Tissue Repair, Immobilization, Disuse and Remobilization

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Introduction

It is vitally important to understand the phases of tissue repair, as well as the way in which different tissues react in each if these phases. Muscle disuse atrophy is the most apparent of all tissues yet immobilization and disuse affect all tissues. So, when faced with injury and subsequent repair, each tissue must be considered. The same applies to remobilization of the affected tissues, as well as the formulation of a rehabilitation program.

Phases of Tissue Repair [1,2,3,4,5]

Injury to tissue initiates a complex series of events, which involve cellular and biomechanical responses, and result in wound healing. The stages are sequential and predictable.

1. Inflammatory Phase
   Following injury most tissues first undergo an acute vascular response. This is followed by cellular infiltration. The vascular response centres around haemostasis and this involves the activation of the coagulation cascade. The cellular aspect follows haemostasis. The haemostatic plug releases cytokines, and cells migrate into the wound. Approximately 6 hours after injury neutrophils move in. Their numbers peak 2 – 3 days later. The role of the neutrophils is initial debridement and phagocytosis of micro-organisms. In this manner the possibility of infection is reduced.

   24 – 48 hours after the neutrophil migration, macrophages move into the site. This influx of macrophages seems to trigger the change from inflammatory to repair phase. The macrophages serve 5 major functions namely; phagocytosis, wound debridement, regulation of matrix synthesis, cell recruitment and activation and angiogenesis.

2. Reparative/Regenerative Phase
   This phase is characterized by cellular response of endothelial cells and fibroblasts (tenocytes/myofibroblasts). Fibroblasts lay down new, small, weak, fibres without organization. Matrix synthesis occurs and increases over the next few weeks resulting in a concurrent increase in strength. Endothelial cells adjacent to the wound proliferate and form new capillaries which migrate into the wound.

   This process results in, what we call, granulation tissue.

3. Remodelling/Maturation Phase
   This is the final phase of wound healing during which collagen fibres reorient parallel to lines of stress, and fibres cross link in a stable formation. This is very important for tensile strength of the new tissue.

Specific Tissues

Although tissues follow the same phases of repair, differences exist between tissues with regards to the time taken to repair and to reach optimum strength. This has bearing on physical rehabilitation because practitioners can apply this knowledge to influence the outcome in a positive manner. To enhance the result, rehabilitation practitioners need to understand the changes that tissues undergo as a result of disuse and immobilization. The final piece of the puzzle is an appreciation of how to safely remobilize tissues in order to avoid damage due to overuse.

Connective tissue is tissue of mesodermal origin.[1] It comprises of:

- Extra cellular components
  - Fibres – collagen, elastin and reticular fibres. These provide structure.
  - Water and glycosaminoglycans (GAGs) which provide lubrication and spacing.
- Cellular components

Rehabilitation practitioners are faced with injuries of connective tissue namely ligaments, tendons, articular cartilage, joint capsules, muscles and bone.

Tendons and Ligaments

Tendons and ligaments are primarily composed of Type I collagen fibres arranged into parallel bundles with a surrounding extracellular matrix.

Collagen is synthesized by fibroblasts. Once collagen is transported out of the cell, these molecules are chemically bound together by cross links. These collagen molecules gather in the extracellular matrix in a parallel formation forming microfibrils, which join together to become fibrils. Fibrils aggregate and ultimately form superstructures (tendons and ligaments).

Newly formed cross links are relatively weak and can be prised apart. As the links mature, they strengthen. Excessive force must be avoided in early stages of tissue repair. Furthermore, the arrangement of collagen matrix is an adaptive process and dependent on directions of forces and loading patterns imposed on the tissue. This means that manual and rehabilitation therapies can influence this process.

