The calcium endocrine system of adolescent rhesus monkeys and controls before and after spaceflight

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EXPERIMENTS CONDUCTED on the Russian biosatellite missions have contributed a great deal of information on the effects of spaceflight on bone in the primate. Although each mission was limited to the participation of only two nonhuman primates in orbit for ~2 wk, the effects of microgravity on bone were evaluated by biopsies after the flight (38, 39). As well, exercise activity, which may confound the interpretation of bone responses, was controlled during the flight. Reduced mechanical stress is known to depress new bone formation in localized areas of the skeleton at any age (2) and to stimulate bone resorption in the mature skeleton (18, 40). The role of the calcium endocrine system in this response of bone tissue has been studied through the analyses of blood samples acquired during ground-based simulations (2, 17, 40) and spaceflight (23, 30). Smith et. al (30) note in their detailed listing of human spaceflight results that the two major calcemic hormones, parathyroid hormone and 1,25-dihydroxyvitamin D, were suppressed and that calcitonin was unchanged. Decreases in parathyroid hormone are initiated by the release of calcium, not always detectable as an increase in serum, from an unloaded skeletal site. Suppressed parathyroid hormone would operate to reduce osteoclastic resorption and bone loss directly and indirectly by reduced intestinal absorption of calcium through decreases in the production of the vitamin D hormone. Collectively, these observations in humans place the calcium endocrine system in a role that responds to the biomechanical effects of weightlessness on bone that initiates increased resorption and decreased formation at different skeletal sites.

In juvenile monkeys, pre- and postflight measurements of parameters of calcium homeostasis and some of the hormones involved in the regulation of bone cell activity have been reported from previous Cosmos flights (16, 26). Comparisons with human data are limited by age, species differences in calcium metabolism, and the lack of in-flight specimens for analysis in the nonhuman primate. Within 24 h of landing, five of six flight animals showed increases in serum calcium. Serum parathyroid hormone and calcitonin were found to be decreased in two monkeys after Cosmos 2044. The nutritional status of vitamin D, as reflected in serum 25-hydroxyvitamin D, decreased within the normal range in two and did not change in another two monkeys whose circulating levels were increased threefold by vitamin supplements before the flight (5). In the monkey, there have been no postflight measurements of the vitamin D hormone 1,25-dihydroxyvitamin D or of 24,25-dihydroxyvitamin D, a derivative of vitamin D that initiates a degradation pathway (33).

Our purpose in evaluating the calcium endocrine system postflight was to confirm reported results and...
extend them to include measurements of 1,25-dihydroxyvitamin D, 24,25-dihydroxyvitamin D, and intestinal calcium absorption in animals with clear differences in bone histomorphometry between flight animals and controls (38).

**METHODS**

_Bion 11 mission and subjects._ In the flight experiment, there were seven juvenile monkeys (_Macaca mulatta_) aged 3–4 yr, each weighing ~4 kg. These animals came from a pool of 10 monkeys from the primate center in Russia. They were trained and observed over a period of 2.5 yr before the flight at the Institute for Biomedical Problems in Moscow (IBMP), the Russian research center for spaceflight. Two were selected for flight (nos. 484 and 357) and five for flight simulation studies carried out at different times in relation to the flight, as shown in Fig. 1 [at the same time as the flight (nos. 447 and 396), 16 days postflight (no. 501 and 534), and 44 days postflight (no. 513)]. One flight monkey (no. 484) was studied on the ground 44 days after landing using the same chair for restraint as during the flight. There were no calcium endocrine data acquired from no. 396. The biosatellite was launched on December 24, 1996, and was recovered on January 7, 1997. Flight animals were transported to the IBMP in Moscow where they were found to be in good condition for postflight tests and blood samples on January 8.

