessed in an attempt to clarify which variables contribute to the increased risk of renal-stone formation, and eventually to allow development of countermeasures that minimize this risk.

MATERIALS AND METHODS

Subjects

This study was approved by the Johnson Space Center Human Research Policies and Procedures Committee, and all subjects gave informed consent before participating. Six male astronauts (mean age, 42.5 y, range 36–49; mean weight 76.8 kg, range 65.7–87.7), who flew on Space Shuttle missions ranging from 11 to 16 days, volunteered for the study.

Urine Collection

Each crewmember collected urine during two 24-h periods before launch, the last within 10 days of launch. During flight, void-by-void urine samples were collected early in the mission (on flight days 3–4) and late in the flight (2–4 days before landing). After landing, urine again was collected for two 24-h periods, once on landing day and once 7 to 10 days thereafter.

Urinary factors associated with renal-stone formation were analyzed by using the methods listed in Table 1, which are described in detail elsewhere.[11] Briefly, preflight and postflight samples were collected into containers and stored at about 4°C. At the end of each period, the contents were mixed and decanted into a graduated cylinder for total volume and pH measurements. A 10 ml aliquot was removed for biochemical analyses. A second 10 ml aliquot was acidified with 6 M hydrochloric acid for the analysis of citrate, oxalate and sulfate. Two additional aliquots were removed and thymol and thimerosal were added to serve as controls for the room temperature storage of the in-flight controls.

During flight, crewmembers collected urine in specially designed collection devices that contained 1.0 mL of 2.5 M lithium chloride as a volume marker. After mixing the contents well, crewmembers withdrew ~7-mL aliquots, placing them into tubes containing 0.05% thymol or 0.1% thimerosal, and stored at ambient temperature for the remainder of the flight. Upon return to Earth, the aliquots were sent immediately to the Johnson Space Center Biochemistry Laboratories and 24-h pools constructed.

Dietary Monitoring

Before and after flight, crewmembers maintained daily handwritten logs of food and fluid consumption for four 48-h periods, i.e., for 24 hours before and 24 hours during each urine-collection period. During flight, consumption of food and fluid was monitored according to the same schedule, but subjects used an automated bar-code scanning system in with each individually packaged food item labeled.

The in-flight diet was designed to meet the Recommended Dietary Allowances (RDAs) as established by the Food and Nutrition Board nutritional recommendations (Table 2). Neither diet nor activity level were restricted from each individual's normal pattern (during any of the sampling periods). In-flight consumption data were stored in the barcode reader and downloaded after landing. Nutrient content of the preflight and postflight foods was calculated with the Minnesota Nutrition Data System (NDS) software Program 2.8, developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis, MN (Food Database version 10A Nutrient Database version 25). Nutrient content of the in-flight foods were calculated from food chemical data generated by the Johnson Space Center Water and Food Analytical Laboratory.

Fluid intake was ad lib during all sampling periods. However, all crewmembers consumed the equivalent of normal saline (in the form of salt tablets swallowed with water) about 90 minutes before landing as part of an established protocol to minimize orthostatic intolerance on re-exposure to gravity.

<< Table 1 to be inserted about here >>

Statistics

Statistical tests included one-way repeated analysis of variance, with significance located by Dunnett's post hoc test. Statistical significance was accepted at the 0.05 level. Statistical analyses was completed using SigmaStat statistical software (Jandel Scientific, San Rafael, CA.). All data reported as means +/- SEM.

RESULTS

Urinary variables for the 6 crewmembers studied are listed in Table 2. Despite the small number of subjects, significant changes were noted in urinary pH, calcium, potassium, uric acid, and the relative supersaturation ratio of calcium oxalate and brushite. Phosphate, magnesium, oxalate and sulfate were unchanged during space flight. Slight but statistically nonsignificant changes that contributed to the overall calculated relative urinary supersaturation ratios included decreased urinary volume and decreased citrate.

All six crewmembers had lower in-flight 24-hour urine volumes than preflight although this decrease was not statistically significant. Total urine volume decreased during the early in-flight phase, from 1.676 L/d before flight to 0.797 L/d during the early in-flight sampling period. Postflight urine volume was equivalent to preflight volume.

