The Problem of Bone Loss During Space Flight and the Need For More Effective Treatments To Make a Mission to Mars Safer

Robert Douglas Bruce III
Life on Mars?
May 28, 2002

A journey into interplanetary space is an undertaking that poses many hazards to astronauts. Dangers such as equipment failure, galactic cosmic radiation and solar particle events, collisions with objects in space, physical and psychological problems, botched calculations, and entering and leaving a planet's atmosphere (to name a few) face astronauts during space travel. Though many of these trials have been successfully overcome there is one hazard in particular on extended voyages that has scientists particularly worried. This is the rapid loss of bone density experienced by astronauts as a result of the zero gravity conditions in space. Mechanical stimulation in the form of physical exercise, though helping to maintain aerobic and muscular capacity, has little affect on the rate of bone loss. For this reason, extended interplanetary space travel such as the long journey to Mars should not be undertaken until new and more effective methods of preventing bone loss have been developed and tested. Such a method may come from alternative forms of treatment such as low-frequency vibrations or bone-enhancing drugs; however, until such a method has been found and proven, extended interplanetary space travel remains too unsafe.

The problem of bone loss during space flight remains, in many ways, a mystery. There is no doubt whatsoever that astronauts experience greatly increased rates of bone loss as a result of the zero g environment. Why exactly this happens still has researchers baffled. Is the mechanical signal of gravity somehow converted to a chemical signal (i.e. a hormone) that then regulates bone growth? Is the loss caused by a decrease in formation rates or an increase in degradation rates? To what extent would the rapid rates of degradation continue? Many of these questions remain unanswered though the problem still remains one of the most prominent physiological hurdles to extended space flight.

The loss of bone in space does not affect the entire body (some bones have actually been shown to gain bone during space flight). The bones subject to degradation experience the most pressure from the downward pull of gravity and are known as the "load-bearing" bones of the body. These include ankles, tibia, femoral neck and greater trochanter, the pelvis, and the lower lumbar vertebrae (Buckey p.28). Though they are unsure exactly why, researchers know that it is the pressure exerted on these bones by gravity in everyday activity that maintains bone density. Exercise subjecting these bones to strong stresses (ex. weight lifting and running) has been shown to actually increase bone density in athletes. In the zero-gravity conditions of space flight, however, these bones experience rapid depletion and calcium loss.

Another problem that certainly does not aid in helping to combat bone loss during space flight is the fact that zero g conditions cause a great decrease in blood pressure to the legs. The presence of gravity on Earth creates a pressure gradient in the body by pulling blood down into the legs. In zero g conditions, this pressure gradient no longer exists causing blood to leave the legs and pool more in the torso and upper body regions. The decreased blood in the legs makes it extremely difficult to heal/build up bones in space if they are getting a much smaller blood supply than they would be on Earth.

Bone begins to deteriorate shortly after astronauts enter space. The combination of zero g, dim lighting in the spacecraft, and high carbon dioxide concentrations all have adverse affects on the skeletal system (Buckey pp. 2-3). Under these conditions, bone loss occurs at rates of up to one and two percent per month (6-24% per year) in load-bearing bones. This is as many as 6 times greater than the rate of bone loss of women with severe osteoporosis (Human Physiology Research and the ISS: Staying Fit Along the Journey p. 2). Some studies have shown that over extended periods of time, this rate of degradation could lead to an overall loss of 40-60% of bone mass in load-bearing bones (Miller p.1). Such effects would be physically devastating to astronauts. Many wonder whether such bone loss would allow astronauts on a long voyage such as a trip to Mars to adequately function on the planet's surface, despite its lower gravity. With such advanced bone loss, astronauts could possibly suffer severe fractures when again subjected to the high gravitational pull of Earth. Even worse, the bone degradation puts astronauts at risk of suffering fractures while on Mars. So far from Earth and any sort of help, such an accident could mean death for an injured astronaut.

The extent of bone loss differs from person to person. Some people seem particularly prone to bone loss while others are not affected as strongly. Though the actual factors determining the extent of bone loss are not known, studies have shown that inherited factors account for up to 80% of bone mass density variability (Vico et. al. p.7). Regardless, no astronaut has ever gone into space and not experienced a certain amount of bone loss. On one extreme, for example, David Wolf, who spent four and a half months on Mir, lost 40% of his muscle mass and 12% of his bone in certain areas. Overall, he lost 23 pounds (Long p.20). One the other extreme, a study of a group of cosmonauts showed that the cosmonaut who had spent the longest time in space and out-of-station missions did not show any significant bone loss (Vico et. al. p.7).

