Fiscal Year:	FY 2004	**Task Last Updated:**	FY 03/30/2006
PI Name:	Whitson, Peggy Ph.D.		
Project Title:	Renal Stone Risk During Spaceflight: Assessment and Countermeasure Validation		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Food and Nutrition**:Risk of Performance Decrement and Crew Illness Due to Inadequate Food and Nutrition (2) **Nutrition**:Risk of Inadequate Nutrition (3) **Renal Stone**:Risk of Renal Stone Formation		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	77058	**Congressional District:**	22
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Project Type:	FLIGHT	**Solicitation / Funding Source:**	99-HEDS-02
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COI Name (Institution):	Pietrzyk, Robert (NASA Johnson Space Center) Sams, Clarence (NASA Johnson Space Center) Jones, Jeffrey (NASA Johnson Space Center)		
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Task Description:	Exposure to the microgravity environment results in many metabolic and physiological changes to humans. Body fluid volumes, electrolyte levels, and bone and muscle undergo changes as the human body adapts to the weightless environment. Changes in the urinary biochemistry occurred as early as flight day 3-4 in the short duration crewmembers. Significant decreases were observed both in fluid intake and urinary output. During and following short duration Shuttle missions, significant changes were observed in the urinary pH, calcium, potassium and uric acid levels. During short duration missions, the risk of calcium oxalate stone formation increased early in the flight, continued at elevated levels throughout the flight and remained in the increased risk range on landing day. The risk returned to preflight levels one week following landing. The preflight calcium phosphate risk was significantly increased early in-flight and remained significantly elevated throughout the remainder of the mission. Results from the long duration Shuttle-Mir missions followed a similar trend. Most long duration crewmembers demonstrated increased urinary calcium levels despite lower dietary calcium intake. Fluid intake and urine volumes were significantly lower during the flight than during the preflight. The calcium oxalate risk was increased relative to the preflight levels during the early in-flight period and continued in the elevated risk range for the remainder of the space flight and through two weeks postflight. Calcium phosphate risk for these long duration crewmembers increased during flight and remained in the increased risk range throughout the flight and following landing. The complexity, expense and visibility of the human space program require that every effort be made to protect the health of the crewmembers and ensure the success of the mission. Results from our investigations clearly indicate that exposure to the microgravity environment of space significantly increases the risk of renal stone formation. These studies have indicated specific avenues for development of countermeasures for the increased renal stone risk observed during and following space flight. Increased hydration and implementation of pharmacological countermeasures should largely mitigate the in-flight risk of renal stones. Maintaining the health and well-being of crewmembers during space flight requires a means of minimizing potential detrimental health effects of microgravity. The formation of a renal stone during flight obviously has severe consequences for the affected crewmember as well as the success of the mission. The studies planned in this investigation will not only provide a better understanding of the stone-forming risk crewmembers experience during and after space flight, but will take the next step to test the efficacy of potassium citrate as a countermeasures to reduce this risk. Based on the known increased risk crewmembers experience, it is imperative that countermeasures to reduce or alleviate this risk are developed and tested.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Relevance to Space and/or Earth Based Research: Previous studies of Skylab and Shuttle crews have demonstrated significant changes in the urinary chemical composition. Increase in urinary calcium and phosphorus are well documented and probably represent bone resorption due to exposure to the weightless environment. Studies of Shuttle mission of varying duration noted significant postflight increases in the urinary stone-forming salts and decreases in the concentration of urinary inhibitors of renal stone formation. This study is expected to show the in-flight effects of microgravity on the risk factors associated with renal stone development. It is expected that space flight will significantly enhance renal stone formation by providing an environment that is saturated with the stone-forming salts, primarily calcium and phosphorus, in the presence of a reduced concentration of renal stone inhibitors. The postflight renal stone profiles completed on Shuttle crewmembers (n = 323) indicated substantial changes from preflight levels and from normal non-stone formers. With the previous in-flight history (n = 6) of some of the known urinary analytes that influence renal stone formation, we expect an increase in calcium-containing stones (both calcium oxalate and calcium phosphate stones), and sodium-containing stones (sodium urate). It is predicted that the increased risk observed during space flight can be minimized and beneficial changes in the urinary chemistry can be accomplished with the use of potassium citrate. Renal stone disease affects approximately 12% of the human population on Earth with recurrence rates of renal stones reaching 75% in untreated individuals. Morbidity is high and related health costs have been estimated to exceed two billion dollars a year. Understanding how the disease may form in otherwise healthy crewmembers under varying environmental conditions may lead to additional clues as to how crystals form in the urine and develop into renal stones.
	E-057: Renal Stone Risk During Spaceflight: Assessment and Countermeasure Validation Principle Investigator: Peggy A. Whitson, Ph.D. NASA Johnson Space Center Houston, Texas 77058 Telephone: 281-244-8950 Fax: 281-244-8873 E-mail: peggy.whitson1@jsc.nasa.gov Co-Investigators/Science Team: Charles Y.C. Pak, M.D. University of Texas Health Sciences Center Dallas, Texas 75235 Robert A. Pietrzyk, M.S. Enterprise Advisory Services, Inc. Houston, TX 77058 Jeffrey A. Jones, M.D. NASA Johnson Space Center Houston, Texas 77058 Clarence F. Sams. Ph.D. NASA Johnson Space Center Houston, Texas 77058 1. PURPOSE: Previous data have demonstrated that human exposure to the microgravity environment of space flight increases the risk of renal stone development during and immediately after space flight. Post-flight changes to the urinary chemical composition increase the risk of uric acid and calcium oxalate stone formation while in-flight assessment has shown a greater risk of calcium oxalate, calcium phosphate and sodium urate stones. Potassium citrate, a proven Earth-based therapy to minimize calcium-containing renal stone development, will be evaluated during space flight as a countermeasure to reduce the risk of renal stone formation. In this study, the renal stone-forming potential of humans will be assessed as a function of mission duration and it will be determined how long after space flight the increased risk exists. 2. BACKGROUND: As of October, 2001, there have been fourteen U.S. crewmembers that have developed renal stones. The Russian Space Program has reported three renal stone events and one in-flight episode of renal stone formation among cosmonauts. Exposure to the microgravity environment results in many metabolic and physiological changes to humans. Body fluid volumes, electrolyte levels, and bone and muscle undergo changes as the human body adapts to the weightless environment. Changes in the urinary biochemistry occurred as early as flight day 3-4 in the short duration crewmembers. Significant decreases were observed both in fluid intake and urinary output. During and following short duration Shuttle missions, significant changes were observed in the urinary pH, calcium, potassium and uric acid levels. During short duration missions, the risk of calcium oxalate stone formation increased early in the flight continued a elevated levels throught the flight and remained in the increased risk range on landing day. The risk returned to pre-flight levels one week following landing. The pre-flight calcium phosphate risk was significantly increased early in flight and remained significantly elevated throughout the remainder of the mission

