Musculoskeletal Adaptation to Space Flight

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Chapter Overview

Clinical and research data from U.S. and Russian short and long duration space missions have clearly demonstrated that humans living and working in space have muscle, connective tissue, and skeletal atrophy when appropriate countermeasures are not used. The atrophy may be continuous or intermittent and possibly progressive until a new homeostatic set point is reached. These changes are manifested in the way the body conserves and activates the muscles, and manages the calcium and other minerals that normally are stored in the skeleton. Loss of total body muscle volume and strength causes decreased muscle force output and early muscle fatigability. In parallel to the muscle atrophy in gravity-dependent muscles and at muscle-bone insertion sites, bone matrix and bone mineral is destroyed leading to possible osteoporosis and the loss of bone strength and increased bone fracture risk. The increased excretion of urinary calcium and phosphorus (bone mineral constituents) may increase the risk for renal stones or dehydration with hypercalcemia. These medical consequences from the musculoskeletal atrophy may cause crew members health problems or limit exploration space mission success. Biomedical research on the International Space Station is helping to maintain the health of astronauts and to develop appropriate countermeasures to protect the musculoskeletal organs of crew members during space flight, when landing on distant planets, and on their return to Earth. This chapter reviews current medical data on how the musculoskeletal organs adapt to space flight and the results of countermeasures to maintain Earth normal bone and muscle form and function.

Learning Objectives

1. Review the mechanisms for musculoskeletal adaptation to microgravity.
2. Review the health risks caused by musculoskeletal adaptation and methods to prevent or treat the potential medical problems that occur because of the space flight adaptation.
3. Review current effective countermeasures being used during space flight.

Introduction

On the International Space Station (ISS) the effective gravity level is 0.0001–0.00001 of that on Earth. A person doing the same work on the ISS that they would do on Earth would have musculoskeletal atrophy because the forces needed to work are so much less in space flight than on Earth.

The muscles and skeletal structures work together to allow human movement and work through locomotion (walking or running) and the ability to apply directional force for activities such as lifting, moving objects from one place to another, and using work tools such as hammers and

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pliers. The single most important force for all Earth-living humans is gravity and all human activity is done within the constant force of gravity. Normal daily living is work against gravity whether the person is moving in an upright position, sitting in a chair, or supine in bed. The level of total exercise depends on the actual activity a person performs and the level of forces generated. Therefore the person who works at a desk all day will be expected to be less strong and have smaller muscles and bones than a person who is doing physical work such as professional athletes (Box 13.1).

The atrophy may be continuous or intermittent and possibly progressive until a new homeostatic set point is reached. These changes are manifested in the way the body conserves and activates the muscles, and manages the calcium and other minerals that normally are stored in the skeleton. Total body muscle atrophy is measured by both volume and strength loss causing both decreased muscle force output and early fatigability. In parallel to muscle atrophy in gravity-dependent and at muscle-bone insertion sites, bone matrix and bone mineral is destroyed with subsequent loss of bone strength and increased excretion of urinary calcium and phosphorus (bone mineral constituents). Clinical consequences from bone atrophy increases the risk for renal stones or hypercalcemia due to dehydration. Musculoskeletal changes have been observed in animals and in people who have spent from 1 week to more than 14 months in space. The loss of bone and muscle when inadequate exercise is performed may be among the most profound physiologic changes associated with long-duration space flight (Box 13.2).

Additionally, the muscle and bone organs are also individually and independently associated with other space travel-induced consequences (Box 13.3). Muscle atrophy and metabolic changes may lead to the metabolic syndrome marked by insulin resistance and changes in cholesterol and triglyceride levels, which could lead to increased cardiovascular risk. Bone atrophy and the development of osteoporosis may lead to changes in blood cell production in the marrow leading to anemia or immunologic dysfunction.

From the earliest human space flight, adequate nutrition and exercises to mimic Earth-based exercise parameters were the goals of the space program; however, the size of the spacecraft and the need of limiting launching weight of food, water, and oxygen in ideal quantities also set a goal of minimizing food and exercise to that necessary to preserve astronaut health and performance for their jobs during space flight. This meant that on return to Earth a rehabilitation program is required and the astronaut would not be expected to be fully back to normal for some period of time (Box 13.4).

The physiologic responses of the human body to the microgravity environment of space flight involve adaptations at numerous levels [1]. A review of how microgravity and its ground-based analogues affect the musculoskeletal system follows.

Space Flight-Induced Muscle Alterations

Human Muscle

It is generally accepted that muscles, involved in the maintenance of an upright posture in terrestrial gravity (antigravity muscles), are most susceptible to space flight-induced adaptations. This susceptibility reflects the almost continuous levels of self-generated (i.e., active) and environmentally generated (i.e., reactive) mechanical loading that these muscles experience under conditions of normal Earth gravity. Thus, the effect of the decrease in the level of mechanical loading that occurs during microgravity exposure logically is reflected most acutely in these muscles.

Box 13.1
The size and strength of the muscles and bones are proportional to the amount of force regularly applied to them.

Box 13.2
Biomedical data from numerous U.S. and Russian short- and long-duration space missions have demonstrated that humans living in space results in muscle, connective tissue, and skeletal atrophy when appropriate countermeasures are not used.

Box 13.3
Information on musculoskeletal adaptation has been obtained from a variety of research and medical monitoring studies conducted in both space flight and in microgravity simulations.

Box 13.4
Although this scenario may also occur during early space exploration missions far from Earth, currently on the ISS there is adequate space for appropriate exercise equipment and more than adequate food, water, and oxygen to allow space crews the ability to "work out" with the required forces in low Earth orbit to potentially maintain their normal Earth physical condition regarding their musculoskeletal organs.

Decreases in skeletal muscle size and function have been reported since humans first began to explore space [2–4]. Space flight results in the loss of lean body mass [5]. Increased glucocorticoids, decreased testosterone (in men), elevated levels of urinary amino acid and nitrogen excretion, and indirect measures of lean body mass catabolism are all changes reported during both brief [6] and long [4, 6–9] duration space flights. Direct measurement of protein synthesis during space flight using ^{15}N-glycine incorporation as a marker has revealed a significant increase in protein synthetic rates. These results indicate that the significant decrease in lean body mass observed after space flight must be associated with a significant increase in protein degradation rates rather than an inhibition of protein synthesis [10]. Decreases in muscle strength, circumference size, and tone have been reported in ISS crews [11] as well as being demonstrated by post-flight magnetic resonance imaging (MRI) of crews on the *Mir* space station [12] (Table 13.1).

Muscle myofiber cross-sectional area (CSA) decreases in parallel to the decline in lean body mass and muscle volume. Pre-flight and post-flight muscle biopsy samples have been obtained from only a few crew members (Box 13.5) [2].