Recovery times seem to vary as much from person to person as the amount of bone loss experienced. Bone loss sometimes continues for a while after a mission before reversing. Recovery times for bone loss are longer than the time of the mission. Two other American astronauts from a group on Mir who were in space longer than four months still have bone deficits more than two years after returning. Other members of the group recovered in times ranging from six months to three years (Long p.22).

While genetic screening of astronauts for low bone degradation rates and post-flight treatments are possible, in-flight treatments for bone degradation are really quite limited. The problem is not as simple as including calcium supplements in the diet of the astronauts because it is the lack of gravity that causes the bone degradation, not a lack of calcium. The increase of calcium caused by taking supplements would simply exit the body along with calcium degraded by the bones in urine.

One possible way to combat the lack of gravity on an extended mission would be to spin the spacecraft around its center point as it makes the voyage. Spinning the spacecraft creates an artificial gravity environment within the ship. Though this would certainly help, it could cause problems as well. Creating artificial gravity in a spaceship would require certain structural changes to the ship to prevent equipment damage. Also, though the spin gives some weight to the astronauts it only provides a fraction of the pull of the Earth's gravity. It would help somewhat in an extended space flight but it would hardly be enough.

Exercise-based treatments are used extensively to slow bone loss. Quite possibly the most important thing that an astronaut can do on an extended journey such as one to Mars is to exercise frequently. Though important on earth, exercise is even more important in a zero g environment to prevent muscle and heart atrophy as well as poor cardiovascular conditioning. Any person would waste away to nothing were they to remain sedentary on a journey as long as the one to Mars. For this reason, astronauts exercise for about two hours each day while in space (Barry p.1). Unfortunately, the very lack of gravity that makes exercise so important also makes it extremely difficult to do.

The majority of exercise-based treatments used attempt to simulate the bone loading experienced during exercise on earth. This type of bone loading is commonly referred to as “impact loading” or “heel strike” loading and attempts to simulate the brief, intense pressure placed on heel, leg, and thigh bones that would be experienced during walking or running (Eisman p.2). The belief is that the higher the amount of load placed on the bone, the greater the effect it will have on bone density. Though such exercises do reduce the rate of bone loss to a degree, mechanical devices created to simulate this heavy loading have met with limited success.

A number of different mechanical devices have been developed to simulate the earth’s gravity during space flight. These generally consist of a variety of straps, cords, and elastic devices to provide load on the legs, hips, and lower back of astronauts. An example of such a device is a Russian experiment that provides resistance by strapping cosmonauts to a treadmill with bungee cords. Similar American-developed equipment uses canisters that can provide up to 300 lbs. of resistance (Miller p. 3). Though these exercise machines have had some effect in battling muscle loss caused during space flight, success has been hindered for a number of reasons. One problem is the fact that the machines often cannot supply sufficient load to the astronauts. The “Russian treadmill” mentioned above can only provide a 60-70% simulation of body weight because it is so uncomfortable (Miller p.3).

In studies done on Earth, placing large strains on the skeletal system can, in some cases, have a negative effect on the skeletal system. While exercise generally increases bone density, too much exercise and load bearing can cause a decrease in bone density. Young women who exercise too heavily sometimes experience a decrease in spinal density. Similarly, a study in which a static load was applied to the ulnae of rats for ten minutes per day slowed growth and decreased density (Eisman p.2).

There have been some models developed that have had somewhat more success in combating bone degradation in space. One such model is the Lower Body Negative Pressure (LBNP) device. An LBNP consists of a chamber within which is a treadmill on which an astronaut can walk. The chamber is sealed around an astronaut's lower body. A simple vacuum motor sucks air from the chamber and creates negative pressure on the lower body. The negative pressure not only simulates 1-1.2 times the Earth's gravity but also increases blood pressure to the legs (Miller p.3). Such a device would be extremely important on an extended voyage such as one to Mars. It serves the multiple purposes of reducing bone loss, providing an aerobic workout, reducing the rate of muscle atrophy also experienced in space, and increasing blood pressure to the legs.

Recently, the focus has shifted from trying to simulate larger loading on bones to instead creating smaller, high frequency loads. One of the newer and perhaps more interesting methods of battling bone loss is standing on a lightly vibrating plate with 10-20 minutes daily. The vibrations are low-frequency vertical oscillations. Studies have been done with frequencies ranging from 30-95 Hz oscillations on a number of animal test subjects. "Currently, most bone researchers believe that stresses placed on bones by e.g. bearing weight or strong physical exertion signal the bone-building cells through some unknown chemical trigger to fortify bones. According to this thinking, the remedy for bone loss in space should be exercises that duplicate stresses on our muscles and skeletons experienced during a daily and active life on Earth." (Barry p.3) This new technology would only use extremely small, high frequency signals for short periods each day as opposed to long workouts that use large loads to simulate the Earth's gravitational pull.