(Whitson et al., 1993, 1997). Results from the long duration Shuttle-Mir missions followed a similar trend. Most long duration crewmembers demonstrated increased urinary calcium levels despite lower dietary calcium intake. Fluid intake and urine volumes were significantly lower during the flight than during the pre-flight. The calcium oxalate risk was increased relative to the pre-flight levels during the early in-flight period and continued in the elevated risk range for the remainder of the space flight and through two weeks post-flight. Calcium phosphate risk for these long duration crewmembers increased during flight and remained in the increase risk range throughout the flight and following landing (Whitson et al., 2001). The complexity, expense and visibility of the human space program require that every effort be made to protect the health of the crewmembers and ensure the success of the mission. Results from our investigations clearly indicate that exposure to the microgravity environment of space significantly increases the risk of renal stone formation. These studies have indicated specific avenues for development of countermeasures for the increase renal stone risk observed during and following space flight. Increased hydration and implementation of pharmacological countermeasures should largely mitigate the in-flight risk of renal stones. Maintaining the health and well-being of crewmembers during space flight requires a means of minimizing potential detrimental health effects of microgravity. The formation of a renal stone during flight obviously has severe consequences for the affected crewmember as well as the success of the mission. The studies planned in this investigation will not only provide a better understanding of the stone-forming risk crewmembers experience during and after space flight, but will take tht enext ste to test the efficacy of potassium citrate as a countermeasures to reduce this risk. Based on the known increased risk crewmembers experience, it is imperative that countermeasure to reduce or alleviate this risk are developed and tested. Whitson, P.A. Pietrzyk, R.A. Pak, C.Y.C. Cintron, N.M. Alteration in renal stone risk factors after spae flight. J Urol 150: 803-807, 1993. Whitson, P.A. Pietrzyk, R.A. Pac, C.Y.C. Renal stone risk factors after space flight. J Urol 158: 2305-2310, 1997. Whitson, PA, Pietrzyk, RA, Morokov, B and Sams, CF. The risk of renal stone formation during long duration space flight Nephron. 89:264-270, 2001.