**Experimental protocols.** All procedures were approved by the IBMP and the Ames Animal Care and Use Committees. Blood samples were obtained from the 10 flight candidates for screening of vitamin D status 6 mo before the flight. Both controls and flight animals had blood samples taken at 113 or 42 days before launch, within 24 h of landing, and before and after each flight simulation study. The flight and five control animals were loosely restrained in a chair (capsule) with a jacket. This allowed some free movement of the legs and arms in the capsule. After the flight, four ground controls and one flight monkey (no. 484) were placed in the identical type of capsule for 2 wk for ground-based data; one control animal (no. 447) was restrained in another type of chair. Animals were fed a paste diet composed of 29.8% dry matter, 0.22% calcium, and 0.29% phosphorus (Covance Laboratories, Madison, WI). The paste diet for flight animals was 26.8% dry matter. The flight paste diet contained 4.7 IU/kg and for the ground experiments 6.7 IU/kg vitamin D. Juice was a flavored drink sweetened with a mixture of fructose, glucose, and sucrose and contained no calcium. Food and juice consumption were recorded for 14 consecutive days during flight and during each simulation study. Fecal samples were not collected from no. 447, since this animal was not chaired in the identical system as the flight animals. Fecal collections, cumulative for 14 days from each of five monkeys (2 separate specimens from flight monkey no. 484), were stored in plastic bags at –20°C until they were analyzed for calcium at Ames Research Center.

_Peptide hormone assays._ Serum parathyroid hormone and calcitonin in the monkey, known to have some cross-reaction with the human hormones (12, 13), were measured by human assays for parathyroid hormone (25) and calcitonin (6). Assays in use were validated for the rhesus monkey (32). We used six mature rhesus monkeys at Ames Research Center to document the response in assayable parathyroid hormone and calcitonin to calcium gluconate [10% for injection, USP (American Regent Laboratories, Shirley, NY) infused at a rate of 3 mg/kg over a period of 10 min]. The monkeys were sedated for infusion with 10 mg/kg ketamine hydrochloride (ketaset). As shown in Fig. 2, the increase in ionized serum calcium stimulated an increase in serum calcitonin (P = 0.01) at the end of the infusion and a decrease in serum parathyroid hormone (P = 0.06) 10 min later.

_Derivatives of vitamin D._ 25-Hydroxy[26(27)-methyl-3H]-cholecalciferol and 24R,25-dihydroxy[26(27)-methyl-3H]cholecalciferol (Amersham, Arlington Heights, IL) were separately purified on a 0.46 × 25-cm Zorbax-Si HPLC column (Du Pont, Wilmington, DE) with dichloromethane-isopropanol (95.5, vol/vol) at 1 ml/min. Synthetic 25-hydroxycholecalciferol [25-(OH)D3] and 24,25-dihydroxycholecalciferol [24,25-(OH)2D3] served as standards. For the assay of 25-(OH)D3 and 24,25-(OH)2D3, 800 dpm of each radiolabeled metabolite were added to the plasma samples before purification to determine recovery. Plasma samples (0.5 ml) were purified using a dichloromethane-methanol liquid-liquid extraction followed by the solid-phase extraction method of Reinhardt and Hollis (27). The solid-phase extraction method employs silica cartridges to separate the vitamin D metabolites. _Fractions 1_ and 2 from the solid-phase extraction were combined and purified on a Zorbax-Si HPLC column, as described above, for the collection of 25-(OH)D3 and 24,25-(OH)2D3 peaks. Aliquots of the 25-(OH)D3 and the 24,25-(OH)2D3 peaks were counted to determine the recovery of tritium. The remainder of the peaks was used for the assays. Protein-binding assay kits, containing rat vitamin D-binding protein and marketed for 25-(OH)D3 (Nichols Institute Diagnostics, San Juan Capistrano, CA), were used in separate assays of the 25-(OH)D3 and 24,25-(OH)2D3 peaks. Standard curves were constructed using 25-(OH)D3 or 24,25-(OH)2D3 (0.639, 0.078, 0.156, 0.312, 0.625, 1.25, and 2.5 ng/tube). The hormone 1,25-dihydroxyvitamin D, extracted with acetonitrile after the addition of tritiated 1,25-dihydroxyvitamin D to monitor recovery, was isolated by batch elution on a Sephadex C-18 column and was assayed with a radioreceptor assay (Nichols Diagnostic Reagent, San Juan Capistrano, CA).

_Parameters of calcium homeostasis and cortisol._ Serum ionized calcium was measured by a calcium/pH analyzer (Ciba-Corning, Medfield, CA). Serum calcium, phosphorus, total protein, creatinine, and alkaline phosphatase were assayed with an automated analytical system (Cobas; Roche Diagnostic Systems, Somerville, NJ). Cortisol was assayed by a commercial RIA (Diagnostic Products, Los Angeles, CA).