Although urinary pH seemed to decline during flight, the drop did not reach statistical significance until landing day (preflight, 6.01 vs. landing-day, 5.14). pH had returned to the preflight value by 7–10 days after landing.

Urinary calcium levels increased during the space flight for all crewmembers with a significant increase at the end of the flight as compared to preflight. Individual variation among subjects was large, with preflight concentrations ranging from 38 to 253 mg/d, and early in-flight values ranging from 73 to 197 mg/d. (No data were available from one subject during the early in-flight period.) Calcium excretion had increased slightly by the late in-flight period (222±34 mg/d, n.s.), but the difference did not reach significance until landing day (245±70 mg/d). Urinary potassium was significantly less during early flight than before (1439 ±256 mg/d during vs. 2620±308 before), and returned to preflight levels after landing. Urinary citrate during flight may have been lower than before flight, but the difference was not statistically significant.

<< **Table 2 to be inserted about here** >>

Relative urinary supersaturation ratios were calculated from the results listed above (Table 2) using the methods of Finlayson.[16] These ratios represent the difference from a normal non-stone-forming population. Relative supersaturation ratios of calcium oxalate, brushite (calcium phopshate), sodium urate and uric acid rose into the increased-risk range (> 2.0) for renal-stone formation during the early in-flight period (Figure 1). (Relative supersaturation values <2 for calcium oxalate, brushite, sodium urate and uric acid saturation and <75 for struvite are in the "low" risk category.) The ratio of calcium oxalate supersaturation significantly increased compared to preflight (1.52±0.4) during the early in-flight period (2.95±0.65) and remained significantly elevated throughout the remainder of the space flight (2.78±0.47). The ratio of calcium oxalate supersaturation remained in the high risk range (> 2.0) on landing day but was not statistically different than preflight. The risk of brushite stone formation was similar to the risk observed for calcium oxalate with levels significantly rising during flight and returning to preflight levels following space flight. The risk of sodium urate and uric acid stone formation increased into the high risk range during the space flight, although the increase was not statistically significant.

The dietary factors that most directly influence renal-stone risk factors are listed in Table 3. Consumption of both fluid and energy (kcal/day) were substantially less during the in-flight periods (45–48% decrease for fluid and 36–46% decrease for energy). A comparison of fluid intake vs. urine output is illustrated in Figure 2. Significant differences in these parameters as compared to before flight were noted for dietary fluid intake throughout the space flight. On landing day, both fluid intake and energy intake still were lower than before flight. However, interpretation of the landing day data should be viewed with caution considering diet records may be incomplete due the heavy schedule of activities associated with Shuttle landing procedures.

Consumption of protein, potassium, phosphorus, and magnesium during flight also was lower than before. No significant differences were noted among sampling periods in consumption of oxalate, sodium, or calcium, although there tended to be a decrease in all of the parameters, consistent with decreases in energy consumption. A comparison of ingested calcium vs. urinary calcium excretion is illustrated in Figure 3. In this case, urinary calcium during the late in-flight phase is elevated as compared to the preflight control, even though ingested calcium levels are below preflight ingestion.

<< Table 3 to be inserted about here >>

DISCUSSION

This study is the first to characterize renal stone-forming potential in astronauts during space flight. In addition, the concurrent examination of the nutritional components allowed us to establish the role of various environmental risk factors associated with space flight.

The renal-stone profile developed by Finlayson[16] to calculate ionic equilibria in urine is used extensively to estimate the relative supersaturation ratio in urine[17] and was used in this study to examine the effects of microgravity on renal stone risk. This risk profile allows assessment of urinary conditions that favor or inhibit crystal formation. Once a crystal has formed, growth and aggregation may cause the formation of renal stones. Estimates of the degree of urinary saturation ratios of calcium phosphate, calcium oxalate, and uric acid are used clinically with patients with disorders of calcium metabolism to evaluate their probability of forming stones.[17] The relative urinary supersaturation ratios of the six subjects examined here was in the low-risk range for renal-stone formation during the preflight period (Figure 1).

Our previous study of astronauts immediately after flight,[11] indicated that the ratios of supersaturation for calcium oxalate and uric acid saturation were elevated after flight as compared to the preflight controls. However, the much lower subject number in this study (6 as compared to 86) probably contributed to the nonsignificance of these increases immediately after landing. Thus, even though these changes immediately after flight in this current study did not indicate a significant change, the trend for elevated ratios of calcium oxalate and uric acid is similar to that observed previously with a much larger study group.

