
**Part I: Summary**

When a bone remains unused for a period of time, one of the resultant effects is a loss of bone. This study investigated the effects of terminating the unloading and allowing normal use of the bone again. The specific effects investigated were whether or not bone loss stopped after it was reloaded and whether or not the process was reversible, as in regaining the bone lost during the period of disuse. The study involved unilateral hindlimb immobilization of growing adult rats for two weeks, followed by removal of the immobilization devices to allow free use of the limb for four weeks, at the termination of the rat.

Two control groups and two study groups existed. The right hindlimbs of the two study groups were immobilized using bandages and padded tape against the abdomen, while the two control groups remained free to use all limbs. All groups were provided the same nutrients throughout the experiment in the form of standard laboratory chow and water. After two weeks, rats in one control group and one study group were terminated and examined. The rats in the second study group were remobilized by removing tape and bandages at this time so that after week six of the study, allowing for four weeks of remobilization, the rats in the second control group and the second study group were terminated and examined. The femora were removed bilaterally from each rat and soft tissues were cleaned and eliminated from the surfaces of the bones. The femora were tested in three-point bending, with maximum bending moment, yield bending moment, work to failure and stiffness being calculated from the data and used in analysis. Then, marrow was removed from the bones, which were dried and placed in a muffled furnace. The ashes were weighed in order to determine mineralization of dry bone tissue.
After two weeks of right hindlimb immobilization bone density of the right femur decreased by 3% and bone density of the left femur decreased by 1.5%, though mass, size and mineralization were not affected and there were no differences in mechanical parameters in three-point bending. After four weeks of remobilization, however, bone density of the right femur was 2.4% lower than that of the control rats who had never been immobilized. Mineralization for the experimental rats was also 1.4% lower in the right femur. In regards to size, the medullary cavity of the right femur was larger than that of the left femur, though the external dimensions of the bone did not differ from the left or between control and experimental groups. In mechanical properties in three-point bending, maximum bending moment was 11.3% lower, yield bending moment was 14.4% lower and stiffness 7.4% lower than the properties for the control rats. In a comparison for rats sacrificed immediately after the immobilization period and rats sacrificed after the remobilization period ended, during the four weeks of remobilization, rats continued to grow in body weight, mass, length and bone density, although improvement of mechanical parameters only occurred in the left femur. The authors concluded that the bone loss process stemming from disuse does not stop after normal mechanical loading of the bone is resumed.

Part I: Critique

The objectives of this study were to determine if reloading a bone, before it reached a steady state from a low activity period, would stop bone loss, as well as to answer whether or not bone loss is temporary and reversible. The study seemed to answer the first question well, though results may be inconclusive for the second question. Regardless of some problems that may exist with the study, however, its findings are still of value to society and could lead to further studies that may apply to human subjects.
In the conclusion of the discussion, the authors state that the results “demonstrate that disuse-induced processes of bone deterioration last longer than immobilization and a resumption of previous loading is not sufficient to stop them.” Because there were improvements in bone density from the end of immobilization (3.5% lower than control) until the end of the remobilization period (2.5% lower than control), it cannot be proven that bone density continues to decrease even after immobilization. However, due to the fact that mechanical properties of three-point bending decreased in experimental rats compared to control rats, it is shown that some part of the bone-loss process is continued into the remobilization period. What is not examined, however, is the cause for this continuation. The continuation of this process may have been due to some behavior in the rats, particular after immobilization. While the study cited that all rats “used all legs while moving” after one day of immobilization, the study does not cite how the level of activity in experimental rats compared with that of the control rats. The assumption, it seems, is that all rats, experimental or control, behaved similarly in movement. However, this is an assumption that should not be made lightly. In humans, sometimes after an injury or some cause of disuse or immobility of a lower limb, the subject adapts and acquires a new gait that compensates for the loss of limb use, such as limping; during the recovery period, this behavior can continue out of habit from adjusting to the injury-phase gait so that normal loading may not occur on the limb after remobilization. Whether or not this was an issue in this study is unknown, since the issue was not mentioned. However, to be able to consider the validity of the conclusion, this should have been addressed.

The second question, whether or not the bone-loss process is temporary and reversible, was answered in the discussion in a statement that “no recovery was noticed... [and] free remobilization appeared to be somewhat harmful to bone properties.” This experiment does not
seem appropriate to meet the scope of this question. The study cites and earlier study using young adult dogs, where a "complete recovery of bone strength" was achieved after 32 weeks of immobilization. Even though this was achieved in that study, the authors of this study accredit the recovery to increased training, which is followed by a decision that free remobilization is harmful and normal loading is not sufficient to stop the bone loss process. This is a very broad statement. It would be interesting to see the study continued for a longer period of time than four weeks, which seems very minimal, considering the rats were still in a growing state and two weeks of immobilization would seem to be a major setback in growth. This study only gathered two data points and they were in a short term. Two data points are not enough to show a trend, so the study should have been conducted for a longer period of time with various data collection points along the way, such as eight, 12, and 16 weeks. The length of time could have been dictated by what was discussed in the introduction to the study; the authors discussed the steady state that is achieved when a change in loading states exists. The study could have continued until a steady state was achieved. The authors cites several studies that support the theory that "complete and permanent" bone recovery is questionable, and this may ultimately be true, but this study would have had more valid results if it had lasted longer and some kind of equilibrium had actually been shown, in order to establish that more recovery would not occur.

Aside from these issues, if further studies show these results to be valid, it could lead to important breakthroughs for aging and bone loss, as it is the aging population whose bone loss is most problematic and dramatic, as well as younger populations. It could often be said that the aging population might be at most risk for immobilization issues, as many have health problems that keep them from exercise, or they are weakened from their age and may be confined to a wheelchair or using assistive devices that keep their legs from being completely weight-bearing.
However, if it can be shown that staying active in old age will keep the elderly safe from bone loss issues, it may encourage people to stay active and healthy as they age in order to try to stay out of situations that will leave them mostly bed- or wheelchair-ridden and sustain an injury. This study used growing adult rats, so in order to help this population a study on elderly adult rats might be the next step in animal studies. If a result came from that study indicated that in old age the bone density and mechanical weakening were still irreversible, this might be helpful to the aging population to remind them that any time spent in an inactive state may result in irreversible bone loss. For younger populations, a long-term study might indicated the best methods of restoring bone density and strength, as well as determining how long complete restoration might take, if it is found to actually be reversible. If it is irreversible, it would still be helpful to discover how to maximize healing. Additionally, studies on non-weight-bearing bones, such as the ulna, would be interesting, in terms of what would qualify as “use” and “inactivity,” as it could lead to better ideas on how to exercise and build bone density in the upper extremities.

Very good summary and excellent effort!

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