**Intestinal calcium absorption.** Dietary calcium was estimated from daily records of food intake and the analysis of diets (Covance Laboratories). Fecal calcium was determined by chemical assay of fecal ash solubilized in 12 N HCl. The ash was prepared from 1-g aliquots of fecal homogenates by

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**Timeline of Bion 11 Studies**

![Timeline of Bion 11 Studies](image-url)

Fig. 1. Time line showing when the 2-wk ground-based simulation studies were done in relation to the launch of the 2-wk spaceflight. Arrow bars with bold outlines indicate flight monkeys. One flight monkey participated in a simulation study >8 wk after the launch.
drying at 110°C (Baxter, Waukegan, IL) for 24 h and then ashing in the furnace at 600°C (model no. CP 18210; Sybron-Thermolyne, Dubuque, IO) for 18 h. The percentage of calcium absorption was calculated as ([dietary calcium – fecal calcium]/dietary calcium) × 100.

Statistical differences of significance. Statistical differences of significance (P < 0.05) were determined by ANOVA, with repeated measures for serial values in the same animals or paired t-tests. Differences in the means as a function of time were evaluated by the Student-Newman-Keuls test. The Student’s t-test was used to estimate differences between the variables in the flight group and controls. Relationships among variables were analyzed by regression analysis using the computer program SPSS/PC+.

RESULTS

Table 1 shows basal parameters of calcium homeostasis, parathyroid hormone, calcitonin, 1,25-dihydroxyvitamin D, and alkaline phosphatase in samples obtained 4–6 mo before the flight in 10 monkey candidates for the mission. The results of these measurements in the five monkeys used for ground controls 6 wk before and 5 wk after the launch show the effects of growth, a consideration because of the age of the flight monkeys, and age dependency of some components of the calcium endocrine system. The expected increases in body weight and in serum creatinine are associated with a significant decrease in the concentration of the vitamin D hormone.

Table 2 compares the pre- and postflight differences in mean values for flight monkeys with the differences in values before and after the ground-

Table 1. Mean body weight, parameters of calcium homeostasis, calcium-regulating hormones, and alkaline phosphatase in the serum of control juvenile rhesus monkeys before and after the Bion 11 mission launch to establish ground-based changes with age and normal growth

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>L - 113</th>
<th>L - 42</th>
<th>L + 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body wt, kg</td>
<td>4.45 ± 0.3</td>
<td>4.76 ± 0.4</td>
<td>4.96 ± 0.2</td>
</tr>
<tr>
<td>Total protein, g/dl</td>
<td>8.0 ± 0.6</td>
<td>8.3 ± 0.3</td>
<td>8.0 ± 0.8</td>
</tr>
<tr>
<td>Total calcium, mg/dl</td>
<td>10.2 ± 0.8</td>
<td>10.4 ± 0.6</td>
<td>10.8 ± 0.8</td>
</tr>
<tr>
<td>Phosphorus, mg/dl</td>
<td>5.9 ± 0.6</td>
<td>5.9 ± 1.0</td>
<td>6.5 ± 1.7</td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>0.52 ± 0.1</td>
<td>0.58 ± 0.1</td>
<td>0.79 ± 0.1*</td>
</tr>
<tr>
<td>Parathyroid hormone, pg/ml</td>
<td>32 ± 30</td>
<td>22 ± 16</td>
<td>20 ± 15</td>
</tr>
<tr>
<td>Calcitonin, pg/ml</td>
<td>40 ± 14</td>
<td>32.6 ± 6</td>
<td>33 ± 6</td>
</tr>
<tr>
<td>1,25-Dihydroxyvitamin D, pg/ml</td>
<td>195 ± 48</td>
<td>163 ± 67</td>
<td>102 ± 29*</td>
</tr>
<tr>
<td>Alkaline phosphatase, IU/l</td>
<td>441 ± 101</td>
<td>517 ± 123</td>
<td>456 ± 123</td>
</tr>
</tbody>
</table>