The relative supersaturation ratios of calcium oxalate and brushite were greater during flight than before even in this small study group. Factors that contributed to this risk included increased urinary calcium (late in flight and on landing day), decreased urine volume (early and late in flight), and decreased citrate (in flight and on landing day). Although urinary calcium —and perhaps phosphate— had decreased by the initial in-flight phase, brushite risk was significantly elevated at that time, probably because of the combination of the diminished urine volume and urinary citrate and the elevated calcium. Thus, even though the changes in urine volume and citrate were not statistically significant in this small group during space flight, the decreases contributed to the overall greater stone-forming potential. The relative supersaturation ratios of calcium oxalate and brushite remained above the preflight levels during the late in-flight phase. Upon return to 1-*g*, the relative supersaturation ratio of brushite declined to below preflight levels, a finding consistent with our previous observations.[11]

The uric acid saturation ratio may have increased during the early in-flight and the immediate postflight phases, though not significantly. The reduction in urine volume (early in flight) and the significant decrease in urinary pH (on landing day) may have contributed to a relative increase in risk, despite a drop in uric acid concentration early in flight. The trend toward higher relative supersaturation of uric acid and the lower urinary pH immediately after flight are consistent with the our previous observations in a much larger study group.[11]

Energy for metabolism, growth, physical activity, excretory processes, and thermal regulation is supplied by the diet; that which the body does not need is stored or excreted. Consumption of fluid, protein, calcium, oxalate, and sodium may play important roles in developing or treating renal stones.[18,19] Consuming large amounts of fluid increases urinary output, which decreases the saturation of the stone-forming salts. For example, a daily urine volume of 2 L or more is typically prescribed for those individuals who have previously formed stones, requiring the ingestion of approximately 3 L of fluid. Although increasing urine volume decreases the risk of stone formation, no evidence exists to support the idea that a high fluid intake would decrease the urinary concentrations of renal-stone inhibitors.[12,15] In the present study, the substantial drops in energy and fluid consumption during flight relative to before may reflect an association between meals and fluid intake and may suggest that little fluid was consumed between meals (Figure 2). This relationship between meals and fluid ingestion is the result of the fact that most space flight foods are rehydrated with water before consumption and this fluid accounts for a large percentage of the total ingested fluid. Reductions in energy, protein, and fluid consumption early during flight may have resulted from symptoms of space motion sickness (not reported), suppressed appetite, or heavy work schedules. Fluid intake on landing day still was less than that before flight, but had increased to preflight levels by 7–10 days after landing.

High calcium intake has long been thought to contribute to the formation of calcium-containing stones; in fact, restrictions on calcium have been prescribed to lower urinary calcium concentrations. However, recent evidence reveals that a diet low in calcium may increase the risk of calcium oxalate stones through increased gastrointestinal absorption of oxalate.[21] If dietary calcium is excessive, healthy individuals excrete the excess in urine. Because space flight induces both bone loss and the resultant hypercalciuria, astronauts are assumed to be at higher risk for renal stones. In this study, large individual differences in calcium intake may have obscured a general tendency for intake to decline during flight. However, urinary calcium concentration seemed to be independent of intake during the late in flight phase in this study (Figure 3). This is consistent with expectations of urinary calcium increases resulting from the space flight-induced bone loss, independent of dietary ingestion of calcium.

Diets high in animal protein also are known to increase urinary concentrations of calcium, oxalate, and uric acid, as well as decreasing the urinary excretion of citrate and lowering the pH of the urine. These changes increase the risk of calcium-oxalate and uric-acid stone formation.[12,22,23] Although the putative decline in in-flight calcium consumption in the crewmembers studied here was not statistically significant, their energy intake was far below the recommended 1000–1200 mg/d, with a correspondingly low protein ingestion. Thus, in this study, it does not appear that dietary protein and oxalate were significant factors in renal stone risk. However, in the future, with the potential resolution of the energy intake (increasing to the recommended daily average) there may be an increase in the stone forming-potential caused by higher protein/oxalate diets.

