

John M. Vogel, M.D. and Ronald J. Friedman, M.D.
Nuclear Medicine Department, U.S.P.H.S. Hospital
San Francisco, California, U.S.A.

Derangement of bone mineral metabolism can be considered to be one of the major threats to the health of astronauts. The hazards are likely to be greatest during prolonged expeditions planned for the future. The integrity of bone and the maintenance of a skeleton capable of resisting the stresses of everyday life are a function of a number of factors:

1. The pulling forces exerted on bone by its attached muscles;
2. The forces exerted along the longitudinal axis of the skeletal system by gravity;
3. Piezoelectric forces, and;
4. The hydrostatic forces which permit the proper flow of blood with its nutrient materials to, and the waste products from, the bone.

This complex set of stimuli is balanced to provide a bone structure capable, by its chemical composition as well as by its architectural deployment of these materials, of supporting the organism and resisting the forces against which the organism must function. Bone is a living organ which continuously remodels itself. When the mechanical forces that are applied to the skeleton during normal activity in a one G environment are removed, bone mineral is lost because bone resorption out-strips bone formation. The loss of bone mineral represents a danger not only because of the risk of fracture in demineralized bones, but also because the associated increased urinary calcium excretion may lead to the formation of kidney stones.

It has been the purpose of our studies to anticipate the effect of weightlessness on bone during prolonged space exploration. To this end, ground-based studies designed to mimic the altered physiologic state have

been used to construct a time-effect curve. Because bed rest most closely resembles the weightless state, the bone mineral changes during periods of up to 9 months of bed rest have been used to predict the magnitude of these changes in a 0-G environment, as well as to determine what remedial measures might be employed to stem the tide of bone mineral loss. The results of these studies have been discussed by Dr. Lockwood in this conference. The results of the studies of 16 control subjects can be summarized as follows:

1. Periods of up to 9 months of bed rest may produce the loss of 40% of the mineral from the central os calcis. This bone is both highly trabecular as well as weightbearing. In contrast, the radius, a primarily cortical and non-weightbearing bone, has failed to exhibit mineral losses during periods of up to 30 weeks of bed rest. Of course bed rest does not reduce the muscular forces on the radius, and may not alter the hydrostatic forces sufficiently to cause a breakdown in homeostasis.

2. The amount of initial mineral content in the os calcis and daily hydroxy proline excretion can influence the rate of mineral loss. Those subjects with high mineral to hydroxy proline ratio had a longer delay in onset of mineral loss and a reduced rate of mineral loss when compared to those having a low ratio.

3. The mean rate of mineral loss in the os calcis was approximately 5% per month, in contrast to a whole body calcium loss of 0.5% per month. The os calcis is therefore not representative of all of the bones in the body. Weight-bearing bones are more likely to lose mineral in the recumbent state than the non-weightbearing bones.

4. The rate of mineral regain after reambulation follows a pattern roughly similar to that of the loss.

5. Little or no os calcis mineral loss has been seen in less than

14-21 days of bed rest.

Using the experience gained with bed rest subjects, we have employed our modification of the gamma ray absorptiometric technique previously described by Dr. Friedman in a study of the Apollo 14 and 15 crews, and a concurrent group of ground-based controls. The mineral content of the central os calcis was determined in mg/cm^2 of hydroxyapatite and expressed as percent of mean baseline. The mineral content of the radius was calculated as grams per centimeter of bone length for the most distal portion of the radius where it can clearly be delineated from the ulna and then expressed as percent of mean baseline.

As shown on the FIRST SLIDE, measurements of the left os calcis and right radius were obtained concurrently, at 30, 15, and 5 days before flight and as soon after recovery as possible and at 1, 5-6, and 14-16 days after recovery. All measurements were corrected to standards measured at the time of each determination. Three ground based controls were measured by the same technique and similarly corrected. Two of the three controls were studied on both missions.

The individual os calcis values for the Apollo 14 mission are shown on the NEXT SLIDE. When the crew is compared with the controls, no evidence of mineral loss resulting from the effects of the mission can be detected. The LEM Pilot (LMP), Mitchell, showed an increase in mineral on each of the post flight measurements which must be considered to be valid. The Apollo 14 radius mineral values are shown on the NEXT SLIDE. A greater variability in the data is evident but again there is no significant difference between the crew and control values. Therefore, no mineral losses can be attributed to the flight.

