

Understanding the Natural Tissue Repair and Regeneration Process

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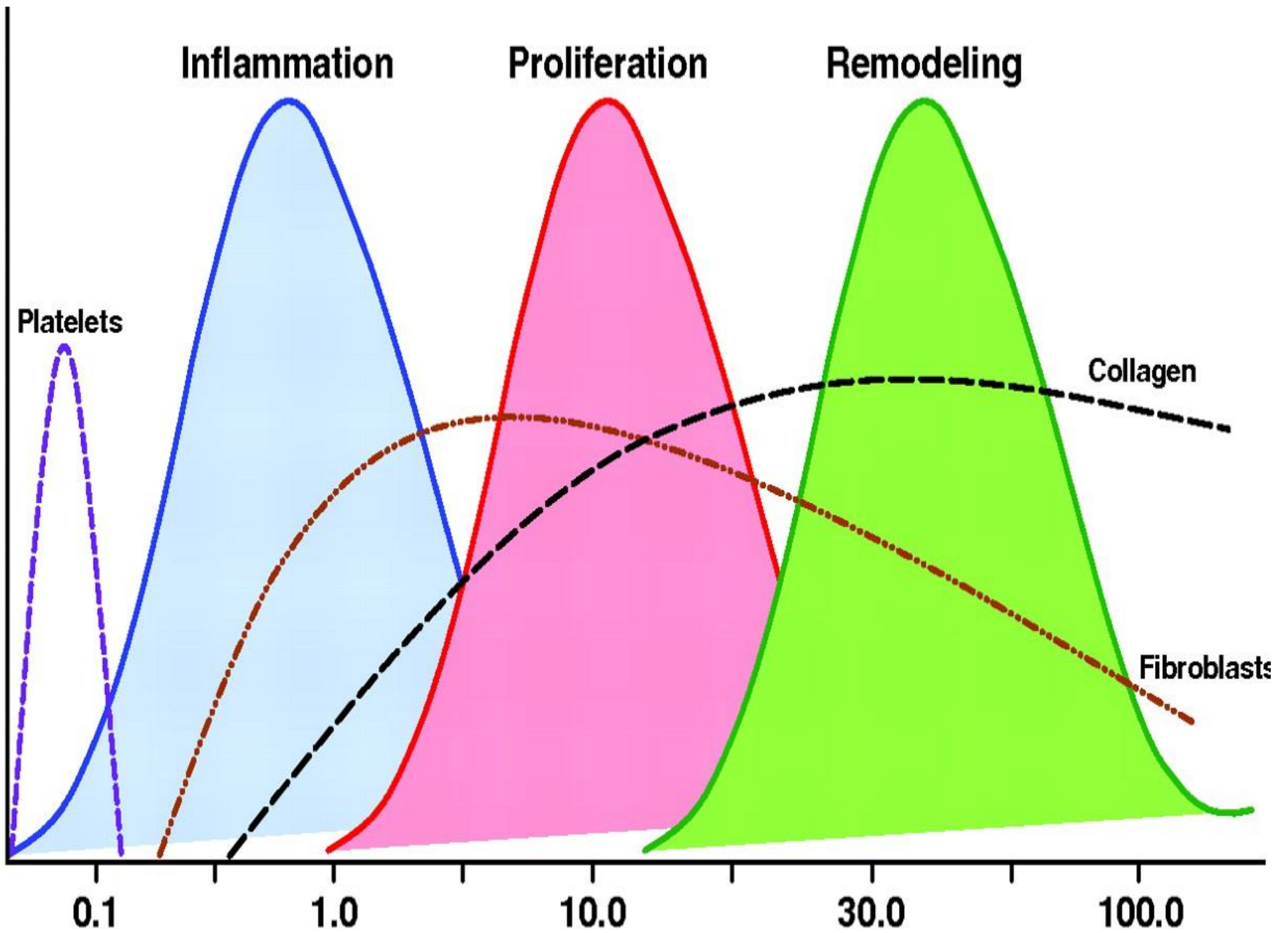
The Natural Tissue Healing Process

- Cleaning up by the immune system
- New blood vessels → O₂ and nutrients
- Regeneration of connective tissue
- Regeneration of epithelial cells

Phases of the Natural Tissue Healing Process

- Hemostasis
- Inflammatory response to heavy exercise
- Proliferation and repair
- Remodeling / maturation

Pakyari M, Farrokhi A, Maharlooei MK, Ghahary A. Critical Role of Transforming Growth Factor Beta in Different Phases of Wound Healing. *Adv Wound Care (New Rochelle)*. 2013 Jun;2(5):215-224



Hemostasis

- Vasoconstriction
- Platelet degranulation and aggregation
- Fibrin deposition

- Clot formation and bleeding cessation

Pakyari M, Farrokhi A, Maharlooei MK, Ghahary A. Critical Role of Transforming Growth Factor Beta in Different Phases of Wound Healing. *Adv Wound Care (New Rochelle)*. 2013 Jun;2(5):215-224