Dietary sodium also promotes renal-stone development. Dietary sodium intake has been correlated in several studies with increased urinary calcium, sodium and reducing urinary citrate.[12,24] Sodium intake during the preflight period was over the upper limit established by NASA for the astronauts and tended to decrease during flight similar to energy intake. However, the correlation between urinary and dietary sodium is not consistent on landing day. Even though dietary sodium is equivlaent to preflight, there is a tendency for urinary sodium to decrease in this group of 6 subjects. Previous studies have demonstrated a significant sodium retention during landing day and the early phases of recovery.[4,11] In this study, urinary sodium was statistically greater 7 to 10 days after landing as compared to preflight levels. Recovery results after previous space flights have varied; however, the 9 Skylab crewmembers and 4 subjects on the SLS-1 mission demonstrated a similar pattern, decreasing initially and then increasing above preflight values.[4,9] On the other hand, urinary sodium in 3 subjects on SLS-2 did not decrease on landing day nor increase thereafter, although postflight concentrations were higher than preflight ones.[9]

By contrast, diets high in potassium or magnesium may provide beneficial effects with regard to stone formation. Potassium generally indicates that a subject is ingesting more alkali (e.g. citrus fruits), which would typically result in increased urinary citrate.[20] Magnesium has been shown to inhibit renal-stone formation by directly complexing with oxalate, reducing the risk of calcium oxalate stones.[25] In our study, dietary potassium and magnesium were significantly less during flight and immediately after as compared to before flight, but returned to preflight levels by 7 days after landing. A parallel decrease in the urinary potassium concentration was noted, however, urinary magnesium did not change over the course of the study. Thus, lower potassium levels, but not magnesium, contributed to the stone-forming potential exhibited by the astronauts during short-term space flight. Longer duration impacts of decreased ingestion of dietary magnesium may further exacerbate risk assessments on extended duration space flights since the magnesium stores in the bone may be altered/depleted.

Probably the key dietary influence on renal-stone risk during flight was the very low fluid intake, which resulted in correspondingly low urine volumes. Urinary output decreased by 22-52% during space flight. In fact, immediate postflight results indicate those crewmembers voiding 2 L or more of urine on landing day are all within the low risk range for stone-forming potential (Whitson et al., unpublished data). While fluid intake prescriptions could potentially alleviate/minimize the in-flight risk as well, there are considerably more physiologic changes that have a negative impact which occur during space flight, as compared to postflight, including metabolic changes that result in hypercalciuria and hypocitraturia. Thus, hydration alone may not be completely effective at eliminating the renal stone-forming risk associated with space flight.

CONCLUSIONS

The complexity, expense, and visibility of the human space flight program necessitates that every effort be made to ensure the success of each mission and protect the crewmembers from unwarranted risk. Having a better understanding of the risk factors involved in stone formation during space flight will allow the development of a means to alleviate/minimize some of these risks. Our results clearly indicate that exposure to microgravity changes the urinary chemical environment so as to favor supersaturation of stone-forming salts, including calcium oxalate and brushite. The increased risk seems to take place quickly upon exposure to microgravity, and to continue throughout space flights of 11-16 days.

Because dietary factors, especially fluid intake, or pharmacologic intervention can significantly influence the urinary chemical composition, countermeasures to minimize the risks of renal-stone development during space flight should be pursued. In addition, correcting the low dietary intake of crewmembers to recommended levels will have to take into account the potential negative effects on the urinary chemical composition and the potential increased risk for renal stone formation. Hydration therapy should be proposed to all crewmembers as a means to reduce the urinary concentration of the stone-forming salts. Potassium citrate also could be used to raise the urinary pH and increase the urinary citrate concentration for short duration missions. For long space missions (>30 days), consideration should be given to bisphosphonate therapies to alleviate hypercalciuria and to minimize microgravity-induced bone loss.

ACKNOWLEDGMENTS

This study was funded as part of the Johnson Space Center Extended Duration Orbiter Medical Project. The authors appreciate the assistance of the JSC Clinical Laboratories in analyzing urine chemistry, Barbara L. Rice of KRUG Life Sciences for dietary analyses, J. Travis Brown and the JSC Flight Projects Office for flight integration and support, and Christine Wogan for editorial input. We also thank the astronauts who made this study possible.