Table 13.1 Comparison of pre- and post-flight change in muscle volume from long duration space flight [11]

	Mir Space Station	ISS
Duration (weeks)	23.0	25.9
Number of subjects	16	4
Total percentage change		
• Quadriceps	−10.0 ± 5.9	−5.4 ± 2.7
• Hamstrings	−13.8 ± 3.9	−7.2 ± 4.0
• Soleus	−14.3 ± 5.8	−18.6 ± 6.9
• Gastrocnemius	−11.7 ± 3.9	−10.3 ± 4.7
• Anterior Calf	−11.7 ± 3.2	−10.5 ± 2.9

Box 13.5
In early U.S. studies, muscle biopsies were obtained before and after flight from the *vastus lateralis* of eight astronauts who completed 5- and 11-day missions [2]. Analysis of the muscle biopsy samples indicated that the myofiber CSA was significantly decreased after space flight; that atrophy was greatest in Type IIB myofibers, followed by Type IIA and then Type I myofibers; that expression of Type II myosin heavy chain (MHC) protein was significantly increased, with an apparent decrease in the amount of Type I MHC protein expressed; and that the number of myonuclei per mm of myofiber length was significantly decreased in Type II myofibers after 11 days of space flight.

In contrast to these findings, long duration missions of 76- and 180-day flights by cosmonauts indicated a large degree of individual variation in the extent of myofiber atrophy, with the decrease in myofiber CSA ranging from about 4–20 % (Box 13.6) [10, 11]. More recent muscle biopsies performed immediately after ISS space flights showed calf muscle volume decreased 13 % with greater atrophy of the soleus muscle (-15 %) compared with the gastrocnemius muscle (-10 %). Peak power was 32 % lower after space flight. Force-velocity characteristics were reduced 20–29 % across the velocity spectrum. There was a 12–17 % shift in MHC phenotype of the gastrocnemius and soleus with a decrease in MHC-I fibers and distribution among the faster phenotypes. These data show a reduction in calf muscle mass and performance along with a slow-to-fast fiber type transition in the gastrocnemius and soleus muscles [12].

Decrements in the aerobic capacity of crew members after space flight, coupled with a reduction in muscle oxidative capacity, indicate that the vascular support to skeletal muscle may also be compromised due to the possibility of lack of gravity hydrostatic pressures and vascular muscular atrophy during space flight. However, at present no consistent relationship is apparent between the degree of muscle atrophy (measured by MRI or myofiber CSA determination after muscle biopsy) and the reported changes in muscle strength and function. This may be due to individual human variation or that these finding are because of physiologic changes associated with return to Earth gravity; e.g., muscle edema and/or landing inflammatory processes.

In addition to the effects of space flight on skeletal muscle, the role of the neural components of skeletal muscle atrophy must not be understated [13]. A functional disruption of neuronal control at the neuromuscular level [14], which seems to be paralleled by a reduction in the overall electrical activity of the muscle after space flight [15], raises the possibility that neuronal-derived factors that play a role in the growth or maintenance of skeletal muscle may be disrupted.

In summary data obtained from astronaut/cosmonaut studies during space flight with minimal exercise countermeasures demonstrate the following:

Box 13.6
Changes at the structural level within skeletal muscle after space flight are paralleled by space flight-induced changes at the functional level such as decreased muscle strength and increased muscle fatigability [10]. Such changes are most clearly observed in the antigravity muscles, where the myofiber atrophy is most pronounced.

1. Loss of muscle mass is most prevalent in the antigravity muscles such as the *soleus*;
2. The atrophic response to short-term space flight does not seem to be specific to myofiber although Type II myofibers may be preferentially atrophied;
3. Myosin heavy chain (MHC) isoform expression does not seem to shift from Type I MHC to Type II MHC during space flights; and
4. Apparent muscle atrophy post flight does not seem proportional to changes in muscle strength.

Animal Muscle

More detail is known about the effects of microgravity on skeletal muscle from short duration space-flown mammals. Tissues harvested 12–48 h after return to Earth revealed significant decreases in muscle mass and myofiber CSA and a shift from Type I to Type II myofibers in the weight-bearing muscles. Similar atrophic changes were observed in the *extensor digitorum longus*, although the degree of atrophy was less than in the weight-bearing muscles from the same animals. These changes were paralleled by large-scale myofiber necrosis in the *soleus*. Similar segmental necrosis and myofiber atrophy, along with denervation and synaptic remodeling at the neuromuscular junction, were observed in the *adductor longus* of rats flown aboard the Kosmos-2044 biosatellite mission. Significant soleus myofiber atrophy was also found after that flight with the decrease in myofiber CSA being greater in Type I than Type II myofibers. This Type I selective atrophy was paralleled by a shift in MHC protein expression from Type I to Type II and an increase in the numbers of myofibers exhibiting a hybrid MHC phenotype. Similar alterations in MHC isoform expression in the *vastus lateralis* and the *vastus intermedius* of the rat have been reported after 9 days of space flight. Skeletal myofiber atrophy after space flight was paralleled by a decrease in the amount of extractable actin mRNA present in the *vastus intermedius* and *lateral gastrocnemius* but not in the *triceps brachii*, indicating that contractile protein synthesis pathways were disrupted (Box 13.7) [16, 17].

Similar results have been reported after a 6-day space flight, specifically a selective atrophy of Type I myofibers, a slight increase in the percentage of Type II myofibers, and an increase in de novo expression of the Type IIx MHC isoform, indicating that microgravity affects rat muscle in as few as 6 days of flight. These biochemical changes correlated with a decrease in myofiber maximal isometric tension and an increase in the maximal shortening velocity after 6 or 14 days of space flight. However, changes in mRNA MHC isoform content were not reflected at the protein level, indicating that in these animals MHC isoform shifting was affected by microgravity exposure at the transcriptional, but not at the translational, and post-translational levels during short-term space flight.

Box 13.7
However, experimental observations on the effects of space flight vary with respect to the muscle studied, the duration of microgravity exposure, and the procedures used to collect the muscle. Studies have been reported from multiple U.S. and Russian space missions, including U.S. Spacelab Space Shuttle missions (7–15+ days) and the Russian Biosatellite missions (10–14 days) [16, 17].

Box 13.8
Some general conclusions that can be drawn from the aforementioned animal studies are as follows:

- First, selective atrophy in weight-bearing muscles, such as the soleus and gastrocnemius, seems to take place during space flight.
- Second, atrophy occurs predominately in Type I myofibers.
- Third, MHC isoform expression shifts from Type I to Type II in the antigravity muscles
- Fourth, the number of myofibers exhibiting a hybrid MHC phenotype is significantly increased in the antigravity muscles after space flight.

Subsequent experiments in which rat skeletal muscle was harvested immediately after landing or during flight (the U.S. SLS-1 and SLS-2 missions, respectively) indicated that the overt muscle damage/necrosis that had been observed previously actually occurred during the reambulation phase after return to 1-*g* rather than during microgravity exposure. These results indicate that the initiation of myofiber atrophy and the shifts in MHC expression observed during space flight occur without overt myofiber damage. In addition, MHC shifting from Type I to Type IIx MHC isoforms (slow to fast transition) occurs after short periods of space flight (i.e., 10 days) and the extent of this adaptation appears to be greater after longer periods of microgravity exposure (i.e., greater amounts of MHC IIx expression after 14 days than after 10 days).

Observations of the effects of space flight on the skeletal muscle of rhesus monkeys data are contradictory: Some have reported no atrophy or fiber type shifting, whereas others found significant myofiber atrophy and a Type I-to-Type II myofiber shift. In addition, short-term space flight resulted in no significant changes in the CSA or myonuclear number of isolated soleus myofibers from Rhesus monkeys [18] (Box 13.8).