Inflammatory Phase

- Increased capillary permeability and cell migration
- Infiltration of phagocytic WBCs that digest and remove invading organisms, fibrin, and extracellular debris
- WBCs produce a range of growth factors and cytokines that promote the next phase

Proliferation Phase

- Primarily involves the generation of repair material and for the majority of musculoskeletal injuries, involves the production of scar tissue
- Involves the generation of repair cells, the most important of which are the fibroblasts
- Fibroblasts synthesize and secrete collagen and produce glycosaminoglycans and proteoglycans needed for the “ground substance”

Proliferation Phase

- Fibroblasts also produce a range of growth factors that induce angiogenesis and endothelial cell proliferation and migration
- Fibroblastic production of new collagen is oxygen dependent and low tissue oxygen will limit the efficacy of the process

Proliferation Phase

- Angiogenesis is essential in the production of collagen as it ↑ local blood flow and thus ↑ oxygen availability → enabling the fibroblasts¹
- Myofibroblasts derived from fibroblasts are responsible for wound contraction and early strength of the repair²

1. Li WW et al. *Adv Skin Wound Care* 2005; **18**(9): 501-502

2. Watson T. *SportEX Med* 2006; **28**: 8-12

Remodeling Phase

- Begins approximately 3 weeks after challenge and continues for 6-24 months
- There is continued remodeling of scar tissue by the simultaneous synthesis of collagen and lysis by collagenase and MMP enzymes
- Resulting in changes in the architecture of the repair to ↑ tensile strength

Factors Affecting the Natural Healing Process

- Infection
- Age
- Nutrition
- Stress
- Diabetes
- Obesity
- Excessive alcohol consumption
- Smoking
- Medications: eg NSAIDS and glucocorticoids

Gao, S and DiPietro, LA, Factors Affecting Wound Healing, 2010,
J Dent Res **89**(3):219-229

Obesity & Natural Muscle Regeneration

- Obesity negatively impacts skeletal muscle maintenance and regeneration
- Muscle satellite cell function is compromised
 - Lipid overload
 - Elevated toxic lipid metabolites
 - Increased pro-inflammatory cytokines
 - Insulin and leptin resistance

Interleukin-6

- Interleukin (IL)-6 is a cytokine and myokine with pleiotropic functions in different tissues and organs
- Skeletal muscle produces and releases IL-6
- Muscle is also an important target of IL-6
- IL-6 can be elevated systemically with negative consequences for muscle health

Muñoz-Cánoves P, Scheele C, Pedersen BK, Serrano AL, Interleukin-6 myokine signaling in skeletal muscle: a double-edged sword? FEBS J. 2013 Sep;280(17):4131-48

Fatigue and ACL Challenges in Men and Women

- Based on our results, it is conceivable that the fatigue-induced decrease in neuromuscular function with a corresponding increase in tibial translation probably contributes to the higher incidence of ACL challenges in women

Behrens M, Mau-Moeller A, Wassermann F, Bruhn S, Effect of fatigue on hamstring reflex responses and posterior-anterior tibial translation in men and women. PLoS One. 2013;8(2)

Muscle Strains

Clinical Classification

- Delayed Onset Muscle Soreness (DOMS)
- Grade I - Mild
- Grade II – Moderate
- Grade III - Severe

Järvinen TA, Järvinen M, Kalimo H, Regeneration of injured skeletal muscle after the injury. *Muscles Ligaments Tendons J.* 2014 Feb 24; **3**(4):337-345

Exercise and Tissue Microtrauma

- The imbalance caused by overly intensive training and inadequate recovery can lead to a breakdown in reparative mechanisms and eventual tissue breakdown
- Approximately 50% of all sports injuries are secondary to overuse and result from tissue microtrauma leading to local tissue damage

Exercise and Tissue Microtrauma

- Insertion sites where tendons and ligaments attach to bones are common sites for injuries
- Exercise induced inflammation in these areas are well documented in a number of sports:
 - Tennis elbow (tendinitis)
 - Runner's knee (patellofemoral pain syndrome)
 - Achilles tendinopathy

Exercise and Tissue Microtrauma

- Sports and exercises that subject joints to a high level of impact loading increase the risk of injury and degeneration
- Intense physical exercise is associated with the development of osteoarthritis

Overtraining Syndrome

- Overtraining Syndrome (OTS) frequently occurs in athletes who train beyond the body's ability to recover, eg for a specific competition or event
- Without adequate rest and recovery, overtraining regimens can backfire and decrease performance
- OTS may extend over weeks and months and in some cases the athlete never recovers

Smith LL. *J Strength Condition Res* 2004; **18**(1): 185-193

Overtraining Syndrome

- There are numerous signs and symptoms associated with OTS which can be grouped under four categories:
 - Psychological
 - Physiological
 - Biochemical
 - Immunological

Smith LL. *J Strength Condition Res* 2004; **18**(1): 185-193

Overtraining Syndrome

- It appears that no single metabolic process is responsible
- However tissue trauma resulting from intense exercise without adequate recovery is associated with oxidative stress and chronic exercise induced inflammation that may underpin many of the metabolic defects associated with OTS

Thank You