The Basics of Soft Tissue Healing and General Factors that Influence Such Healing

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KEY POINTS FROM THIS ARTICLE:

1) Wound healing following overt injury to a tissue follows general “rules” irrespective of the tissue involved.

2) Wound healing and repair of injured tissues follows several steps in the healthy individual. The process is initiated by the inflammatory response and subsequent steps are based on this initial response.

3) “Whereas wound healing generally leads to a repair of the injured site, it does not lead to tissue regeneration. This difference between repair and regeneration has influence on tissues such as ligaments and tendons that function in a mechanically active environment.”

4) “The dynamic interface between mechanics and biology influence the effectiveness of the healing response.” [Important]

5) Factors that impact the outcome of the healing response include the biology of the host, such as:
   A) Age
   B) Sex
   C) Genetics
   D) Tissue history (prior injuries, scar tissue, and disease states)

6) The repair process can lead to a loss of function, primarily from scar tissue, and this can occur in both musculoskeletal and visceral tissue (heart, lung, kidney, liver).

7) Recent investigations have detailed the healing response of many connective tissues (ligaments, tendons, menisci, joint capsules) that function in mechanically diverse environments.

8) The functional outcome of the healing process depends on the extent of “repair” versus “regeneration.”

9) The basic steps in the repair or healing of a tissue following overt injury are:
   A) Hemostasis and a rapid inflammatory phase
   B) A phase of cell proliferation and matrix deposition
C)) A slow remodeling phase, which may take months to years

A)) The Inflammatory Phase

• Following acute injury there is bleeding into the area of injury and pain.

• “Hemostasis is restored by the formation of a fibrin clot, which prevents further bleeding and serves as a provisional matrix for migrating cells.”

• This clotting cascade results in the release of inflammatory molecules and inflammatory cytokines from cells such as platelets.

• There is an influx of fibroblasts, which sets the stage for the second phase (B) of the repair process.

B)) The Matrix Deposition Phase

• Deposition of matrix molecules [fibroblasts] produce collagen proteins that bridge the damaged area with the residual endogenous ligament tissue.

• “If the matrix deposited early during the healing or repair process is altered compared with normal, the organization of the repair tissue is also likely to be altered.” [Important: early best treatment is critical for ultimate quality of healing]

• “The organization of the matrix deposited early following injury is disorganized compared with normal tissue.” [The Fibrosis Of Repair]

• “The tissue deposited early after injury appears to be an attempt to bridge the damaged area without regard to what was present before injury.”

• “Not only does this provisional matrix have a different structural and cellular composition as compared with normal tissue, but in the case of ligament injury, this tissue is not necessarily even localized to the injury gap but also may extend to surround the entire remaining ligament mid substance.”

• “This somewhat amorphous material, resulting from the initiation of an overt inflammatory response and subsequent events is compromised at both the organizational and functional levels, independent of whether it is a ligament, tendon, or skin.”

C)) The Remodeling Phase

• “The remodeling phase is a slow process and is accompanied by alterations not only in matrix remodeling, but also gene expression, cellularity, vascularity, and innervation.”
• The scar tissue in a ligament “undergoes a protracted process where the initially deposited material seems to be turning over and the organization of collagen fibrils become more oriented along the long axis of the ligament.”

• “Because the remodeling phase occurs slowly, and may take months (i.e., skin) or years (i.e., tendon and ligament).” [Important]

• A number of variables seem to influence the rate of remodeling and the final outcome, and it is not always possible to assign potential cause and effect relationships.

• “Even after protracted time post-injury, the mechanical properties of a scar tissue in a ligament ... is still compromised compared with normal.”

• “The scar tissue may be functional for most activities even though it is not ‘normal’.” [Fails during high demand activities]

10) “Normal tissues are organized with respect to collagen alignment and collagen fibril assembly, whereas collagen expressed early following injury is not aligned and heterogeneous with regard to orientation in the tissue. Because the latter is critical for function in a mechanically active environment such as a ligament, it is not surprising that the mechanical properties of the healing ligament are severely compromised compared with normal tissue.” [The Fibrosis Of Repair]

11) The scar cells in the healing ligament are different from normal cells and therefore the scar is intrinsically different. [Key Point]

12) Tissues that do not have an influx of new microvasculature, like the disc and meniscus, do not heal well. [Very Important]

13) “Not all ligaments heal to the same degree, and healing of ligament injuries seems to be influenced by various factors including location (i.e. extra-articular vs. intra-articular), intrinsic aspects (which are largely unknown), mechanical environment, as well as factors discussed in more detail in the following sections.”