Ground-Based Analogues of Space Flight

Human Muscle

Several ground-based paradigms have been used to emulate the effects of microgravity unloading on human skeletal muscle, including complete horizontal or 6° head-down-tilt bed rest, dry immersion, and unilateral upper- and lower limb unloading with or without joint immobilization. In general, skeletal muscle responses to unloading have been comparable in all of these models with minor notable differences.

Bed rest unloading causes a significant loss of body nitrogen and lean body mass [4, 19–22]. A reduction in the size or volume of the muscles used for locomotion accounts for most of the decrease in lean body mass after bed rest. Horizontal and 6° head-down-tilt bed rest protocols of various duration (7 days, 14 days, 30 days, 5 weeks, or 17 weeks) have resulted in significant reductions in lower limb muscle volume as measured by MRI, ranging from a 30 % loss in the ankle extensor muscles [19] to a 12 % loss in the *plantar flexors (gastrocnemius* and *soleus*) [21]. Decreases in muscle volume after bed rest were paralleled by decreases in muscle strength and endurance; i.e., a significant decreases in angle-specific torque, isokinetic muscle strength [19], and fatigue resistance.

At the structural level, the loss of muscle volume in these models correlates with a significant decrease in CSA of both Type I and Type II myofibers [23, 24]. In general, Type II myofibers seem to be more prone to atrophy than do Type I myofibers during short-term unloading, with no significant myofiber type shifting being observed, although alterations in total muscle MHC protein isoform expression have been reported. However, prolonged bed rest (i.e., greater than 80 days) does significantly change the number of MHC hybrid fibers observed in the soleus muscle (Box 13.9) [8].

Again, the decreases in muscle volume and myofiber CSA observed in these ground-based analogues of space flight bring about changes in the neuronal-activation patterns of the unloaded muscles [25], including decreased electrically evoked maximal force, reduced maximal integrated electromyography, and neuromuscular junction dysfunction. Such decreases in the neural drive in unloaded muscle certainly plays a role in the atrophic response.

Some general conclusions that can be drawn from space analog human studies:

1. Terrestrial unloading models produce atrophy in the muscles of the lower limbs, especially the antigravity muscles;
2. This response is greater in the extensor muscles than in the flexor muscles and greater in the calf than the thigh;
3. Muscle atrophy occurs quickly in response to unloading (i.e., within 7–14 days);
4. Loss of muscle mass is paralleled by decrements in muscle strength and endurance;
5. If atrophy is specific to a myofiber type within these muscles, it seems to be Type II myofibers; and
6. Terrestrial unloading does not seem to produce a slow-to-fast shift in absolute myofiber characteristics but does alter the expression of MHC isoforms in human muscle so that an increase in MHC hybrid myofibers is observed.

Box 13.9
Absent from human analog studies are the unique operational and psychological stressors associated with space flight that exacerbate the physiological changes resulting from muscle unloading [8].

Animal Muscle

Ground-based animal models of microgravity-induced skeletal muscle atrophy have for the most part involved the use of small rodents such as rats and mice. These models include hind limb suspension, whole-body suspension, cast immobilization, and joint pinning, all of which mimic many of the gross anatomic and cellular changes associated with microgravity-induced atrophy. Numerous studies with such model systems have illustrated that the responses of skeletal muscle to mechanical unloading depend on many physiologic and environmental factors [26, 27].

Similarities and Differences

Human Muscle: Space Flight vs. Ground-Based

The effects of microgravity exposure on human muscle are not fully understood. However, several salient points can be made with respect to the muscle adaptation that takes place during space flight. First, large-scale tissue remodeling occurs as a response to mechanical unloading of the tissue. Second, this remodeling involves not only the myofibrillar component of the muscle but also the neural and vascular components. However, although unlikely, the shift of body fluids away from the extremities (and hence out of the skeletal muscle vascular bed) into the central core of the body during space flight may also reduce the skeletal muscle nutrient supply or result in muscle microvascular bed remodeling (Box 13.10).

Ground-based analogues of space flight—including bed rest, dry immersion, and unilateral lower limb suspension of humans—produce muscle-adaptation responses that closely but do not totally mimic those observed during space flight

Box 13.10
Tissue remodeling occurs not only in response to the mechanical unloaded state but also to the reduction in neural drive. Vascular remodeling most likely occurs in response to a reduced requirement of the muscle for nutrients because of the reduction in muscle mass.

Box 13.11
The muscle adaptations induced by these models, especially 6°-head-down-tilt bed rest (which also mimics the body fluid shifts observed in space), seem to correlate with those actually detected in crew members.

Box 13.12
However, most studies, either in-flight or on Earth, have used young rats. The skeletal muscle of young rodents clearly reacts differently than does that of older animals, and the effects of unloading in older animals are much less pronounced than are those in young animals.

(Box 13.11). It is possible that the hypodynamic state induced in these models resembles the actual conditions experienced by crew members. The reduction in muscle volume, whole muscle CSA, and myofiber CSA brought about by microgravity exposure accounts at least in part for the reduction in muscle strength associated with space flight and terrestrial hypodynamia in humans. However, the apparent lack of MHC isoform shifting after brief periods of space flight or terrestrial hypodynamia suggests that changes in human muscle contractile activity are influenced to a significant degree by a reduction in neural drive to the muscle.

Rodent Muscle: Ground-Based vs. Space Flight

The effects of microgravity exposure on rodent muscle correlate closely with adaptations observed in hindlimb suspension models. Selective type I myofiber atrophy occurs during both space flight and hindlimb suspension. MHC isoform shifting is common to both situations, with a shift from Type I MHC expression toward Type II MHC expression during both space flight and hindlimb suspension. Given the plasticity of young muscle, the large-scale muscle remodeling observed in young rodents during space flight may be amplified because of age (Box 13.12).

Potential Mechanisms of Microgravity-Induced Skeletal Muscle Atrophy

All of the experimental data collected thus far from ground-based and flight experiments with crew members, other Earth-based human subjects, and animal models suggest that mechanical unloading produces large-scale remodeling of skeletal muscle tissue that results in muscle atrophy.

Among the many muscle growth factors that have been shown to change with microgravity exposure is altered insulin metabolism [28]. Elevated serum insulin levels were reported in both cosmonauts and astronauts after short-duration space flight. In the first 28 U.S. Space Shuttle flights (n = 129 crew members) of 2–11 days of microgravity exposure, circulating levels of insulin were elevated by an average of 55 % on landing day relative to pre-flight levels. Circulating levels of insulin in cosmonauts on landing day have been reported to be twice that observed prior to flight, with elevated levels persisting for up to 7 days. Similar results have been reported in individuals undergoing prolonged bed rest [28]. These data indicate that microgravity exposure may result in skeletal muscle becoming insensitive to the effects of circulating insulin, resulting not only in perturbation of glucose metabolism, but disruption of the anabolic properties of insulin on skeletal muscle (Box 13.13).

Muscle Atrophy Countermeasures

The most direct approach to the prevention of microgravity-induced skeletal muscle atrophy is to be able to duplicate Earth-based exercises in microgravity (Box 13.14).

Although the advantage of artificial gravity loading the whole body would be to counter a variety of microgravity-induced adaptations in addition to skeletal muscle atrophy such as orthostatic intolerance and cardiopulmonary

Box 13.13
Microgravity exposure certainly can induce a rapid response in skeletal muscle tissue that results in large-scale remodeling not only of the myofibrillar components, but also of the neural and (to a lesser extent) the vascular components of the tissue.