Why exactly this type of stimulation has met with such success is still an unanswered question. It is believed that high impact loading may not affect skeletal density as much as thought. Results show that extremely small strains that arise from muscle contractions during less vigorous but more frequent activities such as maintaining posture are strong determinants of bone morphology (Rubin et. al. p.1) While "heel strike" exercises provide intense loading in targeted areas, small, high-frequency vibrations subject the body to horizontal forces and forces in "unusual" directions. These motions cause subtle muscle contractions in the body that have great effect on bone density.

Studies to test the effectiveness of this experiment have produced extremely encouraging results. One study in particular was conducted with groups of female rats subjected to different stimuli over a period of 28 days to study the effects on the rates of bone formation. To simulate zero g, the hind ends of the some of the rats were suspended off the ground. Of these "disuse" groups, some remained suspended for the entire 28 days, some performed weight-bearing exercises for ten minutes a day, and some were subjected to mechanical vibrations for ten minutes a day. Of the control groups not suspended off the ground, one group was also subjected to mechanical vibrations for a day (Rubin et. al. p.1).

The results were surprising. As suspected, the rats that remained in the simulated zero g conditions for the whole time experienced greatly decreased bone formation (-92%). Those that were only allowed 10 minutes of load bearing per day experienced slightly less decrease, though still a significant amount (-61%). Rats who were suspended for all but ten minutes of the day, during which time the were subjected to mechanical vibrations, experienced a decrease of only 3% in bone formation (Rubrin et. al. pp. 1-7).

Similar test done on sheep have had remarkable results. One study was conducted in which the hind limbs of adult sheep were subjected to 20 minutes of high frequency vibration per day for five days a week. The sheep were made to stand on a platform that vibrated at 30 Hz, creating a gravitational force of 0.3 g. When not being treated, the sheep were allowed to roam in the pasture along with the control group. After a year of treatment, the bone density of the femurs of the treated sheep was, on average, 34.2% greater than the bone density of the control sheep (Rubin et. al. p.1). The sheep were actually subjected to greater strains just walking around the pasture than they were when standing on the vibrating plate and yet the effect the treatment had on their hind limbs was enormous.

Experimentation on humans has been very limited thus far. Many question whether or not the therapy would even work on humans due to the great physiological differences between humans and animals. The general feeling is one of optimism, however. If tests have been successfully conducted on species as varied as turkeys, rats, mice, and sheep, it is likely that the same results will hold true for humans.

Some tests have been done on children with cerebral palsy, though compliance was very low and thus the results were poor. Those that did comply used a commercially available vibrating plate 10 minutes per day, 5 days a week, for 6 months. Significant increases were seen in tibial bone density although no such increases were seen in the lower spine (Eisman p.1). Much more extensive studying must be done with human patients, however, before any conclusive results can be obtained.

The implications this experiment has for long term space travel are very exciting. Though this method had not yet been fully tested on humans, it could hold the key to preventing bone loss during long space voyages. Studies done with vibrating plates are extremely simple, non-invasive, and believed to be virtually risk free. Though extremely high vibration frequencies can do damage, the frequencies experimented with thus far are much lower than damaging frequencies. The length of time for which the experiments are conducted is also very small, compared to the two to four hours a day that many astronauts spend on exercise machines to achieve limited results. That is another factor that would make vibration therapy very appealing, not only to astronauts but also to patients on Earth suffering from osteoporosis. Many exercises to combat bone loss and osteoporosis are difficult, time consuming, and invasive. For these reasons, many people do not comply with them and suffer bone loss as a result.

Another possible alternative to physical exercise worth mentioning is the use of drugs to combat bone loss. A number of different drugs have been developed and tested to prevent bone loss (most were developed to treat osteoporosis). A commercial agency sponsored by NASA is testing the use of a drug known as osteoprotegerin (OPG), a protein that regulates bone metabolism, to prevent bone loss. Studies with mice on Earth have shown that, when treated with OPG while in" reduced gravity conditions (created by suspending the hind ends of mice off the ground by their tails to prevent gravitational stresses on "loading" bones) the mice were able to retain their bone density that would otherwise have been lost. Tests with OPG are currently being conducted on a number of mice on the spaceship Endeavor. The mice have been injected with OPG and scientists are hoping to know whether the protein prevents the loss of bone in zero g conditions (Human Physiology Research and the ISS: Staying Fit Along the Journey pp. 3-4).

Since the discovery of the impact of low-frequency mechanical vibrations, researchers have been making a great deal of headway towards the goal of reducing the threat of bone loss to astronauts. The advances are not only important to astronauts. Such knowledge would be incredibly valuable on Earth to help treat people suffering from osteoporosis with non-invasive, risk free methods. Most likely what will evolve is a combination of drug therapy, physical exercise, and vibrations treatment. The combination of the three types of treatments would likely be sufficient to greatly reduce the danger to the astronauts. Until an effective treatment or combination of treatments can be found, however, the risk of injury or death is too great to astronauts to merit sending them into space for long periods of time.