Values are means ± SD. *P < 0.05 for difference from L - 113.
based simulation. Firm statistical differences were found in the responses of monkeys to flight compared with the responses to simulation in decreases in body weight (P < 0.02) and alkaline phosphatase (P < 0.006), increases in cortisol (P < 0.05), and marginal increases in urea nitrogen (P < 0.07). The concentration of serum 1,25-dihydroxyvitamin D was the same in two flight and four ground control animals before (214 ± 24 vs. 204 ± 40 pg/ml; not significant) but not after chair restraint when the flight group average was lower than controls (56 ± 12 vs. 85 ± 15, P = 0.008). The decreases in serum 1,25-dihydroxyvitamin D in ground-based controls, based on repeated-measures ANOVA, were statistically significant (P < 0.006), but not in the smaller flight group (P = 0.190). The percentage decrease in serum 1,25-dihydroxyvitamin D before and after flight was greater than in the ground simulation group (71.5 vs. 57%, P = 0.032). Serum 24,25-dihydroxyvitamin D tended to increase in flight monkeys (P = 0.091) and was unchanged in controls (P = 0.704). Serum 25-dihydroxyvitamin D was the same during the flight and restraint on the ground. Serum calcitonin was clearly decreased in the flight monkeys (P < 0.02), but a similar decrease in ground controls can only be described as a trend (P = 0.062). A decrease in parathyroid hormone in both flight monkeys did not reach significance because of the limited sample size and the high range of values. There were no changes in total serum calcium, except for a modest postsimulation decrease in the ground controls (P = 0.04). Total proteins, serum phosphorus, and creatinine were also unchanged after spaceflight or ground simulation.

Serum cortisol increased in flight monkeys (44 ± 1.5 vs. 59 ± 2.7, P < 0.006) but not in ground controls (20 ± 6 vs. 23 ± 4). Pre- and postflight values were higher than corresponding values in controls (P < 0.05). Flight monkeys also had lower serum creatinine and calcitonin than ground controls before chair restraint (P < 0.05). On landing, serum creatinine remained lower in flight than ground controls (P < 0.002), and urea nitrogen was higher (P < 0.011) in flight animals than controls.

Variables in Table 2 that related to body weight were creatinine (r = 0.475, P = 0.05), alkaline phosphatase (r = 0.696, P < 0.001), and cortisol (r = −0.621, P < 0.005). Alkaline phosphatase correlated with total calcium (r = 0.452, P < 0.001) and with serum phosphorus (r = −0.596, P < 0.001). Serum 1,25-dihydroxyvitamin D correlated with calcitonin (r = 0.493, P < 0.02) and with parathyroid hormone (r = 0.445, P < 0.04.).

Table 3 shows juice and food consumption and intestinal calcium absorption in two flight monkeys and four ground controls. Variations in individual intakes are not reflected in the averages. Flight monkey no. 484 did not eat or drink for the first 2 days after launch and no. 357 drank no juice for the 11th, 12th, and 13th days of the flight. The one monkey studied in space and on the ground consumed 26% less fluid based on estimates of fluid from food plus juice (257 vs. 345 ml). However, average fluid intakes from food and juice in flight monkeys and ground-based controls were similar (294 ± 53 vs. 268 ± 27 ml). Intestinal calcium absorption in two flight monkeys was less than in four controls during simulation experiments on the ground a few weeks after the flight (P = 0.02). There was no relationship between the concentration of 1,25-dihydroxyvitamin D in serum before or after spaceflight and intestinal calcium absorption.

**DISCUSSION**

This investigation was designed to identify the effects of spaceflight on the calcium endocrine system. A comparison of the response of five monkeys on the ground to restraint in the same type of chair used for the two flight monkeys revealed remarkably similar changes in ground controls as flight monkeys, with more pronounced changes in the flight animals. On the
ground, the pelvis was exposed to gravitational forces absent during spaceflight. Bone histomorphometry in the iliac crests of the two monkeys exposed to microgravity showed the characteristic change resulting from unloading (a decrease in bone formation), whereas the ground-based controls did not (38). Some skeletal unloading occurred in the chaired animals on the ground, probably in the legs that were raised off the ground so that the animals could not push against the floor of the capsule. The way in which gravitational forces are transmitted to specific bones is not known, but muscle contractions, possibly fluid shifts and pressures that alter the fluid distribution in bone, are involved. Our data indicate that partial unloading on the ground and more complete skeletal unloading in space caused similar responses in the calcium endocrine system to a different degree that appears to be related to the amount of unloading. The differences between the response of flight monkeys to microgravity and of ground-based controls to chairing were not in the calcium endocrine system per se but in systemic factors affecting it and bone, i.e., losses in body weight, hypercortisolemia, and increases in blood urea nitrogen.