Box 13.14
The two ways to do this is either to design a spacecraft that can produce its own artificial gravity or establish exercise equipment that allows Earth-generated forces on specific muscles as well as the entire human body.

Fig. 13.1 Astronaut Mike Hopkins fixing the treadmill (courtesy of NASA)

deconditioning, currently there is no spacecraft with full or partial artificial gravity available. Therefore the focus remains on preventing or ameliorating the loss of skeletal muscle mass by exercise.

Endurance exercise protocols, such as treadmill running or cycle ergometry (Figs. 13.1, 13.2, and 13.3), have been shown to prevent cardiovascular deconditioning during space flight [29]. However, endurance training does not always counter the loss of skeletal muscle mass observed during space flight (Box 13.15) [8, 30–33].

Muscle mass can be protected or increased with a combination of adequate aerobic and resistance exercise during long duration space flight [34, 35] or bed rest [32, 36] as measured by lean body mass, muscle mass or strength. The resistance exercise device currently being used by crew members on the ISS is the advanced Resistive Exercise Device (aRED), which can allow concentric resistance up to 600 lb, an eccentric–concentric ratio of 60–90 %, and mostly a constant force throughout the range of motion. It is thought that using the aRED also simulates the inertial characteristics of free weights during exercise (Box 13.16) [37].

Data from the ISS aRED use is now being accumulated, and as has been indicated above [34], lean body mass is maintained with adequate exercise. Additional data on specific muscles—e.g., volume and strength—are expected in the near future to show positive results.

Other possible countermeasures include drug therapy. Systemic skeletal muscle growth factors such as pharmacologic doses of human growth hormone, thyroid hormone, insulin-like growth factor-1, or androgens and beta-agonists such as dobutamine and clenbuterol have been given to humans and animals and have promoted gains in skeletal muscle mass and strength [38].

However, both short- and long-term significant adverse side effects have been documented in those using such drugs. Other drug or nutraceuticals (nutrients, dietary supplements, and herbal products) or gene-derived therapies may also help in the prevention of muscle atrophy or enhancement of muscle (lean) body mass, and possibly to maintain or increase muscle strength [39].

In the context of crewed space flight and subsequent microgravity-induced muscle atrophy, operational implications are paramount (Box 13.17). In addition to such operational requirements, the flight crew must be able to respond promptly to any emergency situations that may arise during flight or landing, without their responses being impaired by

Fig. 13.2 Astronaut Sunita Williams completed a triathlon from space using an orbital treadmill to complete the running portion, a stationary bicycle for the biking leg, and a resistance machine to simulate swimming (courtesy of NASA)

loss of muscle strength or function. Such requirements are compounded when mission duration is increased, such as for space station operations and future crewed Mars exploration missions. However, muscle atrophy countermeasures cannot, for obvious reasons, consume large amounts of crew time, use inordinate food or oxygen nor environmental reserves.

Summary

Because the human body evolved in response to, and makes use of, a 1-*g* environment, removal of a gravitational force vector from the whole organism results in a plethora of physiological adaptations. With respect to space flight-induced skeletal muscle atrophy, the removal of mechanical load from muscle tissue and the corresponding reduction in neural input to the muscle results in the loss of muscle mass and strength. Although the use of muscle-unloading models in terrestrial gravity has increased our understanding of the underlying processes involved in the initiation of skeletal muscle atrophy, differences are apparent between the responses observed on the ground and those observed during space flight [32]. Moreover, most experimental observations have been made after only short periods of microgravity exposure. Until tightly controlled experiments during long duration microgravity exposure are possible, our understanding of this crucial physiological adaptation to space flight will remain limited. It is critically important to understand the time course of loss of muscle strength, function, and mass in order to extrapolate to increasingly longer mission durations such as a 3-year Mars mission (Box 13.18).

Space Flight-Induced Skeletal Alterations

Biomedical data from numerous U.S. and Russian space missions have demonstrated that space flight invokes continuous, possibly progressive changes in the skeletal and connective tissue systems.

These changes are manifested in the way the body conserves calcium and other minerals that normally are stored in the skeleton. Loss of total body calcium and skeletal changes have been observed in animals and in people who have spent from 1 week to more than 14 months in space. These changes in bone and mineral metabolism may be among the most profound biomedical changes associated with long-duration

Fig. 13.3 European Space Agency astronaut Alexander Gerst, Expedition 40 flight engineer, exercises on the Cycle Ergometer with Vibration Isolation System (courtesy of NASA)

Box 13.15
Ground-based studies in humans have illustrated that resistance exercise is an efficient method of producing gains in skeletal muscle mass and strength under terrestrial gravity [32, 33].

Box 13.16
The aRED has been shown to increase muscle volume and strength and lean body mass similar to free weights during a 16-week study on Earth [37].

space flight without appropriate musculoskeletal countermeasures. Information on skeletal and mineral changes has been obtained from a variety of studies conducted in space flight and in microgravity simulations. Some of the findings from these studies are reviewed as follows.

Box 13.17
Crews may need to maintain a high level of physical conditioning in order to perform physically demanding mission operations such as ISS and planetary extravehicular activities including construction tasks, habitat maintenance, and science activities.

Box 13.18
The challenge of future space physiological research will be to not just only catalog these adaptations, but to identify and understand the basic cellular and molecular mechanisms that initiate and underlie these changes.

Box 13.19
Bone is lost about 1 % per year after age 30 throughout a person's life. Increased bone loss occurs in women in the first 1–5 postmenopausal years during which 3–5 % bone loss per year can be measured, thereafter the bone loss returns to ~1 % each year. In all humans, illness or confinement-induced inactivity, drugs, and specific other illnesses may cause significant increased bone loss; e.g., glucocorticoid use may increase monthly bone loss up to 2–3 %.

Bone Physiology

In adult humans the skeleton has stopped linear growth by the age of the late teens and the skeleton reaches its greatest mass at about age 30 (Box 13.19). The bones are made up of compact bone (e.g., the long bones of the arms or legs) and trabecular bone (e.g., the body of the vertebral spines and the ends of the long bones). Bone is composed of a support matrix and mineral in approximate equal proportions. Since bone is a dynamic organ, it is always metabolically active and for bone to be either gained or loss, both the matrix and mineral components are involved together. The major support of the body in Earth gravity is the tubular long bones; however, most fractures due to trauma occur through the trabecular bone; i.e., wrist, ankle, hip and spine. Additionally, twofold greater bone loss, can be expected at the areas of bone where muscle tendon and ligaments inserts into the bone [40].

In younger people, including astronauts, their risk for bone fracture increases with less bone loss since they are more active; i.e., work longer, harder, and using more force. Additionally, they may potentially take more risks by participating in active sports and other adventures. Astronauts may be at greater risk for fractures after long duration space flights;

Box 13.20
Osteoporosis is a disease of the atrophy of bone in which either a fracture occurs or the risk of fracture is greatly increased. This usually occurs in older people when their skeletal mass has decreased 30–40 % or more and the skeleton cannot continue to support their usual body weight and physical activity; and less trauma (less force) is needed to cause bone fractures.

i.e., when landing at other planetary bodies, immediately when returning back on Earth, or earlier in old age post working career (Box 13.20).

Human Bone

Skeletal studies on space travelers were started at the dawn of both the space program as well as the development of a way to measure bone density.