The Apollo 15 os calcis mineral changes as shown on the NEXT SLIDE

are different from those seen during Apollo 14. There is a significant mineral loss in the case of the Commander (Cdr) and Command Module Pilot (CMP). The rate of regain of mineral was slower for the CMP who had no interlude of 1/6 G. Both astronauts returned to baseline ranges in 14 days. The Apollo 15 radius mineral changes shown on the NEXT SLIDE were not different from those seen on Apollo 14 in that there were no losses.

It appears that the time response curve obtained from the bed rest studies may be more prolonged with respect to the time of onset of demineralization than is seen in the true weightless state. Yet, this does not appear to be true for all astronauts, in particular the Apollo 14 crew and the LMP of Apollo 15 in whom there were no calcaneal mineral losses in 10-12 days. Repeated studies of normal ambulatory males carried out every 2 to 3 weeks over 6 to 8 months have exhibited a 0.9 to 1.9% standard deviation from the mean. NEXT SLIDE please. Furthermore, the two control subjects studied during both the Apollo 14 and 15 missions had maximal variations from their mean values during both studies of from -2.5% to +2.2% for Vogel and -2.1% to +1.9% for LaPinta. NEXT SLIDE please. It therefore seems reasonable that not only did the three Apollo 14 crewmen and the LMP of Apollo 15 fail to lose calcaneal mineral but that the 2.9% and 2.8% losses for the Gemini 7 crewmen, 2.1 and 3.0% loss for Cdr and CMP of Apollo 8 and 0.8 and 2.3% gain for LMP and CMP of Apollo 7 could also represent minimal or no losses from this bone. These must be contrasted to the 7.8% and 10.3% losses in Gemini 4, 15.1 and 8.9% losses in Gemini 5, 7.0% loss for LMP on Apollo 8 and 5.4% loss for Cdr on Apollo 7 and our reported losses of 6.7 and 7.8% for Cdr and CMP of Apollo 15. The 6.7 and 7.8% mineral losses for this 12 day mission are consistent with the 8.5 and 9.6% losses seen during the 18 day Soyuz 9 mission in which there was no interlude of 1/6 G

lunar gravity.

Losses of this magnitude have not occurred in our bed rest subjects until after the 10th week, with very little change being evident until the 4th week. This appears to be similar to the comparisons made by Biryukov and Krasnykh who considered the Soyuz 9 flight to be comparable to their 62-70 day bed rest confinement. Krasnykh's studies of 70-73 day bed rest subjects resulted in an observed average loss of 11.1% in 5 subjects without total recovery occurring after 20-40 days of reambulation. This observation appears to be comparable to those of our own studies in which an average of 10.5% loss was seen in 8 subjects after 10 weeks bed rest, with recovery after ambulation requiring a time approximately equivalent to the duration of bed rest.

Our Apollo 14 and 15 results contrast most sharply with the previously reported flight mineral data where the radius is concerned. In neither of these missions were there any significant losses in this bone for any of the crewmen or controls. In both of these studies, the most distal available area of the radius was measured. This is the most trabecular area of these bones, albeit minimally so. As seen in this slide, there were variable losses in Apollo 7 of -3.3, +3.4, and -3.6% for the radius, which are not particularly different from our data of -0.7, +2.2, and -0.3% on Apollo 14 and 0.0, -1.9, and -0.7% on Apollo 15. In contrast are the reported radius values of -25.3% and -22.3% for Gemini 5 and -8.8, -11.1, and -11.4% for Apollo 8. Data for this bone have not been reported for Soyuz 9.

It is not possible at this time to attempt any correlations on this conflicting data except those already made when the calcaneal mineral changes were discussed. Clearly, Gemini 7 and Apollo 7 had the greatest similarity

to our Apollo 14 and 15 results and Gemini 4 and 5 and Apollo 8 the least. It would appear that the forces generally applied to the upper extremity bones were still being applied during flight, though significantly reduced. In contrast, except for the lunar excursion periods, compression forces, most vital to the integrity of the os calcis, were completely removed from that bone.

One must conclude that loss of mineral from bones incident to periods of weightlessness can occur earlier than that seen in the bed rest subject and that the magnitude can be potentially severe. If these losses were allowed to continue unabated for a prolonged period of time, the consequences might be severe because the losses are probably not confined to the os calcis. However, because of biological variability between subjects or factors not yet identified, not all astronauts have been so affected during the 10 to 14 day missions. As has been demonstrated on our bed rest studies, baseline mineral to baseline OH-proline excretion ratios can be used to predict mineral loss from the calcaneus. It is reasonable to believe that the preflight mineral content to preflight hydroxy proline excretion ratio may predict mineral loss during the weightless state, but on a compressed time scale. We hope to construct such prediction curves when additional data become available.