17 March 2006

16.423J/HST515J/ESD65J Space Biomedical Engineering and Life Support Systems
Quiz 1

1. (25 points) Exploration in Extreme Environments.

1a. Your best friend has been selected as an astronaut candidate, what advice (or "lessons learned") would you give him/her as he/she embarks on a 12-week (3 month) analog mission to the South Pole in Antarctica? He/she will be living with 5 other crewmates (3 women and 3 men total) (15 points).

Please provide a one-paragraph answer that synthesizes your advice.

Solutions could include:

- Isolated Confined Environments (top 7 categories to be aware of include):
  - Overall hypothesis: Space is an extreme environment where lessons from extreme environments on Earth can be useful.
  - Group interaction (overwhelmingly the most behavioral issue, cooperate, put the team first, unanticipated dynamics, positive outlook and attitude, team goals, how about testing the group before the mission?), communications (can have positive or negative effect, external, internal, mission control), workload (strike a balance, busy and challenging work, not bored), recreation/leisure time (has a positive effect), medical support (limited resources), adjustment, leadership (significantly effects mission success, authority and delegation, how about testing the leaders and managers before the mission who are responsible for making many decisions?), and food (can have a very positive effect)
  - Other important issues include: single/significant events (do not focus on a single activity), organization/management, equipment (use adequately tested equipment), sleep and safety
  - 3rd quarter slump in performance is a known phenomena (anticipate), Stuster's study shows physician 3rd quarter slump and leaders' experiencing the greatest decline in the 2nd quarter.
  - Group interaction themes to watch out for: interpersonal conflicts, not fitting in, problems in crew changes, trivial issues exaggerated, withdrawal; positive responses are seen in celebrations (among crew), balancing team/individual work, group discussions, etc.
  - Knowing your "mission" includes familiarization with: environment (know your environment and be familiar with the effect it has on you, and use it to your advantage), past missions (learn from history), successful outcomes, preparing before the mission (social, communication, expectations, etc.). When in trouble, try lateral thinking. Learn to make errors and learn from them.

1b. Please briefly describe an 'informal' human performance experiment that you would recommend to your colleague to run during his/her Antarctic experience (10 points).

- Choose your own experiment. Example measurements include: subjective (questionnaires), qualitative (journals) and quantitative measurements (physical performance). Suggest an experimental hypothesis, state the objective, and anticipated results.

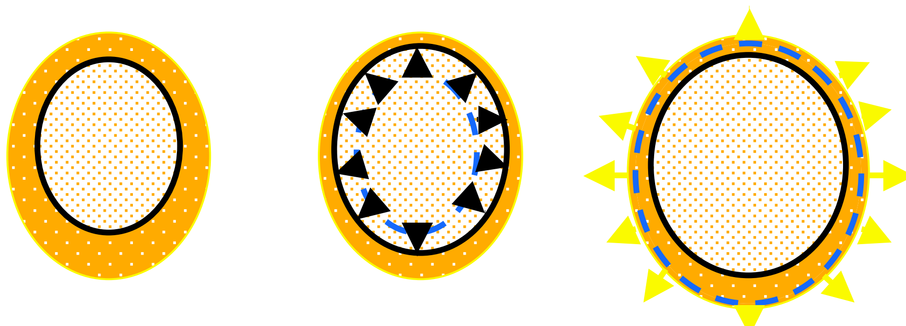
2. (40 points) Describe the skeletal physiological adaptive changes when exposed to long-term microgravity. Include current scientific hypotheses, results, similarities/differences to aging, comparison to 1G)? {illustrations and/or models are encouraged in this answer}

Solutions might include the following:

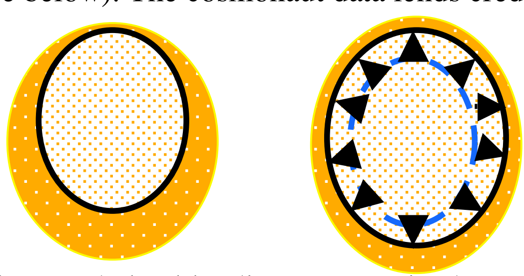
For bone, the signal to demineralize seems to be linked to stress presented by activity of the antigravity muscles, so when posture is no longer the same, muscles are not used, and bone struts no longer needed.