The most striking effect of chairing on calcium-regulating hormones was in the concentration of the vitamin D hormone 1,25-dihydroxyvitamin D. As a percentage of preflight values, the decrease in circulating levels was greater after spaceflight and resulted in lower concentrations in the serum of flight animals than of ground controls. There were no differences in the substrate for the hormone in flight and control groups. Conversion of serum 25-hydroxyvitamin D to the dihydroxylated metabolites of vitamin D takes place in the proximal tubules of the kidney and is depressed by decreases in both trophic hormones for 1,25-dihydroxyvitamin D, parathyroid hormone, and calcitonin (24). Parathyroid hormone values average 74% lower post-flight than preflight and 12% lower in postsimulation than presimulation values. Decreases in calcitonin in both groups are comparable. Two changes in blood that may have depressed \( \alpha_1 \)-hydroxylase are the higher but not significantly different postflight than preflight serum phosphorus and an increase in blood urea nitrogen (\( P < 0.02 \)). This indication of a minor alteration in kidney function was not paralleled by an increase in serum creatinine and was not found in ground controls. Weight loss and reduced muscle mass during the spaceflight probably accounted for lower post-flight than preflight creatinine values. Conversely, the ground controls with higher creatinine values probably had higher lean body mass than flight animals as a result of normal growth (see Table 1).

<table>
<thead>
<tr>
<th>Condition and Animal No.</th>
<th>Juice, g/dl</th>
<th>Diet, g/dl</th>
<th>Calcium, mg/dl</th>
<th>Fecal Calcium, mg</th>
<th>Absorption, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>484</td>
<td>132</td>
<td>305</td>
<td>200</td>
<td>72.3</td>
<td>63.9</td>
</tr>
<tr>
<td>513</td>
<td>50</td>
<td>267</td>
<td>175</td>
<td>55.0</td>
<td>66.9</td>
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<tr>
<td>534</td>
<td>60</td>
<td>242</td>
<td>159</td>
<td>50.0</td>
<td>68.9</td>
</tr>
<tr>
<td>501</td>
<td>165</td>
<td>259</td>
<td>170</td>
<td>72.3</td>
<td>57.5</td>
</tr>
<tr>
<td>Average ± SD</td>
<td>102 ± 57</td>
<td>268 ± 27</td>
<td>176 ± 17</td>
<td>63.2 ± 11</td>
<td>64.2 ± 4.9</td>
</tr>
<tr>
<td>Flight</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>484</td>
<td>91</td>
<td>237</td>
<td>139</td>
<td>73.1</td>
<td>47.5</td>
</tr>
<tr>
<td>513</td>
<td>72</td>
<td>374</td>
<td>220</td>
<td>91.2</td>
<td>51.7</td>
</tr>
<tr>
<td>537</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average ± SD</td>
<td>82 ± 14</td>
<td>294 ± 53</td>
<td>164 ± 56</td>
<td>82.2 ± 13</td>
<td>49.6 ± 3.0*</td>
</tr>
</tbody>
</table>

Dietary calcium estimate calculated by converting diet intakes to dry food (\( \times 0.268 \) for flight paste food and \( \times 0.298 \) for ground paste food) and then multiplying intake by the calcium concentration (0.22%). *\( P = 0.02 \), flight compared with ground group.

The metabolism of vitamin D in the monkey differs from the human, with concentrations of the hormone in the former 10 times the values in the latter (4). This concentration range did not seem to influence the responses of nonhuman primates to chairing in space or on the ground. Our results are in general agreement with the human studies (23, 30), but the decreases are more pronounced. The reason for such high values for 1,25-dihydroxyvitamin D in \( M. \) mulatta is unknown. The renal \( \alpha_1 \)-hydroxylase in the monkey does not appear to be more active than in the human (36). In this mission, adequate vitamin D for growing animals was supplied in the paste diet and was probably not related...
to the high hormone levels that are found in association with a wide range of substrate concentrations. In an earlier Cosmos mission screening for vitamin D deficiency in juveniles fed a variety of foodstuffs without added vitamin D or vitamin D supplements, average values of 173 ± 50 (SD) pg/ml 1,25-dihydroxyvitamin D were associated with 25-dihydroxyvitamin D values averaging 18 ± 9.4 ng/ml (3). Circulating levels of 1,25-dihydroxyvitamin D after spaceflight were not as low as those observed in hypocalcemic simple vitamin D deficiency in monkeys that ranged from 5 to 36 pg/ml (1).