In the Apollo and Skylab [41] programs, a precise method of photon absorptiometry was used to assess bone mineral mass before and after flight. Mineral losses in the *central os calcis*, which is almost all trabecular bone, were compared with whole-body calcium loss during the 84-day Skylab-4 mission. Calcaneal mineral loss was proportional to that calculated from calcium-balance studies. Although no mineral losses were observed in the distal compact radius of any crew member during this mission, it is still unclear if bone loss occurs in all skeletal sites or just in weight-bearing bones during space flight. Early Russian data suggested that compact bone also is lost from the *os calcis*: observed losses from the tubercle and plantar areas of the *os calcis* seemed to increase in rough proportion to mission length, ranging from –0.9 % to –19.8 % over periods of 75–184 days [42].

Cooperative studies between U.S. and Russian investigators began in the 1980s. The initial study measured the spine mineral density using X-ray computed tomography (CT) in four cosmonauts who flew on *Salyut-7*—two cosmonauts after 5 months and two cosmonauts after 7 months in-flight. All four cosmonauts lost total vertebral bone (6.1 %, 0.3 %, 2.3 %, and 10.8 %) as well as posterior-vertebral muscle mass. More bone was lost from the posterior vertebrae, where the muscles are attached, than from the whole vertebrae (8.1 %, 3.7 %, 7.5 %, and 11.9 %) [43].

A formal collaboration began in the 1990s between NASA and the Russian Institute of Biomedical Problems (IMBP) to study Russian cosmonauts after long duration flights on the *Mir* space station. Standardized and monitored for accuracy, a dual energy Hologic whole body bone densitometer was used to evaluate 18 cosmonauts pre- and immediately post-flight [5]. Bone density was measured over the lumbar spine, left hip, and left tibia in all 18 crew members. In 17 crew members, whole body density measurements were also performed. The missions lasted from 4 to 14.4 months.

All Russian crew members followed the Russian national program for exercise and nutrition. Their diet was based on a mass (weight) maintaining eucaloric intake. Their exercise plan repeats a 4-day cycle in which during 3 days there are prescribed exercises and on the fourth day the cosmonaut may rest or exercise according to their personal desires. They worked out on a bicycle ergometer, passive treadmill, and bungee resistive cords. Each exercise day, the cosmonaut has 2 1–1.5 h sessions for a total work out of 2–3 h. There is usually no exercise prescribed during the first 14–30 days. During the early phase of the flight, exercise target heart rate is 160–180 beats per minute. Increased exercise is prescribed toward the end of the mission. Bungee cords are used to secure the exerciser to the treadmill with a force of about 0.6 times the Earth body weight. In addition to these exercises, strength training using the bungee cords for 10–30 min per day are used for specific muscle groups. An elasticized suit, equipped with bungee cords across specific joints, provides passive resistance on the antigravity muscles of the legs and feet and torso. This is worn for up to 8 h per day.

Bone measurements were normalized to loss per month of space flight since the space missions were of different lengths. Total body bone mineral density changed –0.35 % ± 0.25. The total body data represents the total calcium lost from the individual and could be compared to calcium balance from bed rest. Specific gravity-dependent skeletal sites all lost significant bone during the space mission even with an ongoing exercise program. The lower lumber spine lost 1.06 % ± 0.63 per month; in the separate compartments of the hip, the hip femoral neck lost 1.15 % ± 0.84 per month and the trochanter lost 1.56 % ± 0.99 per month; and the entire pelvis lost 1.35 % ± 0.54 per month. If all the cosmonauts had flown for 1 year, the interpolated bone loss would be 12.7 % for the lower spine, 13.8 % for the hip femoral neck (Fig. 13.4), 18.7 % for the trochanter, and 16.2 % for the pelvis. On Earth the usual bone loss with aging is ~1 % per year compared with ~1 % per month in the *Mir* study.

Three cosmonauts flew twice during the study approximately 2 years apart. The average bone loss for the spine, and hip neck and trochanter were not different in each of the flights. The interpolated bone loss for 12 months for cosmonauts who flew twice are spine, 12 % vs. 13.4 %; hip femoral neck, 13.6 % vs. 14.2 %; and hip trochanter, 16.3 % vs. 14.2 %. The microgravity stimulus for bone loss was not modified by a previous space flight in these cosmonauts.

Thus, the Russian exercise countermeasure performed during this study did not seem to protect a major portion of the weight-bearing skeleton.

A most important question is whether the skeleton can recover from the space flight-induced bone loss. The answer

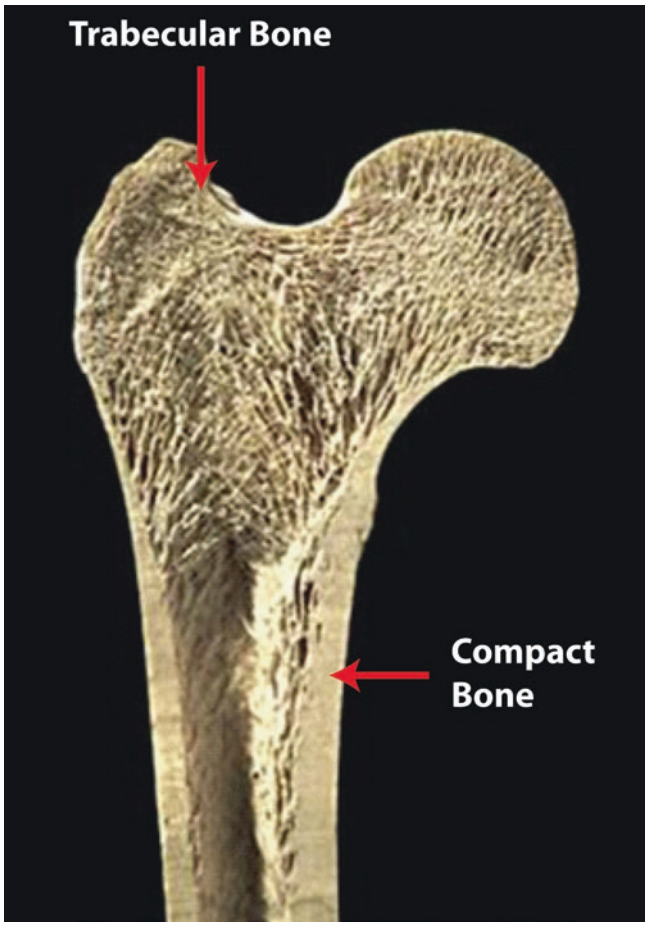

Fig. 13.4 Proximal femur (courtesy of NASA)

is complex [44, 45] in that bone density recovery appears to occur whereas using finite element analysis for bone strength, it does not fully recover. Using existing data on 45 astronauts and cosmonauts in which long-term post-flight measurements had been made, mathematic modeling suggested that 50 % of the bone should be expected to recover by 9 months post-flight. Although individual data show that not everyone actually fully recovers to their pre-flight baseline bone density, the derived curves show 100 % recovery for the spine at 600 days post-flight, the hip femoral neck at 900 days, and the hip trochanter at 1200 days [44]. This group included 7 crew members who participated in space flight missions twice and 2 crew members who participated 3 times. The average interval between space flights was 1381 ± 549 days (774–2347 days). Because of the limited number of crew members flying on multiple missions, no determination could be made of how the multiple missions affected skeletal recovery.