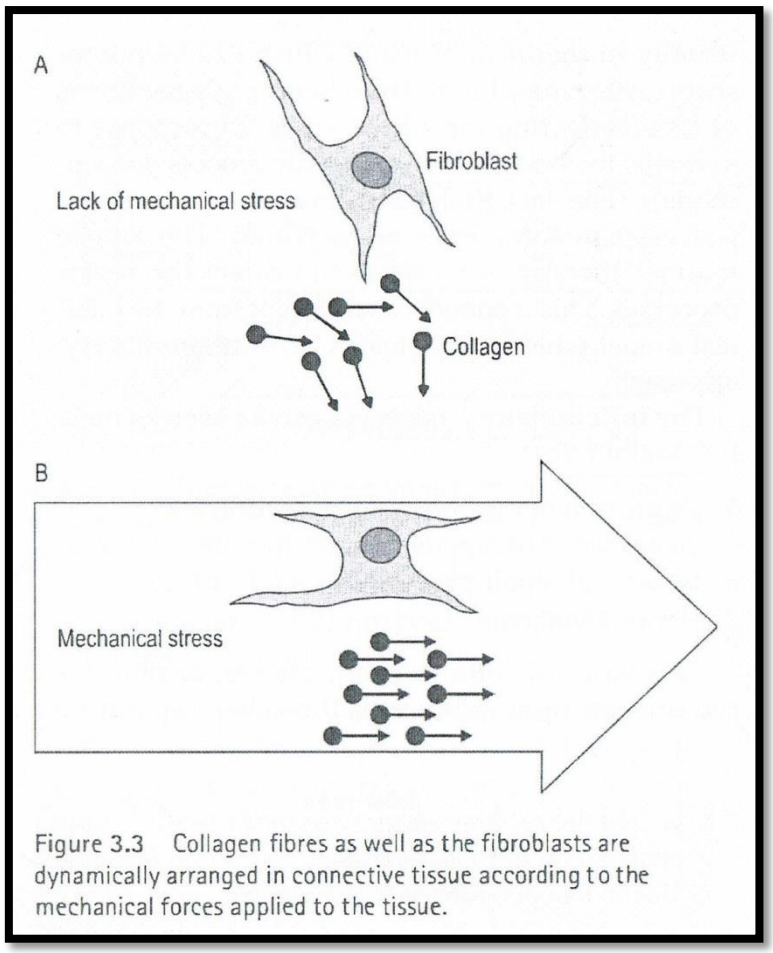

Figure 3.3 Collagen fibres as well as the fibroblasts are dynamically arranged in connective tissue according to the mechanical forces applied to the tissue.

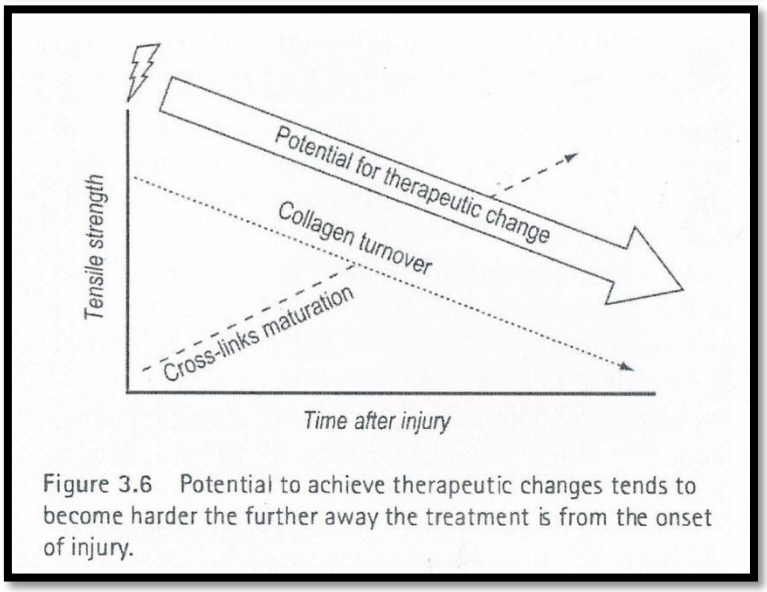

Figure 3.6 Potential to achieve therapeutic changes tends to become harder the further away the treatment is from the onset of injury.

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Tendons attach muscle to bone. They can be classified as vascular (no synovial sheath) or avascular (with a synovial lining). Vascular tendons receive their blood supply from musculotendinous junctions, the osseous point of insertion and adjacent muscle and paratenon. This is extrinsic healing and the formation of adhesions is prevalent. Avascular tendons require a longer period to achieve adequate tensile strength and healing when compared to those without a synovial sheath. Intrinsic

healing occurs (nutrients are received from synovial fluid). It is very important to immobilize avascular tendon repairs to avoid gap formation at the repair site.