BIBLIOGRAPHY

1. Baggs, Albert C. “Portable Bone-Growth Stimulators Go Domestic in USA.” *The Lancet.* 347(1996): 1474-1477.

2. Barry, Patrick L. *Good Vibrations: A new treatment under study by NASA-funded doctors could reverse bone loss experienced by astronauts in space*. 2001. Science @ NASA. 4 May, 2002. <http://science.nasa.gov/headlines/y2001/ast02nov_1.htm>.

3. Barry, Patrick L. and Phillips, Tony. *Mixed Up in Space*. 2001. Science @ NASA. 4 May, 2002. <http://science.nasa.gov/headlines/y2001/ast07aug_1.htm>.

4. *Biomedicine: A Unique Model For Examining Type II Osteoporosis*. (2001). Bioserve Space Technologies. 11 May, 2002. <http://www.colorado.edu/engineering/BioServe/biomedecine.html>.

5. Carey, Sarah. *UF Researcher Launches Experiments on Space Shuttle Columbia*. (1996). UF News. 4 May, 2002. <http://www.napa.ufl.edu/oldnews/spacerat.htm>.

6. Eisman, John A. “Good, good, good…good vibrations: the best option for better bones?” *The Lancet*. 358(2001): 1924-1925.

7. Flieger, J., Karachalios, Th., Khaldi, L., Raptou, P., Lyritis, G. “Mechanical Stimulation in the Form of Vibration Prevents Postmenopausal Bone Loss in Ovariectomized Rats.” *Calcified Tissue International*. 63(1998): 510-515.

8. Goodship, A.E., Cunningham, J.L., Oganov, V., Darling, J., Miles, A.W., and Owen, Gwen. “Bone Loss During Long Term Space Flight is Prevented by the Application of a Short Term Impulsive Mechanical Stimulus.” *Acta Astronautica*. 43(1998): 65-75.

9. Hullander, Doug and Barry, Patrick L. *Space Bones*. (2001). Science @ NASA. 4 May, 2002. <http://science.nasa.gov/headlines/y2001/ast01oct_1.htm>.

10. *Human Physiology Research and the ISS: Staying Fit Along the Journey*. NASA Space Research: The Office of Biological and Physical Research. 4 May, 2002. <http://spaceresearch.nasa.gov/general_info/issphysiology.html>.

11. Long, Michael E. “Surviving in Space.” *National Geographic Magazine* January, 2001:18+.

12. *Measuring Bone Loss in Space and on Earth*. (2001). Space flight Now. 4 May, 2002. <http://www.spaceflightnow.com/news/n0109/30boneloss/>.

13. Miller, Karen. *Gravity Hurts (So Good)*. (2001). Science @ NASA. 4 May, 2002. <http://science.nasa.gov/headlines/y2001/ast02aug_1.htm>.

14. Miller, Karen. *Gravity in the Brain*. (2002). Science @ NASA. 4 May, 2002. <http://science.nasa.gov/headlines/y2002/18mar_playingcatch.htm>.8. Carey, Sarah. *UF Researcher Launches Experiments on Space Shuttle Columbia*. (1996). UF News. 4 May, 2002. <http://www.napa.ufl.edu/oldnews/spacerat.htm>.

15. *Monitoring Bone Loss in Astronauts*. (2001). Space Daily. 4 May, 2002. <http://www.spacedaily.com/news/spacemedicine-01a.html>.

16. Rubin, Clinton, Turner, A. Simon, Bain, Steven, Mallinckrodt, Craig, McLeod, Kenneth. "Anabolism: Low Mechanical Signals Strengthen Long Bones." *Nature*. 412(2001): 603-604.

17. Rubin, Clinton, Xu, Gang, and Judex, Stephan. "The Anabolic Activity of Bone Tissue, Suppressed by Disuse, is Normalized by Brief Exposure to Extremely Low-Magnitude Mechanical Stimuli." *The FASEB Journal*. 15(2001): 2225-2229.

18. *Space Bones*. NASA: Space Product Development News. 19 May, 2002. <http://spd.nasa.gov/news/opg_bones.html>.

19. Vico, Laurence, Collet, Philippe, Guignandon, Alain, Lafarge-Proust, Marie-Helene, Thomas, Thierry, Rehailia, Mohamed, Alexandre, Christian. "Effects of Long-Term Microgravity Exposure on Cancellous and Cortical Weight-Bearing Bones of Cosmonauts." *The Lancet*. 355(2000): 1607-1611.