Task Progress:

4. PROTOCOL:

Twenty-four urines will be collected before, during and after flight. Food, fluid, exercise and medications will be monitored 24 hours prior to and during the 24-hour urine collection in order to assess any environmental influences other than microgravity. Two 10 mEq potassium citrate tablets (total dose 20 mEq) will be ingested daily with the evening meal during the single preflight potassium citrate BDC evaluation session, all days during flight, and following landing through R+14. The following list of urinary biomedical parameters will be measured: total volume, pH, calcium, phosphorus, potassium magnesium, citrate, oxalate, sulfate, uric acid, sodium, creatinine, calcium oxalate, calcium phosphate (brushite), sodium urate, struvite and uric acid saturation. In addition, from the dietary records, the following data will be obtained: fluid intake, kilocalories, dietary calcium, oxalate, sodium, potassium, magnesium and phosphorus.

Preflight and postflight hardware for this investigation will consist of potassium citrate and placebo tablets, urine collection bottles, diet log book, chill pack and cooler. Flight hardware will consist of the urine collection devices, urine storage tubes, urine containment bag, potassium citrate kit, urine storage tube rack and the IMS bar code reader

Crewmembers will collect a 24-hour urine and maintain a 48-hour diet record during three preflight baseline data collection (BDC) session. The last BDC will be in collaboration with the required MedOps requirements for all crewmembers to minimize the demands on crew time. For long duration ISS missions, 24 hour urine collections and 48 hour dietary monitoring will be performed early (< FD 30), mid-mission (> FD30 < FD100) and late (within 30 days of landing). During flight two potassium citrate (20 mEq) or placebo tablets will be taken daily with the last meal of the day. Postflight urine and dietary monitoring will be performed at approximately R+0-2, R+7 and R+14 days.

5. PROGRESS REPORT

Pre-, in- and postflight sessions have been completed for the crewmembers participating in this study during the ISS Expedition 6 mission. Sample and data analysis have been completed and crew science debriefs were presented to the crewmembers.

This study is currently completing the analysis of samples collected during the pre, in- and postflight sessions for crewmembers participating in this study during the ISS Expedition 8 mission. Sample and data analysis is currently underway.

The Renal Stone Study is currently going through the process of pre-positioning for ISS Expedition 11. Preflight baseline data collections sessions will be completed in February, 2005 for the ISS Expedition 11crews.

FUTURE PLANS JULY 2004– OCTOBER, 2005

The study will continue with finalizing the samples and data analysis of the ISS Expedition 8 mission. In addition, crew science debriefs will be completed once all the data is obtained.

The investigation is under the process of being manifested for the ISS Expedition 11mission. The activities planned include pre-flight dietary and urinary assessments, in-flight sessions and postflight dietary records and urinary assessments.

7. PUBLICATIONS

1. Whitson, PA, Pietrzyk, RA, and Sams, CF Urine Volume and its effects on renal stone risk in astronauts. Aviation, Space and Environmental Medicine. 72(4) 368-372, April, 2001. 2. Whitson, PA, Pietrzyk, RA, Morokov, B and Sams, CF. The risk of renal stone formation during long duration space flight Nephron. 89:264-270, 2001. 3. Whitson, PA, Pietrzyk, RA, Jones, JA and Sams, CF. Renal Stone Risk Assessment During Spaceflight: Assessment and Countermeasure Validation. American Institute of Aeronautics and Astronautics International Space Station Utilization – 2001. October 15-18, 2001. Cape Canaveral, Florida. 4. Pietrzyk, RA, Whitson, PA, Jones, JA and Sams, CF. Overview of Renal Stones and Space Flight. 14th Annual Humans in Space Symposium. May 18-23, 2003, Baniff, Alberta, Canada.

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