Additional studies using CT bone densitometry and finite analysis of 16 ISS astronauts who remained in space between 4.5 and 6 months showed that on average they each lost 11.1 % of their proximal femoral total bone mass and lost

Box 13.21
Urinary concentrations of calcium have been shown to increase by up to 79 mg/day during even short space flights [47]. This increase in urinary calcium concentration was observed despite a 30–50 % drop in calcium intake during flight.

14.4–16.5 % of the trabecular bone mass and trabecular bone density. These translated to a sharp decrease in the bones' structural integrity parameters, a loss of 15.7 % in bending strength and a loss of 16.8 % in compressive strength indexes. One year after the space flight, these areas still had bone mass losses. The femoral neck was 91 % of pre-flight value at 1 year and 93% in the proximal femora; however, the total volume increased. The substantial bone mass recovery at 1 year post-flight was not matched by bending (15 % below pre-flight) and compressive strength (20 % below pre-flight) values.

Other Metabolic Parameters

Studies of metabolic balance, during which dietary intake and urinary and fecal excretion were monitored, were conducted on the Skylab missions. Daily intake of calories, minerals, and other nutrients were calculated from individual food-intake reports; and 24-h urine samples and feces were measured back on Earth. Although stools were collected and returned for analysis, enemas were used just before launch and the excreta were discarded. Minerals lost through perspiration were not measured, nor were corrections made for these losses. Despite these problems with the balance technique, these Skylab studies had no other missing data and were as accurate as similar ground-based metabolic studies. They demonstrated that space flight is accompanied by increased excretion of calcium and phosphorus and bone matrix degradation constituents (Box 13.21) [46, 47].

Figure 13.5 illustrates the changes in calcium balance during the Skylab-4 mission [4]. Calcium balance is the net quantity of calcium that enters or leaves the body once calcium excreted in the urine and feces is subtracted from the dietary calcium intake. The amount of calcium excreted in the urine increased rapidly but reached a plateau after 30 days in-flight. A small continuous increase in fecal calcium loss was noted over the duration of the flight. Within 10 days in-flight, pre-flight positive calcium balances became less positive until the body as a whole began to lose calcium. The rate of loss was slow at first but increased to almost 300 mg/day by the 84th day of flight. In a later *Mir* study, crew members' gastrointestinal absorption of calcium was decreased by 38 % on flight day 110 and by 56 % immediately after landing [48].

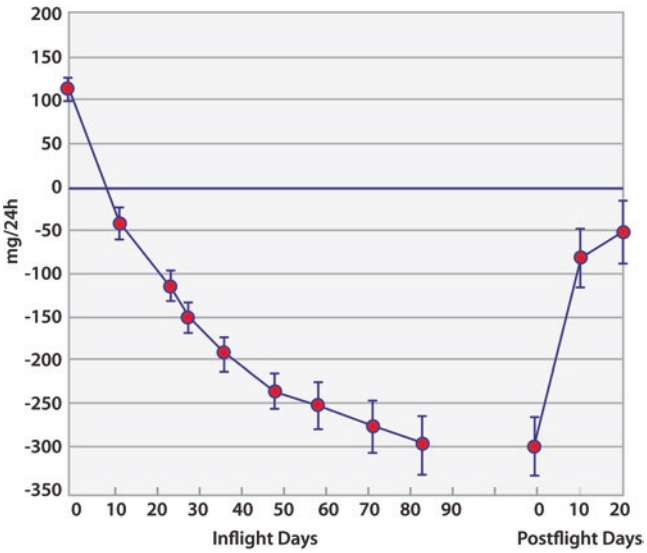

Fig. 13.5 Calcium balance from Skylab 4. Adapted from Ref. [4]

The 3 Skylab-4 crew men lost an average 10 g of calcium each, about 0.8 % of the estimated 1250-g overall body pool.

Recovery of calcium lost during flight begins soon after return to a 1-*g* environment. After the Skylab missions, urine calcium content dropped below pre-flight baselines by 10 days after landing, but fecal calcium content had not dropped to pre-flight levels by 20 days after landing. The crew members' calcium balance, which was markedly negative, also had not returned to zero by 20 days after landing. Nevertheless, calcium balance could return to zero long before losses induced by space flight could be replenished, which might result in irreversible damage to the skeleton.

Additional Biochemical Parameters

Analyses of urine, feces, and blood samples collected during the Skylab, *Mir*, and ISS missions in which there was either inadequate nutrition or exercise revealed changes in several biochemical variables [9, 34, 46, 48]. Urinary output of bone degradation collagen cross-links increased during flight by 33–150 % indicating destruction of the collagenous matrix of bone and bone atrophy. Bone-specific alkaline phosphatase (an indirect marker of new bone formation) levels have been found to decrease during space flight, presumably because of a slowing of bone formation and decrease in osteoblastic function. Observed increases in urinary nitrogen level are thought to reflect muscle atrophy. The proportion of stearic acid in the total fecal fat increased throughout the Skylab flights as more and more calcium became available to form non-absorbable salts. Urinary concentrations of catecholamines decreased, but urinary cortisol levels increased, during the Skylab, *Mir*, and ISS flights (Box 13.22).

Box 13.22
In-flight increases in blood levels of ionized calcium, and decreases in calcitriol, cholecalciferol, and parathyroid hormone suggested that a rise in serum calcium associated with being in-flight triggers a new set point for the calcium regulatory hormones.

Ground-Based Simulation Models

Bed Rest

Although results from space flight balance studies are not identical to those obtained during bed rest, the bed-rest model nevertheless confers several advantages, including the ability to perform a greater number of studies, thereby minimizing individual variations; the ability to monitor subjects more closely than is possible in space, including the control of work/rest schedules, medications, and other variables; and the ability to minimize mineral losses from sweat (and vomitus) during the ambulatory-control, bed-rest, and recovery periods (Box 13.23) [19, 49–52].

This latter point may be a source of error in space flight balance studies: If minerals lost through perspiration and vomitus were not measured throughout the entire flight to account for variations in cabin temperature, space motion sickness, or exercise effort, then mineral balance would be inconsistent, and the amount of calcium loss would be underestimated. Thus, although in-flight balance studies offer useful information, they must be interpreted cautiously (Box 13.24).

Total body calcium stores decrease by 6 g per month after the first month of bed-rest; by the end of 9 months, at least 50 g of calcium are lost. Bed-rest studies also allow investigation of the mechanisms underlying bone loss during longitudinal unloading states.

Improvements in bone mineral absorptiometry techniques have increased the accuracy and precision of whole-body and site-specific measurements. Use of modern instruments in bed-rest studies has shown that greater amounts of bone are lost in the weight-bearing regions of the skeleton than in the non-weight-bearing regions and that more trabecular bone is lost than compact bone. Bone may not be lost from the trunk and upper body [19]. Table 13.2 shows results from 6 male subjects who spent 17 weeks in horizontal untreated bed rest followed by monthly evaluations for the ensuing 6 months. Losses in total body calcium and calcaneal bone were comparable to those in previous studies; the greatest area of bone loss was from the calcaneus. Bone mass was lost at the rate of about 1 % per month in the pelvis, hip, and spine. Recovery was fastest in the calcaneus; and recovery of whole-body calcium and spine and hip mass were slower. With current available therapies,

Box 13.23
Bed rest provides a useful model for studying the effects of weightlessness on bone and mineral [19, 49–52], because the force of gravity on the longitudinal skeleton during bed rest is reduced by approximately 83 %.