REFERENCES

1. Preminger. G. M.: Renal calciuli: pathogenesis, diagnosis and medical therapy. Semin. Nephrol., 12: 200, 1992.

2. Breslau, N. A. and Sakhaee, K.: Pathophysiology of nonhypercalciuric causes of stones. In: Renal Stone Disease. Edited by C. Y. C. Pak. Boston: Martinus Nijhoff Publishing, chapt. 3, pp. 47, 1987.

3. Samuell, C. T. and Kasidas, G. P.: Biochemical investigations in renal stone formers. Ann. Clin. Biochem., 32: 112, 1995.

4. Leach, C. S. and Rambaut, P. C.: Biochemical response of the Skylab crewman: an overview. In: Biomedical Results from Skylab. Edited by R. S. Johnston and L. F. Dietlein. NASA SP-377. Washington, D.C.: National Aeronautics and Space Administration, chapt. 23, pp. 204-216, 1977.

5. Leach, C.S. and Rambaut, P. C.: Biomedical observations of long-duration manned orbital spaceflight. J. Am. Med. Women's Assoc., 30: 153, 1975.

6. Whedon, D., Lutwak, L., Rambaut, P. C., Whittle, M., Leach, C. S., Reid, J. and Smith, M.: Effects of weightlessness on mineral metabolism: metabolic studies on Skylab orbital space flights. Calcif. Tissue Res., 21: 423, 1976.

7. Nicogossian, A. E.: Overall physiological response to space flight. In: Space Physiology and Medicine, 2nd Edition. Edited by A. E. Nicogossian, C. L. Huntoon, and S. L. Pool. Philadelphia: Lea & Febiger, chapt. 7, pp. 139–153, 1989.

8. Whedon, D., Lutwak, L., Rambaut, P. C., Whittle, M., Smith, M. W., Reid, J., Leach, C. S., Stadler, C. R. and Stanford, D. D.: Mineral and nitrogen metabolic studies, experiment M071. In: Biomedical Results from Skylab. Edited by R. S. Johnston and L. F. Dietlein, NASA SP-377. Washington, D. C.: National Aeronautics and Space Administration, chapt. 18, p. 164, 1977.

9. Leach, C. S., Alfrey, C., Suki, W. N., Leonard, J. I., Rambaut., P. C., Inners, L. D., Smith, S. M., Lane, H. W. and Krauhs, J. M.: Regulation of body fluid compartments during short-term space flight. J. Appl. Physiol., 81(1): 105, 1996.

10. Nicogossian, A. E., Pool, S. L. and Uri, J. J.: Historical perspectives. In: Space Physiology and Medicine, 3rd Edition. Edited by A. E. Nicogossian, C. L. Huntoon, and S. L. Pool. Philadelphia: Lea & Febiger, chapt. 1, pp. 3–49, 1994.

11. Whitson, P. A., Pietrzyk, R. A., Pak, C. Y. C. and Cintron, N. M.: Alterations in renal stone risk factors after space flight. J. Urol., 150: 803, 1993.

12. Goldfard, S.: The role of diet in the pathogenesis and therapy of nephrolithiasis. Endocrinol. Metab. Clin. North Am., 19(4): 805, 1990.

13. Curhan, G. C. and Curhan, S. G.: Dietary factors and kidney stone formation. Compr. Ther., 20(9): 485, 1994.

14. Goble, N. M.: Hydration monitoring in the long-term prophylaxis of nephrocalcinosis. West of England Med J., 106: 15, 1991.

15. Pak, C. Y. C., Sakhaee, K., Crowther, C. and Brinkly, L.: Evidence justifying a high fluid intake in treatment of nephrolithiasis. Ann. Intern. Med., 93(1): 36, 1980.

16. Finlayson, B.: Calcium stones: some physical and clinical aspects. In: Calcium Metabolism in Renal Failure and Nephrolithiasis. Edited by D. S. David. New York: John Wiley & Sons, p. 337, 1977.

17. Pak, C. Y. C., Skurla, C. and Harvey, J.: Graphic display of urinary risk factors for renal stone formation. J. Urol., 134: 867, 1985.