Ligaments attach bone to bone. They tend to widen at the insertion to blend with the periosteum. Ligaments support articulating surfaces. There are currently many questions regarding rehabilitation information because of the location. The location of the ligament affects its ability to heal. The medial collateral ligament (MCL) of stifle has a very good healing potential. The cranial cruciate ligament (CCL) does not. The CCL never reaches its original tensile strength following repair, hence the need for alternative surgeries which rather address stifle biomechanics.

The importance of this for rehabilitation is that the time to begin a program for ligament injury depends on the ligament involved. Equine studies show that rehabilitation should focus on low duration (30 minutes) and high frequency (6 days per week) to have the greatest benefit. Sprain-avulsion fractures at the ligament-bone interface have the best prognosis for return to normal tensile strength. The surgical requirement is as small a gap as possible at the wound site, to minimize scar formation. Bone resorption occurs at bone-ligament/tendon interface and can take as long as one year to recover.

Stress deprivation (immobilization) rapidly reduces the mechanical properties of tendons and ligaments. There is a drop in cross sectional area which is as a result of a decrease in fibril size and density i.e. atrophy.[2] The synthesis and degradation of collagen (part of a healthy balance) also decreases. Fibrils laid down are haphazard and disorganised. This causes a weakening at bone-tendon and bone-ligament complexes because of the formation of abnormal cross links. Furthermore, the GAG level is reduced so there is less water absorption which translates into less extensibility.

Tendons are less affected by immobilization than ligaments. With immobilization of tendons there is an obliteration of space between the tendon and its sheath which decreases the gliding motion, and so results in decreased ROM. Immobilization affects the regeneration of vascular supply to the tendon therefore impairing healing. Research shows that healing of tendon ends by collagen deposition takes at least 28 days. Collagen bundles, however, are distinguishable from normal tendons for 112 days after injury.[4] But, complete immobilization for more than 21 days resulted in reduced vascularisation at the wound site. In the case of tendons physical rehabilitation is a balancing act. The goals of rehabilitation include strengthening and prevention of the formation of adhesions. A good result requires an appropriate choice of surgical technique so as to minimise the gap and prevent haematoma formation.

Current research supports the application of periodic, moderate stress to the injured tendon/ligament to aid nutritional haemostatis and repair. ROM of the tendon should be maintained (movement of 1 - 2 mms) to combat the deleterious effects of immobilization. These passive mobilization exercises can begin as soon as 5days after injury but beware not to perform excessive excursions. In the case of Achilles tendon injuries the area can be splinted (immobilized) with no tension on the tendon, but allow for movement of the digits. The device should not allow weight bearing.[4] This small ROM prevents adhesion formation. Remove splints 3 weeks post-

operatively to gain the most benefits from healthy repair. Once removed, limit the amount and type of exercise. Progressively increase the frequency and magnitude of loading to the healing tendon/ligament. . Apply low, cyclic loads to promote matrix formation and enhance remodelling. Light weight bearing can begin at 6 weeks because the tendon will have 20 – 25% of its tensile strength. This is adequate to withstand normal muscle force. Wait at least 12 weeks before allowing less restrained, more active loading. Light exercise is required to maintain the range of motion (ROM) and for maturation. Sufficient tensile strength for normal activity may take months to return.

Passive ROM in early stages is most beneficial. Early mobilization results in higher tensile strength and these tendons are less inclined to rupture than immobilized tendons. The movement reduces the formation of adhesions and organises vascular regeneration into a normal pattern.

Joints

The following processes and structures are responsive to mechanical stimulation:

- Articular cartilage haemostasis and repair
- Synovial fluid formulation and flow
- Connective tissue supporting the joints

When discussing joints the articular cartilage, joint capsule, synovium and ligaments are included.

The role of the synovial fluid is to lubricate moving articular and synovial surfaces, as well as to supply nutrients to avascular articular cartilage. A physiological mechanism exists called the trans-synovial pump, which aids in the formation and drainage of synovial fluid in the joint.[1] It is activated by both active and passive movement. Chondrocytes are totally dependent on synovial fluid to supply required nutrients. Different joint pathologies will impede transport of these nutrients. Joint injuries can vary from mild damage of the synovial lining, capsular or ligamentous structures (sprains) to severe damage of the articular surface. Damage to any of these structures will initiate a repair process.