Box 13.24
Bed-rest studies, on the other hand, offer reliable and reproducible evidence that bone loss continues unabated for at least 36 weeks, with no indication of the expected new steady state.

Box 13.25
Studies using animals to mimic space flight-induced bone changes have also played a significant role to elucidate the nature of microgravity-induced osteoporosis.

Box 13.26
The most pronounced changes in animal models of weightlessness occur in weight-bearing bones. Mechanical stimulation has a critical effect on bone structure and metabolism. The relative rates of bone formation and resorption also seem to vary depending on the age and prior activity of the animal.

Table 13.2 Percent bone gain or loss in 6 men after 120 days of bed rest. Adapted from [5]

	Recovery day 1	Recovery day 180
Region	% of Baseline	% of Baseline
Head	+3.2	+4.2
Arms	−2.4	−6.7
Ribs	−1.4	+0.4
Thoracic spine	−1.2	−0.5
Lumbar spine	−5.8	−2.4
Total spine	−3.1	−1.6
Femoral neck	−3.6	−3.6
Trochanter	−4.6	−3.4
Calcaneus	−10.4	−1.8

substantial bone recovery is possible in individuals with clinical osteoporosis and continued development and evaluation of new physical and pharmaceutical therapeutics are ongoing.

Animal Studies

Animal research has been very important to ascertain the mechanisms related to bone remodeling (repair) in adults and to develop the important therapeutics that are now and will be used in clinical practice (Box 13.25). A variety of animal models have been used that have similar bone parameters to humans including rodents, rabbits, pigs, sheep, dogs, and primates both on Earth [27, 40, 53–55] and in microgravity [56, 57]. Studies of animals with immobilized limbs have suggested that disuse causes changes in both the formation and resorption of remodeling bone depending on the length of the immobilization period. *Macaca nemestrina* monkeys "couched" for long periods lost trabecular and cortical bone in weight-bearing areas. Moreover, recovery of the cortical bone deficiencies may not have been complete even after 40 months of ad libitum activity during the recovery phase.

These and other results indicate that immobilization or unloading produces several time-dependent changes in bone accretion and resorption and suggest that proportionately larger increases in resorption must be a key factor in loss of bone mineral mass as the cause of disuse osteoporosis. Skeletal losses in space are also likely due to larger increases in bone resorption relative to bone formation (except in immature growing animals) (Box 13.26).

In-Flight Animal Experiments

Animal and bone-cell culture studies performed in space have generally shown decreases in osteoblastic activity [58–61]. Monkeys experiencing 11.5 days of weightlessness lost more bone mineral than did ground control animals and had decreases in iliac trabecular bone volume and perhaps thinner trabeculae as well [62]. Young rats studied on the Spacelab-3 mission, as well as others on the Kosmos biosatellites, showed marked skeletal changes after as few as 7 days in-flight [61], including decreases in bone growth, mineralization, bending strength, and weight of the lumbar spine (L3). Rats flown on an 18.5-day Kosmos mission or the 7-day Spacelab-3 mission showed 30 and 28 % decreases in mechanical bending strength, respectively [56]. These and other findings suggest that the loss of bone in growing rats might be due primarily to inhibited bone formation rather than to increased bone resorption.

Bone Atrophy Countermeasures

NASA research and development activities to reduce the potential skeletal-associated risks from space flight include: (1) the development for devices and protocols for mass-loading (resistive) exercises, (2) pharmaceuticals to

Fig. 13.6 Astronaut Carl Walz uses the short bar on the interim Resistive Exercise Device (iRED) (courtesy of NASA)

counteract the loss of gravitational- and muscle-associated forces exerted on the skeleton while doing work or exercising, and (3) nutritional and atmospheric, and (4) engineering manipulations that lower the mass, volume, and storage problems of bringing everything that is needed to support life on exploration missions beyond low Earth orbit.

Once it became apparent that the exercise plan used on the *Mir* was insufficient to maintain Earth-level skeletal mass, NASA developed an elastomer-based resistance exercise device (iRED) consisting of 2 canisters capable of producing up to ~150 lb of force per canister (see Fig. 13.6). Additional bungee cords can also be attached to increase the load characteristics [63]. Limitations of the iRED included: (1) It was found that cable extension beyond 22 in. at high resistance resulted in excessive wear and breakage of the elastomer spokes. To perform exercises involving a larger range of motion (ROM), adjustable straps were attached between the iRED cables and a pulley on each side of the shoulder harness to allow a full ROM without overextension of the FlexPacks; and (2) the FlexPacks could be damaged if the force exceeded 150 lb. Therefore, for subjects who required training forces greater than 150 lb from a single canister (a total resistance of 300 lb), the resistance was "augmented" by attaching bungee cords in parallel with the iRED cable. Each pair of bungees provided an additional 100 lb of force when fully extended. Additionally on the ISS, (3) iRED calibration was difficult if not impossible during space flight and (4) there was no way to monitor actual iRED work. Results from Earth-based research showed that the iRED was able to build muscle almost similar to free weights but there was no anabolic bone result (Box 13.27) [34, 64].

Box 13.27
Previously it was clearly demonstrated that high resistive exercise during bed rest could prevent most if not all of the disuse bone loss [64]. ISS bone density measurements showed that in the eight crew members who participated in the study and used the iRED there was continued bone loss at about the same rate as seen in the *Mir* study [34].

The aRED discussed in the muscle section is currently being used on the ISS (see Figs. 13.7 and 13.8). It has the ability to fulfill resistive exercise to meet almost all the crew members' requirements. Results in 11 subjects are very

Fig. 13.7 Astronaut Koichi Wakata exercises on the advanced Resistive Exercise Device (aRED) (courtesy of NASA)

Fig. 13.8 Astronaut Kevin Ford exercises on the advanced Resistive Exercise Device (courtesy of NASA)

Box 13.28
Diet plays a major role in maintaining bone; the main diet constituents required are adequate protein, bone minerals (calcium and phosphorus), and vitamin D. There are many more as well. Additionally there may be too much salt and meat with sulfur containing amino acids, which are known to increase the risk of osteoporosis.

promising [34]. In addition to minimizing bone loss, the additional exercise has normalized endocrine status for parathyroid hormone; i.e., it does not drop during flight indicating elevation of blood calcium and bone formation markers are increased; however, there continues to be increased urinary bone matrix degradation products indicating continued increased bone turnover.

In almost all previous space flight missions, there were dietary problems of under eating and "weight" (mass) loss (Box 13.28) [6, 7, 30, 34]. The aRED also appears to increase appetite in space crews, indirectly assuring adequate protein and mineral consumption [34].

There are also environmental factors important in maintaining bone. Bone is used by the body to acutely buffer an acid load either from food, exercise, or the environment. *Sulfur containing amino acids is an acid load* at meal time. On the ISS, the atmosphere contains tenfold higher CO_2 atmospheric levels than on Earth. Moreover, without adequate ventilation (moving air by fans) CO_2 may locally build up to be breathed by crew. The increased CO_2 is converted to carbonic acid and requires increased buffering causing bone loss. This may also increase the risk for kidney stones.