18. Brown, W. W. and Wolfson, M.: Diet as culprit or therapy. Clinical Nutrition 77(4): 783, 1993.

19. Hill, J. M., Harvey, P.W. and Fleming, S.J.: Dietary treatment of idiopathic urolithiasis. Med. J. Aust., 159: 366, 1993.

20. Wabner, C.L. and Pak, C.Y.C..: Effect of orange juice consumption on urinary stone risk factors. J. Urol. 149: 1405, 1993.

21. Massey, L. K., Roman-Smith, H. and Sutton, R. A.: Effect of dietary oxalate and calcium on urinary oxalate and risk of formation of calcium oxalate kidney stones. J. Am. Diet. Assoc., 93: 901, 1993.

22. Breslau, N. A., Brinkley, L., Hill, K.D. and Pak, C.Y.C.: Relationship of animal protein to kidney stone formation and calcium metabolism. J. Clin. Endocrionol. Metab. 66(1): 140, 1988.

23. Wainer, W., Resnick, V. A. and Resnick, M. I.: Nutritional aspects of stone disease. In: Renal Stone Disease. Edited by C. Y. C. Pak. Boston: Martinus Nijhoff Publishing, chapt. 4, pp. 85–120, 1987.

24. Massey, L. K. and Whiting, S. J.: Dietary salt, urinary calcium and kidney stone risk. Nutr. Rev., 53(5): 131, 1995.

25. Linberg, J., Harvey, J. and Pak, C.Y.C.: Effects of magnesium citrate and magnesium oxide on crystallization of calcium salts in urine: changes produced by food-magnesium interaction. J. Urol., 143: 248, 1990.

Table 12. Nutritional Recommendations (RDAs*) for Crewmembers During Space Flight

Energy:	Men (30–60 y): 1.7(11.6W+879) kcal/day	
	Women (30–60 y): 1.6(8.7W + 829) kcal/d	
	where W = weight in kg; e.g., a 70-kg man would need 2875 kcal/d	
Protein:	12–15% of total calories; e.g., a 70-kg crewmember would need 86–108 g/d	
	Short-Term Missions *	Missions > 30 days **
Fluid:	At least 2000 mL/d	At least 2000 mL/d
Calcium:	800 mg/d	1000-1200 mg/d
Sodium:	< 3500 mg/d	< 3500 mg/d
Potassium:	3500 mg/d	3500 mg/d
Magnesium:	350 mg/d (males) 280 mg/d (females)	350 mg/d

* RDA, Recommended Daily Allowances as determined by National Research Council, Food and Nutrition Board, 10th Edition, 1989.

** NASA Nutritional Advisory Committee, 1995.

Table 2. Renal-Stone Risk-Assessment Profile for Six Male Astronauts Before, During, and After 11- to 16-Day Space Shuttle Missions

	Before Flight	Early In Flight	Late in Flight	Landing Day	7–10 Days After Landing	Signif-icance
Total volume (L/d)	1.676 (0.09)	0.797 (0.08)	1.303 (0.17)	1.524 (0.35)	1.572 (0.31)	ns
pH	6.01 (0.18)	5.95 (0.19)	5.92 (0.13)	5.14 (0.05)*	6.09 (0.14)	$p < 0.05$
Calcium (mg/d)	166.2 (32.7)	131.8 (22.0)	221.8 (34.4)	245.2 (70.2)*	227.1 (50.0)	$p < 0.05$
Phosphate (mg/d)	884.8 (110)	822.8 (170)	920.5 (104)	678.0 (165)	933.2 (166)	ns
Oxalate (mg/d)	32.1 (4.6)	27.2 (2.7)	31.0 (2.4)	23.4 (3.6)	28.5 (5.4)	ns
Sodium (mg/d)	2597 (443)	1807 (104)	2127 (285)	1704 (410)	4029 (654)*	$p < 0.05$
Potassium (mg/d)	2620 (308)	1439 (256)*	1675 (177)*	1713 (395)	2157 (331)	$p < 0.05$
Magnesium (mg/d)	93.5 (6.6)	89.2 (6.0)	101.8 (10.3)	71.2 (13.3)	97.8 (9.7)	ns
Citrate (mg/d)	717.7 (115)	468.8 (109)	522.3 (66)	456.3 (82)	671.3 (148)	ns
Sulfate (mmol/d)	20.8 (1.7)	13.3 (1.8)	20.7 (2.4)	21.9 (3.9)	17.0 (2.2)	ns
Uric Acid (mg/d)	593.5 (49.0)	321.6 (32.3)	454.3 (72.4)	267.2 (74.2)*	556.2 (63.7)	$p < 0.05$
Creatinine (mg/d)	1621 (159)	1237 (182)	1408 (61)	1598 (195)	1710 (152)	ns
CALCULATED RELATIVE SUPERSATURATION						
Calcium Oxalate	1.52 (0.40)	2.95 (0.65)*	2.78 (0.47)*	2.07 (0.40)	1.60 (0.28)	$p < 0.05$
Brushite	1.11 (0.32)	2.20 (0.32)*	2.10 (0.43)*	0.32 (0.07)	1.92 (0.31)	$p < 0.05$
Sodium Urate	1.83 (0.47)	2.66 (0.50)	1.77 (0.42)	0.66 (0.42)	3.59 (0.88)	ns
Struvite	1.29 (0.78)	3.46 (1.44)	0.99 (0.28)	0.05 (0.04)	1.05 (0.32)	ns
Uric Acid Saturation	1.96 (0.69)	2.31 (0.75)	1.68 (0.31)	2.84 (0.76)	1.21 (0.38)	ns