- decrease in osteoblast function and osteoclast function remains the same
- bone connected to force bearing muscle seems to be most affected, i.e. hips, pelvis, vertebrae (illustrate or reference Russian figure below).
- bone demineralization and remodeling, decrease in bone formation etiology: skeletal unloading or because trabecular bone is metabolically more active
- possibility of irreversible changes (need longitudinal database on astronauts/cosmonauts)

Adaptive modeling, or Wolf's Law (which follows Frost's Mechanostat in the materials), describes a relationship between bone structure and function. Throughout life, bone is constantly broken down and rebuilt to accommodate changing mechanical demands on the skeleton. From an engineering perspective, reduced bone strength could occur for two reasons: 1. The material is less able to withstand loading stresses OR 2. The structure is altered to increase loading stresses. **Stress and strain** must be major players in this evolving story. If we think geometrically, bone density (BMD) does not measure strength, rather, strength is determined by shape and dimensions of bone cross-sections. The homeostatic endpoint that the body strives to maintain appears to be the section modulus. Ah ha, we might **hypothesize that strain magnitude (and frequency) are the stimuli for bone resportion and formation**. Furthermore, we **hypothesize that stress and particularly, bending might be essential** to understand the mechanisms of bone loss in space. **Buckling** might really need to be understood for bone fractures in the elderly. We need a model. Why? Our measured properties do not uncover the essential mechanisms. We now discuss the relation to **aging**. A young bone is shown on the left with an elderly schematic in the center and right where the endiosteal (inner diameter) expands (loss) as well as trabecular bone loss and there is **appropriate adaptive** periosteal (outer diameter) bone formation. The bottom line result in aging is that there is BMD loss, but not necessarily section modulus reduction, therefore strength can be maintained. We become more mechanically efficient as we age (nice human design!). If we go into microgravity and reduce loading,



In the Figures, we hypothesize that the lack of loading will result in: 1) accelerated internal bone loss, 2) no periosteal expansion, and that both BMD and bone strength would be reduced (See below). The cosmonaut data lends credit to our hypothesis.



In **conclusion**, depending on skeletal loading, geometric changes may compensate for net bone loss. Reduced skeletal loading is a form of disuse like spaceflight. Bone loss in disuse leads to reduced structural strength. Wolff is still right today! Limitations to our studies include: Structural geometry can be measured with current DXA scanners but they don't do it very well. Small changes in dimensions are structurally relevant, but can't be reliably measured with current DXA scanners. We are able to show significant changes but we do it with statistical power (large change (spaceflight) or large N (elderly or NHANES studies).

3. (25 points) Give short, but complete definitions of the following:
   (a) the size principle;
   (b) nuclear chain and nuclear bag fibers;
   (c) illustrate $\alpha-\gamma$ coactivation (use a sketch with labels and some narrative);
   (d) describe how muscle fiber types might adapt in long-duration spaceflight;
   (e) Will the L-T (length-tension) and F-V (force-velocity) curves be affected by spaceflight? How?

Solutions (detailed descriptions included for completeness, but not in Quiz answer)
a. Size Principle – states that the motor units that generate the smallest forces are activated first. The largest motor units, with the greatest number of muscle fibers, originate in the largest nerve cell bodies and require the greatest amplitude of stimulus before becoming active. (Henneman et al., 1965) The small motor units - mostly supply red muscle fiber w/ high density of mitochondria are highly fatigue resistant on always "on". The large motor units supply most white or pink muscle fibers and are capable of high velocities and high forces for short periods. Nice symmetry here - motor units are recruited from small to large, the increment in forces as the new one comes in is always proportional to the level of force at the time. The sequence is reversed when the force level falls (largest units dropping out first).

b-c. Within that motor unit are muscle spindles (stretch receptors) subject to the same relative stretch as the whole muscle. **The muscle spindle is made up of nuclear bag and nuclear chain fibers**. Golgi tendon organs, sensitive to tendon stretch, are usually found near the muscle-tendon junction. Nuclear bag (~ 2) and nuclear chain (~ 3-5 per spindle = 2-3 mm long, 1.5 mm in diameter). Small muscles for fine control hive a high density of spindles (some hand muscles w/ 120 spindles per gram of muscle) vs. Large muscles, gastroc., fewer than 5 spindles per gram. The spindle functions include position and rate of change of length signaling**. Alpha (α) motoneurons inervate the main muscle mass (extrafusal fibers) while, gamma (γ) motoneurons inervate the interafusal fibers within the spindle organs.** Spindles attach at both ends to the main muscles and act as strain guages. The gammas are much smaller and have slower conduction velocities than alpha motoneurons. Muscle spindle afferents are of 2 types: Ia and II. **The Ia come from the nuclear bag fibers (possibly the chains) and the II come from the nuclear chain fibers. The nuclear bag is associated with gamma dynamic (γ_d) and gamma static (γ_s) efferents with both bag and chains, therefore, built-in velocity and length sensors, respectively.** Small muscles for fine control have many spindles compared to large muscles that may have few spindles. Group I fibers have large axons and therefore high conduction velocities. Group II fibers are smaller with lower conduction velocities.