The ideal may be to make space flight as Earth-like as possible; however, this is unlikely to happen. Artificial gravity continues to be studied but there are no current plans for its use for exploration missions. Adequate or near-adequate nutrition and exercise are certainly possible as ISS data shows when the aRED is used; however, there still needs to be other countermeasures available, namely pharmaceuticals.

Bone antiresorptive drugs are currently extensively used on Earth to treat or prevent osteoporosis. A bisphosphonate drug used in volunteers on the ISS clearly showed the same excellent results [65] as on Earth to prevent bone loss. Table 13.3 shows that the bisphosphonate therapy may have completely prevented space flight-induced bone loss. The drug was used in addition to either the iRED and aRED exercise protocols; the data shows an improvement in maintaining bone over those who used only one or the other exercise devices. There are several reasons why this is important for space missions: (1) the antiresorptive drug could be used when the astronaut could not exercise for an extended period of time, e.g., illness, injury, exercise equipment is broken, too busy with other work; or (2) for operational purposes to conserve on food supplies, oxygen use, CO_2 removal, and removal of other substances increased by exercise into the atmospheric.

Table 13.3 Bone mineral and bone strength % change immediately after ISS space flight. Comparing ISS results prior to the use of the aRED with Bisphosphonate Rx. Adapted from [65]

	Pre aRED (n = 18)	Bisphosphonate Rx (n = 7)
Total hip		
• Trabecular bone	−13.6 % ± 6.4	−1.1 % ± 9.8
• Cortical bone	−3.2 % ± 3.5	−0.6 % ± 4.7
• All of the hip bone	−9.8 % ± 5.9	−1.6 % ± 6.4
Computed strength		
• Strength fall (n = 14)	−9.5 % ± 5.6	−0.1 % ± 7.6

Summary

Information obtained from long duration space missions, particularly Skylab, Salyut, *Mir*, and the continuing ISS missions, clearly indicates that bone and mineral metabolism changes substantially during space flight. Space crews will increase the living and working time in microgravity from the current 6-month tours to 1-year ISS missions. Bone atrophy from the weight-bearing bones occurs without adequate nutrition and exercise. The major health hazards associated with the bone loss include signs and symptoms of hypercalcemia and rapid bone turnover, the risk of kidney stones from hypercalciuria, the lengthy recovery of lost bone mass after flight, the possibility of irreversible bone loss (particularly in trabecular bone), possible calcification in the soft tissues, and perhaps an increase in fracture potential. For these reasons, risk reduction efforts are being directed toward elucidating additional information regarding bone health during long duration space flight and toward developing more effective countermeasures to prevent both short-term and long-term complications.

Conclusion

Musculoskeletal adaptation during space flight without adequate continuing nutrition, exercise, and the control of environmental parameters may lead to problematic consequences including significant decrements in work or mental performance, ill health, and loss of mission. The current biomedical programs at NASA and other spacefaring national agencies have been studying the effects of space flight on musculoskeletal physiology and developing a set of countermeasures to prevent or mitigate potential problems from occurring during long duration space flight.

Case Studies from the Aeromedical Practice

Case 1

A crew member on the ISS reported that he had "pulled" his back and was in pain at rest. He was especially in pain when he used the aRED or ran on the treadmill. He actually felt better when walking on the treadmill or in the sleeping bag at night. He has taken NSAIDs on a regular basis with only minimal relief. He has taken no other medicines and he continues to try to do his prescribed exercises each day with great difficulty. The initial discussion is to determine if a more serious underlying condition that is associated with systemic ailments or neurologic deficits is present. Identifying the symptoms, along with an accurate diagnosis of the underlying cause of the pain, is the first step in obtaining effective pain relief. While lower back pain is extremely common, the symptoms and severity of lower back pain vary greatly. A lower back muscle strain might be excruciating, while a degenerating disc might cause only mild, intermittent discomfort. Assuming that it is believed that the pain is only lumbar muscular strain or sprain, what advice should be given regarding pain control and use of the exercise equipment, since it is known that rapid muscle strength and size loss may occur if the person cannot follow his usual exercise protocol? The flight surgeon prescribed more acute pain relief and medication to help treat low back muscle spasm. Exercise was suspended for a few days. Since body position and exercise forces are different in microgravity, the crew member should be encouraged to self-explore as to what activities he is able to do and at what level of forces exerted through the body harness system can be used with no pain when he restarts exercise. He should be encouraged to increase his exercise activity as soon as possible as he recovers.

Case 2

In a prior space flight 1 year earlier, a crew member had a bone loss of 10 % from his hip femoral neck. Now the crew member is being considered for another ISS mission a year hence. What should be considered regarding the crew member's current bone health state, and what possible therapies could be used prior to flight to correct the previous space flight-induced bone loss (if the loss is still present)? A bone density measurement (DEXA) should be obtained. In the evaluation of the DEXA, current medical and drug use and history will be important as well as the person's current exercise program and their physical condition. The DEXA results should be compared with other individuals who are similar to the crew member regarding age and sex from the general population DEXA database. Since limited data shows similar losses will occur in the second space flight mission and if there is still significant bone loss apparent from the previous flight, increased exercise and drug therapy should be considered during the time prior to the new space flight.

Self-Study Questions

1. What causes muscle atrophy in space?
2. What causes bone atrophy in space?
3. Does musculoskeletal deconditioning and atrophy increase with longer duration space missions?
4. What specific types of exercises can prevent muscle atrophy during space flight?
5. What specific type of exercise is required to prevent bone atrophy during space flight?
6. How are forces generated for exercises in space flight that are equivalent to forces on the musculoskeletal organs during Earth-based exercise?
7. Why would other countermeasures be need for preventing microgravity-induced muscle or bone atrophy?
8. How do ground-based microgravity simulations studies help to clarify the biomedical adaptation results from space travel?
9. What are the environmental factors on the ISS that affect skeletal health?
10. What other conditions or situations can occur in space that influence the rate and amount of musculoskeletal atrophy measured in returning crews?

Key Points to Remember

The following is the summary of the current robust evidence reflecting the adaptation of the musculoskeletal system to space flight:

1. Muscle and bone atrophy without sufficient exercise.
2. Muscle strength declines and the muscle tires much earlier in work.
3. Bone loss may cause osteoporosis, which means that there has been a bone fracture or that the risk of a bone fracture is high.
4. Most of the atrophy during space flight occurs in the gravity-dependent torso and lower limbs.
5. Skeleton size and strength in the adult animal is due to both direct gravitation forces generated during exercise and separate forces of muscle contracting (pulling) on the bone through the ligaments and tendons at the insertion sites at the bone and muscle junction.
6. Nutrition is very important in maintaining the ability to exercise effectively and to stay in good physical conditioning.

7. Bone loss is prevented on Earth with drugs that reduce bone breakdown. Preliminary research in space indicates that the same drugs are effective in microgravity when combined with aerobic and resistive physical training.
8. Medical concerns for the consequences of musculoskeletal atrophy in space flight include pathological levels of potassium or calcium in the blood, which can cause cardiac arrhythmias or neurological problems and renal problems such as kidney failure or kidney stones.
9. Muscle size and strength returns to normal with rehabilitation (if necessary) on Earth.
10. The knowledge base on the bone strength recovery after space flight is inconclusive and requires additional investigations.

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