The limiting factor for the repair of articular cartilage is its avascular nature. Two different responses can be expected.[4]

- Partial thickness damage does not illicit an inflammatory response. The defect can remain unfilled for up to one year.
- Full thickness damage (to subchondral bone). Repair takes from 5 – 7 days to 2 months, with remodelling taking 2 – 6 months to complete. Repaired tissue is not hyaline cartilage but passive ROM (PROM) can positively affect this outcome. Adolescents are likely to have a better outcome than adults.

Much of the treatment of articular cartilage defects revolves around surgical debridement and then the application of PROM post operatively.

Joints are designed to be mobile and to work under repetitive, mechanical stress. As such, they are sensitive to immobility which results in atrophy of capsule, ligaments, synovial membrane and articular cartilage. This atrophy presents as a decrease in matrix, cellular components, GAGs, water and therefore the cartilage loses thickness. A thinner cartilage layer does not have the protective cushioning of the

water within the matrix and injury becomes more prevalent, especially at areas of weight bearing. A decrease in synovial fluid leads to a decrease in nutrition and the joint heads into a downward spiral of disease. Total immobility can also cause fibro-fatty changes that result in adhesions around the patellar fat pad. Immobility can cause a 20 – 30% reduction in PROM, lameness and muscle atrophy. Another downside is vascular proliferation of the joint capsule, which can become a contracture, usually at the flexor aspect.

Passive motion as soon as possible has a hugely positive effect in that it stimulates the synovial pump, helps to manage pain, reduce swelling, removes waste products and potentially damaging by-products whilst supplying nutrients. It also helps to prevent the formation of adhesions. If a joint must be immobilized research in canine stifles suggests that immobilization in flexion results in fewer osteoarthritic changes and those changes are reversible.

Another model maintained active stifle motion, without weight bearing, in dogs for a duration of eight weeks. There was no evidence of atrophy or resorption of soft tissue, including the meniscus. Absence of weight bearing resulted in bone atrophy. Weight bearing with no stifle motion led to atrophy of the lateral meniscus. The conclusion was that motion may be more important than loading to prevent meniscal atrophy.

Frequent, regular therapeutic exercises are more effective in improving joint mobility than free activity. Crating with controlled movement is better than immobilization. When considering remobilization after immobilization then a low intensity, controlled activity is vital in the early stages. Cartilage recovery can be as soon as 3 weeks but may take 50 weeks, and some patients may never fully regain cartilage health. Avoid vigorous exercise.

<u>Muscle</u>

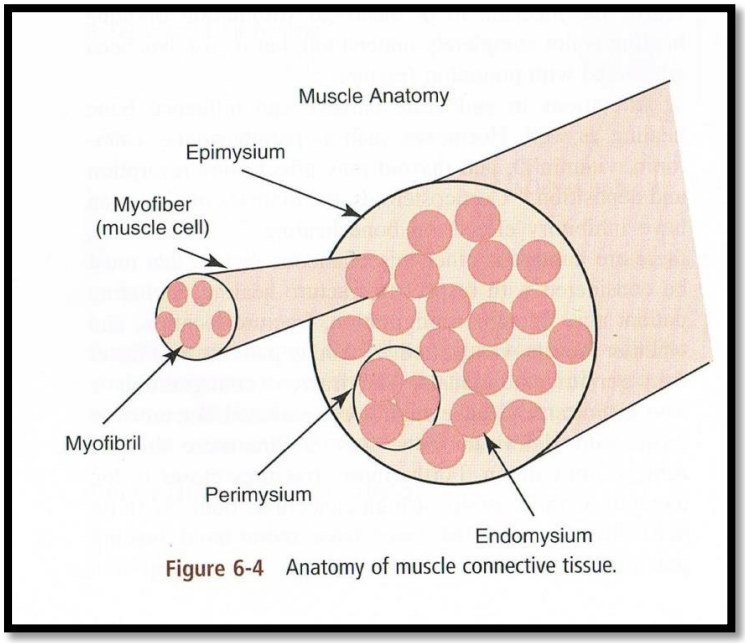

Figure 6-4 Anatomy of muscle connective tissue.

Canine Rehabilitation and Physical Therapy 2nd Ed. 2014 Millis D.L. Levine D.

Muscle fibres are richly supplied with capillaries, nerves and lymphatics which traverse through surrounding connective tissue sheath. Injuries to muscle occur as a result of lacerations, contusions, ruptures, ischaemia and strains. A strain tends to occur close to the myotendinous junction. Muscle healing processes follow the same basic principles of tissue repair.