Muscle commands are signaled by simultaneous increases in both α and γ activity by higher order motor centers. This alleviates the problem of contraction of the main (extrafusal) muscle mass and a slackening of the spindles if only a motor activity changed (say increased). The stretch reflex would then come into play as the Ia afferent activity dropped, causing the a motor activity to fall, thus turning the muscle force off. $\alpha-\gamma$ coactivation alleviates this problem. Needle electrodes in the intrafusal and extrafusal muscle fibers of the hand show that an increase in discharges from the spindle afferents occurs at the same time or only slightly after the beginning of electrical activity in the extrafusal muscle. The slight delay is accounted for by the time required for the intrafusal fibers to contract. (Additional answer covered in Muscle Homework Solutions)

d. Long-duration spaceflight shows selective atrophy of the slow twitch muscle fibers (SO, or 'red'), of the antigravity muscles. **Extensor muscles** have the majority of slow fibers types and these are the **primary antigravity muscle**, therefore, they are most affected. Significant atrophy of both fiber types can be seen in spaceflight, and the extent of atrophy is confounded by the level of countermeasures (exercise). There is less need (and therefore use) of the fast fibers (FG, or 'white') during spaceflight 'locomotion' in microgravity and there is a shift toward slow fibers. FG (fast glycolytic), white fibers (palest staining, look for presence of mitochondrial ATPase in stains); fastest=time required for the tension to rise to its peak value in a twitch is less than other types, low density of mitochondria and blood capillaries, anaerobic glycolysis to resynthesize muscle phosphagens. Fast oxidative glycolytic (FOG, or pink fibers), intermediate size between white and red, similar to FG, but more mitochondria, oxidative enzymes present, partially aerobic. Slow oxidative, or red muscle fibers are the smallest axon diameter fibers, which require the lowest tetanic tension of activation, slow contraction velocity, rich in mitochondria (red blood cell) concentration and oxygen carrying capacity, high oxidative enzymes, aerobic processes, fatigue resistant.

e. The L-T (length-tension) relationship is based on Huxley's physiological quantitative model of the actin-myosin crossbridges, so we don't expect a change in the relative sense T (%) vs. Length, (Note: assuming no cellular structural changes.), BUT if you plot L-T on an absolute scale you will notice reduced Tension levels from the loss of strength and atrophy (I imagine most will give this answer). Hill's F-V (force-velocity) curve will be affected by spaceflight. From class lectures, notes and the Russian muscle data a considerable decrease was noted in the F/V ratio during spaceflight. As measured by a dynomometer, you expect the force to have a higher slope (steeper dropoff) giving less force per velocity for shortening. Thus, the power curve (T &V) will also be decreased. You might need to take this in to consideration for the design of a lunar or Martian bicycle! You can think of the 3D relationship between Tension-Length-Velocity to capture the changes all at once:

4. (10 Points) Realizing the unified physiology of the musculoskeletal system, comment and/or illustrate how your answers for questions 2 and 3 above interact in a systems sense.
Musculoskeletal system: The muscles and bones are connected via tendons and stress, strain and force are critical parameters for performance. Consider the interaction of the muscles and bones, particularly in the most significant regions (i.e., the vertebrae, long bones, hip). In bone, the imparted stress signals bone formation, resorption, and steady-state homeostasis. Bone demineralization seems to be linked to stress presented by external loading and to musculature. The activity of muscles is greatly reduced when posture control is no longer the same (or no longer needed in spaceflight), therefore, altering the stress-strain profile. This phenomena gives rise to the result above (slow twitch fibers atrophy more, especially the extensor muscles since they have the majority of slow fibers types and these are the primary antigravity muscles). The stress-strain musculoskeletal response is critical, especially subjected to bending moments and torsion. Frost's mechanostat theory suggests that bone maintains a certain strain level. The system witnesses a decrease from the musculature and, therefore, reduced strain on the skeleton, which results in an exacerbated physiological deconditioning of the musculoskeletal system. There is an integrated physiological effect going on dependent on gravity as well as each other (musculo-skeletal dependence).

Physiological deconditioning from spaceflight manifests itself as the need for an adaptive response to 1G upon return from spaceflight. CNS recruitment of muscle fibers necessary for movement in 1G for musculoskeletal performance and motor control. The need in 1G to maintain upright posture has to account for altered posture etiology: atrophy due to a decrease in CNS recruitment of antigravity muscles and perhaps a concomitant decrease in the contractile proteins synthesized in muscle. You also have an instantaneous skeletal loading in 1G that requires an adaptive response, not to mention orthostatic intolerance.[1]

[1] In general, the **illustrations** provided were much appreciated and demonstrated your learning.