Parathyroid hormone is a potent regulator of renal \( \alpha_1 \)-hydroxylase which has a major role in the adaptation to immobilization and disuse, limiting bone resorption, new bone formation, and mineralization (31). After parathyroid hormone assays became reliable enough to reflect biological activity, investigators demonstrated reduced circulating levels at the end of 7 days in space (23) and during the final days of a 3-mo spaceflight (30). Measurements in two monkeys at the launch of Cosmos 2044 showed an average decrease from 125 to 37 pg/ml (16). Although our low postflight values cannot really be compared with baseline specimens that were obtained >1 mo before launch and we do not have statistical evidence for a decrease in circulating hormone because of the small sample size, both flight monkeys showed a decrease, i.e., from 94 to 11.6 pg/ml in one and 22 to 11.6 pg/ml in the second. Samples from the ground-based chair restraint study show considerable variation and are not different. The inverse relationship between serum calcium and parathyroid hormone in serial samples of this study tends to validate the human assay we used. A correlation between circulating parathyroid hormone and 1,25-dihydroxyvitamin D tends to support the idea that parathyroid hormone had a role in suppressing the formation of 1,25-dihydroxyvitamin D in this study.

The decrease in serum calcitonin is similar to the observation of Korolkov et al. (16) in the two juveniles flown on the Cosmos 2044 mission, a change not reported in human adults (30). Calcitonin originates in the C cells of the thyroid gland. Because one of its primary functions is to inhibit osteoclastic bone resorption (7), one can expect reduced circulating calcitonin to favor bone loss or have little influence. The precise regulation and role of the hormone in calcium homeostasis is uncertain. Relevant to this study are recent investigations that find 1,25-dihydroxyvitamin D, and not serum calcium, in contrast to parathyroid hormone, has the dominant role in the regulation of calcitonin gene expression in vivo in the rat (24). Because we found calcitonin and 1,25-dihydroxyvitamin D to be correlated, we can speculate that circulating calcitonin responds to or is the result of the changes in vitamin D in spaceflight.

Changes in body weight and in the concentration of cortisol in the serum distinguished the response in two flight animals from that of five ground-based controls chaired in a similar manner. The flight animals lost an average of 14% of their body weight, similar to the losses reported by Korolkov et al. (16) in five young monkeys from other Cosmos missions. Lobachik et al. (19) found decreases averaging 8% for total body water before and after this spaceflight. This represented decreases in interstitial fluids rather than plasma volume that appeared to increase. They found similar trends that were not significant in the control animals. Because weight loss was accompanied by an increase in urea nitrogen in the flight animals, a reflection of an increase in protein breakdown or impaired excretion, lean body mass may also have been reduced. This is suggested by a lower postflight serum creatinine in the flight monkeys than controls and increased urinary creatinine excretion during the flight (20).

The measurements of cortisol in serum clearly separated the flight from the control monkeys. There was evidence of hypercortisolism before the launch of the flight. This may have been related to a higher level of attention, training, and testing of flight animals compared with ground controls in preparation for the 2 wk in space. Restraint of adult male rhesus monkeys is followed initially by increases in the excretion of 17-hydroxysteroids or of serum cortisol that tend to normalize during the period of chairing (9, 10, 21). Serum cortisol remained constant in the juveniles on the ground but was increased after the spaceflight. The postflight increase may well have been an effect of the landing or circadian variation, and not the consequence of weightlessness per se.

The endocrine response of the juvenile male rhesus monkey to chair restraint on the ground or in space appears to be appropriate for maintaining calcium homeostasis and responding to the reduced need for calcium to mineralize bone in an unloaded skeleton. The 1,25-dihydroxyvitamin D-parathyroid hormone axis is suppressed, a situation favoring a decrease in bone formation and intestinal calcium absorption. These changes were more pronounced in the flight than the ground controls, consistent with the decrease in bone formation at the iliac crest in this flight (38) and our finding of reduced intestinal calcium absorption. There is no evidence that the modest decrease in calcitonin actually affected bone resorption based on bone morphology or the urinary excretion of markers of bone resorption (20). In juveniles, bone resorption is likely to be at a maximum because of growth and is unaffected by the modest decrease in calcitonin postflight, which could simply reflect the decrease in 1,25-dihydroxyvitamin D and the priority of the calcium endocrine system to regulate calcium.

We acknowledge the excellent work of Shawn Bengston in coordinating and handling the logistics of these experiments. We thank M. Eyestone and Teclemicael K. Tewolde for some of the biochemical analyses.

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