14) “The large scar tissue mass gradually remodels, likely under the influence of the mechanical environment.” [Very Important: supports the contention that the mechanics of the chiropractic adjustment can enhance the timing and quality of scar remodeling]

15) “Scar-like” tissue is “functionally ineffective.”

16) “Maturation of the scar tissue requires mechanical loading to continue the remodeling phase of healing.” [Very Important]

17) “Normal connective tissues that function in a mechanically active environment (actually most tissues) subscribe to the “use it or lose it” paradigm of tissue
integrity.” “Increased loading leads to adaptation, whereas decreased loading below a threshold leads to atrophy.” “The same principle likely also holds for scar tissue and immobilization beyond the initial phases of healing could have a detrimental impact on outcome.” [Very Important]

18) “Too much loading of a scar at too early a time point may have a detrimental impact on the maturation of the scar.”

19) Post healing joint instability and the loss of function leads to increased expression of inflammatory mediators, “likely caused by microinjuries to the scar tissue, and resulted in a protracted healing response.” There is a delicate balance between biology and mechanical environment when it comes to optimizing the basic healing response in tissues such as ligaments, tendons, or skin.”

20) “Some tendon and ligament injuries lead to formation of scar tissue that is partially functional, but to regain as much function as possible requires physiotherapy to ‘facilitate’ the return to function after the scar tissue has formed.” [Very Important]

21) The inflammatory response associated with overt injury or surgery can lead to formation of adhesions, where “the ligament/tendon scar tissue is “bonded” to the surrounding tissue and thus, such restrictions compromise function in situations where movement is required.” [Adhesions, Fibrosis Of Repair]

22) This “emphasizes the need to minimize the induction of a vigorous inflammatory response in some environments to assist in the repair process without side effects such as adhesions.” [Very Important: the resolution of inflammation is fibrosis; reducing inflammation reduces the fibrosis]

23) “It is clear that the outcome is repair and not regeneration in all soft connective tissues, except for muscle and of course the hard tissue, bone.” [Most Important: ligaments and tendons repair (with scar tissue) rather than regenerate (heal with normal pre-injury tissue)].

24) Writings from ships’ captains from the 17th to 19th centuries whose men suffered from scurvy noted: “Under conditions of vitamin C deficiency, scars on men that had formed greater than 20 years prior seemed to dissolve before normal skin was affected, leaving gaping wounds where once there were scars. Thus, even after many years, scar tissue is more ascorbate dependent than normal skin for maintenance of integrity in humans.” [Both acute injury and the long-term integrity of healed tissues are Vitamin C dependent].

25) “The healing process is influenced by age.”

26) “It is known that the biomechanical properties of ligaments and tendons change with age (become stiffer) because of accumulated stresses and the
incidence of injuries, and degenerative processes in many of these tissues increase with age (aside from those associated with athletics).” [Very Important]

27) The authors present evidence that indicates that different tissues and different individual [animals] have phenotypes that allow them to genetically heal better or worse. Apparently, genetics in part, determines if the healing occurs by regeneration or by scar tissue, which is linked to the “severity and extent of the inflammatory response.” [Very Important]

28) Women tend to have a more vigorous inflammatory response than males, [and therefore more fibrotic and mechanical (scar) healing residuals]. This response is probably linked to estrogen levels.

29) Normal ligament and joint function (laxity) can be influenced by the menstrual cycle in some women.

30) Pregnancy is associated with changes in several hormones qualitatively and quantitatively, impairing the metabolism of cells in the healing ligament, and also affecting the functioning of the normal ligament (i.e. laxity).

31) Genetic factors play a role in some pathologic scarring or wound healing such as keloid formation.

32) “It is apparent from talking with orthopedic surgeons that there is a body of anecdotal information that has implicated genetics in wound healing following ligament injuries and surgical interventions.”

