HISTOLOGY OF WOUND HEALING: MICROSCOPIC STAGES FROM GRANULATION TISSUE TO SCAR FORMATION

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https://doi.org/10.5281/zenodo.22881895

Abstract: Wound healing is a complex biological process involving coordinated cellular and molecular changes. It generally progresses through overlapping stages of hemostasis, inflammation, proliferation, and tissue remodeling. Histologically, the transition from granulation tissue to mature scar tissue is characterized by changes in fibroblasts, collagen deposition, vascularity, and extracellular matrix organization. This article reviews the main microscopic stages of wound healing and explains the structural changes that occur during the formation and maturation of scar tissue.
Keywords: wound healing, histology, granulation tissue, fibroblasts, collagen, inflammation, angiogenesis, scar tissue, tissue remodeling.

INTRODUCTION

Wound healing is an essential protective mechanism that restores tissue integrity after injury. It involves a coordinated interaction between inflammatory cells, fibroblasts, endothelial cells, epithelial cells, extracellular matrix components, and numerous signaling molecules [1].

Although wound healing is traditionally divided into several stages, these stages overlap considerably. The process begins immediately after tissue injury and includes hemostasis and inflammation, followed by proliferation and tissue formation, and finally remodeling and scar maturation [2].

From a histological perspective, one of the most important transitions is the development of granulation tissue and its subsequent transformation into a relatively dense and less vascular scar. Understanding these microscopic changes is important for explaining normal healing as well as pathological conditions such as chronic wounds and excessive scar formation.

MATERIALS AND METHODS

This article is based on a review of scientific literature concerning the histological and cellular mechanisms of wound healing. Information was obtained from peer-reviewed publications and established medical and histological sources. The analysis focused on the microscopic characteristics of inflammation, granulation tissue formation, collagen deposition, angiogenesis, fibroblast activity, re-epithelialization, and scar maturation.

RESULTS AND DISCUSSION

Hemostasis and the early inflammatory phase. Wound healing begins immediately following tissue injury. Damage to blood vessels causes vasoconstriction and platelet activation. Platelets aggregate and form a temporary blood clot that limits blood loss and provides an initial extracellular matrix for migrating cells [3].

Histologically, the early wound contains fibrin, platelets, erythrocytes, and inflammatory cells. The clot acts as a provisional scaffold and also contains growth factors that participate in subsequent repair processes. During the inflammatory phase, neutrophils are among the first cells to enter the injured area. They help remove microorganisms, damaged tissue, and cellular debris. Later, macrophages become increasingly important. They remove remaining debris and release cytokines and growth factors that stimulate fibroblast proliferation, angiogenesis, and tissue repair [4].

Formation of granulation tissue. The proliferative phase is characterized by the formation of granulation tissue. Histologically, granulation tissue is composed of numerous newly formed small blood vessels, proliferating fibroblasts, inflammatory cells, and a loose extracellular matrix [5].

Angiogenesis is particularly important during this stage. Endothelial cells proliferate and migrate into the wound, forming new capillary networks. As a result, granulation tissue often appears red and has a soft, granular microscopic structure. Fibroblasts are another major cellular component. They migrate into the wound and begin synthesizing extracellular matrix proteins, particularly collagen. Initially, the collagen matrix is relatively immature and loosely organized.

Granulation tissue therefore serves as a temporary structural and metabolic environment in which new tissue can develop. It gradually fills the wound and provides a foundation for subsequent remodeling.

Re-epithelialization. At the same time, epithelial cells at the edges of the wound begin to proliferate and migrate across the wound surface. This process is known as re-epithelialization. Keratinocytes detach partially from their normal attachments and migrate over the provisional matrix. Once the wound surface is covered, epithelial proliferation and differentiation contribute to the restoration of the epidermal structure [6]. The rate of re-epithelialization depends on the depth and size of the injury, the availability of viable epithelial cells, blood supply, and the presence or absence of infection.

Transition from granulation tissue to scar tissue. As healing progresses, granulation tissue gradually becomes less cellular and less vascular. Fibroblasts continue to synthesize collagen, while many newly formed capillaries regress. The extracellular matrix becomes increasingly dense, and collagen fibers become thicker and more organized. Type III collagen, which is relatively abundant during early repair, is gradually replaced and reorganized with a greater proportion of type I collagen during maturation [7].