Asterisk denotes significant differences from before flight, $p<0.05$.

Values for before flight are the means (± SEM) from two separate preflight urine-collection sessions. All other values are the average of 6 subjects (except early in-flight, n=5).

Table 3. Nutrient Consumption in Six Male Crewmembers Before, During, and After 11- to 16-Day Space Shuttle Missions

	Before Flight	Early In Flight	Late in Flight	Landing Day	7–10 Days After Landing
Fluid (g /d)	3127 (211.1)	1632 (91.3)*	1704 (219.1)*	2499 (265.5)	2403 (236.5)
Energy (kcal/d)	2752 (278.6)	1485 (179.2)*	1754 (187.4)*	1733 (306)*	2323 (316)
Protein (g/d)	110 (13.3)	41.9 (6.3)*	67.1 (11.9)	51.8 (7.5)*	90.9 (10.9)
Oxalate (mg/d)	193.6 (62.1)	138.8 (37.5)	164.8 (53.4)	133.4 (66.7)	156.5 (50.1)
Sodium (mg/d)	3666 (374.4)	2292 (414)	2714 (405.8)	3501 (286.1)	3711 (623)
Potassium (mg/d)	3644 (407.7)	1101 (155.4)*	1536 (225.8)*	1859 (208.2)*	3003 (368.9)
Calcium (mg/d)	905 (207.2)	450 (67.9)	523 (37.5)	705 (105.5)	918 (232.9)
Phosphorus (mg/d)	1572 (284.9)	616 (112.1)*	887 (102.1)*	1043 (43.8)	1386 (210.0)
Magnesium (mg/d)	398 (70.3)	161 (35.5)*	215 (32.4)*	205 (8.7)*	312 (22.7)

Data shown are the 48-h mean (± SEM) dietary intake for 24 hours before and during the 24-h urine-collection period. Asterisk indicates significantly different than before flight ($p < 0.05$).

FIGURE LEGENDS

Figure 1. Urinary supersaturation of calcium-containing stone-forming salts in 6 male Space Shuttle crewmembers before flight (PRE), early (E-FLT) and late (L-FLT) in flight, on landing day (R+0), and 7–10 days after landing (R+7–10). Data are means with standard error bars. *Significantly different from before flight, $p < 0.05$. The horizontal line indicates the transition from low risk stone forming potential to high risk.

Figure 2. Fluid intake and urine output in 6 male Space Shuttle astronauts before flight (PRE), early (E-FLT) and late (L-FLT) in flight, on landing day (R+0), and 7–10 days after landing (R+7–10). Data are means with standard error bars. *Significantly different from before flight, $p < 0.05$.

Figure 3. Calcium intake and urinary excretion in 6 male Space Shuttle astronauts before flight (PRE), early (E-FLT) and late (L-FLT) in flight, on landing day (R+0), and 7–10 days after landing (R+7–10). Data are means with standard error bars. *Significantly different from before flight, $p < 0.05$.