33) “The quality of the tissue prior to overt injury may play a role in the wound healing process and the final outcome, and therefore should be considered.” “The presence of previous injury, either overt or subclinical, could also impact the healing outcome. The healing outcome following re-injury could impact both the quality of the outcome and the functioning of the healed tissue.” [Very Important]

34) “Mechanobiology is likely important in the healing outcome in tissues such as ligaments, tendons, and related tissues. That is, depriving healing ligaments of mechanical loading likely has a detrimental impact on healing outcome.” [Very Important: improved with chiropractic adjustments]

35) Ligaments and tendons adapt to increases in mechanical loading within a physiologic window; therefore, decreased loading decreases function. [Important]

36) When loading is consistently decreased, the quality of the tissue is decreased; this may influence the ability of these injuries to heal and their functional residuals.

37) Aging influences healing outcomes. [Very Important]
38) Re-injury of an acutely healing ligament increases inflammatory molecules, which could worsen the long-term consequence of the mechanical properties of the tissue. [Very Important]

39) “Because not all injuries to a tissue are overt, it is possible that the accumulated cycles of injury and repair to a tissue could impact the starting material following an overt injury. If one extends this to the situation of a second acute injury, the starting material following a second injury is really scar tissue rather than normal tissue. This could impact the functional outcome in at least 2 ways; first, the quality of the scar may be compromised compared with the original scar tissue; and second, the size of the scar may be increased and thus could impact the functional outcome.” [Very Important]

40) “The size of the wound and the resulting scar tissue has a dramatic impact on the biomechanical outcome.”

41) “Diabetes can impact the healing outcome.”

42) “Many patients with diabetes have a compromised wound healing response due in part to an impaired inflammatory response and elaboration of growth factors.”

43) In conditions such as diabetes, “the disease could affect the quality of the connective tissue directly via derivatization of the tissues and formation of advanced glycation endproducts [AGEs] by carbohydrates.”

44) “Many individuals with diabetes exhibit impaired wound healing and can develop chronic wounds that do not readily heal.”

45) In animals, “a single local glucocorticoid treatment of a healing ligament resulted in reduced biomechanical properties of the scar, possibly because of a delay in the maturation/remodeling of the healing tissue.”

46) “It is readily apparent that wound healing in the adult under the most optimal conditions should be considered tissue repair not regeneration.” “For tissues like a ligament or tendon, the mechanical outcome may be less than ideal, depending on the expectations of tissue use post-injury and the occurrence of side-effects such as adhesions.” [Very Important]

47) Improved understanding and application of the regulation of the inflammatory response may improve the subsequent healing processes improving the functionality of the reparative outcome. [Lasers, Omega-3, Antioxidant Status, etc.]

48) Regulation of the interface between biology and biomechanics (i.e. mechanobiology) may also affect the functionality of the reparative outcome. [Chiropractically Very Important]
COMMENTS FROM DAN MURPHY

This article reiterates that ligaments are important sources of proprioception. This is important because proprioceptive afferents control joint muscle tone; there is appreciative evidence from other sources that indicate that joint proprioception influences sympathetic autonomic tone and immunology.

This article reiterates that soft tissue healing occurs over a period of 12 months or more.

Ligaments and tendons heal with scar tissue (repair) as a rule, and not with normal pre-injury tissue (regeneration). This scar tissue causes permanent loss of function.

Scar tissue is mechanically and neurologically functionally inferior to normal tissue. Its inherent weakness makes the tissue prone to failure at previously normal load levels, and subsequent new trauma to scarred tissue will result in greater injury.

Scar tissue (fibrosis) is linked to the intensity of the initial inflammatory response. Consequently, early inflammation control could improve the timing and quality of healing.

Scar tissue, to varying degrees, is remodelable with the application of controlled motion, which I believe includes and even requires chiropractic adjustment.

Mechanical loading is critical for scar tissue remodeling and maturation.

Lack of symptoms is not synonymous with full healing and functional recovery.

There are definitive reasons as to why some patients heal slowly or incompletely with functional residuals. These reasons include:

A)) Age
B)) Female Sex
C)) Genetics
D)) Tissue history (prior injuries, scar tissue, and disease states)
E)) Diabetes
F)) Disc injuries heal poorly, primarily as a consequence of poor blood supply
G)) Pregnancy
H)) Vitamin C levels
I)) Menstrual cycle hormonal changes
J)) Any reason that deprives the healing tissues from mechanical loading
K)) Re-injury of a prior injury or prior tissue that has sustained repetitive stress
L)) Excess carbohydrates that increase glycation (AGEs) [Hb-A1c]
M)) Any treatment with corticosteroids
N)) Anything that exaggerates the inflammatory response [omega-6/omega-3 or AA/EPA ratio]