Microscopically, this transition results in a change from highly vascular, cellular granulation tissue to denser connective tissue with fewer blood vessels and fewer inflammatory cells. An important feature of this stage is the activity of myofibroblasts. These specialized cells have characteristics of both fibroblasts and smooth muscle cells. They produce extracellular matrix and contribute to wound contraction, reducing the size of the wound [8].

Scar maturation and remodeling. The final stage of healing is tissue remodeling. It may continue for months or even longer after the wound has apparently closed. During remodeling, collagen fibers undergo continuous degradation and synthesis. The fibers become progressively more organized and aligned according to mechanical forces acting on the tissue. At the same time, cellularity and vascularity decrease [9]. A mature scar is therefore histologically different from normal tissue. It contains relatively dense collagen bundles, fewer blood vessels, and fewer cells. However, scar tissue usually does not completely reproduce the original architecture and functional properties of the tissue.

The mechanical strength of a healing wound increases gradually but does not normally return completely to the strength of uninjured tissue [10].

Histological abnormalities of wound healing. The normal sequence of wound healing can be disrupted by infection, poor blood supply, diabetes, nutritional deficiencies, repeated trauma, or excessive inflammation.

Delayed healing may be associated with persistent inflammation and inadequate formation of granulation tissue. In contrast, excessive collagen production can result in hypertrophic scars or keloids. A hypertrophic scar generally remains within the original boundaries of the wound, whereas a keloid extends beyond them. Histologically, both conditions are characterized by abnormal collagen deposition and altered extracellular matrix organization [11]. These conditions demonstrate that successful wound healing requires a balance between extracellular matrix production and degradation.

CONCLUSION

Wound healing is a dynamic histological process involving inflammation, angiogenesis, fibroblast proliferation, collagen deposition, re-epithelialization, wound contraction, and tissue remodeling. Granulation tissue represents a highly vascular and cellular stage of repair, while mature scar tissue is characterized by reduced vascularity, lower cellularity, and more organized collagen fibers.

The transition from granulation tissue to scar is therefore not a single event but a gradual remodeling process. Fibroblasts and myofibroblasts play important roles in extracellular matrix

production and wound contraction, while collagen synthesis and degradation determine the structure and strength of the final scar.

Understanding these microscopic changes is important for recognizing normal tissue repair and explaining pathological wound healing. Further knowledge of cellular and molecular mechanisms may contribute to improved approaches for treating chronic wounds and preventing excessive scar formation.

REFERENCES

1. Gurtner G.C., Werner S., Barrandon Y., Longaker M.T. Wound repair and regeneration. Nature. 2008;453:314–321.
2. Eming S.A., Martin P., Tomic-Canic M. Wound repair and regeneration: mechanisms, signaling, and translation. Science Translational Medicine. 2014;6(265):265sr6.
3. Rodrigues M., Kosaric N., Bonham C.A., Gurtner G.C. Wound healing: a cellular perspective. Physiological Reviews. 2019;99(1):665–706.
4. Koh T.J., DiPietro L.A. Inflammation and wound healing: the role of the macrophage. Expert Reviews in Molecular Medicine. 2011;13:e23.
5. Reinke J.M., Sorg H. Wound repair and regeneration. European Surgical Research. 2012;49:35–43.
6. Pastar I., Stojadinovic O., Yin N.C., et al. Epithelialization in wound healing: a comprehensive review. Advances in Wound Care. 2014;3(7):445–464.
7. Xue M., Jackson C.J. Extracellular matrix reorganization during wound healing and its impact on abnormal scarring. Advances in Wound Care. 2015;4(3):119–136.
8. Hinz B. Formation and function of the myofibroblast during tissue repair. Journal of Investigative Dermatology. 2007;127:526–537.
9. Wynn T.A., Ramalingam T.R. Mechanisms of fibrosis: therapeutic translation for fibrotic disease. Nature Medicine. 2012;18:1028–1040.
10. Gonzalez A.C.O., Costa T.F., Andrade Z.A., Medrado A.R.A.P. Wound healing — A literature review. Anais Brasileiros de Dermatologia. 2016;91(5):614–620.
11. Ogawa R. Keloid and hypertrophic scars are the result of chronic inflammation in the reticular dermis. International Journal of Molecular Sciences. 2017;18(3):606.