The extent of the injury will determine the outcome of functional muscle fibre versus scar tissue. Partial tears have a better probability of returning to function and tensile strength. There is a competition (during repair) between regeneration of functional muscle fibres and the production of fibrous scar tissue. This process can be influenced by immobilization and mobilization. Timing of appropriate mechanical stress is hugely important to a final outcome.

For the best result (optimum muscle fibre healing to return to maximal function) mobility across the injury site should not begin until healing is well under way (late reparative/early remodelling phase). In this stage muscle fibres can be aligned parallel to action if appropriate stressors are allowed. Muscle regeneration is dependent on longitudinal dynamic muscle tension (stretching/muscle contraction). This promotes normal parallel alignment of myotubes to lines of stress and the connective tissue component is restored. The connective tissue is vital for the development of internal tendons, fascicule and adequate, well-defined skeletal attachments. This connective tissue must develop in order for the muscle to function after damage.

The postural muscles (extensor muscles and those which cross a single joint) contain mostly Type 1 fibres (slow twitch) and are the most prone to atrophy. There is a decrease in fibre size and number. The size and number of mitochondria decreases. There is a drop in total muscle weight. The muscle contraction time is prolonged and the muscle tension produced is less, which translates into a decrease in strength. Immobilization reduces the chronic load on these muscles with a resultant rapid loss of strength in the first week. Further losses occur more gradually. It is preferable to immobilize in an elongated position and usually only for 3 – 5 days.

Fortunately remobilization rapidly overcomes these effects and changes are reversible. It is generally expected that a remobilization period twice that of the immobilization period will return the limb circumference to normal values. In the case of partial tears controlled activity can be allowed from 2 – 3 weeks. With total ruptures only allow this at 4 weeks. Expect to return to unrestricted activity in 8 – 12 weeks.

Mechanical loading is essential for muscle regeneration. The potential to regenerate muscle is less in older animals. More intense training will result in more rapid recovery of muscle mass. Therapy 3 – 6 times per week is preferable to once a week. Treadmill walking and swimming are useful exercises because resistance stimulates muscle protein synthesis and the activation of muscle satellite cells.

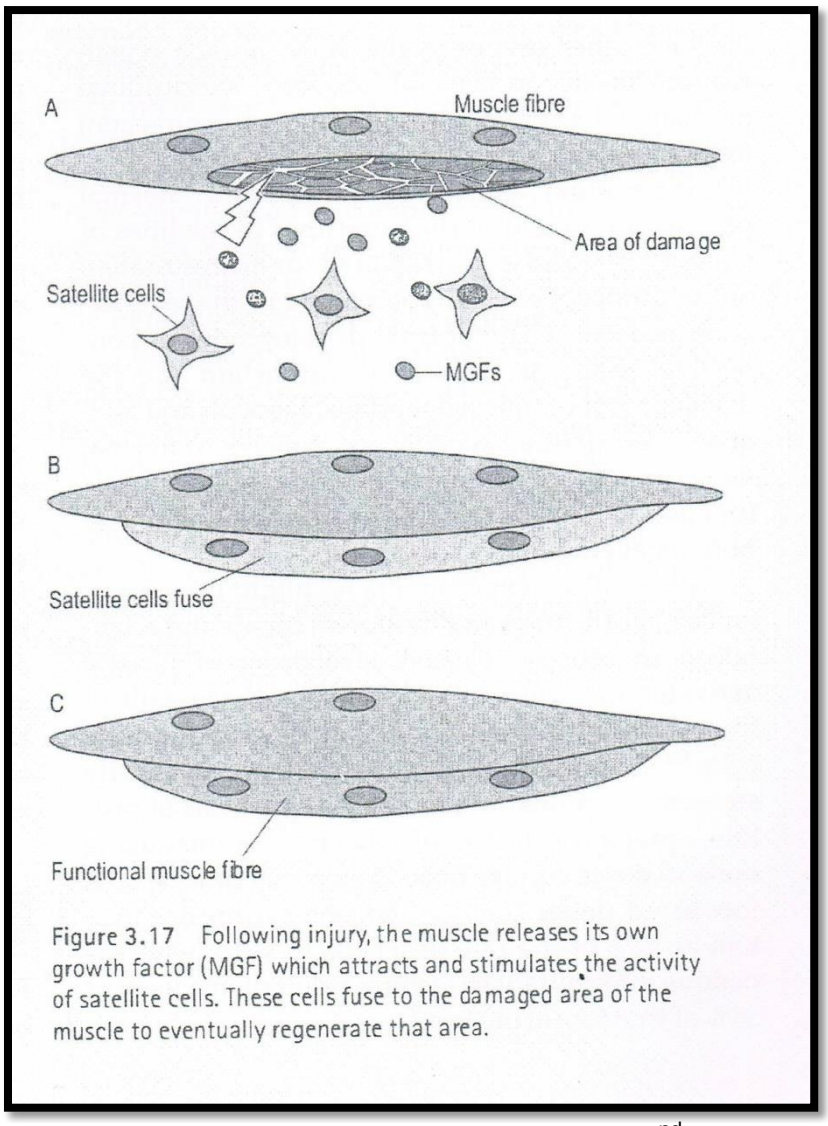

Figure 3.17 Following injury, the muscle releases its own growth factor (MGF) which attracts and stimulates the activity of satellite cells. These cells fuse to the damaged area of the muscle to eventually regenerate that area.

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<u>Bone</u>

Bone is dynamic tissue. It comprises of the following:

- 35% organic
  - Osteocytes
  - Osteoclasts
  - Osteoblasts
  - Bone matrix
  - Type I collagen
- 65% mineral
  - Calcium
  - Phosphorous which are deposited in association with the collagen fibres.

The collagen gives bone its tensile strength and visco-elastic property. The mineral deposition provides structural rigidity and enables bone to withstand compressive forces. Bone can adapt to forces according to Wolff's Law. The blood supply is primarily from nutrient artery and also periosteal attachments.

Two types of bone healing can take place.[4]

- Primary bone healing occurs when the gap between fractured ends is less than 0.1mm. Contact healing bone forms across the fracture line. Healing can also occur if the gap is between 0.1 and 0.5mms. This is gap healing but in both instances the repair is rigid and no callus is formed. This close alignment does not reduce the time required for healing.
- Secondary bone healing occurs when the gap between ends is greater than 0.5mms. The reduction is less rigid an a callus is formed. The degree of callus formation is dependent on the amount of instability at the fracture site.

Because bone can regenerate, it is possible to regain 100% of tensile strength. Clinical union is defined as the ability to withstand the load so the fixation can be removed. Intramedullary pins and external fixators can usually be removed earlier than plates.

General healing times are:

Pups	< 3 months	2 – 4 weeks
Pups	3 – 6 months	4 – 12 weeks
Pups	6 – 12 months	5 – 8 weeks or 3 – 5 months
Adults	>1 year	7 – 12 weeks or 5 – 12 months

Local immobilization occurs due to casting, splinting, denervation, paralysis, disarticulations, limb suspension and stress shielding following plating. Systemic immobilization occurs with body casting, bed rest and space flight.

Patterns of bone loss are similar regardless of the area but amount of bone loss differs depending on the location and the degree of unloading. Immobilization[2] creates the following changes:

- Increased bone resorption but decreased bone deposition
- A drop in cancellous and cortical bone mass
- Decrease in cortical bone density and stiffness
- The loss is more extensive in distal weight bearing bones

Changes are dependent on length of immobilization, age of animal and the bone involved. The longer the immobilization the greater the bone loss, up to 32 weeks whereafter bone loss stops progressing. If trabecular bone structure is lost, it is difficult to regain.

Longer immobilization times translate into longer recovery times. Older animals may have less bone mass than younger ones, prior to immobilization. Younger animals recover more quickly.

Initial rehabilitation during early immobilization is aimed at maintaining joint ROM, reducing pain and decreasing tissue inflammation. Safe, controlled mobility must be established to increase loading and thus callus formation. If, however, the load is too high then there is a drop in osteoid production. More is not always better.

Training after remobilization results in a more complete and rapid recovery. Begin with mild treadmill three times a week, and follow with higher intensity training as the

injury strengthens. Jump training MAY result in recovery of more normal trabecular bone mass.

Conclusion

From this brief overview it can be appreciated that a thorough understanding of basic tissue healing is imperative to successful physical rehabilitation practice. Furthermore, an appreciation of the healing process in the different tissue types, as well as the understanding of mechanical stressors and how they affect tissue repair, will yield the best recovery possible. Finally, an awareness of the time frames of healing of the various tissues will also result in fewer complications and a strong, positive outcome.

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